U.P.Rajarshi TandonOpen University, Prayagraj

PGZY-108 (N)

Genetics and Evolution

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Course Introduction

We welcome you to the study of this course on Genetics and Evolution.Genetics is the science of heredity that relates to the study of the structure and function of genes and the mechanisms of their transmission from one generation to the next.

It is studied at the level of whole organisms (classical or transmission genetics), the DNA itself (molecular genetics) or whole populations (population and evolutionary genetics).

With our increasing knowledge of genetics, we can better understand what controls and contributes to our development and individuality. Our improved understanding of the genetic basis for life has opened up new approaches for the investigation, diagnosis and treatment of disease.

Mendelian inheritance involves the understanding of **genes**, **alleles**, and how they combine during sexual reproduction. Genes are units of heredity, located on chromosomes, while alleles are different versions of a gene. For instance, a gene might control flower color, while alleles determine whether the flower will be purple or white.

- Transmission genetics deals with the study of gene from one generation to the next.
- Molecular genetics is the study of molecular structure of genes as well as nature, expression and regulation of these molecules.
- Population genetics deals with the study of behaviour of genes in population. The population genetics define evolution as changes in gene frequencies.

The course aims at presenting the subject matter of genetics and evolution. It examines not only the inheritance of genes, which affect the characters of organisms but also the developmental processes where by the characters are produced.

This course also deals with evolution. It is founded on the concept, that morphological similarities descend from a common evolutionary ancestor. Evolutionary systematics or Darwinian classification is branch of biological classification.

In this course you will learn about Lamarckism and Darwinism and study about different type of mutation, molecular basis of mutation, human evolution, tracing the journey of life from its usy beginnings to the present day. You will explore the forces that shaped our species, the genetic adaptations that made us human, and the cultural innovations that set us apart from all other life forms.

The course is divided into two blocks. The first block deals with genetics and the second block deals with evolution.

Block I- Genetics

Block II- Evolution

Block 1 – Genetics

This is the first block of the course that contains eight units dealing with the concept of genetics.

Unit 1: This unit deals with the Mendelian inheritance, features of Chromosomes, Sex chromosomes, Chromosome theory of inheritance, Extension of Mendelian inheritance, Gene interactions,Maternal effect, Extranuclear inheritance and linkage

Unit 2: It deals with Bacterial transformation, selection and mapping, Bacterial conjugation, and mapping via Hfr strains and Bacterial transduction

Unit 3: Eukaryotic chromosome, Deletions and duplications, Inversions and translocations, and also deals with the Changes in chromosome number and Aneuploidy

Unit 4: This unit deals with theNucleotide structure, Discovery and structure of DNA double helix, RNA structure and types

Unit 5: It deals with Prokaryotic DNA replication, Eukaryotic DNA replication and Regulation of DNA

replication

Unit 6: It deals with Transcription in prokaryotes, Transcription in eukaryotes, RNA modification and Structure and function of tRNA,

Unit 7: It deals with Genetic basis of protein synthesis, Genetic code and amino acids, Ribosome structure and assembly and Stages of translation

Unit 8: The last unit of this block deals withOverview of transcriptional regulation Lac operon- model and regulation, Trp operon- model and regulation, translational and post-translational regulations

Objectives:

After studying this block you will be able to –

- discuss the patterns of inheritance and genetic transfer and mapping in Bacteria
- discuss the variation in chromosome structure and number
- describe molecular structure of nucleic acids andDNA replication
- describe gene transcription and RNA modification
- discuss the translation of mRNA andgene regulation

Block- II- Evolution

In previous block you have studied about the genetics. This block deals with the evolution. This block comprises of 5 units (unit 9 to 13),including flowing topics.

Unit 9: This unit deals with the early concepts and theories, modern concept of origin of life, Miller's experiments andevidences in favour of organic evolution

Unit 10: Lamarck's theory, Analysis of Lamarck's theory, Criticism of Lamarckism, Neo-Lamarckism, Darwin's theory- natural selection and origin of new species Criticism and objections of Darwinism and Neo-Darwinism

Unit 11: This unit deals with the Mutation, molecular basis of mutation, Types of mutation, Causes of mutation, Mutagenic agents and Significance of mutation.

Unit 12: It deal with Isolating mechanisms, reproductive isolation, Genetic basis of isolation, role of isolation in evolution, Different kinds of adaptation, Kinds of variations, sources of variation, and significance of variation.

Unit 13: The last unit of this block deals withAncestral apes, fossil human, Origin of modern human, races of modern human, Distribution of human diversity and colonization

Objectives:

After studying this block you will be able to –

- discuss the origin of life
- discuss the Lamarckism and Darwinism
- describe Mutation theory
- describe Isolation, adaptation and variation
- discuss the Evolution of Human

Unit-1Patterns of inheritance

1.1 Introduction

Mendelian inheritance is a set of principles explaining how traits are transmitted from parents to their offspring. It was first discovered by Gregor Johann Mendel, an Austrian monk, in the 19th century. Mendel's groundbreaking experiments on pea plants laid the foundation for modern genetics.

Mendelian inheritance involves the understanding of **genes**, **alleles**, and how they combine during sexual reproduction. Genes are units of heredity located on chromosomes, while alleles are different versions of a gene. For instance, a gene might control flower color, while alleles determine whether the flower will be purple or white.

Objectives:

After studying this unit you should be able to know-

- Mendalian inheritance
- Features of Chromosomes, Sex chromosomes
- Gene interactions, Maternal effect
- Extranuclear inheritance
- Linkage

1.2 Mendelian Inheritanceand Non-Mendelian Patterns of Inheritance

Meiosis is a specialized form of cell division that reduces the chromosome number by half, resulting in gametes (sperm and egg cells) that are haploid (containing a single set of chromosomes). The behavior of chromosomes during meiosis provides a physical explanation for Mendel's laws.

A. Law of Segregation

Mendel's Law of Segregation states that each individual has two alleles for each gene, and these alleles separate during the formation of gametes. As a result, each gamete carries only one allele for each

gene.

For example based on the Chromosome theory are-

- during meiosis I, homologous chromosomes (one from the mother and one from the father) align and then segregate into different cells. Each resulting gamete gets only one chromosome from each pair, explaining how one allele of a gene segregates into a gamete.
- This is why offspring inherit one allele from each parent, providing the genetic basis for Mendel's first law.

B. Law of Independent Assortment

Mendel's Law of Independent Assortment states that the alleles for different genes assort independently of one another during gamete formation.

For example based on the Chromosome theory are-

- During meiosis I, homologous chromosome pairs line up independently of one another. This independent alignment of chromosomes ensures that the inheritance of one gene (on one chromosome) does not affect the inheritance of another gene (on a different chromosome).
- This independent segregation of chromosomes explains how genes on different chromosomes assort independently, corresponding to Mendel's second law.

However, genes located close to each other on the same chromosome may not assort independently, leading to the phenomenon of **genetic linkage**.

For examples based on the Mendelian Inheritance in Humans

- Eye color is often cited as an example of Mendelian inheritance. The brown eye color allele (B) is dominant, and the blue eye color allele (b) is recessive. If a child inherits the genotype Bb, the child with brown eyes because the brown allele is dominant. A child with the genotype bb will have blue eyes.

Example 1:

- **Parent 1**: Bb (brown eyes)
- **Parent 2**: Bb (brown eyes)
- **Possible offspring genotypes**: BB (brown), Bb (brown), bb (blue)

There is a 25% chance the child will have blue eyes and a 75% chance they with brown eyes.

2. Cystic Fibrosis:

Cystic fibrosis (CF) is a genetic disorder caused by a recessive allele. In this case, the dominant normal allele (F) and the recessive allele causing CF (f) are present. An individual must inherit two copies of the recessive allele (ff) to have the disorder.

Example 2:

- **Parent 1**: Ff (carrier)
- **Parent 2**: Ff (carrier)
- **Possible offspring genotypes**: FF (normal), Ff (carrier), ff (affected)

There is a 25% chance the child will have cystic fibrosis and a 50% chance the child will be a carrier.

3. Albinism:

Albinism is a condition where the body produces little to no melanin, the pigment responsible for skin, hair, and eye color. It follows Mendelian inheritance, with the allele for normal pigmentation (A) being dominant, and the allele for albinism (a) being recessive.

Example 3:

- **Parent 1**: Aa (normal pigmentation)
- **Parent 2**: Aa (normal pigmentation)
- **Possible offspring genotypes**: AA (normal), Aa (normal), aa (albinism)

There is a 25% chance of an albino child.

Mendelian Inheritance in Humansnumerous traits and genetic disorders follow

Mendelian inheritance refers to the patterns of inheritance first described by **Gregor Mendel** in the mid-19th century, based on his experiments with pea plants. These patterns follow the laws of **segregation** and independent assortment, where traits are passed from parents to offspring via distinct units of inheritance (genes). In humans, numerous traits and genetic disorders follow Mendelian inheritance patterns, categorized into autosomal dominant, autosomal recessive, X-linked dominant, and X-linked recessive traits.

1. Autosomal dominant inheritance

In autosomal dominant inheritance, a single copy of the mutant allele is sufficient to cause the phenotype or disorder. The mutant gene is located on one of the **autosomes** (chromosomes 1-22), so the trait is equally likely to affect males and females. Affected individuals often have one affected parent, and there is a 50% chance of passing the trait to offspring.

A. Huntington's Disease

- **Gene**: Mutations in the **HTT(Huntingtin)** gene cause Huntington's disease.
- This neurodegenerative disorder typically begins in mid-adulthood and leads to progressive motor dysfunction, cognitive decline, and psychiatric symptoms. Individuals with Huntington's disease inherit one mutant allele from an affected parent, and the presence of just one defective allele is enough to cause the disease.

B. Marfan Syndrome

- **Gene**: Mutations in the **FBN1**(Fibrillin-1) gene, which encodes the protein fibrillin-1, lead to Marfan syndrome.
- Marfan syndrome is a genetic disorder that affects connective tissues and can cause elongated limbs, joint hypermobility, and life-threatening heart and aortic complications. An individual with Marfan syndrome typically inherits the mutant allele from one parent.

C. Achondroplasia

- **Gene**: Mutations in the **FGFR3**(Fibroblast Growth Factor Receptor-3) gene cause achondroplasia, most common a form of dwarfism, disproportionately short limbs, and normal intelligence. The disorder is caused by a dominant mutation, and those with one mutated allele exhibit the phenotype.

2. Autosomal Recessive Inheritance

In **autosomal recessive inheritance**, two copies of the mutant allele (one from each parent) are required to express the trait or disorder. Carriers, who have only one copy of the mutant allele, do not show symptoms but can pass the allele to their offspring. Autosomal recessive traits affect both sexes equally. For examples

A.Cystic Fibrosis is caused by mutation in the CFTR (cystic fibrosis Transmembrane Conductance Regulator) gene

- Cystic fibrosis is characterized by thick, sticky mucus production that leads to respiratory and digestive problems.

B. Sickle Cell Anemia caused HBB (Haemoglobin subunit Beta) gene, which codes for the β-globin subunit of hemoglobin, cause sickle cell anemia.

- Sickle cell anemia causes red blood cells to adopt a sickle shape, leading to pain, anemia, organ damage, and increased risk of infection. Individuals who inherit two copies of the mutant allele develop the disease, while carriers (heterozygotes) are typically asymptomatic but can experience mild symptoms under certain conditions, such as low oxygen levels.

C. Phenylketonuria (PKU)-Mutations in the **PAH**(Phenylalanine Hydroxylase) gene, which encodes the enzyme phenylalanine hydroxylase, lead to phenylketonuria.

- PKU causes the inability to break down the amino acid phenylalanine, resulting in intellectual disabilities if untreated. Affected individuals inherit two defective alleles, while carriers do not show symptoms.

3. X-linked Dominant Inheritance

In X-linked dominant inheritance, a mutation in a gene located on the X chromosome causes the trait or disorder. Since females have two X chromosomes, they are more likely to be affected, but males (with one X and one Y chromosome) can also be affected.

Some examples are

A. Rett Syndrome

- Mutations in the **MECP2**(Methyal-cytosine binding Protin 2) gene on the X chromosome cause Rett syndrome.
- Rett syndrome primarily affects females and is characterized by developmental regression, intellectual disability, and loss of motor skills. Males with the mutation often do not survive past infancy, as they lack a second X chromosome to counterbalance the defective gene.

B. Fragile X Syndrome-

Geneexpansions in the FMR1(Fragile X Mental Retardation-1) gene on the X chromosome lead to Fragile X syndrome.

- This condition is the most common cause of inherited intellectual disability. Symptoms include developmental delay, learning disabilities, and behavioral challenges. Both males and females can be affected, but males typically have more severe symptoms because they have only one X chromosome.

4. X-linked Recessive Inheritance-

The mutant allele must be present on both X chromosomes in females to express the trait, while in males, only one copy of the mutant allele is necessary because they have only one X chromosome. As a result, X-linked recessive disorders are much more common in males than in females.Some examples are

A. Hemophilia A and B

- Mutations in the F8 (Fator-VIII) gene (Hemophilia A) and F9 (Factor-IX)gene (Hemophilia B) on the X chromosome cause these conditions.
- Hemophilia is characterized by an inability to properly clot blood, leading to excessive bleeding and bruising. Males with the mutation on their X chromosome are affected, while females are usually carriers unless they inherit the mutation from both parents.

B. Duchenne Muscular Dystrophy (DMD)-

Mutations in the **DMD** gene, which encodes dystrophin, cause Duchenne muscular dystrophy. That leads to progressive muscle weakness, loss of motor skills, and early death. The condition primarily affects males, as they inherit a defective X chromosome from their mother.

C. Red-Green Color Blindness

- **Gene**: Mutations in the **OPN1LW**(Opsin 1 long wave) and **OPN1MW**(Opsin 1 medium wave) genes, located on the X chromosome, cause red-green color blindness.
- Individuals with red-green color blindness have difficulty distinguishing between red and green hues. The condition is more common in males because they have only one X chromosome.

5. Y-linked Inheritance

In **Y-linked inheritance**, the gene responsible for the trait or disorder is located on the **Y chromosome**, which is only present in males. Since only males inherit the Y chromosome from their fathers, Y-linked traits are passed exclusively from father to son.

Example:

A. Y-Linked Hearing Impairment

- **Gene**: Mutations in a gene on the Y chromosome can lead to certain forms of hearing impairment.
- **Symptoms**: Affected males inherit the mutation from their father and experience hearing loss. Since the Y chromosome is passed directly from father to son, the trait follows a strict paternal lineage.

Non-Mendelian Patterns of Inheritance or Extrachromosomal inheritance

Extrachromosomal inheritance, also known as cytoplasmic or non-Mendelian inheritance, involves the transmission of genetic material not found in the nuclear chromosomes but in organelles like mitochondria and chloroplasts, or in plasmids and viruses. Here are the key characteristics of extrachromosomal inheritance:

1. Maternal Inheritance:

- **Mitochondrial and Chloroplast DNA**: In many organisms, the extrachromosomal DNA found in mitochondria and chloroplasts is inherited almost exclusively from the mother. This is because the egg cell provides most of the cytoplasm to the zygote, whereas the sperm contributes primarily nuclear DNA.
- **Example**: Mitochondrial diseases are often passed down from mother to offspring, regardless of the offspring's sex.

2. Non-Mendelian Inheritance Patterns:

- **Deviation from Mendel's Laws**: Unlike nuclear genes, which follow Mendelian inheritance patterns, extrachromosomal genes do not segregate in the typical 1:2:1 or 3:1 ratios seen in Mendelian genetics.
- **Example**: All offspring of a female with a mitochondrial mutation may inherit the condition, while none of the offspring from a male with the mutation will inherit it, regardless of Mendelian expectations.

3. Lack of Biparental Inheritance:

- **Uniparental Inheritance**: Generally, only one parent (typically the mother) passes on the extrachromosomal DNA. This contrasts with chromosomal inheritance, where offspring inherit one set of chromosomes from each parent.
- **Example**: In most cases of mitochondrial inheritance, both male and female offspring receive their mitochondrial DNA solely from the mother.

4. High Copy Number:

- **Multiple Copies**: Organelles like mitochondria and chloroplasts contain multiple copies of their DNA. This means that a cell can have a large number of mitochondrial or chloroplast genomes.
- **Implication**: The presence of many copies of the DNA can buffer the effects of mutations, but it can also lead to situations where some cells have a mix of normal and mutated DNA (heteroplasmy).

5. Cytoplasmic Segregation:

- **Unequal Distribution**: During cell division, the cytoplasmic components, including organelles with extrachromosomal DNA, can be distributed unevenly between daughter cells.
- **Result**: This can lead to variation in the expression of traits linked to extrachromosomal DNA, as different cells (and therefore different tissues) may end up with different amounts of normal or mutated DNA.

6. Horizontal Gene Transfer:

- **Plasmid Exchange**: In bacteria, plasmids (extrachromosomal DNA) can be transferred between individuals via horizontal gene transfer mechanisms like conjugation, transformation, or transduction.
- **Example**: Antibiotic resistance genes are often spread among bacterial populations through plasmid transfer, which allows for rapid adaptation to environmental changes.

7. Epigenetic and Environmental Influences:

- **Expression Variability**: The expression of extrachromosomal genes can be influenced by environmental factors and epigenetic modifications. This can lead to variability in the manifestation of traits or diseases associated with extrachromosomal DNA.
- **Example**: The severity of mitochondrial diseases can vary depending on the energy demands of different tissues and the proportion of mutated mitochondrial DNA they contain.

8. Involvement in Specific Traits and Diseases:

- **Specialized Roles**: Extrachromosomal DNA often plays a role in specific cellular functions, such as energy production in mitochondria or photosynthesis in chloroplasts.
- **Example**: Mutations in mitochondrial DNA can lead to disorders that affect energy-demanding organs like the heart, brain, and muscles.

9. Heteroplasmy:

- **Mixed Populations of DNA**: In some cases, cells can contain both normal and mutated versions of mitochondrial or chloroplast DNA. The proportion of mutated DNA can vary between cells, leading to variable phenotypic expression.
- **Example**: In mitochondrial diseases, heteroplasmy can result in a range of symptoms depending on the distribution of mutated and normal mitochondrial DNA.

10. Rapid Evolution:

- **High Mutation Rates**: Mitochondrial DNA, in particular, has a higher mutation rate compared to nuclear DNA. This can lead to rapid evolutionary changes and genetic diversity within populations.
- **Example**: Mitochondrial DNA is often used in studies of human evolution and population genetics due to its high mutation rate and maternal inheritance pattern.

These characteristics of extrachromosomal inheritance contribute to the diversity of genetic inheritance patterns and have significant implications for understanding genetic diseases, evolution, and cellular function.

SAQ.1

a) Chromosome abnormalities can cause genetic disorders with changes in chromosome number or structure, often leading to …….

b) Abnormal number of chromosomes. where chromosomes fail to separate properly during ……. It occurs due to nondisjunction.

c) Genes that are located close to each other on the same chromosome tend to be inherited together, a phenomenon known as……..

d) Extranuclear inheritance, or the inheritance of genetic material from organelles like mitochondria and chloroplasts, plays a crucial role in many biological processes and deviates from classical ……. This form of inheritance follows different patterns, primarily maternal inheritance

e) Extrachromosomal inheritance, also known as cytoplasmic or non-Mendelian inheritance, involves the …… material located outside the nucleus. There are several types of extrachromosomal inheritance, each associated with different organelles or genetic elements.

Types of Extrachromosomal Inheritance

Extrachromosomal inheritance, also known as cytoplasmic or non-Mendelian inheritance, involves the transmission of genetic material located outside the nucleus. There are several types of extrachromosomal inheritance, each associated with different organelles or genetic elements. Here are the main types:

1. Mitochondrial Inheritance

- **Location**: Mitochondria, the organelles responsible for energy production in eukaryotic cells.
- **Inheritance Pattern**: Typically maternal, as mitochondria are inherited almost exclusively from the mother.
- **Examples**:
    - **Leber's Hereditary Optic Neuropathy (LHON)**: A disease that affects vision, caused by mutations in mitochondrial DNA.

- **Mitochondrial Myopathy**: A group of neuromuscular diseases caused by defects in mitochondrial DNA.

2. Chloroplast Inheritance

- **Location**: Chloroplasts, the organelles responsible for photosynthesis in plants and some algae.
- **Inheritance Pattern**: Usually maternal, similar to mitochondrial inheritance, although in some species it can be biparental or paternal.
- **Examples**:
  - **Variegation in Plants**: The appearance of different colors in leaves, often due to mutations in chloroplast DNA.
  - **Leaf Color Patterns**: Certain color traits in plants are determined by chloroplast genes.

3. Plasmid Inheritance

- **Location**: Plasmids, small, circular DNA molecules found primarily in bacteria, but also in some fungi and plants.
- **Inheritance Pattern**: Plasmids can be inherited vertically (from parent to offspring) or horizontally (between organisms via processes like conjugation, transformation, or transduction).
- **Examples**:
  - **Antibiotic Resistance**: Many bacteria acquire antibiotic resistance genes through plasmids.
  - **Toxin Production**: Some bacteria carry plasmid-encoded genes that enable them to produce toxins.

4. Episomal Inheritance

- **Location**: Episomes, which are extrachromosomal DNA elements that can replicate independently of the chromosomal DNA or integrate into the host genome.
- **Inheritance Pattern**: Episomes can be inherited by daughter cells during cell division, either as free elements or after integration into the chromosomal DNA.
- **Examples**:
  - **Herpesviruses**: Certain viruses, such as Epstein-Barr virus, can exist as episomes within the host cell nucleus.

5. Cytoplasmic Inheritance (Cytoplasmic Factors)

- **Location**: Involves the inheritance of traits determined by factors present in the cytoplasm of the cell, which could include small RNAs, proteins, or other molecules.
- **Inheritance Pattern**: Maternal or, less commonly, paternal.
- **Examples**:
  - **Maternal Effect Genes**: In some organisms, the phenotype of the offspring is determined by the mother's genotype due to the presence of certain molecules in the egg's cytoplasm.

6. Virus-Mediated Inheritance

- **Location**: Viral genomes that can integrate into the host’s genetic material or exist independently as extrachromosomal elements.

- **Inheritance Pattern**: Viral DNA can be passed from parent to offspring if integrated into germline cells, or it can be maintained in somatic cells.
- **Examples**:
    - **Endogenous Retroviruses**: Viral sequences that have become a permanent part of the host genome.
    - **Bacteriophages**: Viruses that infect bacteria can carry genes that influence the bacterial phenotype.

These types of extrachromosomal inheritance contribute to genetic diversity and allow for unique inheritance patterns that differ from classical Mendelian genetics. Each type has specific implications for evolution, disease, and biotechnology.

Modes of Extrachromosomal Inheritance

The modes of extrachromosomal inheritance describe how these genetic elements are passed from one generation to the next or between organisms. Here are the main modes:

1. Maternal Inheritance

- **Description**: In this mode, the genetic material is inherited exclusively from the mother. This is common for organelles like mitochondria and chloroplasts, which are found in the cytoplasm and are typically passed on from the egg cell.
- **Example**:
    - **Mitochondrial Inheritance**: Mitochondrial DNA (mtDNA) is inherited from the mother because the sperm's mitochondria are usually destroyed after fertilization.
    - **Chloroplast Inheritance in Plants**: Chloroplast DNA (cpDNA) is often maternally inherited, determining traits like leaf color.

2. Paternal Inheritance

- **Description**: In rare cases, genetic material can be inherited from the father. This mode is less common than maternal inheritance and usually involves specific species or circumstances.
- **Example**:
    - **Paternal Leakage**: Occurs in some plants and animals where paternal mitochondria are not entirely destroyed and contribute to the offspring's mitochondrial DNA.
    - **Certain Algae and Gymnosperms**: Some species of algae and gymnosperms exhibit paternal inheritance of chloroplast DNA.

3. Biparental Inheritance

- **Description**: In this mode, genetic material from both parents is inherited. Although rare, biparental inheritance can occur in some species, particularly with organelles like chloroplasts.
- **Example**:
    - **Chloroplast Inheritance in Certain Plants**: In some species, both maternal and paternal chloroplasts are passed to the offspring, leading to biparental inheritance of chloroplast DNA.

4. Horizontal Gene Transfer

- **Description**: This mode involves the transfer of genetic material between organisms that are not parent and offspring, typically seen in bacteria. Horizontal gene transfer allows for the spread of traits like antibiotic resistance among populations.
- **Example**:

- **Plasmid Transfer in Bacteria**: Plasmids, which carry extrachromosomal DNA, can be transferred between bacterial cells through processes like conjugation, transformation, or transduction.
- **Viruses as Vectors**: Certain viruses can transfer genes between different organisms, facilitating horizontal gene transfer.

5. Cytoplasmic Segregation

- **Description**: This mode occurs during cell division, where the distribution of organelles like mitochondria or chloroplasts is uneven between daughter cells. This can result in different cells or tissues having varying amounts of normal or mutated DNA.
- **Example**:
  - **Heteroplasmy in Mitochondria**: Some cells might contain a mixture of normal and mutated mitochondria, leading to variable expression of mitochondrial diseases.
  - **Variegation in Plants**: Some plant cells may receive different amounts of chloroplasts with mutated DNA, leading to variegated (multicolored) leaves.

6. Viral-Mediated Inheritance

- **Description**: Certain viruses can integrate their genetic material into the host's genome or exist as episomes (independent genetic elements) in the host cell. This viral DNA can be passed to the next generation if integrated into the germline cells.
- **Example**:
  - **Endogenous Retroviruses**: Retroviruses can integrate their DNA into the host genome, and this viral DNA can be inherited by the host's offspring.
  - **Bacteriophages**: Viruses that infect bacteria can carry genes that are inherited by subsequent generations of bacteria.

7. Uniparental Inheritance

- **Description**: In this mode, genetic material from only one parent (either the mother or the father) is passed on to the offspring, without contributions from the other parent. This is a broader category that includes maternal, paternal, and some cases of biparental inheritance, where one parent's contribution is dominant.
- **Example**:
  - **Uniparental Mitochondrial Inheritance**: Typically maternal, as mentioned earlier, but in rare cases can be paternal.

Summary of Modes:

- **Maternal Inheritance**: Mitochondria and chloroplasts typically passed from the mother.
- **Paternal Inheritance**: Rare, with organelles like mitochondria sometimes passed from the father.
- **Biparental Inheritance**: Both parents contribute organelles, though this is uncommon.
- **Horizontal Gene Transfer**: Transfer of genes between non-parental organisms, common in bacteria.
- **Cytoplasmic Segregation**: Uneven distribution of organelles during cell division.
- **Viral-Mediated Inheritance**: Viral genes integrated into the host genome or passed as episomes.
- **Uniparental Inheritance**: Genetic material is passed from one parent only.

These modes of extrachromosomal inheritance demonstrate the diverse mechanisms by which genetic information can be transmitted outside of traditional chromosomal inheritance.

Differences Between Extrachromosomal and Chromosomal Inheritance:

1. **Location of Genetic Material**:
    - **Extrachromosomal**: Genetic material is located outside the nucleus (e.g., in mitochondria, chloroplasts, or plasmids).
    - **Chromosomal**: Genetic material is located on chromosomes within the nucleus.
2. **Inheritance Pattern**:
    - **Extrachromosomal**: Inheritance can be maternal (e.g., mitochondrial or chloroplast DNA) or through horizontal gene transfer (e.g., plasmids in bacteria).
    - **Chromosomal**: Inheritance follows Mendelian principles, with genes located on chromosomes being inherited from both parents.
3. **Genetic Recombination**:
    - **Extrachromosomal**: Recombination can occur, but the mechanisms differ (e.g., plasmid exchange in bacteria).
    - **Chromosomal**: Recombination occurs during meiosis, contributing to genetic diversity.
4. **Functional Impact**:
    - **Extrachromosomal**: Often involves specific traits or functions related to the organelles or plasmids, such as energy production or antibiotic resistance.
    - **Chromosomal**: Affects a wide range of traits and functions related to overall organism development and inheritance.

The Significance of Extrachromosomal Inheritance

The significance of extrachromosomal inheritance lies in its impact on genetics, evolution, disease, and biotechnology. Here are the key aspects:

1. Understanding Non-Mendelian Inheritance Patterns

- **Explanation**: Extrachromosomal inheritance provides insights into inheritance patterns that deviate from classical Mendelian genetics. It explains how certain traits and diseases are passed down through generations in ways that do not fit the traditional dominant, recessive, or sex-linked models.
- **Significance**: This understanding is crucial for diagnosing and managing diseases that follow these non-Mendelian patterns, such as mitochondrial disorders.

2. Implications for Genetic Diseases

- **Explanation**: Many genetic diseases are linked to mutations in extrachromosomal DNA, particularly mitochondrial DNA. These mutations can lead to a wide range of disorders, often affecting energy-demanding organs such as the brain, heart, and muscles.
- **Significance**: Knowledge of extrachromosomal inheritance is essential for genetic counseling, predicting disease risk, and developing targeted therapies. For instance, treatments that address mitochondrial dysfunction are being explored for various conditions.

3. Evolutionary Insights

- **Explanation**: Extrachromosomal DNA, such as that found in mitochondria and chloroplasts, evolves at a different rate than nuclear DNA. Mitochondrial DNA, for example, accumulates mutations more rapidly, making it a valuable tool for studying evolutionary relationships and tracing maternal lineage.
- **Significance**: Mitochondrial DNA is widely used in population genetics, evolutionary biology, and anthropology to study human origins, migrations, and the evolutionary history of species.

4. Role in Horizontal Gene Transfer

- **Explanation**: In bacteria, plasmids (extrachromosomal DNA) facilitate horizontal gene transfer, allowing for the rapid spread of traits such as antibiotic resistance across bacterial populations.
- **Significance**: Understanding horizontal gene transfer is critical for addressing public health challenges, such as the spread of antibiotic-resistant bacteria, which is a major concern in treating bacterial infections.

5. Impact on Plant Breeding and Agriculture

- **Explanation**: Chloroplast inheritance in plants can influence traits such as leaf color, resistance to herbicides, and other agronomically important characteristics. Manipulating chloroplast DNA can lead to the development of crops with desirable traits.
- **Significance**: Plant breeders and agricultural biotechnologists can exploit extrachromosomal inheritance to create more robust and productive crop varieties, which is vital for food security.

6. Biotechnological Applications

- **Explanation**: Plasmids are essential tools in genetic engineering. They are used to introduce new genes into bacteria, plants, and even animal cells, enabling the production of pharmaceuticals, biofuels, and genetically modified organisms (GMOs).
- **Significance**: The ability to manipulate plasmid DNA has revolutionized biotechnology, leading to advancements in medicine, agriculture, and industrial processes.

7. Potential for Gene Therapy

- **Explanation**: Extrachromosomal inheritance pathways, particularly those involving mitochondrial DNA, offer potential targets for gene therapy. By replacing or editing defective mitochondrial DNA, scientists hope to treat or cure mitochondrial disorders.
- **Significance**: Gene therapy targeting extrachromosomal DNA could provide new avenues for treating genetic diseases that currently have limited options.

8. Contribution to Personalized Medicine

- **Explanation**: Variations in mitochondrial DNA can affect how individuals respond to certain drugs or their susceptibility to specific diseases.
- **Significance**: Understanding these variations allows for the development of personalized medical treatments that are tailored to an individual's unique genetic makeup.

9. Insights into Cellular Function and Aging

- **Explanation**: Mitochondrial DNA plays a crucial role in energy production and cellular metabolism. Mutations and dysfunctions in mitochondrial DNA are associated with aging and age-related diseases.
- **Significance**: Research into mitochondrial function and inheritance provides insights into the biological processes of aging, with potential implications for extending healthy lifespan and treating age-related conditions.

10. Understanding Cytoplasmic Inheritance in Development

- **Explanation**: Cytoplasmic inheritance, involving molecules like RNA or proteins in the egg cytoplasm, can influence early embryonic development and the expression of certain traits.
- **Significance**: This has implications for developmental biology and reproductive technologies, such as in vitro fertilization (IVF), where the cytoplasmic environment of the egg can affect the outcome.

Conclusion

In every cell, the Chromosomes are thread-like structures located within the nucleus. Who carry genetic information in the form of genes and are crucial in heredity, cell division, and the functioning of living

organisms.

1.3 Features of Chromosomes, Sex chromosomes

1. Composition of Chromosomes

Chromosomes are made of **DNA** (Deoxyribonucleic Acid) and **proteins**, primarily **histones**, that help in packaging the DNA tightly to fit into the cell nucleus. Each chromosome contains a single long molecule of DNA, which holds thousands of genes.

2. Structure:

A chromosome is a **double-helix** structure, with DNA tightly coiled around histones to form nucleosomes. In a condensed form, a chromosome is visible under a microscope during cell division. The parts of a chromosome are:

- **Chromatid**: Each chromosome consists of two sister chromatids joined at the centromere. The chromatids contain identical genetic information.
- **Centromere**: The region that connects two sister chromatids. It plays a crucial role in the movement of chromosomes during cell division (mitosis and meiosis).
- **Telomeres**: The protective caps at the ends of chromosomes that prevent DNA from degradation and fusing with other chromosomes.
- **Kinetochore**: A protein complex that forms at the centromere and attaches chromosomes to the spindle fibers during cell division.

3. Number of Chromosomes:

Different species have different numbers of chromosomes. In humans, the diploid number (total number of chromosomes) is **46**, arranged in **23 pairs**. Of these, **22 pairs** are autosomes (non-sex chromosomes), and 1 pair are sex chromosomes.

4. Function:

Chromosomes carry **genes**, which encode proteins and determine an organism's traits. They are essential in:

- **Transmission of Genetic Information**: During reproduction, chromosomes ensure that genetic material is passed from parents to offspring.
- **Cell Division**: Chromosomes replicate during cell division (mitosis and meiosis) to ensure that each new cell has the correct genetic information.
- **Evolution**: Chromosome mutations, rearrangements, or variations contribute to genetic diversity and evolution over time.

5

. Homologous Chromosomes:

In diploid organisms, chromosomes come in pairs called **homologous chromosomes**, chromosomes that are similar in size, shape, and genetic content, although the specific alleles they carry may differ, one inherited from each parent.

Types of Chromosomes

1. Autosomes:

Autosomes are the 22 pairs of chromosomes in humans that do not determine an individual's sex. These chromosomes contain genes responsible for most of the body's functions, such as metabolism, immune responses, and physical traits like height and eye color.

2. Sex Chromosomes:

Sex chromosomes, or allosomes, determine the sex of an individual. Humans and most animals have two types of sex chromosomes: **X** and **Y**.

- **Females** typically have two X chromosomes (**XX**).
- **Males** have one X and one Y chromosome (**XY**).

Sex chromosomes not only determine sex but also carry genes responsible for sex-linked traits and some non-sexual traits.

Structure and Features of Sex Chromosomes

X Chromosome

1. **Size and Genes**:
    - The X chromosome is significantly larger than the Y chromosome, containing over **1,100 genes**.
    - It carries genes responsible for various functions beyond sex determination, including development of the brain, muscles, and immune system.
    - Some traits controlled by the X chromosome are **color blindness** and **hemophilia**.
2. **Dosage Compensation (X-inactivation)**:
    - In females (XX), one of the X chromosomes in each cell becomes inactive to prevent double the dose of X-linked genes. This process is called **X-inactivation** or **lyonization**.
    - The inactivated X chromosome forms a **Barr body**, visible in the cell nucleus.
3. **Inheritance**:
    - Males inherit the X chromosome from their mother and pass it to all their daughters but none of their sons.
    - Females inherit one X chromosome from each parent.

Y Chromosome

1. **Size and Genes**:
    - The Y chromosome is much smaller than the X chromosome, containing about **50-200 genes**.
    - Its primary function is sex determination and male development. The **SRY gene** (Sex-determining Region Y) located on the Y chromosome triggers the formation of testes, leading to male characteristics.
    - The Y chromosome carries genes related to sperm production and other male-specific traits.

2. **Inheritance**:
    - The Y chromosome is passed exclusively from father to son, making it a critical marker

for tracing paternal lineage in genetic studies.

3. **Degeneration**:
    - Over time, the Y chromosome has degenerated and lost many of its original genes. It is significantly smaller than the X chromosome, though it still contains essential genes for male fertility.

Sex Determination Systems

Sex chromosomes play a crucial role in determining the biological sex of an organism. There are several sex determination systems across different species:

1. XY System (Humans, Mammals, Some Insects)

- **Females**: XX
- **Males**: XY
- The presence of the Y chromosome determines maleness. The SRY gene on the Y chromosome triggers male development.

2. ZW System (Birds, Some Reptiles, Some Fish)

- **Females**: ZW (heterogametic sex)
- **Males**: ZZ (homogametic sex)
- In contrast to the XY system, females are the ones with two different sex chromosomes.

3. XO System (Some Insects):

- **Females**: XX
- **Males**: XO (only one sex chromosome, X)
- In this system, the presence of two X chromosomes leads to female development, while having only one X chromosome results in a male.

4. Environmental Sex Determination:

- In some species, such as certain reptiles, sex is determined by environmental factors like temperature during egg incubation, rather than by the presence of specific sex chromosomes.

1.4 Gene interactions, Maternal Effect

Chromosome Disorders

Chromosome abnormalities can cause genetic disorders with changes in chromosome number or structure, often leading to genetic disorders.

1. Aneuploidy:

Abnormal number of chromosomes. where chromosomes fail to separate properly during cell division It occurs due to **nondisjunction**.

Common aneuploidies include:

- **Down Syndrome (Trisomy 21)**: Individuals have three copies of chromosome 21, leading to developmental delays, characteristic facial features, and other health issues.
- **Turner Syndrome (45, X)**: Individuals with Turner Syndrome typically have only one X chromosome (instead of two sex chromosomes, i.e., 45 chromosomes total). They develop as

females but often have short stature, infertility, and other health issues.

Turner Syndrome is a chromosomal condition that affects individuals who are phenotypically female. It results from the complete or partial absence of one of the X chromosomes, leaving the individual with only **45 chromosomes** instead of the usual 46.

- **Chromosome Complement**: 45, X (Monosomy X)
- **Sex Chromosome Pattern**: Female (because there is no Y chromosome), but with one X chromosome missing or partially missing.

Symptoms and Features:

- **Physical Characteristics**: Short stature, a webbed neck, a broad chest with widely spaced nipples, and low-set ears.
- **Reproductive Development**: Ovaries fail to develop properly, leading to **infertility** and lack of menstruation (primary amenorrhea). Many individuals require hormone therapy to initiate puberty.
- **Other Health Concerns**: Increased risk of congenital heart defects, such as coarctation of the aorta, and kidney abnormalities. They may also have a higher risk of developing type 2 diabetes, hypothyroidism, and osteoporosis.
- **Cognitive Development**: Most individuals with Turner Syndrome have normal intelligence, but there may be specific learning difficulties, especially with spatial reasoning or math.

Causes:

- Turner Syndrome occurs when a random error in cell division (nondisjunction) results in the loss of an X chromosome in either the sperm or the egg. It is not typically inherited
- and is usually a sporadic genetic event.
- **Klinefelter Syndrome (47, XXY)**: Males have an extra X chromosome, leading to symptoms such as reduced fertility, taller height, and mild cognitive impairment.

Klinefelter Syndrome is a chromosomal condition affecting males, characterized by the presence of an **extra X chromosome**. The genotype is **47, XXY**, leading to a total of 47 chromosomes instead of the usual 46.

- **Chromosome Complement**: 47, XXY
- **Sex Chromosome Pattern**: Male, due to the presence of the Y chromosome.

Symptoms and Features:

- **Physical Characteristics**: Taller than average height, longer limbs, and reduced muscle mass. Individuals may have broader hips and less facial and body hair than typical males.
- **Reproductive Development**: Underdeveloped testes, leading to **low testosterone levels** and reduced fertility. Some individuals may also develop gynecomastia (enlarged breast tissue).
- **Cognitive Development**: Individuals with Klinefelter Syndrome may have normal intelligence but often experience mild learning disabilities, especially in language and executive functioning (organization, planning). They may also have challenges with reading and writing.
- **Psychosocial Impact**: Boys with Klinefelter Syndrome may experience delayed puberty, leading to feelings of social isolation or low self-esteem due to differences in physical development.

Causes:

- Klinefelter Syndrome is caused by **nondisjunction**, where the X chromosomes fail to separate properly during the formation of egg or sperm cells. It can occur in either the mother's egg or the father's sperm and is generally not inherited.

Treatment:

- **Hormone Therapy**: Testosterone replacement therapy can help induce more typical male secondary sexual characteristics, such as increased muscle mass, deepening of the voice, and facial hair growth.
- **Educational Support**: Early intervention for learning difficulties is important for managing the cognitive effects.

2. Structural Abnormalities:

Structural abnormalities in chromosomes can result from deletions, duplications, inversions, or translocations.

Maternal Effect Genes: A Key to Early Developmental Processes

Maternal effect genes are a specialized class of genes where the genotype of the mother directly influences the phenotype of her offspring through the products she provides to the egg during oogenesis. Unlike most genes, where the offspring's own genotype determines its traits, maternal effect genes exert their influence at the very earliest stages of embryonic development, often before the zygotic genome becomes active. These genes are crucial in setting up the developmental blueprint that will guide the formation and organization of the embryo.

Mechanisms of Maternal Effect Genes

Maternal effect genes function primarily by encoding proteins, RNAs, or other molecules that the mother deposits into the egg. These molecules are typically involved in the regulation of early developmental processes, such as:

1. **Axis Formation**:
    - In many species, maternal effect genes help establish the body axes of the embryo (e.g., anterior-posterior, dorsal-ventral). For example, in *Drosophila melanogaster* (fruit fly), the *bicoid* gene is a well-known maternal effect gene. The *bicoid* mRNA is localized at the anterior end of the egg, and after fertilization, it is translated into a protein that forms a gradient. This gradient of Bicoid protein determines the anterior structures of the embryo.
2. **Cellular Differentiation**:
    - Maternal effect genes can also influence the early differentiation of cells. In the nematode Caenorhabditis *elegans*, the maternal effect gene *glp-1* encodes a protein involved in cell signaling that directs the fate of certain cells in the early embryo.
3. **Epigenetic Regulation**:
    - These genes can affect the epigenetic state of the embryo by influencing DNA methylation patterns or histone modifications, which can regulate gene expression patterns throughout development. For example, certain maternal effect genes in mammals are involved in establishing the correct imprinting patterns, which are critical for normal development.

Examples of Maternal Effect Genes

1. *Drosophila melanogaster* (Fruit Fly):

- ***Bicoid***: This gene is responsible for setting up the anterior-posterior axis of the embryo. *Bicoid*

mRNA is localized at the anterior pole of the egg, and its protein product forms a concentration gradient that determines head and thorax development. Offspring from mothers lacking functional *bicoid* fail to develop anterior structures properly, regardless of their own genotype.

- ***Nanos***: Another key maternal effect gene in *Drosophila*, *nanos* is localized at the posterior end of the egg and is crucial for abdomen formation. Like *bicoid*, *nanos* mRNA is deposited in the egg by the mother, and its translation after fertilization creates a gradient that determines the posterior structures.

2. *Caenorhabditis elegans* (Nematode):

- ***Glp-1***: This gene is critical for the proper development of germ cells and early embryonic cells. The *glp-1* protein is involved in cell-cell signaling that determines the fate of various cells during the early stages of the embryo's development.

3. Mammals:

- **Zona Pellucida Genes**: In mammals, maternal effect genes are involved in the formation of the zona pellucida, a protective glycoprotein layer surrounding the oocyte. The genes encoding the proteins that make up the zona pellucida, such as *ZP1*, *ZP2*, and *ZP3*, are expressed during oogenesis, and mutations in these genes can result in infertility due to defective egg development.
- ***Stella* (Dppa3)**: In mice, the maternal effect gene *Stella* is important for the regulation of DNA methylation and the preservation of genomic imprinting during early development. Offspring from *Stella*-deficient mothers exhibit severe developmental defects, despite having a normal genotype.

Evolutionary and Developmental Significance

Maternal effect genes are not just essential for normal development but also play a significant role in the evolution of developmental processes. They can contribute to evolutionary change by allowing rapid adaptation to environmental conditions. For instance, changes in the regulation or expression of maternal effect genes can lead to significant changes in the developmental pathways and resulting phenotypes without altering the zygotic genome.

Moreover, maternal effect genes provide a mechanism for transgenerational inheritance of traits, where the mother's genotype can influence the phenotype of multiple generations. This can be particularly important in fluctuating environments, where maternal effects can provide a form of phenotypic plasticity that allows offspring to better cope with environmental challenges.

Conclusion

Maternal effect genes are a fascinating and crucial component of developmental genetics. They represent a unique intersection between the mother's genotype and the offspring's phenotype, influencing the earliest stages of development through the provision of essential gene products. The study of maternal effect genes has provided deep insights into the mechanisms of development and evolution, highlighting the intricate ways in which life is shaped from the very beginning. Understanding these genes continues to be a vital area of research, with implications for everything from developmental biology to evolutionary theory.

1.6 Linkage

The principle of linkage was discovered by Willium Bateson and R.C. Punnet in 1906 in sweet pea. But it was put forward as a regular concept by T. H. Morgan in 1910 in *Drosophila melanogaster*. Linkage is defined as the tendency of two or more genes to remain together in the original combination

in the same chromosome during the process of inheritance for a number of generations. Such genes are called as linked genes.

According to linkage theory some of the main principle are as follows

- Linkage involves two or more genes which are linked in same chromosomes in a linear fashion.
- Linked genes are inherited together from the parents to the off springs.
- Linkage reduce variability
- Linkage is a rare phenomenon
- Linkage involve either dominant or recessive alleles (coupling phase) or some dominant and some recessive alleles (repulsive phase)
- Linkage is usually involves those genes which are located close to each other.
- The strength of linkage depends on the distance between the linked genes. If genes are closely related it shows strong linkage and if genes are widely located it shows weak linkage.
- The linked genes do not show Mendel's law of independent assortment.
- If the dominant genes are located on one homologous chromosome and the recessive genes on the other homologous chromosome, the arrangement of linked genes is called cis-arrangement.
- If the dominant genes and recessive genes are linked in one chromosome, the arrangement is called trans-arrangement.
- All the genes on a pair of homologous chromosomes collectively form a linkage group. The number of linkage group of any species of plant or animal will be equal to the number of chromosome pairs. This hypothesis was given by Sutton (1903) and confirmed by Morgan
  - *Drosophila* have 4 pairs of chromosomes therefore 4 linkage group
  - Human has 23 pairs of chromosomes and therefore 23 linkage group
  - Sweet pea has 7 pairs of chromosomes and therefore 7 linage group

T. H. Morgan and co-workers have found 2 types of linkage in *Drosophila*

(a)Complete linkage

(b)Incomplete linkage

(a)Complete linkage : If the chances of separation of two linked genes are not possible those genes always remain together as a result, only parental combinations are observed. The linked genes are located very close together on the same chromosome such genes do not exhibit crossing over. This phenomenon is called complete linkage. It is rare but has been reported in male *Drosophila*.

The example of complete linkage in *Drosophila* is grey body vestigial wing was cross with black body normal wing.

According to T.H. Morgan when a cross of Drosophila A male with grey body vestigial wing (b^+vg/b^+vg) crossed with female having black body and normal wings were found.

The male of F1 generation with grey body and normal wing was crossed with a female of black body with vestigial wing, it is a test cross here in male only two types of gametes i.e. b^+vg and bvg^+ were formed due to complete linkage and lack of crossing over in male *Drosophila* and in female only two types of progeny was formed one with grey body and vestigial wing (b^+vg/bvg) and other black body with normal wing (bvg^+/bvg). As four types of phenotypes were supposed to form but due to complete linkage only 2 types of phenotypes are formed and ration is 1: 1.

(b)Incomplete linkage : If two linked genes are sufficiently apart, the chance of their separation are possible. As a result parental and non-parental combinations are observed. The linked genes exhibit some crossing over. This phenomenon is called incomplete linkage. If accidental breakage in the chromosome takes place in one place or many and the characters do not remain together even for few generation.

For example In female *Drosophila* grey vestigial wing (b^+vg / b^+vg) and black normal wing (bvg^+/bvg^+) were test crossed to double recessive (bvg/bvg) males. It shows as follows

Parents : Grey, Vestigial Wing — Black long Wing

b^+vg / b^+vg — bvg^+/ bvg^+

Gametes : b^+vg — bvg^+

F1 : b^+vg / b^+vg

Grey & Normal wing

Test cross : F1 female grey long X Male Black, vestigial wing

b^+vg / b^+vg — bvg / bvg

Gametes : (b^+vg) (bvg^+) = Non crossovers (bvg)

(b^+vg) (bvg) = Recombinants

Test cross ratio :

1. Grey, Vestigial	b^+vg / bvg	= 41.5 %
2. Black, long	bvg+ / bvg	= 41.5 %
3. Grey long	b^+vg^+/ bvg	= 8.5 %
4. Black, Vestigial	bvg / bvg	= 8.5 %

In such cases when parents of grey body vestigial wing (b^+vg/b^+vg) was crossed with black body normal wing (bvg^+/bvg^+). In F_1 generation all of the them were with grey body and normal wing. When this F1 generation female grey body normal wing (b^+vg /bvg) were crossed with recessive wing (bvg / bvg). The following four types of phenotypes were found

1. Grey body Vestigial wing	b^+vg / bvg	= 41.5 %
2. Black body long wing	bvg+ / bvg	= 41.5 %
3. Grey body long wing	b^+vg^+/ bvg	= 8.5 %
4. Black body Vestigial wing	bvg / bvg	= 8.5 %

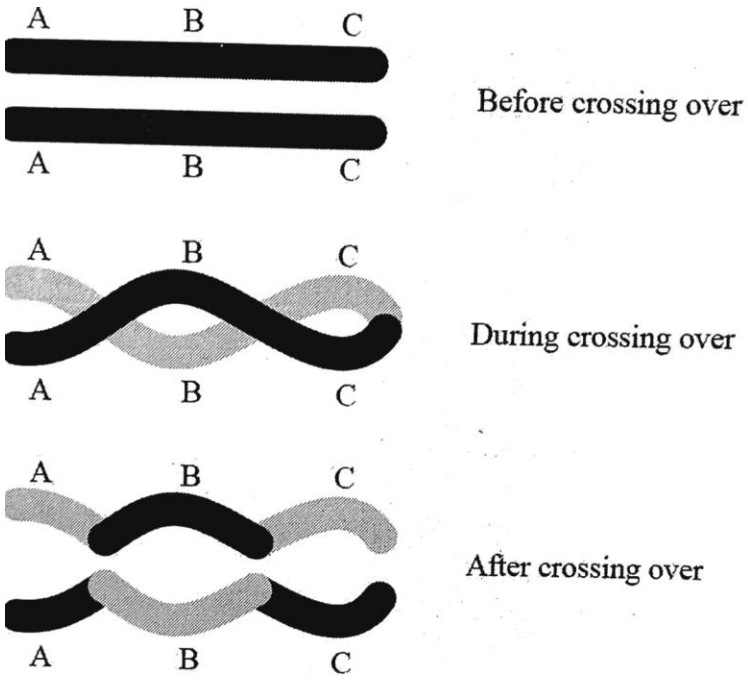
From above 83% parental combination grey body, vestigial wing and black body long wing showed linkage, while 17 % of them with phenotype grey body long wing and black body vestigial wing showed recombination.

Crossing over

The term crossing over was given by T.H. Morgan. Crossing over is a process that produces new combination or recombination of genes by interchanging of corresponding segments between non-sister chromatids of homologous chromosomes. Crossing over occurs during meiosis or gametogenesis. The number of crossing over depends upon the length of the chromosome. The longer the length, the higher the percentage of crossing over. The number of chromosome over between two genes is represented by percentage of crossing over. The percentage of crossing over is directly proportional to the distance

between two genes. It can express.

$$\text{Crossing over} = \frac{\text{Percentage of total number of offspring in F2}}{\text{Total number of recombination}} \times 100$$



The recombination accomplished through crossing over

(1) Crossing over occurs at two levels, when crossing takes place at gross chromosomal level, it is called chromosomal crossing over and when it take place at DNA level called genetic recombination.

(2) A reciprocal exchange of material between homologous chromosomes in heterozygotes is reflected in crossing over.

(3) The crossing over results basically from an exchange of genetic material between non-sister chromatid by break and exchange following replication.

(4) The frequency of crossing over appears to be closely related to physical distance between genes on chromosome and serves as a tool in constructing genetic maps of chromosomes.

Types of crossing over

(a)Mitotic or somatic crossing over : When the process of crossing over occurs in the chromosomes of body or somatic cells of an organism during the mitotic cell division it is called mitotic or somatic crossing over.

(b)Meiotic or germinal crossing over : When the crossing over occurs in germinal cells during the gametogenesis during the meiotic cell division.

Mechanism of crossing over

It include following steps

(1)Synapsis

(2)Duplication of chromosomes

(3)Crossing over

(4)Terminalization

(1) Synapsis : Pairing between two homologous chromosome one from paternal and one maternal in presence of synaptonemal complex. The homologous chromosome undergo lengthwise pairing occur. The pairing start at one or more points and proceeds along the whole length in a zipper fashion called synapsis. Synapsis may be terminal, procentric or random. The paired homologous chromosomes are called bivalent and it takes place during prophase.

(2) Duplication of chromosomes : Such take place during pachytene phase of meiosis. After synapsis duplication of chromosome take place in which change of bivalent chromosome into tetravalent stage. The two sister chromatids are attached with unsplitted centromeres.

(3) Crossing over : In such stage, exchange of segment between the non-sister chromatids of homologous chromosomes at tetravalent stage. In such the two non sister chromatids first break at particular point due to endonuclease enzyme then a segment on one side of each break connects with a segment on the opposite side of the break, so that the two non-sister chromatids cross each other. The crossing of two chromatids is known as chiasma formation.

(4) Terminalization : After the chiasma formation the non sister chromatids starts repel each other due to the force of synapsis attraction between them decreases. Chiasma itself moves in a zipper fashion towards the end of tetrad. This movement of chiasma is known as terminalisation.

Types of crossing over : It depend upon the number of chiasma is appeared. The crossing over is of 3 types.

(1) ***Single cross-over*** **:** In such case when only one chiasmata develop. These chiasmata may appear between the chromatids.

(2) ***Double cross over*** **:** In such type two chiasmata develop. These chiasma may appear between the chromatids.

(3) ***Multiple cross over*** **:** In such types when more than two chiasmata are formed.

There are many **theories** to explain the mechanism of crossing over

(1)Chiasma Theory : This theory was proposed by Janssens. According to this theory before crossing over, the chromosome of each bivalent get duplicated to form tetrad. Now crossing over takes place between non-sister chromatids of a tetrad, which overlap with one another and form chiasma. In the chiasma the chromatids break and they rejoin with the mutual exchange segment, while the other two chromatids remain intact.

(2)Breakage theory : This was proposed by Muller. According to this, the non sister chromatids of homologous chromosome break off first without crossing over, then the broken segments rejoin to form new combination.

(3)Contact Theory : This was proposed by Serebrovsky. According to this non-sister chromatids first touch and cross each other, then breakage occur at the chiasma of chromatid. The broken segments rejoin to form new combination.

Factor affecting crossing over

(a)Mutation : It reduces crossing over

(b)X-ray effect : X-ray increases frequency of crossing over.

(c)Temperature : Increase or decrease in temperature will effect frequency of crossing over. High temperature increases frequency of crossing over.

(d)Age : Age is inversely proportional to the crossing over as age increases there is decrease in frequency of recombination.

(e)Sex : There is a tendency of reduction of crossing over in male.

Significance of crossing over

(i) Due to change of segment from one chromosome to another chromosome, give rise to the origin of new characters

(ii) There is strong proof in favour of linear arrangement of genes on the chromosomes.

(iii) Crossing over generates genetic difference within a population

(iv) Crossing over help in making of linkage map & genetic map.

Extra chromosomal Inheritance

It has been observed that phenotypic characters are controlled by the chromosome present in nucleus. But it is also seen that some characters are also expressed by the factor present in the cytoplasm. So these factors which are present in cytoplasm are called plasmagenes. The plasmagenes transmit characters from one generation to generation. Hence as plasmagenes are present in cytoplasm, so this phenomenon is called cytoplasmic inheritance or Extrachromosomal inheritance. This was proposed by Correns in 1908.

Characteristics of extra chromosomal inheritance

(1) It does not follow the typical Mendelian inheritance pattern.

(2) The inheritance of extrachromosomal factors is independent of genes located within the cell nucleus.

(3) In some cases egg contributes more cytoplasm to the zygote as compared to male gametes. Hence the plasmagenes of female parent alone contributed to the offspring. So such cytoplasm inheritance is also called maternal inheritance.

(4) Plasmagenes are self-replicating.

(5) Plasmagenes are transmitted by means of cytoplasm only.

(6) Plasmagenes are capable of mutation.

Example of cytoplasmic inheritance

(1) Kappa particles in Paramecium

(2) Shell coiling in snail

(1)Kappa particles in Paramecium : There are two strains in Paramecium. One is killer strain and other is sensitive strain. The killer strain produces a toxic substance called paramecin that kills the sensitive strain. The production of paramecin in killer type is controlled by kappa particle present in cytoplasm. The sensitive strain does not contain kappa particles in its cytoplasm. The kappa particles are passes from one generation to the next generation in the process of cell division. The kappa particles are also multiplied with cell division. The kappa particles are transmitted from one cell to another through the cytoplasm. The multiplication of kappa particles is controlled by a dominant nuclear gene K and the sensitive strain have the recessive allele k. The kappa particle is dependent for its continued existence on K. The gene K can only maintain the kappa particles and cannot initiate its production.

When the killers KK conjugate with non killer kk, the ex-conjugants are Kk. But the development of a particular type depends upon the duration of cytoplasmic exchange. In normal

conjugation process only nuclear material is exchanged, no cytoplasm material exchange take place. In such situation each conjugants give rise to the organism of its own type i.e. killer ex-conjugant produce killer type and nonkiller produces non killer type.

Some time conjugation period is long and cytoplasmic bridge between two conjugants is larger. In such situation, nuclear material along with the cytoplasmic materials are also exchanged. During this cytoplasmic exchange, the kappa particle which is present in killer type enters into the non killer type and convert non killer into killer type. So all the offspring produce by the ex-conjugants are of killer type.

This shows that a Paramecium becomes a killer when it receives kappa particles and when it does no recessive kappa particle it become sensitive type.

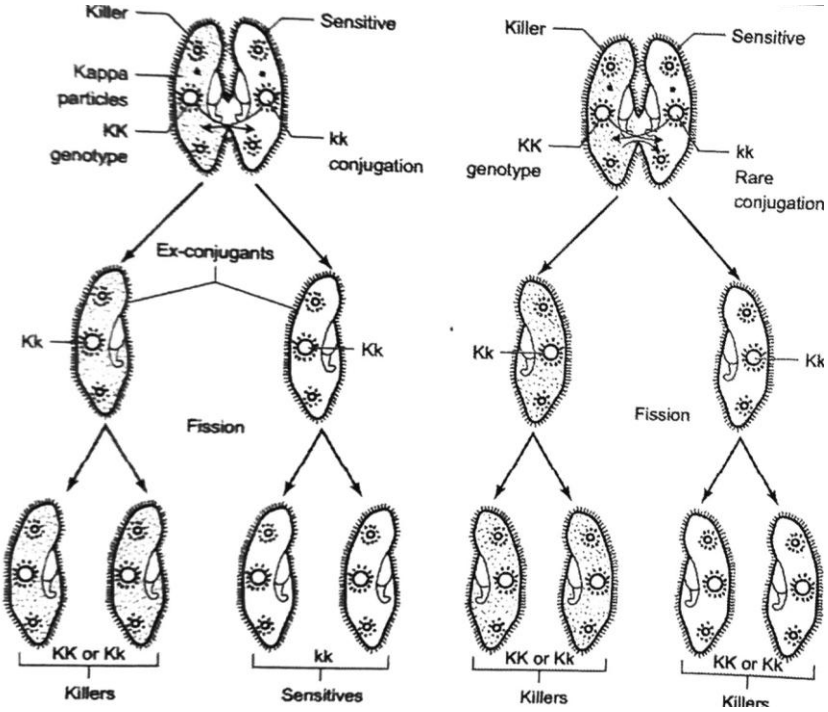


Fig : Conjugation without and conjugation with cytoplasmic exchange

(2)Shell coiling in Snail : The snail *Limnaea* shows two types of coiling i.e. dextral (toward right side) and sinistral (towards left side). The dextral coiling is due to dominant alleles "DO" while the sinistral coiling is due to recessive alleles "do". The coiling is determined by the gene of the mother and not by the individuals own gene.

If a dextral female is crossed with sinistral male, all the F1offspring develop dextral shell like the mother. When a cross occurs between sinistral female and dextral male, the eggs will develop into sinistral type like the mother. It clearly indicates that the offspring, irrespective of their own genotype, exhibit the effect of their mother's genotype. This maternal influence is due to the presence of some cytoplasmic bodies in the egg cell. The phenotype of the offspring is determined by the genotype of the female parent. In the crosses, it is evident that the genotype "Dd" can be dextral as well as sinistral depending on the genotype of the female parent. Similarly dd can be dextral if the genotype of the female parent is dominant (Dd). It should be carefully noted that the phenotype of the female parent does not have any effect on the phenotype of the offspring. It is the genotype of the female parent which determines the phenotype of the offspring. This is an example of the delayed effect of the genotype.

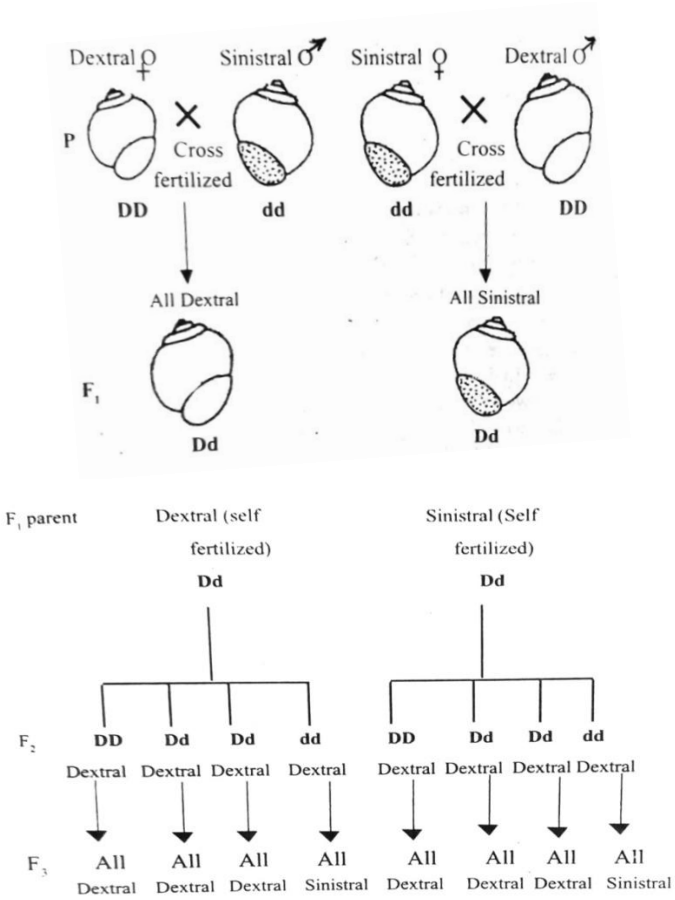


Fig : Maternal effect in direction of coiling of the shell in *Limnaea* –Inheritance of Shell coiling

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1.7 Summary

- Mendel's Law of Segregation states that each individual has two alleles for each gene, and these alleles separate during the formation of gametes. As a result, each gamete carries only one allele for each gene.
- Mendel's Law of Independent Assortment states that the alleles for different genes assort independently of one another during gamete formation.
- Incomplete dominance is intermediate between the two homozygotes because neither allele is completely dominant, and the heterozygote exhibits a phenotype.
- Autosomes are the 22 pairs of chromosomes in humans that do not determine an individual's sex. These chromosomes contain genes responsible for most of the body's functions, such as metabolism, immune responses, and physical traits like height and eye color.
- Chromosome abnormalities can cause genetic disorders with changes in chromosome number or structure, often leading to genetic disorders.

- Abnormal number of chromosomes. where chromosomes fail to separate properly during cell division It occurs due to nondisjunction.
- Genes that are located close to each other on the same chromosome tend to be inherited together, a phenomenon known as genetic linkage.
- Extranuclear inheritance, or the inheritance of genetic material from organelles like mitochondria and chloroplasts, plays a crucial role in many biological processes and deviates from classical Mendelian inheritance. This form of inheritance follows different patterns, primarily maternal inheritance
- Extrachromosomal inheritance, also known as cytoplasmic or non-Mendelian inheritance, involves the transmission of genetic material located outside the nucleus. There are several types of extrachromosomal inheritance, each associated with different organelles or genetic elements.

1.8 Terminal Questions

1. Explain the Mendalian inheritance and Non-Mendelian Patterns of Inheritance

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2. Explain the Features of Chromosomes, Sex chromosomes

   Explain the Gene interactions, Maternal effect.

   Explain the Extranuclear inheritance.

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3. Explain the Linkage and Genetic Mapping.

1.9 Answers

Reference 1) Gardner, E.J. Simmons, M.J. Snustad, D.P. (2008), Principles of Genetics. VIII Edition. Diley India.

2) Gupta P.K. 2007 Genetics.

3) Verma P.S. and V.K. Agrawal 2004 Cell Biology, Genetics, Molecular Biology, Evolution and Ecology.

4) Winchester A.M. – Genetics.

SAQ. 1

a) genetic disorders.
b) cell division
c) genetic linkage.
d) Mendelian inheritance
e) transmission of genetic

Unit 2Genetic transfer and Mapping in Bacteria

2.1Introduction

Bacteria are known to adapt and evolve to changing environments. One of the key mechanisms that contribute to this adaptability is genetic transfer, which allows bacteria to acquire new traits and evolve at a much faster rate than through mutation alone. The transfer of bacterial genetic material can be done through numerous mechanisms. The most common mechanisms are transformation, transduction, and conjugation. It is significant to know the definition of these three processes and the mechanism by which the genes are transferred.

Transformation is the uptake of free DNA by bacteria from the environment. This process can occur naturally, where bacteria take up DNA fragments released by dead cells, or artificially, where laboratory techniques are used to introduce DNA into bacterial cells.

Conjugation is the direct transfer of genetic material between bacteria through a physical connection between the cells. This transfer is mediated by a round DNA known as plasmid, a molecule that has the capacity to replicate independently. The plasmid contains genes that encode the transfer machinery, allowing the plasmid to be transferred between bacterial cells.

Transduction is a process in which the transfer of genetic material occurs from one bacterium to other via a bacteriophage (bacterial cell infected by virus). During transduction, the bacteriophage inserts its DNA into the host cell's genome. As the virus replicates, it can pick up fragments of the host DNA and package them into new viral particles. These particles can then infect other bacteria, transferring the genetic material. In this unit the phenomenon of transformation, conjugation and transduction will be discussed in detail highlighting the essential pathways through which these phenomena occur.

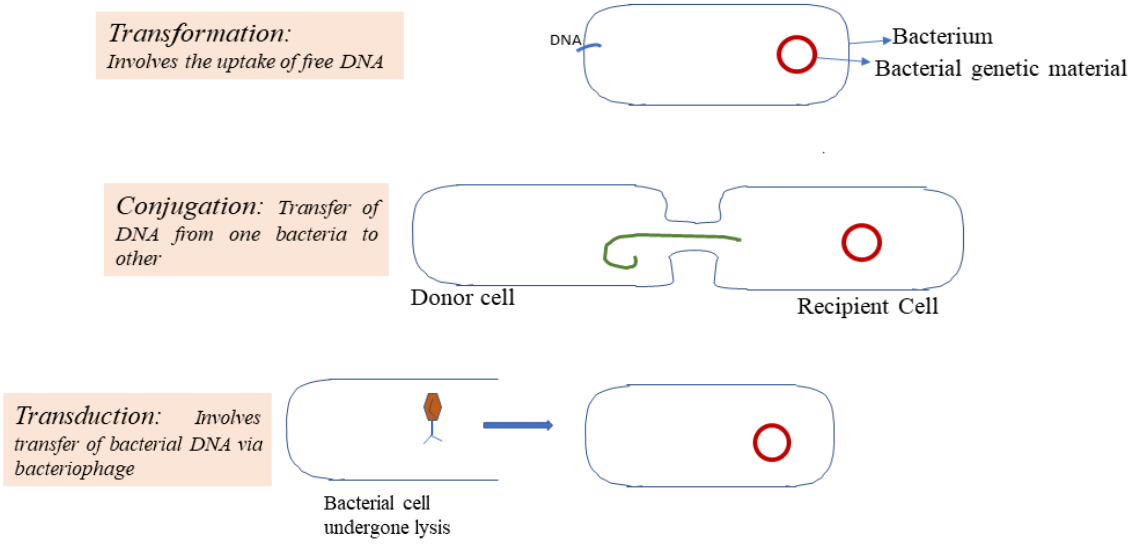

Figure 1. Transformation, conjugation and transduction are the three major types of gene transfer in bacteria.

Objective:

After studying this unit, you will be able to know-

- Bacterial transformation, selection and mapping
- Bacterial conjugation and mapping via Hfr strains
- Bacterial Transduction

2.2 Bacterial transformation, selection and mapping

Bacteria are an incredibly diverse group of organisms that can be found in almost every environment on Earth. They are known for their ability to adapt and evolve rapidly, which is in part due to their ability to transfer genetic material between cells. One of the most important mechanisms of gene transfer in bacteria is transformation, which allows bacteria to take up DNA from the environment and incorporate it into their own genome. This essay will explore the process of bacterial transformation, as well as how selection and mapping are used to study the genetic changes that result from this process.

- **Bacterial Transformation**:

Transformation is the process by which bacteria take up DNA from their environment and incorporate it into their own genome. This process was first discovered by Frederick Griffith in 1928, when he observed that heat-killed virulent bacteria could transfer their genetic material to live non-virulent bacteria, causing them to become virulent. Later, Oswald Avery, Colin MacLeod, and Maclyn McCarty identified DNA as the genetic material responsible for this transformation.

In the year 1928, Griffith was the scientist who discovered the phenomenon of transformation in bacteria named Streptococcus pneumoniae (pneumococcus). When cultured on blood agar medium, pneumococci with capsules form large, smooth colonies are the S type. This is the virulent group with encapsulated pneumococci which causes pneumonia in mice and humans. The other group referred as R contains nonencapsulated, avirulent medium, such nonencapsulated, avirulent pneumococci produce small, rough-surfaced colonies. The two strains virulent and avirulent are classified depending on the presence of a polysaccharide capsule and its absence. Virulent strains have it and avirulent lack it. The bacteria which lack the coating are easily engulfed and destroyed by the phagocytic cells present in host animal's circulatory system. Virulent bacteria are not easily engulfed due to the presence of polysaccharide coat and thus multiply and cause pneumonia. The virulent or encapsulated bacteria form smooth colonies and are referred as S and are cultured on agar culture plate whereas the other avirulent or nonencapsulated strains produce rough colonies (R).

Griffith along with the previous work knew that the live virulent cells are needed for the onset of pneumonia in mice. The heat-killed virulent strains of bacteria when injected into mice leading to no pneumonia. The same was with the live avirulent bacteria. In addition to it the major experiment was to inject the living IIR (avirulent) cells combined with heat-killed IIIS (virulent) cells into mice. Assuming that the earlier experiments suggested that neither cell type caused death in mice when injected alone the same would happen here in this case of double. The outcome was unexpected when after 5 days, all of the mice were dead on receiving both types of cells. Further the scrutiny of their blood discovered a large number of living type III*S* (virulent) bacteria. This experiment and its interpretations were the crucial to understand the phenomenon of transformation.

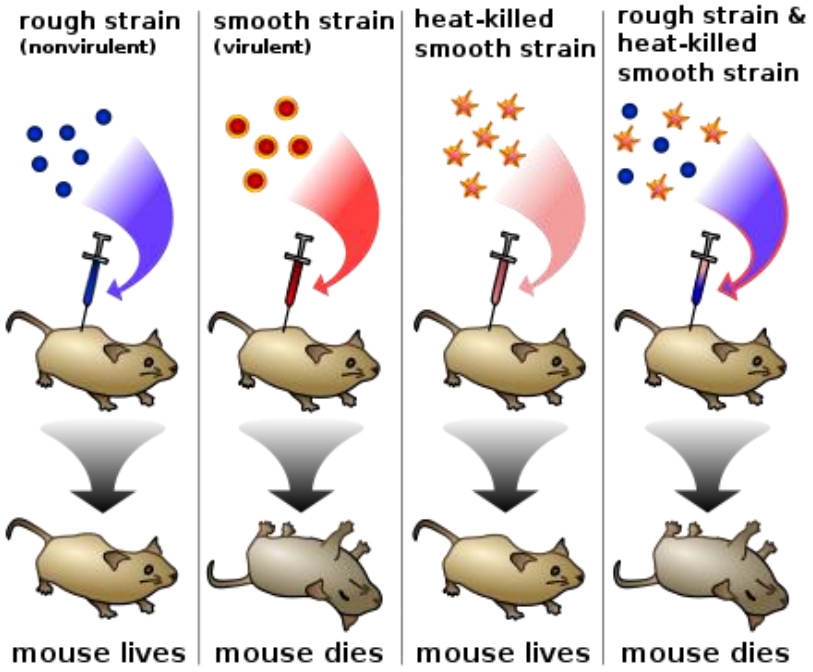

Figure 2. Griffith's experiment demonstrating transformation in bacteria.(**Source**:*https://en.wikipedia.org/wiki/Griffith%27s_experiment*)

There are two main types of transformation: natural transformation and artificial transformation. Natural transformation occurs when bacteria take up DNA from the environment, while artificial transformation is the process by which DNA is introduced into bacteria in the laboratory.

(a) Natural Transformation: Natural transformation occurs when bacteria take up DNA fragments from their environment. This process is facilitated by the presence of specific DNA uptake sequences on the bacterial cell surface, which bind to DNA fragments in the environment. Once bound, the DNA is transported across the cell membrane and incorporated into the bacterial genome through recombination with the recipient chromosome. Natural transformation is most commonly observed in certain bacterial species, such as *Streptococcus pneumoniae* and *Haemophilus influenzae*. In these organisms, natural transformation plays an important role in genetic diversity and evolution, allowing the bacteria to acquire new traits that can help them survive in changing environments.

(b) Artificial Transformation: Artificial transformation is the process by which DNA is introduced into bacteria in the laboratory. This process is often used to introduce specific genes or genetic elements into bacteria for research purposes. One of the most common methods of artificial transformation is electroporation, which involves applying a high-voltage electric field to bacterial cells that have been made competent (able to take up DNA). This electric field creates pores in the bacterial cell membrane, allowing DNA to enter the cell. Alternative common method of artificial transformation is chemical transformation, which includes treating bacterial cells with a chemical that makes them more permeable to DNA.

Selection: After transformation, the bacteria that have taken up the DNA must be selected from those that have not. This process is known as selection and is often used to isolate bacteria that have acquired a specific genetic trait, such as antibiotic resistance.

The most common method of selection is antibiotic resistance selection. This method involves growing bacteria on a medium that contains an antibiotic to which only the transformed bacteria are

resistant. Bacteria that have not taken up the DNA will not survive on this medium, while those that have taken up the DNA and developed resistance will grow and form colonies.

Another method of selection is fluorescence-activated cell sorting (FACS). This method involves tagging the transformed bacteria with a fluorescent marker and then using a machine to sort the bacteria based on their fluorescence.

Mapping: Mapping is the process of determining the relative positions of genes on a chromosome or plasmid. In bacteria, mapping can be used to identify the location of genes that have been acquired through transformation.

There are two main types of mapping: linkage mapping and physical mapping.

(a) Linkage Mapping: Linkage mapping follows the principle of genetic linkage, where genes that are physically close together on a chromosome are more likely to be inherited together. This mapping technique involves crossing two bacterial strains that differ in a particular trait, such as antibiotic resistance. The resulting offspring are then screened to identify which traits are linked and which are not. By analyzing large numbers of these crosses, researchers can build a genetic map of the bacterial genome.

(b) Physical Mapping: Physical mapping involves determining the physical location of genes on a chromosome or plasmid. This technique is based on the fact that different DNA fragments have different sizes and can be separated by electrophoresis. Physical mapping can be done using two main methods: restriction mapping and sequencing. Restriction mapping involves cutting the DNA into fragments using restriction enzymes and then analyzing the resulting fragments by electrophoresis. By comparing the sizes of the fragments produced by different restriction enzymes, researchers can determine the relative positions of the genes on the chromosome or plasmid.

Sequencing involves determining the precise order of nucleotides in the DNA. This technique can be done using a variety of methods, including Sanger sequencing and next-generation sequencing. By comparing the sequences of different strains or plasmids, researchers can identify the genes that have been acquired through transformation and determine their precise locations on the chromosome or plasmid.

Bacterial transformation, selection, and mapping have a wide range of applications in both basic and applied research. For example:

(a) Basic Research: Bacterial transformation, selection, and mapping are important tools for studying the genetics and evolution of bacteria. By mapping the bacterial genome, researchers can identify the genes responsible for important traits, such as virulence and antibiotic resistance. This information can be used to understand the molecular mechanisms underlying bacterial adaptation and evolution.

(b) Biotechnology research: Bacterial transformation, selection, and mapping are important tools for biotechnology. By introducing new genes or genetic elements into bacteria, researchers can produce new proteins, enzymes, or other biotechnologically important products. This technique is used in the production of a wide range of products, including antibiotics, vaccines, and industrial enzymes.

(c) Medicine: Bacterial transformation, selection, and mapping are important tools for medical research. By mapping the genome of bacterial pathogens, researchers can identify the genes responsible for virulence and antibiotic resistance. This information can be used to develop new treatments and vaccines for bacterial infections.

(d) Environmental Cleanup: Bacterial transformation, selection, and mapping are important tools for environmental remediation. By introducing new genes or genetic elements into bacteria, researchers can produce bacteria that are capable of breaking down environmental pollutants, such as oil spills or toxic chemicals.

By mapping the bacterial genome and identifying the genes responsible for important traits, researchers can develop new strategies for improving human health and the environment. As our understanding of bacterial genetics and evolution continues to grow, these techniques will become increasingly important for a wide range of applications.

2.3 Bacterial conjugation and mapping via Hfr strains

Bacterial Conjugation:

Bacterial conjugation is the transfer of genetic material from one bacterium to other. This process of genetic recombination is important for development of chromosome mapping. It involves physical mating between different strains for transfer of genetic material unidirectionally. DNAtransfer from a donor cell to arecipient cell occurs during conjugation by formation of a channelor bridge. Conjugation helps in the spread of antibiotic resistance genes and other virulence factors. In this section, we will discuss bacterial conjugation and mapping via Hfr strains, a technique used to study bacterial genetics and gene transfer.

Bacterial conjugation was first discovered by Joshua Lederberg and Edward Tatum in 1946. They observed that two varied strains of *Escherichia coli* could exchange genetic material when they were grown together in a culture medium.

The two scientist Lederberg and Tatum findings were used to design many experiments for explaining the process of conjugation. Through these arrangements it was evident that bacterial strains are involved in unidirectional transfer of genetic material. Cells those who serve as donor of parts of their chromosomes are F+ cells (F is for fertility).

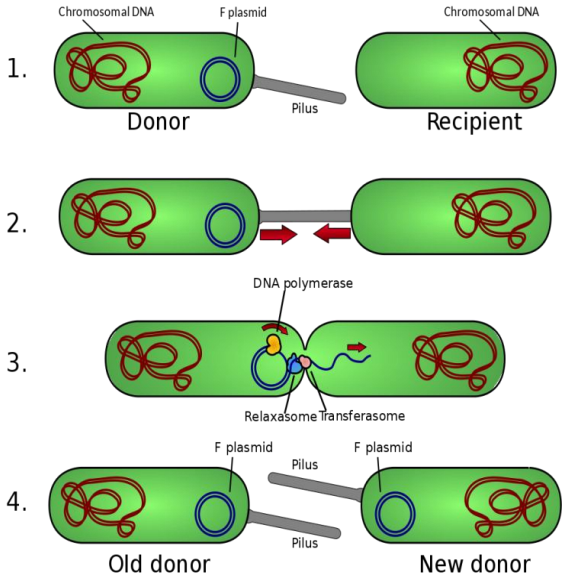

Figure 3. Bacterial conjugation (**Source**:*https://en.wikipedia.org/wiki/Bacterial_conjugation*)

Recipient bacteria obtain the donor chromosome (DNA) and recombine it by part of their own chromosome known as F^- cells. It was proved that the cell contact is important for the chromosome transfer. This was established by a simple experiment performed by Bernard Davis. The tube used was U shaped tube for growing F^+ and F^- cells.

Lederberg started his study by an experiment including two double mutant strains. One of the strains was not able to synthesize amino acids like threonine (thr-) and leucine (leu-). The second strain could synthesize them but were unable to make vitamins such as biotin (bio-) and amino acid methionine (meth-). Thus, the genotypes of the two strains were:

&

bio^+	$meth^+$	thr^-	leu^-
bio^-	$meth^-$	thr^+	leu^+

Here (+) sign denoted the wild gene which has the capacity to synthesize the required substance. Both the strains were unable to flourish or grow on the minimal medium. These strains which are mutants are called auxotrophs. The wild strains from which they are derivative are prototroph. An experiment was performed where the two auxotrophs mentioned above were plated together on a minimal medium, growth was observed. The time when the growing cells were analyzed the appeared to be the wild type cells with genotype bio^+ $meth^+$ thr^+ leu^+. Frequency was very low for such cells. Further it was concluded by Lederberg and Tatum that the growing cells of this genotype are the recombinants produced by the combination of genes.

The process of conjugation involves the transfer of plasmids from one bacterium to another through a specialized structure called a conjugation bridge or pilus.In conjugation, the donor cell contains a plasmid that carries genes for the synthesis of the pilus and for the transfer of the plasmid. The pilus is a long, thin appendage that extends from the donor cell to the recipient cell. The transfer of the plasmid occurs through the pilus, and the recipient cell becomes a donor cell after the transfer is complete. The plasmids that are transferred during conjugation can carry a variety of genes, including antibiotic resistance genes, virulence factors, and metabolic genes. The transfer of these plasmids can have important implications for human health, as it can lead to the spread of antibiotic resistance and other harmful traits.

- **High frequency of recombination (Hfr) Strains:**

A cell which carries an F factor linked to it is termed an **Hfr cell** (*h*igh-*fr*equency *r*ecombination).In its condition the F factor facilitates transfer of the chromosome from Hfr cell to a recipient (F−) cell through conjugation (Hfr × F− mating). These cells usually detach before the transfer of chromosome iscomplete. It is rare to find an intact complete chromosome being transferred from an Hfr cell to a recipient cell.

Hfr strains are important tools for studying bacterial genetics and gene transfer. The integration of the F plasmid into the bacterial chromosome allows for the transfer of chromosomal genes during conjugation. The transfer of these chromosomal genes can be used to map the location of genes on the bacterial chromosome.

The process involved in the transfer of DNA from donor cell to a recipient cell remain same in conjugation when only F factor gets transferred such as (F+ × F− matings) or in case of bacterial chromosome transfer, as in (Hfr × F− matings). A specific site is known to be involved in the initiation of transfer referred as *oriT*—the *ori*gin of *t*ransfer present on the F factor. On the oriT site the DNA replication initiates. In addition to these two additional sites are present- *oriV* and *oriS* for initiating replication during cell division, not at the time of conjugation.

Mapping via Hfr Strains:

The process of mapping via Hfr strains involves conjugating an Hfr strain with a recipient strain that is deficient in the genes that are being mapped. The Hfr strain will transfer its entire chromosome to

the recipient strain, including the F plasmid that is integrated into the chromosome. The transfer of chromosomal genes occurs in a linear fashion, starting at the site where the F plasmid is integrated. The transfer of chromosomal genes occurs at a high frequency, but it is not complete. The transfer of genes is interrupted when the conjugation bridge is broken, either by the physical separation of the two cells or by the degradation of the pilus. As a result, only a portion of the chromosome is transferred to the recipient strain.

The order of gene transfer can be determined by analyzing the time at which each gene is transferred. The gene that is transferred first is the closest to the site of integration of the F plasmid, and the gene that is transferred last is the farthest away from the site of integration. By analyzing a large number of conjugation events, researchers can build a map of the bacterial chromosome, showing the relative locations of the genes.

To understand the mapping, we need to study the classic experiment performed involving a specific Hfr strain referred as Hfr H (isolated by William Hayes an English microbial geneticist). F factor in this strain is integrated near the *thr* (threonine) and *leu* (leucine) loci.Two researchers Elie Wollman and Francois Jacob in the year 1957 working at the Pasteur Institute, Paris, crossed Hfr H cells with genotype *thr+ leu+ azis tons lac+ gal+ strs* to F− cells with genotype *thr− leu− azir tonr lac− gal− str r*.

Amino acids like threonine and leucine are synthesized by genes *thr* and the *leu* respectively. Sensitivity (*s*) or resistance (*r*) to sodium azide are controlled by allele pairs *azis*/*azir, tons*/*tonr,* and *str s*/*str r* bacteriophage T1, and streptomycin, respectively. In the experimental setup firstly at various time interval the Hfr H and F− cells were mixed to initiate mating. After this the two Wollman and Jacob removed the samples and further agitated it vigorously by using a blender for breaking the conjugation bridges. This separated the conjugating cells. The cells after vigorous agitation during mating were plated on medium with antibiotic streptomycin. They lacked the amino acids threonine and leucine. It was seen that selective recombinant cells with *thr+* and *leu+* genes on Hfr H parent and the *str r* gene of the F− parent could only grow on the *selective medium.* The Hfr H donor cells were killed by streptomycin, and the F− recipient cells were not able to grow in absence of threonine and leucine.

For the identification of the donor markers presence, colonies by *thr+ leu+ str r* recombinants were shifted to series of plates containing different selective media.Medium containing specific supplements were plated in a series of plates that allowed Wollman and Jacob to study whether the recombinants contained donor or recipient alleles of each of the genes. A specific medium containing sodium azide was used to differentiate among *azi s* and *azir* cells. Medium with bacteriophage T1 was used to have the data of recombinant bacteria as *tons* or *tonr*.Two mediums were taken the first medium with lactose was used as the sole carbon source for knowing whether recombinants were *lac+* or *lac−*, and other medium was galactose as the sole carbon source to recognize *gal+* and *gal−* recombinants.While interruption in the conjugation prior to 8 minutes was done after mixing the Hfr H cells and F− cells, no *thr+ leu+ str r* recombinants were noticed. Few recombinants (*thr+ leu+ str r*) appeared early at about 8 1/2 minutes after the mixing of Hfr H and F− cells and got accumulated to a maximum frequency within a few minutes.It was observed that the donor alleles were transferred to recipient cells in a specific temporal sequence. The first gene which got expressed was Hfr H *azi s* gene after mixing the Hfr and F− bacteria at about 9 minutes. After 11, 18, and 25 minutes of mating markers those who first appeared where *tons, lac+,* and *gal+* respectively. The outcomes revealed that genes from Hfr H are being transferred to the F− cells. This sequence reflects the gene order on the chromosome.The F factor has the tendency to integrate at various sites in the *E. coli* chromosome. The site of integration or joining decides the initiation of gene transfer in each Hfr strain. The orientation of F factor is either *d c b a* reading clockwise or *a b c d* reading clockwise governs the transfer of genes is clockwise relative to the *E. coli* linkage map or counterclockwise. The transfer of a complete

chromosome from an Hfr to an F− cell takes about 100 minutes, and transfer appears to proceed at a fairly constant rate. For mapping the genes on bacterial chromosomes, the time taken during the transfer of genes during conjugation can be used. Conjugation mapping is used to determine a new mutation in *E. coli.*

One of the most important features of mapping via Hfr strains is that it allows for the determination of the orientation of the genes on the chromosome. This is because the direction of gene transfer is always from the site of integration of the F plasmid to the end of the chromosome. By analyzing the order of gene transfer in both clockwise and counterclockwise directions, researchers can determine the directionality of the genes on the chromosome.

Mapping via Hfr strains has been used extensively to study the genetics of E. coli and other bacteria. It has been used to map the location of genes involved in antibiotic resistance, metabolism, and virulence. This information has been critical for understanding the mechanisms of bacterial pathogenesis and for developing new strategies for treating bacterial infections.

Finally, mapping via Hfr strains is limited to bacteria that are capable of undergoing conjugation. Not all bacteria are capable of conjugation, and some may require special conditions in order to do so. This means that mapping via Hfr strains may not be applicable to all bacterial species.

SAQ

1. ……is the process by which bacteria take up DNA from their environment and incorporate it into their own genome.
2. There are two main types of transformation: ……transformation and……. transformation.

2.4 Bacterial Transduction

Bacterial transduction is a type of horizontal gene transfer in bacteria that involves the transfer of genetic material from one bacterium to another by a bacteriophage, a virus that infects bacteria. Bacterial transduction plays an important role in bacterial evolution and adaptation, and has been extensively studied as a mechanism of gene transfer and genetic manipulation.

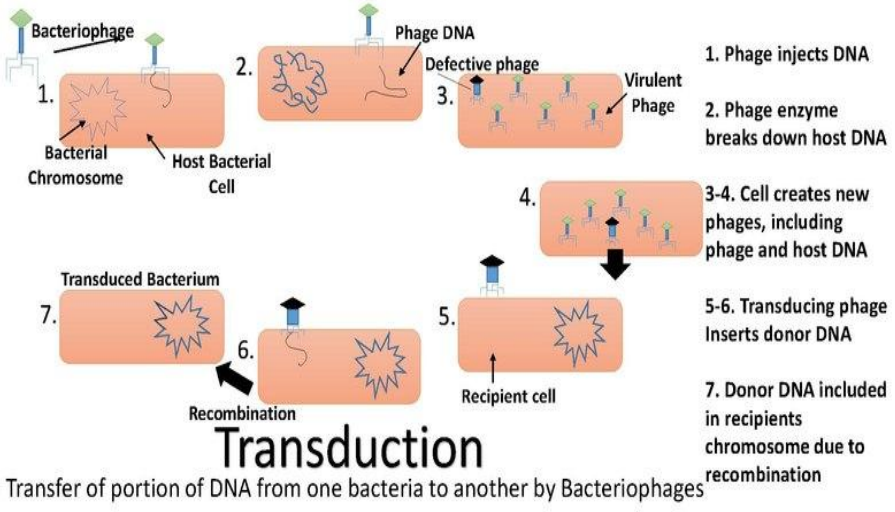

Figure 4. The process of transduction being shown by the schematic diagram (**Source**:https://en.wikipedia.org/wiki/Transduction_%28genetics%29)

Norton Zinder and Joshua Lederberg (1952), were exploring the probable recombination in the bacterium *Salmonella typhimurium*. The discovery suggested the phenomenon of bacterial

recombination mediated by bacteriophages referred as **transduction**.

Bacterial transduction involves the transfer of genetic material from a donor bacterium to a recipient bacterium with the help of a bacteriophage. During the process of transduction, the bacteriophage infects the donor bacterium and takes over its genetic machinery. As the bacteriophage replicates, it may accidentally package some of the donor bacterium's DNA into its viral particles. When these viral particles infect a recipient bacterium, they deliver the donor DNA into the recipient cell.

There are two main types of bacterial transduction: generalized transduction and specialized transduction. Generalized transduction occurs when any random piece of donor DNA is packaged into the viral particles and transferred to the recipient bacterium. Specialized transduction, on the other hand, occurs when specific genes near the site of viral integration are packaged into the viral particles and transferred to the recipient bacterium.

a) Generalized Transduction:

Generalized transduction is a mechanism of bacterial transduction that involves the random packaging of donor DNA into the viral particles. The well-known examples of generalized transducing phages include P22 in *S. typhimurium* and P1 in *E. coli*. During generalized transduction, a bacteriophage infects a donor bacterium and begins to replicate. As the bacteriophage replicates, it may accidentally package some of the donor bacterium's DNA into its viral particles. When these viral particles infect a recipient bacterium, they deliver the donor DNA into the recipient cell.

Generalized transduction can occur with any DNA sequence in the donor bacterium, including plasmids, chromosomal DNA, and phage DNA. However, because the process is random, only a small fraction of the donor DNA is successfully transferred to the recipient bacterium. The transferred DNA may be integrated into the recipient chromosome, where it can be expressed and passed on to subsequent generations of bacteria. The phenomenon is very inefficient and so the frequency of transduction for any given bacterial gene is around 1 per 106 phage particles.

b) Specialized Transduction:

Specialized transduction is a mechanism of bacterial transduction that involves the transfer of specific genes near the site of viral integration. During specialized transduction, a bacteriophage infects a donor bacterium and integrates its viral DNA into the bacterial chromosome at a specific site. When the viral DNA is excised from the bacterial chromosome, it may carry with it some of the adjacent bacterial genes. When these viral particles infect a recipient bacterium, they deliver the donor DNA into the recipient cell.

The transferred DNA may be integrated into the recipient chromosome, where it can be expressed and passed on to subsequent generations of bacteria. The well-known example of specialized transducing phage is the bacteriophage lambda (λ).

Specialized transduction is less efficient than generalized transduction because it requires the viral DNA to integrate into a specific site in the bacterial chromosome. However, specialized transduction is important because it can transfer specific genes, such as antibiotic resistance genes, from one bacterium to another.

The difference among the two types of transductions is depicted by the help of a figure.

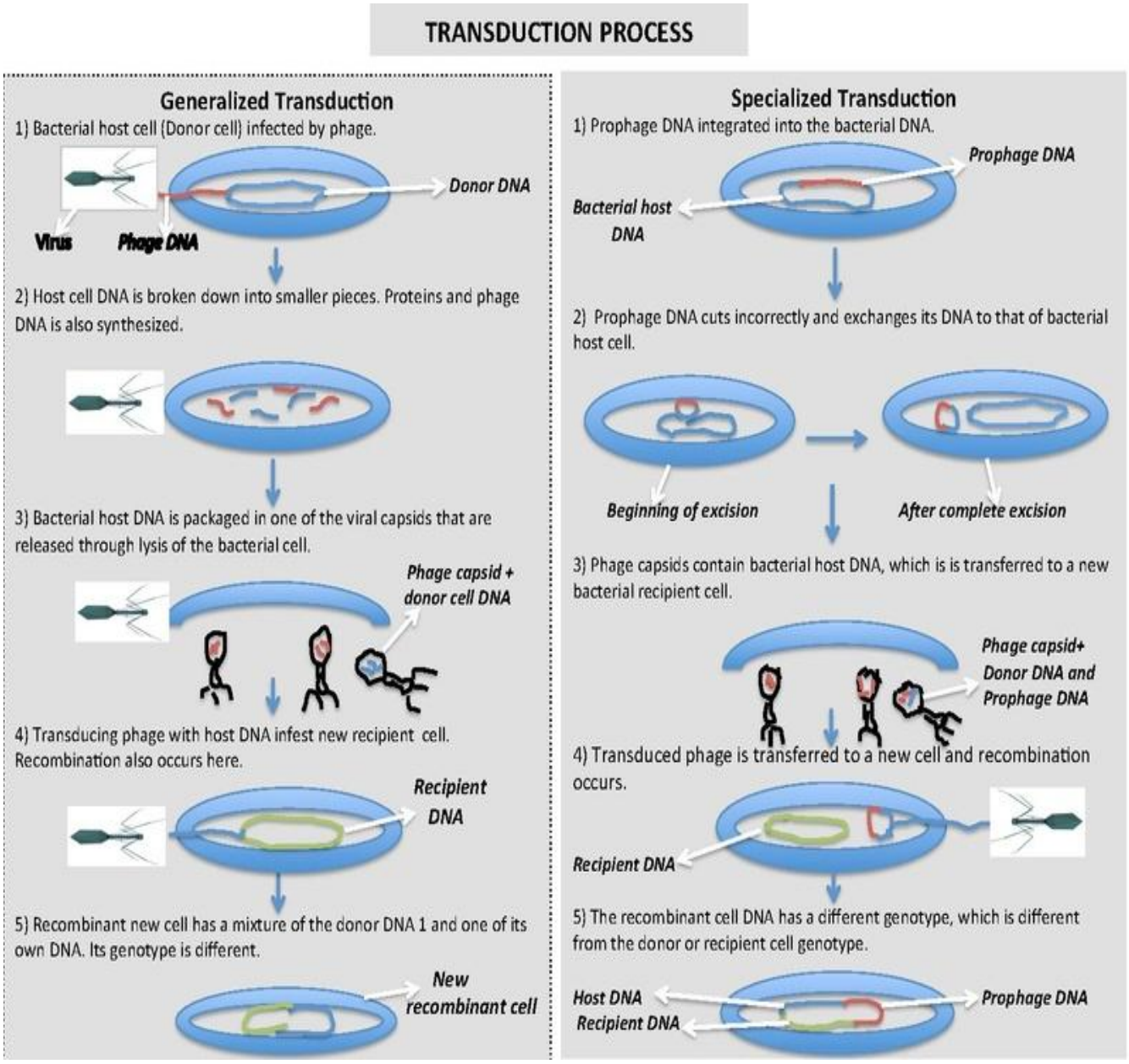

Figure 5. Difference among generalized transduction and specialized transduction (**Source**:*https://en.wikipedia.org/wiki/File:Transduction_illustration.pdf*)

Bacterial transduction has a number of significant applications in microbiology and biotechnology. These applications include:

Genetic manipulation: Bacterial transduction has been used as a tool for genetic manipulation in bacteria. Scientists can use bacteriophages to deliver specific genes or plasmids to bacteria, allowing them to manipulate bacterial gene expression or produce recombinant proteins.

Gene mapping: Bacterial transduction can be used to map the location of genes on bacterial chromosomes. By analyzing the transfer of genetic material from donor to recipient bacteria, researchers can determine the location and orientation of genes on the bacterial chromosome.

Antibiotic resistance: Bacterial transduction plays an important role in the spread of antibiotic resistance genes among bacterial populations. Antibiotic-resistant bacteria can transfer their resistance

genes to other bacteria through horizontal gene transfer, including bacterial transduction. Understanding the mechanisms of bacterial transduction and the transfer of antibiotic resistance genes can help researchers develop strategies to combat antibiotic resistance.

Viral therapy: Bacterial transduction can also be used in viral therapy, a type of treatment that uses bacteriophages to target and kill bacterial infections. By engineering bacteriophages to carry specific genes or enzymes, researchers can create customized viral therapies that target specific bacterial strains or virulence factors.

For the study of genetics and evolution in bacteria it is important to understand the process of transformation, conjugation and transduction. Due to these processes novel genotypes are created which helps the microorganism to adapt to the changing environment and respond to various drugs or antibiotics.

Certain changes which are beneficial to bacterial cell may be lethal to mankind. Multiple drug resistance strains of bacteria are also an outcome from such processes.

With the changing environmental condition certain genetic transfer are useful to the mankind. Thus, the understanding of such phenomenon is necessary for the better research in field of bacterial genetics and its evolution. Transfer of genes involving any of the following phenomenon produce new combination of genes and enhance the capability of bacteria to adapt to the changing environment.

2.5 Summary

- Conjugation is the direct transfer of genetic material between bacteria through a physical connection between the cells. This transfer is mediated by a round DNA known as plasmid, a molecule that has the capacity to replicate independently.
- Transduction is a process in which the transfer of genetic material occurs from one bacterium to other via a bacteriophage (bacterial cell infected by virus).
- During transduction, the bacteriophage inserts its DNA into the host cell's genome. As the virus replicates, it can pick up fragments of the host DNA and package them into new viral particles. These particles can then infect other bacteria, transferring the genetic material.

2.6 Terminal Question

Q.1 Explain Bactrial Transduction.

Q.2 Explain Bacterial Transformation

Q.3 Describe in detail high frequency of recombination.

Q.4 Explain Bacterial conjugation.

2.7 Answer

SAQ

1. Transformation
2. natural and artificial

Suggested Readings:

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Unit 3Variation in Chromosome Structure and Number

3.1 Introduction

Eukaryotic chromosomes are structures found in the nucleus of cells that include the genetic material of the organism. They store, organize and transmit the genetic information vital for the development and functioning of the cell and the organism as a whole. It is important to know the structure, composition, and functions of eukaryotic chromosome.

Eukaryotic chromosomes are long, thread-like structures that are visible during cell division when they condense and become visible under a microscope. Each eukaryotic chromosome consists of a complex of DNA and proteins known as chromatin. Chromatin is the combination of DNA molecules and histone proteins, which help in organizing and packaging the DNA. The chromatin undergoes additional folding and coiling to form a highly compact and condensed structure during division.

Objectives

After studying this unit, you will be able to know-

- Eukaryotic chromosomes
- Chromosomal aberrations

3.2 Eukaryotic chromosome

The primary component of eukaryotic chromosomes is deoxyribonucleic acid (DNA) the genetic material. It is a double-stranded helical molecule that carries the genetic information in the form of genes. Genes are specific segments of DNA that encode the instructions for producing proteins and controlling various cellular processes. The DNA in eukaryotic chromosomes is organized into linear structures, unlike prokaryotic chromosomes, which are typically circular.

Histones are a group of proteins that play a crucial role in DNA packaging. The DNA molecule wraps around histone proteins to form structures called nucleosomes. A nucleosome consists of DNA wrapped around an octamer of histone proteins. This octamer comprises two copies each of four core histones: H2A, H2B, H3, and H4. The DNA between nucleosomes, known as linker DNA, is associated with another histone called H1. The nucleosome structure helps in compacting the DNA and maintaining its stability.

Eukaryotic chromosomes are organized into distinct areas. In the center the chromosome has a centromere which is a specialized region and plays a crucial role in the segregation of chromosomes during cell division. Telomeres are located at the ends of chromosomes and are essential for protecting the genetic information from degradation and ensuring proper replication.

The number of chromosomes varies among different eukaryotic species. Humans, for example, have 46 chromosomes organized into 23 pairs, known as homologous chromosomes. These pairs consist of two chromosomes, one inherited from each parent. The number and structure of chromosomes are essential for maintaining genetic stability and proper cell division.

Eukaryotic chromosomes serve several critical functions. Eukaryotic chromosomes store and transmit the genetic information necessary for the inheritance of traits from one generation to the next. This genetic information is crucial for protein synthesis, cell growth, and development.

During the cell cycle, eukaryotic chromosomes undergo DNA replication, which ensures that each daughter cell receives an identical copy of the genetic material. This process is vital for maintaining genetic stability and continuity.

Chromosomes play a role in gene regulation by controlling the accessibility of genes to the cellular machinery responsible for gene expression. Different regions of chromosomes can be selectively condensed or decondensed to regulate gene activity.

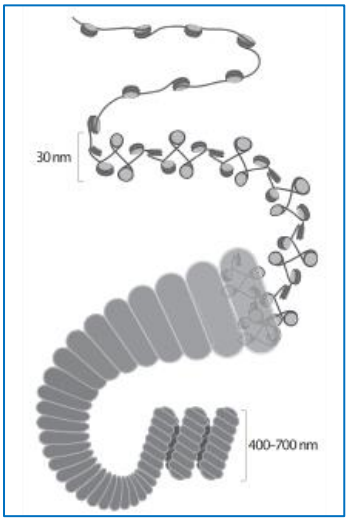


Fig1.A picture showing the packaging of nucleosomes into higher order chromatin structures.

Source:https://en.wikipedia.org/wiki/Eukaryotic_chromosome_structure

Karyotype:

A karyotype is an arrangement of an individual's chromosomes in a particular pattern. It is based upon the size, banding patterns, and centromere position. It is an essential technique used in cytogenetics to study chromosomal abnormalities, such as numerical or structural changes in chromosomes, which can be associated with genetic disorders or diseases. There are four types of chromosomes. Metacentric, submetacentric, acrocentric and telocentric.

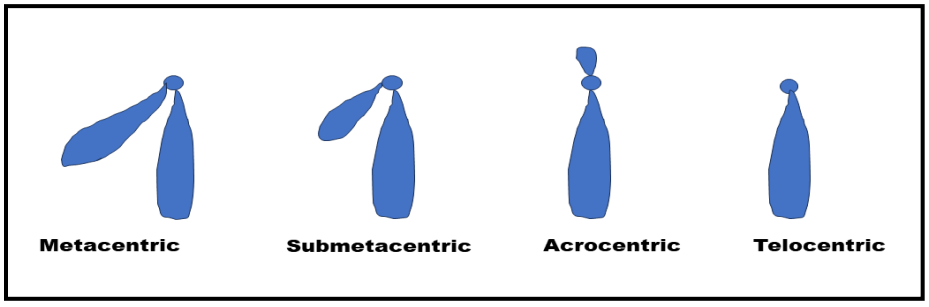
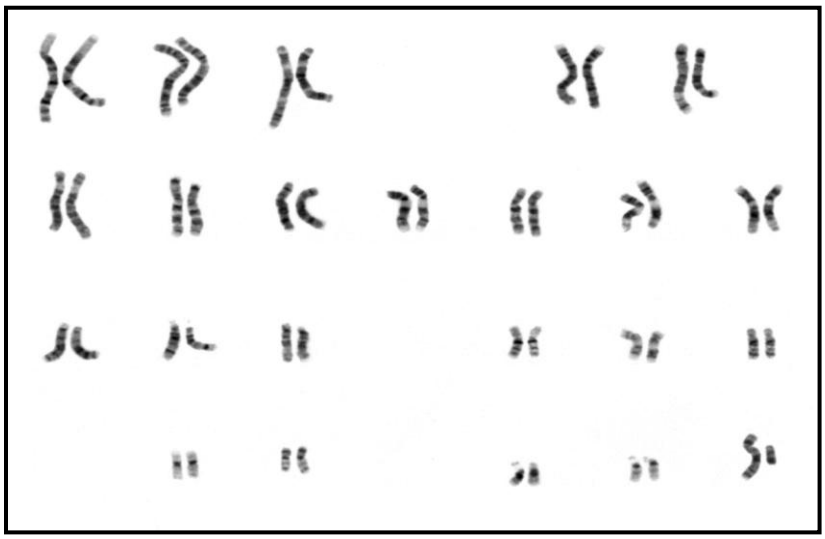


Fig 2. The four different types of chromosomes

To prepare a karyotype there are certain steps which are usually considered and a protocol is followed. Firstly, cells are obtained from an individual through various methods, like blood sample, amniocentesis, or chorionic villus sampling, depending on the purpose of the karyotype. The cells are then cultured in the laboratory to stimulate cell division. The other crucial step is to trat the cells by a mitogen, a substance that promotes cell division. This is done to obtain a satisfactory number of actively dividing cells.After cell division is induced, the cells are arrested at metaphase, a stage of cell division where the chromosomes are most condensed and visible. The cells are further treated with colchicine, to prevent further cell division and to arrest cells at metaphase. Following this, the cells are gently swelled and fixed on a glass slide.

As the cells get fixed, the chromosomes are stained with a dye. The two commonly used staining techniques for creating karyotypes are Giemsa staining (G-banding) and Wright staining (W-banding). These banding patterns provide a unique identification for each chromosome and help in their classification and analysis.Under a microscope, the stained chromosomes are observed, and high-quality images of individual chromosome spreads are captured. These images are then analyzed and arranged in pairs, according to their size, centromere position, and banding patterns.The chromosomes are typically arranged in a standardized format known as the International System for Human Cytogenetic Nomenclature (ISCN), which allows for consistent and uniform reporting of chromosomal abnormalities.Karyotyping plays a crucial role in the identification and characterization of chromosomal abnormalities. Structural abnormalities, such as translocations, inversions, deletions, or duplications, can be visualized and identified through karyotyping.Additionally, numerical abnormalities, such as aneuploidy (an abnormal number of chromosomes), can also be detected. For example, conditions like Down syndrome (trisomy 21), Patau syndrome (trisomy 13), or Turner syndrome (monosomy X) can be diagnosed through karyotyping.Karyotyping has diverse clinical applications, including prenatal diagnosis of genetic disorders, investigation of infertility or recurrent pregnancy loss, identification of chromosomal abnormalities in cancer cells (cytogenetics), and research purposes. It provides valuable information for genetic counseling, prognosis determination, and treatment planning.



A normal human karyotype depicting the arrangement of chromosomes.

Source: https://en.wikipedia.org/wiki/Karyotype

3.3 Chromosomal aberrations

Chromosomes are discrete structures which can be properly seen in metaphase of cell division. Every species of animals and plants possess a fixed number of chromosomes that can be identified individually because of their specific size and shape. The identity of chromosomes remains unaltered

while they pass from one generation to the other. However, changes in the number and structure of chromosome may occur due to one or other reasons. Such gross level changes are referred as aberrations and therefore, numerical as well as structural chromosomal aberrations are known to occur in the members of a species.

Structural chromosomal aberrations are mainly of four types: Deletion, duplication, inversion and translocation.

Deletion-

It denotes to the deficiency of a chromosome segment that in fact results due to loss of a chromosome part. Deletions may be of two types, i.e., terminal or interstitial. A single break close to the terminal portion of the chromosome results into a terminal deletion. However, the interstitial deletion results due to two breaks in a chromosome arm and the reunion of the broken ends losing the small broken segment of the chromosome. Terminal deletions are very rare whereas, interstitial deletions are more common. Syndromes which are the examples of deletion include Cri-du-chat syndrome, Prader-Willi syndrome, Angelman syndrome and others. Let us first understand the basic difference among these disorders.

Cri-du-chat syndrome: In this syndrome deletion occurs on the short arm of chromosome 5 (specifically, the region known as 5p). Individuals suffering with this syndrome show characteristic features like high-pitched cry resembling a cat's cry (hence the name "cri-du-chat" meaning "cry of the cat"), intellectual disability, developmental deformity and distinctive facial features.

Prader-Willi syndrome: It is typically caused by the loss of genes on the long arm of chromosome 15 from the father. It leads to developmental delays, intellectual disability, short height, increased appetite and obesity. Individuals with Prader-Willi syndrome may also experience behavioral and psychological challenges.

Angelman syndrome: It is also associated with a deletion on the long arm of chromosome 15 from the mother's side. This disorder leads to severe intellectual disability, developmental delays, speech impairment, seizures. Angelman syndrome suffering child may also have problems pertaining to balance and movement.

Williams syndrome: This results from a deletion on chromosome 7 (typically in the region 7q11.23). Characterized by distinct facial features, cardiovascular abnormalities, intellectual disability, and a unique cognitive profile. Individuals with Williams syndrome often exhibit exceptional verbal and social skills but may have difficulties with spatial tasks and certain cognitive processes.

These are just a few examples of deletion chromosomal aberrations and the associated disorders. Genetic testing and counseling are typically employed to diagnose and manage these conditions appropriately.

Duplication-

As the term indicates, duplication or addition of chromosome refers to the repetition of a segment of chromosome. The duplication may involve a segment of the chromosome being represented two or more times in the chromosome of a homologous pair.

Charcot-Marie-Tooth disease type 1A (CMT1A): CMT1A is a peripheral neuropathy caused by a duplication of a segment on chromosome 17. The duplication involves the PMP22 gene, which is meant for the production of a protein called peripheral myelin protein 22. The extra copies of this gene disrupt the normal function of peripheral nerves, leading to muscle weakness, loss of sensation, and other symptoms.

Duplication 15q syndrome: This syndrome involves the duplication of a region on chromosome

15, typically resulting from a structural abnormality called isodicentric 15). This duplication can lead to a range of symptoms, including intellectual disability, developmental delays, seizures, behavioral issues, and characteristic features such as a prominent forehead and widely spaced eyes.

Pallister-Killian syndrome: Pallister-Killian syndrome is a rare genetic disorder caused by a mosaic tetrasomy of chromosome 12p. It involves the duplication of a segment of chromosome 12 in some cells of the body. The syndrome is characterized by intellectual disability, developmental delays, distinctive facial features, hypotonia (low muscle tone), and other systemic abnormalities.

Potocki-Lupski syndrome: This syndrome is caused by a duplication of a specific region on chromosome 17, involving the dosage-sensitive retinoic acid-induced 1 (RAI1) gene. It is associated with developmental delays, intellectual disability, autism spectrum disorder, distinctive facial features, and other symptoms.

Duplication 8p syndrome: Duplication 8p syndrome is caused by the duplication of a segment of chromosome 8. The syndrome is characterized by intellectual disability, developmental delays, distinctive facial features, and other anomalies such as cardiovascular defects, kidney abnormalities, and skeletal anomalies.

The duplications may not be deleterious. Moreover, the duplication is useful in evolution of new genetic material. The example of bar eye is most appropriate to explain this phenomenon. In *Drosophilamelanogaster,* the wild type eye is large and has about 810 facets. Flies with bar eyes have lesser number of facets. The number of eye facets gets highly reduced in flies having more duplications. Perusal of polytene chromosome bands in *Drosophila melanogaster* have revealed that the specific region in X-chromosome identified as 16A is found to be one in normal condition whereas, in bar eye, it undergoes duplication.

Inversion–

It is an intra-chromosomal aberration, in which a section of the chromosome becomes changed by rotation through 180 degrees. Due to inversion in the chromosome, the order of the genes in the inverted part is thus reversed. The inverted segment may or may not contain centromere and therefore, inversions if do not include centromere are called as paracentric inversions whereas, inversions with centromere are pericentric inversions. When crossing over occurs within the inverted segment of a paracentric inversion, then acentric and dicentric chromatids are formed. The acentric chromatids fail to move to either pole due to lack of centromere. The dicentric chromatids have two centromeres and are connected by a bridge, break and contain duplications and deficiencies. Thus, only fifty percent of gametes are seen to be viable. If crossing over occurs in the inverted loop of a pericentric inversion, then chromatids with deletion and duplication of genes are formed in fifty percent of gametes.

Inversions occur randomly during cell division. They may or may not have obvious effects on a health or development of an individual, based upon specific genes and genetic material involved.

Translocation–

In this type of chromosomal aberration a part of a chromosome breaks off and attaches to another non-homologous chromosome. Thus, shifting of a part of a chromosome to a non-homologous chromosome or exchange of parts of chromosomes between non-homologous chromosomes are referred as translocation. There are mainly two types of translocations. a. Simple translocation where the broken piece gets attached to another chromosome and b. Reciprocal translocation in which a segment from one chromosome is exchanged with a segment from another non-homologous one, so that in reality two translocation chromosomes are simultaneously formed.

Robertsonian translocations occur when two acrocentric chromosomes fuse at their short arms. This type of fusion results in the formation of a single chromosome with a larger size and further loss of

genetic material from the short arms of the original chromosomes. These are among the balanced type of translocations and are common in the general population.

Screening of translocation aberrations can be done by genetic testing, such as karyotyping, fluorescence in situ hybridization (FISH), or chromosomal microarray analysis.

The numerical chromosomal aberrations are mainly categorized as:

Aneuploidy

Aneuploidy refers to the type of numerical changes in the chromosome which is either in the form of absence of one or two chromosomes or addition of some of the chromosomes in the diploid sets of chromosomes. Monosomy, Nullisomy, trisomy, tetrasomy etc. are the cases of aneuploidy. There are many examples of trisomy which are discussed in detail in the upcoming paragraphs.

Aneuploidy usually occurs due to random errors in cell division, specifically during meiosisor mitosis. One of the common causes of aneuploidy is non-disjunction. In non-disjunction chromosomes fail to separate properly during cell division thus lead to an unequal distribution of chromosomes in the subsequent cells. Aneuploidy occurs in autosomes as well as sex chromosomes.Aneuploidy signifiesaimportant aspect of chromosomal aberrations along withnegative effects on human health and progress. Tremendous advances in ongoing research and medical progressions improves our understanding and ability to diagnose and manage such disorders.

Euploidy

In case of euploidy, a complete set of chromosomes is either missing or gets added to the diploid set of chromosomes. Haploidy, triploidy, tetraploidyetc. are considered the cases of polyploidy.Euploidy is known to be for the viability and reproductive success of organisms.

<table>
<tr><td colspan="4">Ploidy</td></tr>
<tr><td colspan="2">Euploidy</td><td colspan="2">Aneuploidy</td></tr>
<tr><td colspan="2">Haploidy (n)</td><td>Hypoploidy</td><td>Hyperploidy</td></tr>
<tr><td colspan="2">Diploidy (2n)</td><td>Monosomy(2n-1)</td><td>Trisomy(2n+1)</td></tr>
<tr><td colspan="2">Polyploidy: Triploidy (3n), Tetraploidy (4n) etc.</td><td>Double Monosomy(2n-1-1)</td><td>Tetrasomy(2n+2)</td></tr>
<tr><td>Autopolyploidy</td><td>Allopolyploidy</td><td>Nullisomy (2n-2)</td><td>Pentasomy(2n+3)</td></tr>
</table>

There exists variation at the level of occurrence of such aberrations in different species of animals and plants. Plants may tolerate euploidy, particularly polyploidy whereas, due to dosage effect such euploid variations are intolerant to animals. A number of numerical chromosomal aberrations are known in humans causing phenotypic as well as other disorders. However, almost in all kind of numerical chromosomal aberrations varying degree of mental retardation is involved.

Table depicting different types of numerical chromosomal aberrations and the specific term used for them.

Numerical Chromosomal Aberrations	
Aneuploidy	
(i) Monosomy	2n - 1
(ii) Trisomy	2n + 1
(iii) Tetrasomy	2n +2

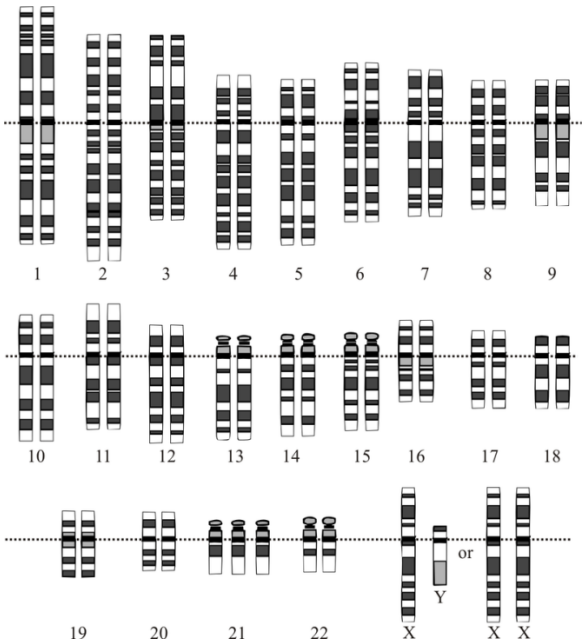
(iv)	Nullisomy	2n - 2
(v)	Double Trisomy	2n +1 +1
Polyploidy		
(vi)	Haploidy	n
(vii)	Diploidy	2n
(viii)	Triploidy	3n
(ix)	Tetrasomy	4n

Some of the cases in humans with numerical abnormalities whose frequency is substantially high are as follows:

Down syndrome:

Down syndrome is a case of trisomy in humans. In this disorder presence of extra chromosome 21 is observed.British physician, Langdon Down in the year 1866 was first to describe it. The characteristic feature of Down syndrome includes short stature, broad skull, large protruding tongue with furrows, stubby hands with crease on palm, hearing and vision problems and mental retardation. Individuals with Down syndrome are prone to develop diseases such as Alzheimer's disease(dementia) early compared to other humans. Irregular speech which is difficult to understand is also seen in children with Down syndrome.

Individuals with Down syndrome are known to have intellectual and developmental delays as common feature. They exhibit mild to moderate intellectual disability, and their cognitive skills can differ significantly.



Karyotype of Down syndrome individual showing trisomy of 21 chromosome.

Source:https://en.wikipedia.org/wiki/Down_syndrome

Prenatal ultrasoundis used diagnose for Down syndrome. Several blood test markers can be done to predict for this syndrome in the first or second trimester. In addition to these amniocentesis and chorionic villus sampling are some of the most effective ways to diagnose it but are also dangerous as they increase the chance of miscarriage.

Patau Syndrome:

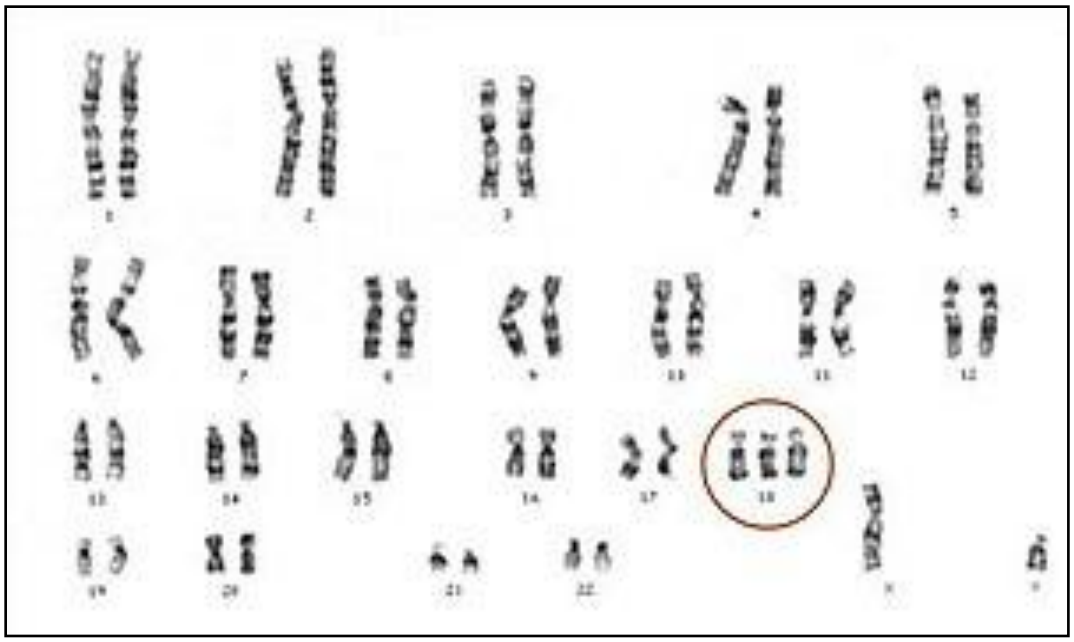
Patau syndrome is also a case of trisomy of chromosome number 13. Trisomy of 13 is caused by the nondisjunction of chromosomes. This syndrome is associated with a wide range of physical and developmental abnormalities. The severity of these features can vary among affected individuals. Infants with Patau syndrome often have cleft lip or palate, small eyes (microphthalmia), small head size (microcephaly), and a prominent ridge on the forehead. Intellectual disability and seizures are common. Heart defects, kidney abnormalities, gastrointestinal abnormalities and genitourinary abnormalities. Skeletal defects are also visible which include extra fingers or toes, fused fingers or toes, and abnormalities of the bones. Such individuals have poor growth and reduced body weight. In addition to these they have eye abnormalities, hearing loss, respiratory problems, and various other congenital anomalies.

Prognosis and Management:It is associated with high mortality rate and many affected individuals do not survive beyond the first year of life. The severity of the syndrome and the prognosis can vary depending on the specific features and organ involvement. The presence of severe heart defects and brain abnormalities often contributes to the poor prognosis.

For management of Patau syndrome involves a multidisciplinary approach, including medical interventions to address specific health issues, early intervention programs for developmental support, and supportive care to enhance the quality of life for affected individuals and their families.

Edward Syndrome:

Edward syndrome is also a case of trisomy of chromosome number 18. Edward syndrome suffering individuals are known to have multiple congenital abnormalities. Babies with this syndrome are prone to have heart disease.Additional featuresare small head, clenched fists are with overlapping fingers, and suffer from intellectual disability.This syndrome is associated with anincreased rate of infant mortality resulting in very early death of affected babies. In addition to this it is observed that medical care and interventions help to prolong the life of some individuals with trisomy 18 up toteenage years or till adulthood. The severity of the condition can vary widely among affected individuals.



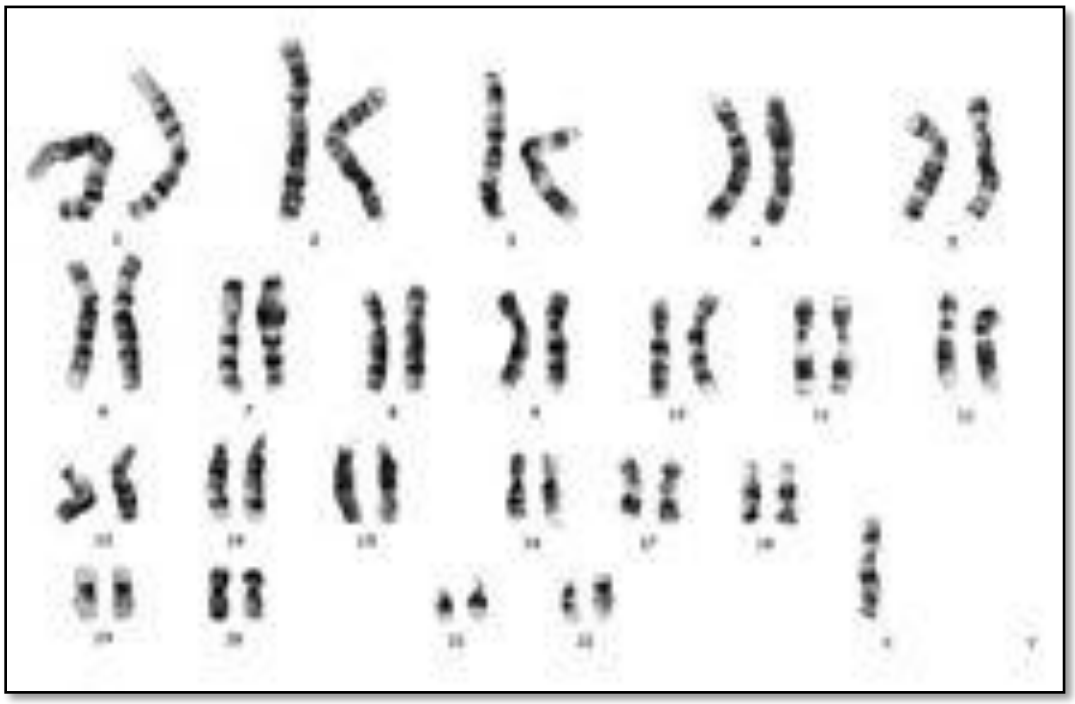
The above karyotype is of trisomy of 18.

Source: https://en.wikipedia.org/wiki/Trisomy_18

Turner syndrome:

Turner syndrome is with 45, X, or 45, X0. It is a genetic disorder in which partial or complete loss of X chromosome occurs.

Females affected by Turner syndrome have external genitalia and internal ducts and the ovaries areundeveloped or rudimentary. In addition to these some other features are short height (usually under 5 feet), underdeveloped breasts and presence of skin flaps on the backof the neck. Broad chest is usually present which is shieldlike. These females have usually normal intelligence.



The above karyotype is of a Turner syndrome

(Source: https://en.wikipedia.org/wiki/Turner_syndrome)

Diagnosis of this syndrome is often during childhood. It is based on physical characteristics and growth patterns. Karyotype analysis is performed to confirm the diagnosis by identifying the absence or abnormalities in the X chromosomes.

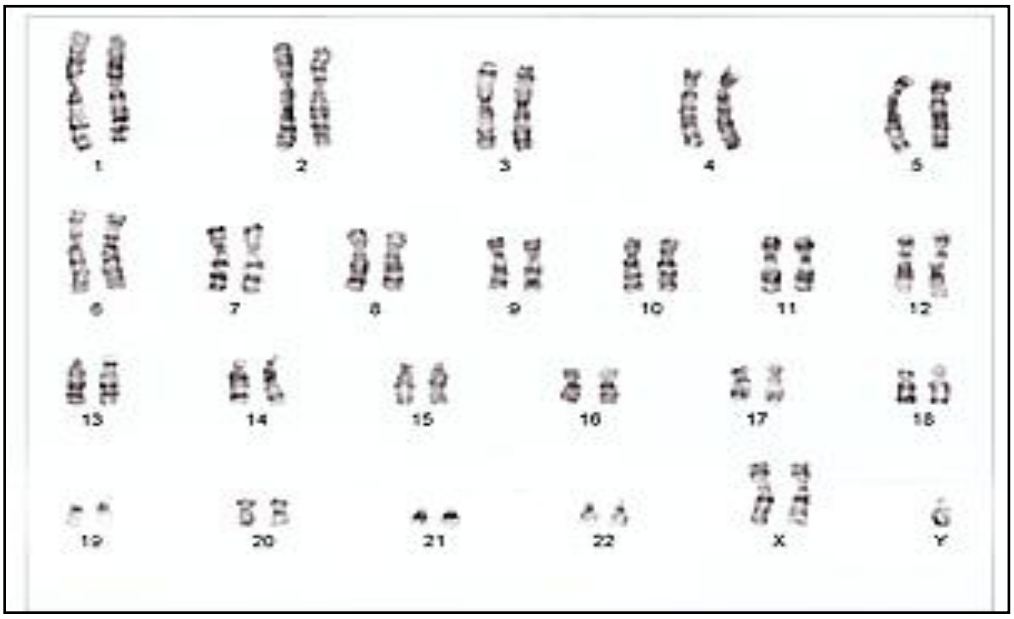
Treatment for Turner syndrome aims to address specific health concerns and manage associated symptoms. This may include growth hormone therapy to improve height, estrogen replacement therapy to induce puberty and promote sexual development, and regular monitoring and management of cardiac and renal issues. Psychological support and educational interventions are also essential to address any social or learning difficulties that may arise.

Klinefelter syndrome:

In this syndrome the male is known to have an extra copy of X chromosome (47, XXY). Such individuals have small and poorly developed testis. Other symptoms than these are increased height, poor motor coordination, breast growth and less body hairs. At the level of intelligence, they are average but have difficulty in speech and expression.

The formation of Klinefelter syndrome (XXY) karyotype is by the fertilization of an egg XX and a Y bearing sperm or it may be due to thefertilization of an X-bearing eggwith an exceptional XY sperm. Other than this XXY genotype the other complex karyotypes are XXXY, XXYY, XXXYY, XXXXYY,

and XXXXXY. It is seen that all these individuals have one or more Barr body. Individuals with a combination of more than two X chromosomes are usually mentally impaired to some extent.



The above karyotype is of Klinefelter syndromeindividual having an extra copy of X chromosome

Source: https://en.wikipedia.org/wiki/Klinefelter_syndrome

XYY syndrome:

The Karyotype 47, XYY is other example of viable trisomy in human.This syndrome is also known as Jacob's syndrome, is a genetic condition that affects males.The condition is estimated to occur in approximately 1 in 1,000 male births.

These individuals exhibit certain characteristic feature such as taller stature, delayed speech and language development, learning difficulties and behavioral and emotional challenges.

3.4 Summary

- Down syndrome is a case of trisomy in humans. In this disorder presence of extra chromosome 21 is observed.
- Patau syndrome is also a case of trisomy of chromosome number 13.
- Turner syndrome is with 45, X, or 45, X0. It is a genetic disorder in which partial or complete loss of X chromosome occurs.
- Klinefelter syndrome the male is known to have an extra copy of X chromosome (47, XXY).

3.5 Terminal Question

Q1. Down syndrome in mostly caused by an extra copy of which chromosome:

(a) 5(b)21 (c) 18 (d) 13

Q2. Match the following:

A- Down's syndrome 1- presence of additional sex chromosome

B- Cri-du chat syndrome 2- loss of a part of chromosome

C- Klinefelter's syndrome 3- absence of sex chromosome

D- Turner's syndrome 4- presence of 1 extra chromosome

(a) A-4, B-2, C-3, D-1 (b) A-4, B-2,C-1, D-3 (c) A-4, B-1, C-2, D-3 (d) A-3, B-4, C-1, D-2

Q3. What is karyotype? Explain the human karyotype in detail.

Q4. Describe various types of chromosomal deletions with appropriate examples?

3.6 Answer

1. (b)21
2. (a) A-4, B-2, C-3, D-1 (b) A-4, B-2,C-1, D-3 (c) A-4, B-1, C-2, D-3 (d) A-3, B-4, C-1, D-2

Suggested Readings:

1. Alberts, B., Johnson, A., Lewis, J., Raff, M., Roberts, K., & Walter, P. (2014). Molecular biology of the cell (6th ed.). Garland Science.
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Unit 4- Molecular Structure of Nucleic Acids

4.1Introduction

Imagine a world where life is not composed of flesh and blood but instead is built upon an intricate, almost magical code. A world where tiny structures hold the secrets of life itself and where these structures are made up of the tiniest of building blocks - nucleotides.

In this chapter, we will delve into the wondrous world of nucleotide structure, exploring the remarkable details that make up the building blocks of life. From the seemingly simple structure of the nucleotide to the complex interactions between nucleotides within the DNA and RNA strands, we will journey through the fascinating world of these molecular marvels.

At first glance, nucleotides may appear to be nothing more than small, unremarkable chemical compounds. However, when we zoom in to the molecular level, we discover a universe of complexity, beauty, and wonder. From the elegant shape of the sugar-phosphate backbone to the intricate patterns formed by the nitrogenous bases, the structure of nucleotides is a sight to behold.

But beyond their visual appeal, the structure of nucleotides holds the key to understanding the mysteries of life. The arrangement of these tiny building blocks is what creates the genetic code, which determines the physical traits and characteristics of all living beings. The structure of nucleotides also plays a critical role in the process of replication, ensuring the continuity of life from generation to generation. As we contemplate the beauty and complexity of nucleotides, we are reminded of the remarkable creativity and ingenuity of nature. The composition of nucleotides is not arbitrary but rather the result of eons of evolution, selection, and adaptation. Through countless generations of trial and error, nature has sculpted the precise arrangement of atoms and bonds that give rise to the wondrous properties of nucleotides.

As we journey through this chapter on nucleotide structure, we will uncover the intricate details that make up these molecular wonders. We will explore the chemical bonds that hold them together, the unique properties of each nitrogenous base, and the significance of their arrangement within the DNA and RNA strands. Through this exploration, we will gain a newfound appreciation for the beauty and complexity of the world of nucleotides, and the vital role they play in the story of life. So let us begin this journey of wonder and discovery, as we explore the remarkable world of nucleotide structure.

In the grand tapestry of life, a magnificent, intricate, and enigmatic design weaves together the essence of all living organisms: nucleic acids. These elegant structures, at once delicate and robust, whisper the secrets of existence from the smallest microbe to the towering sequoia. This breathtaking chapter, "Molecular Structure of Nucleic Acids," invites you to embark on an awe-inspiring journey into

the heart of this cosmic code, exploring the ethereal beauty and divine complexity that define the very blueprint of life.

Our odyssey begins with the humble nucleotide, the fundamental unit of nucleic acids that serves as the cornerstone for the construction of these breathtaking molecular masterpieces. We will explore the intricate architecture of these building blocks, delving into the chemical bonds and atomic interactions that imbue them with their unique and vital characteristics. As we scrutinize the structural nuances of the purines and pyrimidines that constitute the genetic alphabet, we will stand in awe of the remarkable simplicity and elegance with which nature communicates its most profound messages.

As we delve into the mesmerizing world of nucleotide structures, we will retrace the footsteps of pioneering scientists who illuminated the path to our understanding of these miraculous molecules. We will journey alongside the giants of molecular biology, like Watson, Crick, Franklin, and Wilkins, who peered deep into the heart of life's mysteries and uncovered the enigmatic double helix. The discovery and unveiling of the DNA double helix will unfold before our eyes like a sacred revelation, its graceful form echoing the harmonious dance of life itself. We will witness the birth of the central dogma, the cornerstone of modern biology, and ponder the profound implications of this discovery for our understanding of the origins of life, the nature of inheritance, and the eternal bonds that unite all living creatures.

As we traverse the realms of RNA, we will marvel at the myriad forms and functions it assumes, each type a testament to nature's boundless creativity and ingenuity. We will explore the role of messenger RNA as the bearer of genetic information, relaying the instructions encoded within DNA to the cellular machinery responsible for assembling the proteins that govern life's myriad processes. We will delve into the world of transfer RNA and ribosomal RNA, the unsung heroes of the protein synthesis process, whose remarkable structures and interactions form the basis for the exquisite choreography of translation. As we encounter the diverse array of non-coding RNAs that play essential roles in regulating gene expression, splicing, and countless other cellular processes, we will stand in awe of the vast symphony of molecular interactions that underlie the harmonious functioning of the living cell.

In an age where the mysteries of the universe seem ever more distant and elusive, the study of nucleic acids offers a profound connection to the sacred, a spiritual anchor that grounds us in the miracle of existence. To explore the molecular structure of nucleic acids is to unravel the delicate threads that weave together the fabric of life, to bear witness to the divine language that echoes through every cell, and ultimately, to rediscover our own place within the vast, interconnected cosmos.

As you journey through this chapter, may you be filled with a sense of wonder and reverence for the astonishing beauty that lies hidden within the realm of nucleic acids. May you find inspiration in the exquisite complexity and elegant simplicity of the molecular structures that form the foundation of life. As we delve deeper into the mysteries of DNA and RNA, may you experience a profound sense of interconnectedness with all living beings, and an appreciation for the sacred web of existence that unites us all.

As we discuss the groundbreaking experiments and discoveries that have shaped our understanding of nucleic acids, may you be inspired by the tenacity, curiosity, and collaborative spirit of the scientists who have dedicated their lives to unraveling life's deepest secrets. Let their stories remind us of the power of human ingenuity and the potential for collective wisdom to illuminate even the darkest corners of the unknown.

In conclusion, this chapter on the "Molecular Structure of Nucleic Acids" is an invitation to embark on a profound and transformative journey into the heart of life's most enigmatic and essential molecules. As we delve into the mesmerizing world of DNA and RNA, may we be humbled by the awe-

inspiring beauty and complexity of the molecular structures that underpin our existence, and may we find renewed inspiration to cherish, protect, and celebrate the sacred tapestry of life that connects us all.

So let us together immerse ourselves in this journey, this exploration of the very fabric of life. Let us stand in awe of the mysteries that unfold before us and revel in the opportunity to glimpse the inner workings of the living world. In the pages that follow, we shall uncover the intricate designs and divine symphony that lie hidden within the molecular structure of nucleic acids, and in doing so, may we find a renewed sense of wonder, purpose, and connection to the living world that surrounds and sustains us.

Objective

After studying this unit, you will be able to know-

- Nucleotide Structure
- Discovery and Structure of DNA Double Helix
- Structure of DNA Double Helix
- RNA structure and types

4.2 Nucleotide Structure

Discovery

Figure 1 : Friedrich Miescher

The discovery of nucleotides was a gradual process that involved the contributions of many scientists over several centuries. The first hint of the existence of nucleotides came in the late 19th century when the Swiss chemist Friedrich Miescher isolated a substance from the nuclei of white blood cells that he called "nuclein." Miescher later discovered that nuclein was composed of both protein and a previously unknown acidic substance that he named "nucleic acid."

In the early 20th century, the British biochemist Frederick Gowland Hopkins discovered that the nucleic acids found in yeast contained a component that he called "purine." He also identified another component of nucleic acids that he called "pyrimidine."

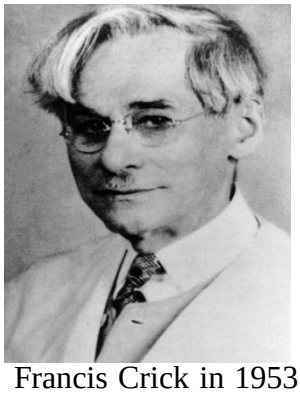


Figure 2: Phoebus Levene

The American biochemist Phoebus Levene, who was working at the Rockefeller Institute for Medical Research in New York, continued the study of nucleic acids in the early 1900s. Levene discovered that nucleic acids were composed of repeating units that he called "nucleotides." He also identified the three basic components of nucleotides: a nitrogenous base, a sugar molecule, and a phosphate group.

Further research in the mid-20th century led to the discovery of the structure of DNA by James Watson and Francis Crick in 1953. They proposed that DNA consisted of two strands of nucleotides that were held together by hydrogen bonds between the nitrogenous bases. This discovery revolutionized the field of biology and led to many advances in genetics and biotechnology.

Since then, further research has revealed the complexity and diversity of nucleotides and their role in the regulation of gene expression, as well as their importance in many cellular processes such as energy transfer and signaling. The study of nucleotides continues to be a vibrant area of research in the fields of biochemistry, molecular biology, and genetics.

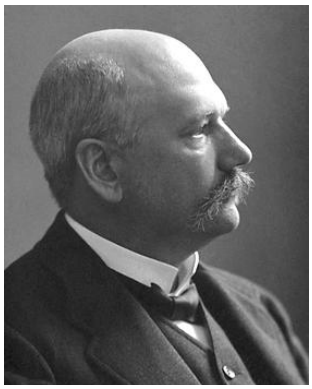


Figure 3: Albrecht Kossel

Albrecht Kossel, a German biochemist, was awarded the Nobel Prize in Physiology or Medicine in 1910 for his work on the chemistry of the cell nucleus and its constituents. One of his notable achievements was isolating and describing the five nitrogenous bases that are the building blocks of nucleic acids.

In 1885, Kossel extracted the first nitrogenous base, adenine, from the pancreas of a calf. He went on to isolate guanine from fish scales, cytosine from the glandular tissues of birds, and thymine from the thymus gland of a calf. Finally, in 1900, Kossel isolated the fifth nitrogenous base, uracil, from yeast.His discovery of the nitrogenous bases paved the way for the discovery of DNA and RNA, which are the carriers of genetic information in all living organisms. The Composition of Nucleotides

Nucleotides are the building blocks of DNA and RNA, and each nucleotide consists of three basic components: a sugar molecule, a phosphate group, and a nitrogenous base. The chemical structure of each component of nucleotides is critical for the stability and function of DNA and RNA. Understanding the chemical properties and interactions of these components is essential for understanding the structure and function of nucleotides, which in turn is critical for understanding the nature of life itself.

Sugar

The sugar molecule in nucleotides is a pentose sugar, meaning it contains five carbon atoms. The sugar molecule in DNA is called deoxyribose, while the sugar molecule in RNA is called ribose. These two sugar molecules differ in the presence or absence of an oxygen atom at the 2' carbon position. Deoxyribose, which is the sugar molecule in DNA, has a five-carbon ring structure with four carbon atoms and one oxygen atom. The carbon atoms are numbered 1' through 5', with the nitrogenous base attached to the 1' carbon and the phosphate group attached to the 5' carbon. The 2' carbon of deoxyribose is missing an oxygen atom, which gives DNA its name. Ribose, which is the sugar molecule in RNA, also has a five-carbon ring structure with four carbon atoms and one oxygen atom. However, the 2' carbon of ribose has an **additional** oxygen atom, which is why it is called a "ribose" sugar. The presence of the extra oxygen atom in ribose is important for the structure and function of RNA. The sugar molecule is a critical component of nucleotides because it forms the backbone of DNA and RNA. The sugar molecules in adjacent nucleotides are joined together by a phosphodiester bond, which connects the 3' carbon of one sugar molecule to the 5' carbon of the next sugar molecule. This forms a long, stable, and flexible backbone that provides the structural support for the nitrogenous bases. The unique structure of the sugar molecule in nucleotides is important for the stability and function of DNA and RNA. The differences between deoxyribose and ribose contribute to the differences in the structure and function of DNA and RNA. Understanding the structure and properties of the sugar molecule is, therefore, critical for understanding the structure and function of nucleotides and for understanding the nature of life itself.

Phosphate group:

The phosphate group consists of a phosphorus atom (P) bonded to four oxygen atoms (O), three of which are single bonds (P-O) and one of which is a double bond (P=O). In the context of nucleotides, the phosphate group is bonded to the 5' carbon of the sugar molecule through a phosphodiester bond, forming the backbone of DNA and RNA.The phosphate group contributes to the overall negative charge

of nucleotides due to the presence of multiple negatively charged oxygen atoms. This negative charge is essential for the structure and function of DNA and RNA, as it allows the molecules to interact with positively charged ions and other molecules and also helps to stabilize the double helix structure.In addition to its structural role, the phosphate group also plays a crucial role in energy transfer in cells. Adenosine triphosphate (ATP) is a nucleotide that contains three phosphate groups linked together by phosphoanhydride bonds. When these bonds are broken, energy is released that can be used to power cellular process

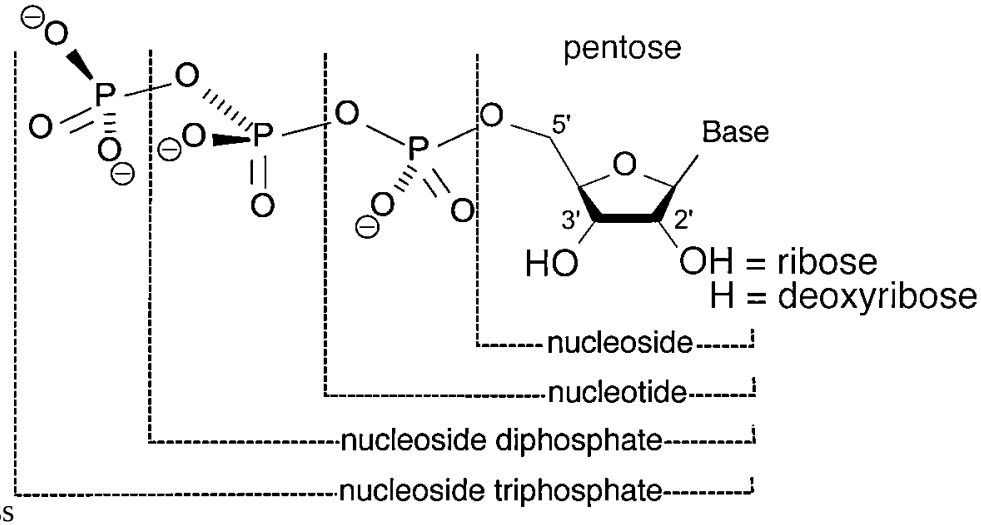


Figure 4: General depiction of nested nucleoside, nucleotide, nucleoside diphosphate, nucleoside triphosphate.

Such as muscle contraction, nerve transmission, and synthesis of macromolecules like proteins and nucleic acids.Overall, the phosphate group is a critical component of nucleotides that contributes to their structure, function, and energy transfer properties. Its importance in regulating cellular processes and its role as a limiting nutrient in the environment make it a fascinating subject of study in the field of biochemistry.

Nitrogenous base:

he nitrogenous bases are one of the three basic components of nucleotides, along with the sugar and phosphate groups. There are two types of nitrogenous bases: purines and pyrimidines.Purines are larger bases that consist of two fused rings of carbon and nitrogen atoms. The two purines found in DNA and RNA are adenine (A) and guanine (G). In DNA, A always pairs with T (thymine) via two hydrogen bonds, while G always pairs with C (cytosine) via three hydrogen bonds. In RNA, uracil (U) replaces T and pairs with A via two hydrogen bonds.

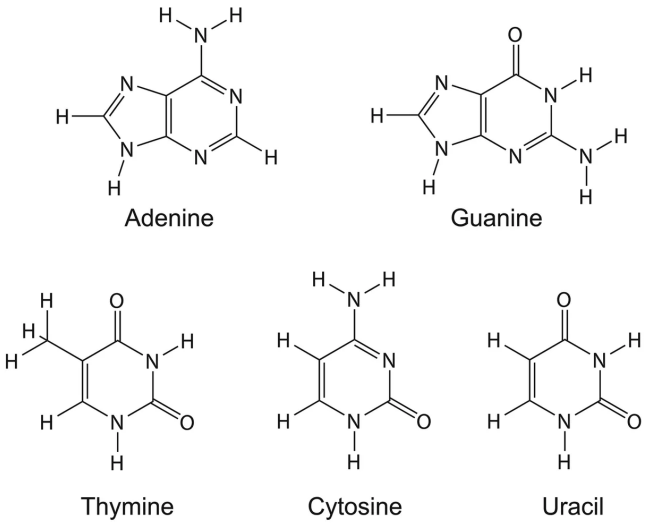


Figure 5: Nitrogenous bases found in living

Pyrimidines are smaller bases that consist of a single ring of carbon and nitrogen atoms. The three pyrimidines found in DNA and RNA are cytosine (C), thymine (T), and uracil (U). As mentioned above, C pairs with G via three hydrogen bonds, and T (or U in RNA) pairs with A via two hydrogen bonds.

The nitrogenous bases contribute to the overall chemical and structural properties of nucleotides. The size and shape of the bases affect the geometry of the nucleotide moleculeand how it interacts with other molecules. The specific pairing of the bases, as mentioned above, is essential for the stability and fidelity of DNA and RNA replication and transcription.

Interestingly, the nitrogenous bases have a distinct UV absorption spectrum that allows for their detection and quantification in nucleic acid samples. This has led to the development of many techniques for studying DNA and RNA, such as gel electrophoresis and polymerase chain reaction (PCR), that rely on the properties of the bases.

Additionally, variations in the nitrogenous bases can affect the genetic code and the expression of genes. For example, mutations in the DNA sequence can lead to changes in the amino acid sequence of a protein, affecting its structure and function.

In summary, the nitrogenous bases are critical components of nucleotides that contribute to the structure, function, and properties of DNA and RNA. Their specific pairing, size and shape, and UV absorption properties make them important subjects of study in biochemistry and molecular biology.

Structure And Properties of Nitrogenous Bases.

Adenine Structure:

Adenine is a nitrogenous base that is one of the four building blocks of DNA and RNA. It was first isolated in 1885 by a German biochemist named Albrecht Kossel. Adenine is a purine, which means that its structure contains a double ring of carbon and nitrogen atoms.

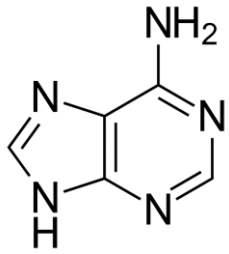


Figure 6: Structure of Adenine

The chemical formula of adenine is $C_5H_5N_5$. Its molecular weight is 135.13 g/mol. Adenine is a white crystalline powder that is soluble in water and other polar solvents. Its melting point is 360-365°C, and it has a density of 1.6 g/cm³.

The structure of adenine can be visualized as a flat molecule with two fused rings. The larger ring, which contains four nitrogen atoms and two carbon atoms, is called the purine ring. The smaller ring, which contains two nitrogen atoms and three carbon atoms, is called the imidazole ring.

The nitrogen atoms in adenine are arranged in a specific pattern, which gives the molecule its unique properties. The two nitrogen atoms in the imidazole ring are part of a group called an amino group, which can form hydrogen bonds with other molecules. The four nitrogen atoms in the purine ring are arranged in a way that allows them to participate in hydrogen bonding as well.

In DNA and RNA, adenine always pairs with thymine or uracil, respectively, through two hydrogen bonds. This pairing is essential for the stability and replication of genetic material.

In conclusion, adenine is a purine nitrogenous base that is an essential component of DNA and RNA. Its structure contains a double ring of carbon and nitrogen atoms, with two nitrogen atoms in an imidazole ring and four nitrogen atoms in a purine ring. Understanding the structure of adenine is crucial to understanding the properties and functions of DNA and RNA.

Guanine Structure:

Guanine is another nitrogenous base that is one of the building blocks of DNA and RNA. It was first isolated in 1846 by a German chemist named Julius Bodo Winkler. Guanine, like adenine, is also a purine and has a

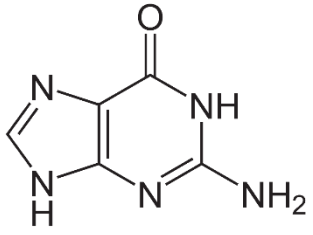


Figure 7: Structure of Guanine

similar structure.

The chemical formula of guanine is $C_5H_5N_5O$. Its molecular weight is 151.13 g/mol. Guanine is a white or off-white crystalline powder that is soluble in water and other polar solvents. Its melting point is 360-365°C, and it has a density of 2.2 g/cm³.

The structure of guanine can be visualized as a flat molecule with two fused rings. The larger ring, which contains four nitrogen atoms and two carbon atoms, is the purine ring. The smaller ring, which contains one nitrogen atom, is the imidazole ring.

The nitrogen atoms in guanine are arranged in a specific pattern, which gives the molecule its unique properties. The nitrogen atom in the imidazole ring is part of a group called an amino group, which can form hydrogen bonds with other molecules. The four nitrogen atoms in the purine ring are arranged in a way that allows them to participate in hydrogen bonding as well.

In DNA and RNA, guanine always pairs with cytosine through three hydrogen bonds. This pairing is also essential for the stability and replication of genetic material.

In conclusion, guanine is a purine nitrogenous base that is an essential component of DNA and RNA. Its structure contains a double ring of carbon and nitrogen atoms with two nitrogen atoms in an imidazole ring and four nitrogen atoms in a purine ring. Understanding the structure of guanine is crucial to understanding the properties and functions of DNA and RNA.

Thymine Structure:

Thymine is a nitrogenous base that is one of the building blocks of DNA. It was first isolated in 1893 by a German chemist named Albrecht Kossel. Thymine is a pyrimidine, meaning its structure contains a single ring of carbon and nitrogen atoms.

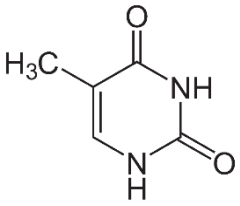


Figure 8: Structure of Thymine

The chemical formula of thymine is $C_5H_6N_2O_2$. Its molecular weight is 126.11 g/mol. Thymine is a white or yellow crystalline powder that is slightly soluble in water but more soluble in organic solvents. Its melting point is 316-317°C, and it has a density of 1.66 g/cm³.

The structure of thymine can be visualized as a flat molecule with a single ring. The ring contains two nitrogen atoms and four carbon atoms. Thymine also has a methyl group attached to one of the nitrogen atoms. It is also known as 5-methyl uracil.

The nitrogen atoms in thymine are arranged in a specific pattern, which gives the molecule its unique properties. The nitrogen atom with the methyl group is called methylated nitrogen. This methyl group can participate in hydrogen bonding with other molecules, making thymine more hydrophobic than other pyrimidines. The other nitrogen atom in the ring can also participate in hydrogen bonding.

In DNA, thymine always pairs with adenine through two hydrogen bonds. This pairing is essential for the stability and replication of genetic material.

In conclusion, thymine is a pyrimidine nitrogenous base that is an essential component of DNA. Its structure contains a single ring of carbon and nitrogen atoms, with a methyl group attached to one of the nitrogen atoms. Understanding the structure of thymine is crucial to understanding the properties and functions of DNA.

Cytosine Structure:

Cytosine is a nitrogenous base that is one of the building blocks of DNA and RNA. It was first isolated in 1894 by Albrecht Kossel. Cytosine is a pyrimidine, which

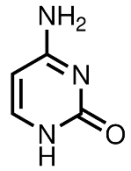


Figure 9: Structure of Cytosine

means that its structure contains a single ring of carbon and nitrogen atoms.

The chemical formula of cytosine is $C_4H_5N_3O$. Its molecular weight is 111.1 g/mol. Cytosine is a white crystalline powder that is slightly soluble in water but more soluble in organic solvents. Its melting point is 320-325°C, and it has a density of 1.45 g/cm³.

The structure of cytosine can be visualized as a flat molecule with a single ring. The ring contains two nitrogen atoms and three carbon atoms. Cytosine also has a carbonyl group attached to one of the carbon atoms.

The nitrogen atoms in cytosine are arranged in a specific pattern, which gives the molecule its unique properties. One nitrogen atom in the ring can participate in hydrogen bonding, while the other nitrogen atom can accept a hydrogen ion to become a negatively charged ion. The carbonyl group can also participate in hydrogen bonding.

In DNA and RNA, cytosine always pairs with guanine through three hydrogen bonds. This pairing is essential for the stability and replication of genetic material.

Cytosine can undergo a chemical modification called deamination, where the amino group is removed and replaced with a carbonyl group. This modification can change the genetic code, as the modified cytosine can pair with adenine instead of guanine.

In conclusion, cytosine is a pyrimidine nitrogenous base that is an essential component of DNA and RNA. Its structure contains a single ring of carbon and nitrogen atoms, with a carbonyl group attached to one of the carbon atoms. Understanding the structure of cytosine is crucial to understanding the properties and functions of DNA and RNA.

Uracil Structure:

Uracil is a nitrogenous base that is one of the building blocks of RNA.Uracil is a pyrimidine, which means that its structure contains a single ring of carbon and nitrogen atoms.

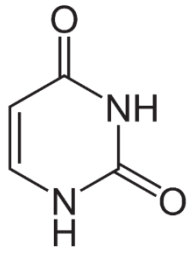


Figure 10: Structure of Uracil

The chemical formula of uracil is $C_4H_4N_2O_2$. Its molecular weight is 112.1 g/mol. Uracil is a white or colorless crystalline powder that is slightly soluble in water but more soluble in organic solvents. Its melting point is 335-338°C, with a density of 1.33 g/cm³.

The structure of uracil can be visualized as a flat molecule with a single ring. The ring contains two nitrogen atoms and four carbon atoms. Uracil also has a carbonyl group attached to one of the carbon atoms.

The nitrogen atoms in uracil are arranged in a specific pattern, which gives the molecule its unique properties. One nitrogen atom in the ring can participate in hydrogen bonding, while the other nitrogen atom can accept a hydrogen ion to become a negatively charged ion. The carbonyl group can also participate in hydrogen bonding.

In RNA, uracil always pairs with adenine through two hydrogen bonds. This pairing is essential for the stability and replication of genetic material.

Compared to thymine, which is found only in DNA, uracil is more reactive due to the absence of the methyl group. Uracil can be easily modified by enzymes or chemical agents, leading to changes in the genetic code and protein synthesis.

In conclusion, uracil is a pyrimidine nitrogenous base that is an essential component of RNA. Its structure contains a single ring of carbon and nitrogen atoms, with a carbonyl group attached to one of the carbon atoms. Understanding the structure of uracil is crucial to understanding the properties and

functions of RNA.

- **Biological Importance of Nucleotides**

Nucleotides play a crucial role in cellular processes and have a diverse range of functions. Here are some of the key functions of nucleotides in detail:

1. Building blocks of nucleic acids: Nucleotides serve as the basic building blocks of DNA and RNA. In DNA, the sequence of nucleotides determines the genetic information that is transmitted from one generation to the next. In RNA, nucleotides play a critical role in the process of gene expression by carrying information from DNA to the protein synthesis machinery.
2. Energy storage: Nucleotides such as adenosine triphosphate (ATP) serve as a primary energy carrier in cells. The high-energy bonds between the phosphate groups in ATP store energy that can be used to power cellular processes such as muscle contraction and nerve impulse transmission. When ATP is hydrolyzed, energy is released that can be used to drive biochemical reactions.
3. Enzyme cofactors: Some nucleotides can act as cofactors for enzymes, helping them perform their functions. For example, nicotinamide adenine dinucleotide (NAD+) and flavin adenine dinucleotide (FAD) are important coenzymes that play a role in electron transfer reactions in metabolism.
4. Intracellular signaling: Nucleotides can act as second messengers, transmitting signals within cells. For example, cyclic adenosine monophosphate (cAMP) and guanosine triphosphate (GTP) can activate protein kinases and other signaling pathways that regulate cellular processes such as cell growth and division.
5. Regulation of gene expression: Nucleotides can affect gene expression by binding to regulatory proteins such as transcription factors and modulating their activity. For example, cyclic AMP can activate protein kinase A, which phosphorylates transcription factors and promotes the transcription of genes involved in glucose metabolism.
6. Structural role: In addition to their role in nucleic acids, nucleotides can also play a structural role in molecules such as coenzymes and ATP-binding proteins. For example, the coenzyme NAD+ can bind to enzymes and help them perform their functions, while ATP-binding proteins such as myosin use the energy from ATP hydrolysis to perform mechanical work.

In summary, nucleotides are essential components of cellular processes and play diverse roles ranging from genetic information storage and transmission to energy storage and intracellular signaling. Their functions are critical for the proper functioning of cells and organisms.

4.3Discovery and Structure of DNA Double Helix

Deoxyribonucleic acid (DNA) is the molecule responsible for carrying genetic information from one generation to another. The discovery of the double helix structure of DNA is one of the most important scientific breakthroughs of the 20th century. This chapter will explore the history and significance of the discovery of the double helix structure of DNA.

Figure 11: Friedrich Miescher

History of DNA Research

Contrary to popular belief, James Watson, an American biologist, and Francis Crick, an English physicist, were not the discoverers of DNA in the 1950s. Rather, Swiss chemist Friedrich Miescher first identified DNA in the

late 1860s. In the years that followed, other scientists, such as Phoebus Levene and Erwin Chargaff, conducted extensive research on DNA, uncovering significant information about the chemical components and how they bonded. Without the foundational work of these early researchers, Watson and Crick would likely not have arrived at their groundbreaking conclusion in 1953, which identified DNA as a three-dimensional double helix.

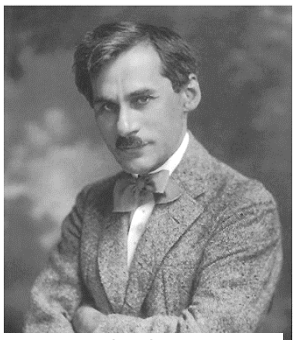


Figure 12: Phoebus Levene

In 1869, Swiss physiological chemist made a significant breakthrough in genetic research when he identified a substance he called "nuclein" in the nuclei of human white blood cells. Miescher's original plan was to isolate and study the protein components of leukocytes by washing used, pus-coated patient bandages and filtering out the white blood cells. However, when he discovered a substance in the cell nuclei with chemical properties unlike any protein, including a high phosphorous content and resistance to proteolysis, Miescher realized he had found a new substance. He predicted that a family of phosphorous-containing substances, known as nucleins, would be equivalent to proteins. Erwin Chargaff in 1971, noted that Miescher's discovery of nucleic acids was unique among the discoveries of the four major cellular components, which include proteins, lipids, polysaccharides, and nucleic acids.

As the 20th century arrived, Johann Friedrich Miescher's work on nuclein was all but forgotten, but scientists continued to explore the chemical structure of this mysterious molecule. Among them was Russian biochemist Phoebus Levene, a physician-turned-chemist who made significant contributions to the field, publishing over 700 papers on the chemistry of biological molecules during his career. Levene's many accomplishments include being the first to identify the order of nucleotide components (phosphate-sugar-base), discovering the carbohydrate components of RNA (ribose) and DNA (deoxyribose), and correctly identifying how RNA and DNA molecules are composed. In the early years of Levene's career, scientists did not know how individual nucleotides in DNA were arranged in space, and it would be years before the discovery of the sugar-phosphate backbone of DNA. Several scientists proposed different ways in which the nucleotide components of DNA might combine, but Levene's "polynucleotide" model proved to be the correct one. Levene suggested that nucleic acids were composed of a series of nucleotides, each consisting of a nitrogen-containing base, a sugar molecule, and a phosphate group. However, Levene's proposal underwent revisions as new evidence emerged, and it was discovered that the order of nucleotides along a stretch of DNA (or RNA) is highly variable.

Despite these alterations, Levene's polynucleotide structure accurately described the basics of DNA. It is now known that DNA is composed of a series of nucleotides, each containing a phosphate group, a ribose or deoxyribose sugar, and a single nitrogen-containing base. There are two categories of nitrogenous bases: purines (adenine [A] and guanine [G]), with two fused rings, and pyrimidines (cytosine [C], thymine [T], and uracil [U]), with a single ring. RNA contains only A, G, C, and U, whereas DNA contains only A, G, C, and T.

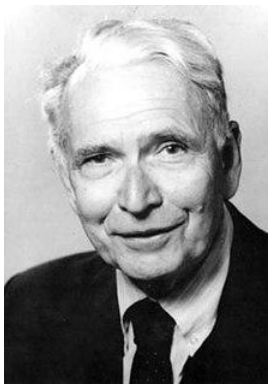


Figure 13: Erwin Chargaff

Erwin Chargaff played a crucial role in advancing the understanding of DNA's structure and composition, building upon the research of his predecessor, Levene. Chargaff, a biochemist from Austria, was deeply inspired by the groundbreaking 1944 study by Oswald Avery and his colleagues at Rockefeller University, which showed that genes consist of DNA. Chargaff considered this discovery to herald the advent of a new era in heredity research, and he was driven to investigate the chemistry of nucleic acids. According to Chargaff, Avery's work offered the first hints of a novel language, and he resolved to decipher it.

In his quest to uncover the language of DNA, Chargaff set out to compare

DNA from different species. He made two significant discoveries using a new technique he developed for identifying small amounts of organic matter. First, he observed that the nucleotide composition of DNA varies among species, which contradicts Levene's proposal that nucleotides repeat in the same sequence. Second, Chargaff found that DNA has certain consistent properties regardless of its source or tissue type. Specifically, the amount of adenine (A) is usually similar to that of thymine (T), and the amount of guanine (G) is usually close to that of cytosine (C). This finding is now known as "Chargaff's rule," where the total amount of purines (A + G) and pyrimidines (C + T) are nearly equal. Chargaff's discoveries proved to be pivotal for the later work of Watson and Crick, though he himself could not have predicted the explanation of these findings, namely, that A binds with T and C with G within the DNA molecule.

The Discovery of the Double Helix

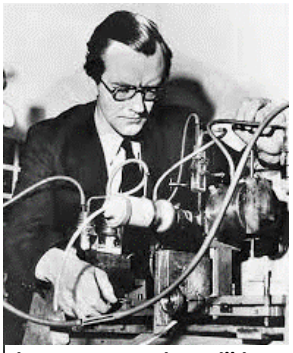


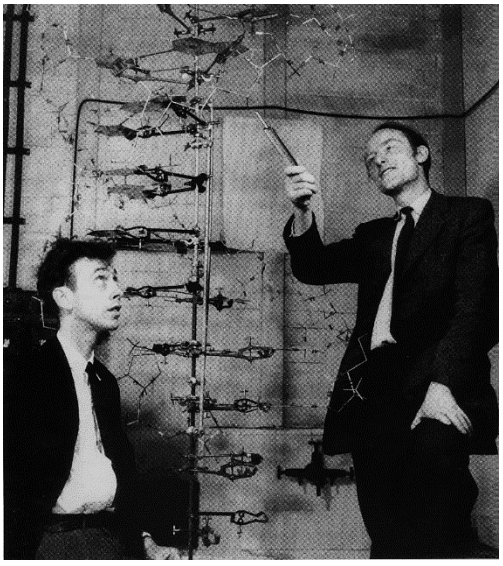
Figure 14: Maurice Wilkins

In the early 1950s, there were three main groups of scientists working on the structure of DNA: Linus Pauling at Caltech, Maurice Wilkins and Rosalind Franklin at King's College London, and James Watson and Francis Crick at the Cavendish Laboratory at Cambridge University.

Linus Pauling proposed a triple helix structure for DNA based on his knowledge of chemical bonding. However, his model was later proven incorrect. Meanwhile, Maurice Wilkins and Rosalind Franklin were using X-ray crystallography to study the structure of DNA at King's College London. It was Wilkins's idea to study DNA by X-ray crystallographic techniques. Their images provided crucial information about the helical shape of DNA, as well as the distance between the nitrogenous bases and the width of the helix. At the same time, James Watson and Francis Crick were also studying the structure of DNA at the Cavendish Laboratory at Cambridge University.


Figure 15: Rosalind Franklin

Watson and Crick's proposal of the double-helical model for the structure of DNA was largely built upon Chargaff's findings that A = T and C = G, as well as the X-ray crystallography work of Rosalind Franklin and Maurice Wilkins. In addition, Watson and Crick were able to utilize recent advances in model building, which involved assembling potential three-dimensional structures based on known molecular distances and bond angles, a technique developed by Linus Pauling. Despite initially fearing that Pauling might beat them to the punch, Watson and Crick ultimately found that Pauling's prediction of the structure of DNA was incorrect. By manipulating cardboard cutouts representing the chemical components of the four bases and other nucleotide subunits, Watson and Crick were able to piece together a model of DNA structure as if it were a puzzle. However, they initially made a mistake in their understanding of how the different elements in thymine and guanine were configured. They eventually realized their error thanks to the suggestion of American scientist Jerry Donohue, who urged them to make new cardboard cutouts of the two bases with a different atomic configurations. This led to the realization that the complementary base pairs, A with T and C with G, fit together perfectly, held together by hydrogen bonds, and the final structure of DNA matched Chargaff's rule.



Ultimately they proposed the double helix structure of DNA in 1953. Watson, Crick, and Wilkins were awarded the Nobel Prize in

Figure 16: James Watson and Francis Crick with their DNA double helix model, 1953

Physiology or Medicine in 1962 for their work on the structure of DNA. However, Rosalind Franklin, who passed away from cancer in 1958, did not receive the award. The debate surrounding the reasons for her exclusion from the Nobel Prize still remains unclear. However, it is worth noting that the Nobel Prize stipulates that no more than three people can be awarded the prize. Additionally, the fact that Franklin passed away before the prize was awarded may have also played a role, although it is important to mention that the rule against posthumous awards was not established until 1974. Today, her contributions to the discovery of DNA are widely recognized and celebrated.

In conclusion, the discovery of the structure of DNA has had a profound impact on the field of biology and beyond. The contributions of many scientists, including Friedrich Miescher, Phoebus Levene, Erwin Chargaff, Rosalind Franklin, Maurice Wilkins, Linus Pauling, James Watson, and Francis Crick, paved the way for the understanding of the genetic code and the development of biotechnology. The double helix structure of DNA and the rules that govern base pairing have opened up new avenues for scientific inquiry and technological advancement, from genetic engineering and gene therapy to personalized medicine and forensics. While there is still much to be learned about the intricacies of DNA and its role in life, the pioneering work of these scientists has set the stage for many exciting discoveries and breakthroughs in the years to come.

The Watson and Crick model has undergone minor changes and elaborations since its creation in 1953, but its four major features remain unchanged.

1. The double-stranded helix of DNA is held together by hydrogen bonds, with A bases always paired with Ts and Cs paired with Gs to account for Chargaff's rule.
2. Most DNA double helices are right-handed, except for the left-handed Z-DNA.
3. The DNA double helix is anti-parallel, with nucleotides linked by their phosphate groups to connect the 3' end of one sugar to the 5' end of the next.
4. The nitrogen-containing bases of DNA are exposed and available for potential hydrogen bonding, allowing easy access for other molecules, including proteins involved in DNA replication and expression.

4.5 Summary

4.6 Terminal Question

Question1

Timeline of the key events in the discovery of the DNA double helix:

1869*: Friedrich Miescher, a Swiss biochemist, discovers a substance in the nucleus of white blood cells that he calls "nuclein." This substance is later identified as DNA. He was the first to identify DNA as a distinct molecule.*

1928*: Frederick Griffith performs experiments with bacteria that show that genetic information can be transferred between cells.*

1944*: Oswald Avery, Colin MacLeod, and Maclyn McCarty demonstrate that DNA is the genetic material that carries the hereditary information in cells.*

1950*: Erwin Chargaff discovers that the amount of adenine (A) in DNA is equal to the amount of thymine (T), and the amount of guanine (G) is equal to the amount of cytosine (C). This is known as Chargaff's rule.*

1952*: Rosalind Franklin and Maurice Wilkins use X-ray crystallography to produce images of DNA that provide crucial information about its structure.*

***1953**: James Watson and Francis Crick at the Cavendish Laboratory at Cambridge University use Franklin and Wilkins' X-ray images, as well as information from other scientists, to propose the double helix structure of DNA. Their findings are published in the scientific journal Nature.*

***1962**: Watson, Crick, and Wilkins are awarded the Nobel Prize in Physiology or Medicine for their work on the structure of DNA.*

Today, the discovery of the DNA double helix continues to have a profound impact on the fields of genetics, molecular biology, and medicine.

4.4 Structure of DNA Double Helix

The structure of DNA is a remarkable and uniform double-stranded helix that consists of two polynucleotide strands coiling around each other. This helix is characterized by a consistent orientation, width, nucleotide spacing, length, and number of nucleotides per helical turn, which were first described by Watson and Crick. The double helix resembles a twisted ladder, with the sides of the ladder being composed of alternating sugar (deoxyribose) and phosphate molecules, and the rungs made up of nitrogen base pairs. The nitrogenous bases that make up the DNA molecule include Adenine (A), Thymine (T), Guanine (G), and Cytosine (C).

These bases pair up in a specific pattern, with A always pairing with T and G always pairing with C. The complementary base pairing between adenine and thymine, and between cytosine and guanine, is a fundamental aspect of DNA structure and function. The two strands of DNA are bound together by hydrogen bonds, with two hydrogen bonds linking adenine to thymine and three hydrogen bonds linking guanine to cytosine.

Each strand has a 5′end and a 3′end, with a phosphate group and a hydroxyl group, respectively. The two strands are anti-parallel, meaning that they run in opposite directions. The strands are held together by hydrogen bonds, and they are complementary to each other. The DNA is composed of deoxyribonucleotides, which are linked together by 3′-5′ phosphodiester bonds.

The base pairing occurs due to the nature of these nitrogenous bases. Adenine always pairs with thymine (A-T) via two hydrogen bonds, while cytosine pairs with guanine (C-G) via three hydrogen bonds. Hydrogen bonding and hydrophobic interactions between bases stabilize the shape of the helix. The diameter of the double helix is 2nm, and the double helical structure repeats at an interval of 3.4nm.Thus the vertical separation between two base pairs in DNA is 3.4 Å (0.34 nanometers). A full turn of the DNA helix is 34 Å (3.4 nanometers). Each base pair rotates 36 degrees clockwise in relation to the previous base pair. Studies have shown that there are actually 10.4 base pairs per turn, rather than the previously assumed 10.0.

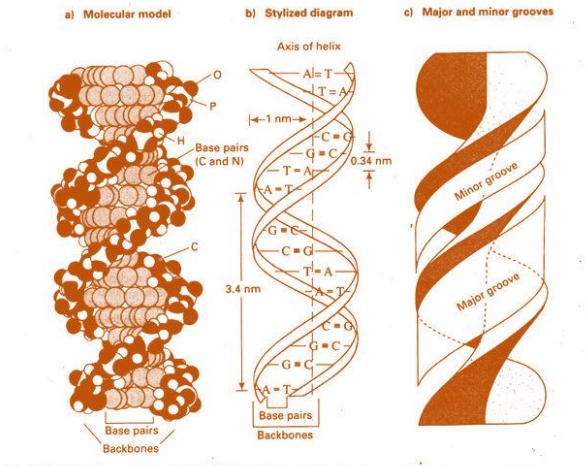


Figure 17A-DNA B-DNA Z-DNA

DNA has two grooves due to its double helical structure, with one groove being larger than the other. The asymmetry of the grooves is caused by the geometric configuration of the bonds between the phosphate, sugar, and base groups, which result in base groups attaching at 120-degree angles instead of 180 degrees. The larger groove, called the major groove, occurs when the backbones are far apart, while the smaller groove, called the minor groove, occurs when they are close together. Since the major and minor grooves expose the edges of the bases, they can be used to identify the base sequence of a specific DNA molecule. This recognition is crucial because proteins

need to recognize specific DNA sequences to bind and carry out the proper functions of the body and cell.

In summary, the structure of DNA is a remarkable and uniform double-stranded helix composed of nucleotides that are linked together by phosphodiester bonds. The two strands are held together by hydrogen bonds, and the complementary base pairing between adenine and thymine, and between cytosine and guanine, is a fundamental aspect of DNA structure and function. The helix shape is stabilized by hydrogen bonding and hydrophobic interactions between bases.

Structural variations of DNA

B-DNA is the classic Watson-Crick model of DNA and is the most common form of DNA found in living organisms. However, different forms of DNA, such as A-DNA, Z-DNA, C-DNA, D-DNA, and E-DNA, can appear under certain conditions. The deviation in DNA forms is based on their structural diversity, which can be attributed to changes in the conformation of the sugar-phosphate backbone, base pair orientation, and helical parameters.

A-DNA: A-DNA is a type of DNA that has a right-handed helix, similar to B-DNA, but with a few differences. It has 11 base pairs per turn, a 0.26 nm axial rise, a 28° helix pitch, a 20° base-pair tilt, a 33° twist angle, and a 2.3 nm helix diameter. A-DNA forms when humidity is low, and salt concentration is high. The major differences between A-DNA and B-DNA are in the conformation of the deoxyribose sugar ring and the placement of base pairs within the duplex. The sugar ring in A-DNA is in the C3′ endo conformation, while in B-DNA, it is in the C2′ endo conformation. Additionally, in A-DNA, the base pairs are displaced away from the central axis and closer to the major groove, resulting in a ribbon-like helix with a more open cylindrical core compared to B-DNA.

Z-DNA: It is a left-handed double helical structure that winds to the left in a zig-zag pattern. Z-DNA is a unique form of DNA that was discovered by Rich and Wang in 1984. It features left-handed helices and a pronounced zig-zag pattern in the phosphodiester backbone, which gives it its name. Similar to B-DNA, it has anti-parallel strands but is longer and thinner. Z-DNA forms when the DNA is in an alternating purine-pyrimidine sequence, such as GCGCGC, where the G and C nucleotides are in different conformations, resulting in the zig-zag pattern. The difference lies in the G nucleotide, which has the sugar in the C3′ endo conformation and the guanine base in the syn conformation. This positions the guanine back over the sugar ring, which is not typically seen in A- and B-forms, where it readily forms H-bonds with the complementary base. The duplex in Z-DNA must accommodate the distortion of this G nucleotide in the syn conformation. The cytosine in the adjacent nucleotide of Z-DNA is in the normal C2′ endo, anti-conformation. Z-DNA has 12 base pairs per turn, a 0.45 nm axial rise, 45° helix pitch, 7° base-pair tilt, -30° twist angle, and a 1.8 nm helix diameter.

C-DNA: This specific type of DNA forms under specific conditions - at 66% relative humidity and in the presence of Li+ and Mg2+ ions. It features a right-handed helix with an axial rise of 3.32 Å per base pair and a total of 33 base pairs per turn. The helical pitch is calculated to be 30.97 Å, and the base pair rotation is 38.58°. In comparison to A-DNA and B-DNA, it has a smaller diameter of 19 Å and a base tilt of 7.8°.

D-DNA: This form of DNA is an uncommon variation with only 8 base pairs per helicalturn. It is only found in certain DNA molecules that lack guanine. The axial rise per base pair is 3.03 Å, and the tilt from the helix axis is 16.7°. D-DNA has a unique structure due to its atypical base pair arrangement, which leads to variations in its helical parameters. The rarity of D-DNA and its specific conditions for formation make it a less well-known and less studied DNA form.

E-DNA: Eccentric DNA is characterized by a long helical axis rise and base pairs that are perpendicular to the helical axis. It has a deep major groove and a shallow minor groove, which result from the unique orientation of the base pairs. Interestingly, if allowed to crystallize for an extended

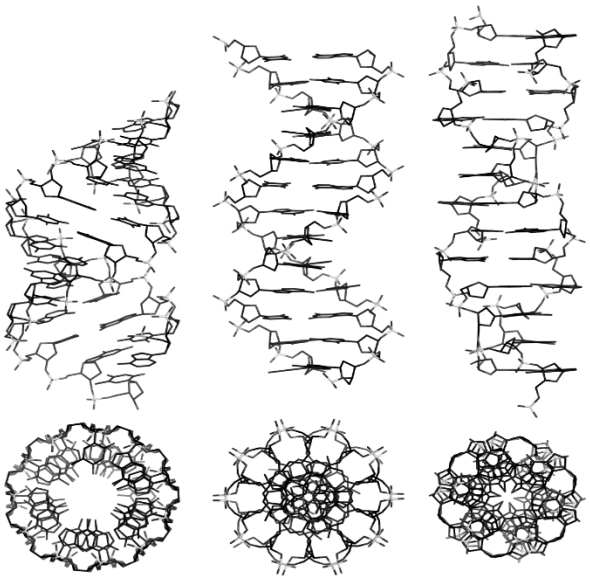


Figure 18Figure 18:Figure 19: The depicted illustration exhibits three different conformations of DNA, namely A-DNA, B-DNA, and Z-DNA, with a focus on 12 base-pair steps that are composed of 13 base pairs. The image displays both side and top views of the confor

period of time, the methylated sequence of eccentric DNA forms the standard A-DNA structure. This type of DNA is an intermediate in the crystallographic pathway from B-DNA to A-DNA and can provide valuable insights into the structural transitions between the two forms.

These different structural variations of DNA contribute to the dynamic and diverse nature of the DNA molecule, allowing it to adopt various conformations in response to specific environmental conditions or molecular interactions. Understanding the distinct structural features of these DNA forms and the factors that influence their formation can help researchers uncover the molecular mechanisms that govern DNA function, stability, and interactions with other biomolecules. Moreover, these insights can facilitate the development of new therapeutic strategies and diagnostic tools that target the unique structural properties of specific DNA forms, ultimately leading to improved healthcare and personalized medicine

4.5 RNA structure and types

RNA (Ribonucleic acid) is a versatile biological molecule that plays a crucial role in gene expression and protein synthesis. RNA molecules are composed of a long chain of nucleotides that are linked together by covalent bonds. RNA is single-stranded, and it is usually shorter than DNA. RNA is synthesized from a DNA template by the process of transcription. The structure of RNA is similar to that of DNA, but there are some differences. RNA contains uracil instead of thymine as one of its nucleotides and is usually single-stranded. RNA comes in different types that perform different functions. The three major types of RNA are messenger RNA (mRNA), transfer RNA (tRNA), and ribosomal RNA (rRNA).

This chapter will provide an in-depth discussion of RNA structure and types. The first section will discuss the chemical structure of RNA and how it differs from DNA. The second section will introduce the three major types of RNA and describe their functions in gene expression and protein synthesis. The third section will cover other types of RNA with important biological functions, including microRNA, small interfering RNA, and long noncoding RNA.

Understanding the structure and types of RNA is crucial for comprehending how genetic information is expressed and how proteins are synthesized. This chapter will provide a comprehensive overview of RNA, from its chemical structure to its biological functions. In addition to the three major types of RNA, other types play essential roles in various biological processes. Some of these RNA molecules are involved in gene regulation, while others have structural or catalytic functions.

- ### Chemical structure of RNA

The chemical structure of RNA is similar to that of DNA, with a few key differences. Like DNA, RNA is composed of nucleotides, which are made up of three parts: a nitrogenous base, a sugar, and a phosphate group. The four nitrogenous bases found in RNA are adenine (A), guanine (G), cytosine (C), and uracil (U). In DNA, thymine (T) replaces uracil. The nitrogenous bases form the "rungs" of the nucleic acid ladder, with the sugar-phosphate backbone forming the "rails".

The sugar in RNA is ribose, while in DNA it is deoxyribose. The difference between the two sugars is that ribose has a hydroxyl (-OH) group attached to the 2' carbon atom, whereas deoxyribose has a hydrogen (-H) atom in its place. This difference in the sugar molecule affects the stability and structure of RNA.

Another key difference between RNA and DNA is that RNA is usually single-stranded, while DNA is double-stranded. This difference in structure is due to the fact that RNA molecules can fold back on themselves to form complex three-dimensional structures. These structures are essential for many of the functions of RNA, including catalyzing chemical reactions and regulating gene expression.

In addition to these differences, there are some similarities between RNA and DNA. Both molecules are composed of nucleotides, which are linked together by covalent bonds between the 3' carbon of one nucleotide and the 5' carbon of the next. Both RNA and DNA can form hydrogen bonds between complementary base pairs, which allows them to maintain their double-stranded structure. Overall, the chemical structure of RNA is similar to that of DNA, with a few key differences. These differences in the nitrogenous bases, sugar, and structure affect the stability and function of RNA and are essential for its role in gene expression and protein synthesis.

- ## Type of RNA

The three major types of RNA are messenger RNA (mRNA), transfer RNA (tRNA), and ribosomal RNA (rRNA). Each type of RNA plays a crucial role in the process of gene expression and protein synthesis.

- ## Messenger RNA (mRNA):

The structure of mRNA is a complex and fascinating subject. It is a key part of the genetic code and the process of protein synthesis.

Messenger RNA (mRNA) is synthesized during the process of transcription from DNA. It carries genetic information from the DNA in the nucleus of a cell to the ribosome, the site of protein synthesis in the cytoplasm. The mRNA sequence is determined by the sequence of nucleotides in the DNA template, and it provides the instructions for assembling a specific sequence of amino acids to form a protein.

Messenger RNA (mRNA) is a single-stranded molecule that is complementary to the DNA template from which it is transcribed. It is the molecule that carries the genetic code from the nucleus to the ribosome, where it is used to translate the code into proteins.

mRNA is made up of a series of nucleotides, which are the building blocks of nucleic acids. The nucleotides in mRNA are adenine (A), guanine (G), cytosine (C), and uracil (U). The order of the nucleotides in mRNA determines the amino acid sequence of the protein that will be translated.

mRNA is a linear molecule, with a 5' end and a 3' end. The 5' end is the end that is first transcribed from the DNA template, and the 3' end is the end that is last transcribed. The 5' end of mRNA is capped with a ribose sugar that is attached to a guanine nucleotide. This cap protects the mRNA from degradation and helps to stabilize it. The 3' end of mRNA is polyadenylated, which means that a series of adenine nucleotides are added to the end of the molecule. This polyadenylation helps to stabilize the mRNA and makes it more efficient for translation.

The structure of mRNA can be divided into three main regions: the 5' untranslated region, the coding region, and the 3' untranslated region. The 5' untranslated region is a region of mRNA that is not translated into protein. It contains regulatory sequences that control the transcription of mRNA and the processing of mRNA. The coding region is the region of mRNA that is translated into protein. It contains the genetic code for the protein that will be synthesized.The 3' untranslated region is a region of mRNA that is not translated into protein. It contains regulatory sequences that control the degradation of

mRNA and the stability of mRNA

- **Transfer RNA (tRNA):**

Transfer RNA (tRNA) is a small RNA molecule that plays a key role in protein synthesis. It is responsible for carrying amino acids to the ribosome, where they are incorporated into the growing polypeptide chain.

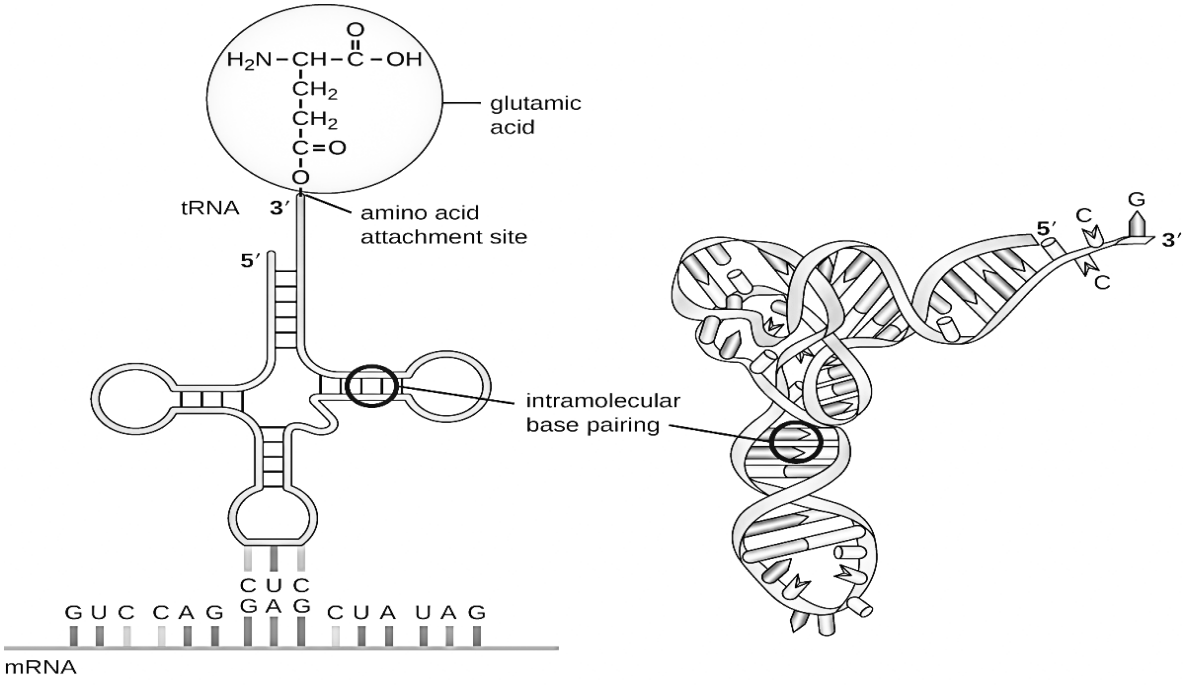
tRNA molecules are cloverleaf-shaped, with three hairpin loops and a variable loop. The anticodon loop is the loop that contains the tRNA's anticodon, which is a triplet of nucleotides that is complementary to the codon on the mRNA that it is binding to. The anticodon loop is also the loop that binds to the ribosome.

The acceptor loop is the loop that contains the tRNA's amino acid attachment site. The amino acid is attached to the tRNA by a peptide bond.

The variable loop is the loop that contains the tRNA's other nucleotides. The variable loop is important for the tRNA's function, as it helps to determine the tRNA's affinity for the ribosome and its ability to bind to the mRNA codon.

tRNA molecules are synthesized in the nucleus of the cell. The process of tRNA synthesis is called tRNA transcription. tRNA transcription is similar to mRNA transcription, in that it is a process of copying the genetic information from DNA to RNA. However, tRNA transcription is different from mRNA transcription in that it is a much shorter process, and it only produces a single strand of RNA. tRNA molecules are then transported to the cytoplasm of the cell, where they bind to the ribosome. The ribosome is a large molecule that is made up of proteins and RNA. The ribosome is responsible for translating the genetic code in mRNA into proteins. When a tRNA binds to the ribosome, the anticodon loop binds to the codon on the mRNA that it is complementary to. The amino acid attachment site is then exposed to the ribosome, and the amino acid is added to the growing polypeptide chain. The ribosome then moves along the mRNA, and the tRNA is released. The ribosome then binds to the next codon on the mRNA and repeats the process.

tRNA molecules are essential for protein synthesis. Without tRNA, proteins could not be synthesized and cells could not function.



tRNA 2-dimensional structure

tRNA 3-dimensional structure

- **Ribosomal RNA (rRNA):**

Ribosomal RNA (rRNA) is a type of RNA that is essential for protein synthesis. It is found in ribosomes, which are the organelles that are responsible for translating mRNA into proteins.

rRNA is a large molecule, with a molecular weight of up to 6 million daltons. It is made up of a number of different subunits, which are encoded by different genes. The subunits come together to form the ribosome, which is the site of protein synthesis. rRNA has a number of different functions. It is responsible for binding to mRNA and bringing it into the ribosome. It also helps to catalyze the process of protein synthesis. In addition, rRNA is responsible for the stability of the ribosome. The structure of rRNA is complex and has been the subject of much study. The molecule is made up of a number of different regions, each of which has a specific function. The regions are:

- The 5' ribosomal subunit: This subunit is responsible for binding to mRNA and bringing it into the ribosome. It also contains the site where the first amino acid is added to the growing polypeptide chain.
- The 3' ribosomal subunit: This subunit is responsible for binding to the mRNA and bringing it into the ribosome. It also contains the site where the last amino acid is added to the growing polypeptide chain.
- The central region: This region contains the site where protein synthesis takes place. It is also responsible for the stability of the ribosome.
- The linker region: This region connects the 5' and 3' ribosomal subunits.

The structure of rRNA is essential for its function. The different regions of the molecule interact with each other in a specific way in order to carry out the process of protein synthesis.

In summary, the three major types of RNA play critical roles in gene expression and protein synthesis. Messenger RNA carries genetic information from DNA to the ribosome and provides the instructions for assembling a specific protein sequence. Transfer RNA delivers amino acids to the ribosome during protein synthesis, and ribosomal RNA catalyzes peptide bond formation and helps to position the tRNA molecules. Together, these three types of RNA form a complex machinery that allows cells to produce the proteins they need to carry out their functions.

In addition to the three major types of RNA, there are other types of RNA that play important roles in a variety of biological processes. Some of these RNA molecules are involved in gene regulation, while others have structural or catalytic functions.

MicroRNA (miRNA):

MicroRNA (miRNA) is a class of small RNA molecules that play a critical role in gene regulation. miRNAs are transcribed from DNA by RNA polymerase II and processed by cellular machinery to produce short RNA molecules of approximately 22 nucleotides in length. The processing involves cleavage by the enzyme Drosha, which creates a precursor miRNA (pre-miRNA) hairpin structure. Pre-miRNAs are then transported to the cytoplasm where they are further processed by Dicer, resulting in the mature miRNA molecule.

miRNAs bind to complementary sequences on target mRNA molecules, leading to their degradation or inhibition of translation. The binding of miRNAs to their targets is facilitated by the RNA-induced silencing complex (RISC), which is composed of the miRNA and several proteins, including Argonaute proteins.

miRNAs play a role in a variety of biological processes, including development, differentiation, and disease. They are also involved in the regulation of gene expression in response to environmental

stimuli, such as stress or infection. Dysregulation of miRNA expression has been implicated in a variety of diseases, including cancer, cardiovascular disease, and neurodegenerative disorders.

Small interfering RNA (siRNA):

Small interfering RNA (siRNA) is another class of small RNA molecules that play a role in gene regulation. siRNAs are usually derived from exogenous sources, such as viruses or transposons, and are processed in a similar manner to miRNAs.

siRNAs also bind to complementary sequences on target mRNA molecules, leading to their degradation or inhibition of translation. The use of siRNAs as tools for gene silencing has been widely adopted in both research and medical applications.

siRNAs also play a role in the defense against viral infection, as they are involved in the RNA interference (RNAi) pathway, which targets and degrades viral RNA.

Long noncoding RNA (lncRNA):

Long noncoding RNA (lncRNA) is a class of RNA molecules that are more than 200 nucleotides long and do not code for proteins. lncRNAs play various roles in gene regulation, including acting as transcriptional regulators, modulating mRNA stability, and interacting with other RNA molecules.

lncRNAs are transcribed from DNA by RNA polymerase II and can be processed in various ways. Some lncRNAs undergo splicing and polyadenylation, similar to protein-coding mRNA molecules, while others are processed by alternative mechanisms.

lncRNAs have been implicated in various biological processes, including development, differentiation, and disease. They are also involved in the regulation of cellular stress responses and the maintenance of genome stability. Dysregulation of lncRNA expression has been associated with a variety of diseases, including cancer, cardiovascular disease, and neurological disorders.

Overall, these other types of RNA highlight the diverse roles that RNA molecules play in the regulation of gene expression and cellular function. By understanding the functions of these RNA molecules, we can gain insights into the complex mechanisms that govern biological processes and develop new therapeutic strategies for a variety of diseases.

4.6 Summary

In conclusion, RNA is a versatile molecule that plays a crucial role in gene expression and protein synthesis. The chemical structure of RNA is distinct from DNA and allows it to perform unique functions in the cell. The three major types of RNA, mRNA, rRNA, and tRNA, are involved in different stages of protein synthesis, including transcription, processing, and translation. In addition, other types of RNA, such as miRNA, siRNA, and lncRNA, play important roles in gene regulation, defense against viral infection, and maintenance of genome stability.

The study of RNA has advanced our understanding of the molecular mechanisms that govern biological processes, and has provided insights into the etiology of a variety of diseases. Research on RNA has also led to the development of novel therapeutic strategies, such as RNA interference and RNA-based drugs. As our knowledge of RNA continues to expand, we can expect to uncover new functions and mechanisms of RNA molecules in the cell. The future of RNA research is promising, and the potential for RNA-based therapies in treating human diseases is enormous. The study of RNA will undoubtedly continue to be a key area of research in the field of molecular biology and biotechnology.

4.7 Terminal Question

Question-1 describe in details structure of DNA.

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Question-2 describe in detail biological importance of nucleotides.

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Question-3 explain structure and properties of nitrogenous base.

4.8 Answer

4.9 Suggested books

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UNIT- 5 DNA Replication

5.1 Introduction

The story of DNA replication is a tale of scientific discovery that spans several decades. It is a

story that begins in the early 20th century, with the identification of DNA as the molecule of heredity, and culminates in the late 20th century with the elucidation of the detailed mechanisms of DNA replication.

The journey towards understanding DNA replication began with the discovery of DNA itself. In 1869, Swiss physician Friedrich Miescher isolated a novel substance from the nuclei of white blood cells, which he named "nuclein". This substance, rich in phosphorus and nitrogen, was later renamed deoxyribonucleic acid (DNA).

However, the role of DNA as the molecule of heredity was not immediately recognized. For many years, proteins, with their diverse structures and complex chemistry, were considered the most likely candidates for the carriers of genetic information. The turning point came in 1944, when Oswald Avery, Colin MacLeod, and Maclyn McCarty demonstrated that DNA from a virulent strain of bacteria could transform a non-virulent strain into a virulent one. This experiment provided the first definitive evidence that DNA carried genetic information.

Objectives

After studying this unit, you will be able to know-

- The Double Helix and Complementary Base Pairing
- Elucidation of the Mechanism of DNA Replication
- Prokaryotic and Eukaryotic DNA Replication
- Regulation of DNA Replication

5.2 The Double Helix and Complementary Base Pairing

The next significant milestone in the history of DNA replication was the discovery of the structure of DNA. In 1953, James Watson and Francis Crick, building on the X-ray diffraction data collected by Rosalind Franklin and Maurice Wilkins, proposed the double helix model of DNA. This model suggested that DNA was composed of two antiparallel strands twisted into a helix, with the bases on the inside and the sugar-phosphate backbone on the outside.

The double helix model also proposed the principle of complementary base pairing, with adenine (A) pairing with thymine (T), and cytosine (C) pairing with guanine (G). This principle was crucial for understanding how DNA could be replicated.

The Semi-conservative Model of DNA Replication

The next question was how DNA replicated itself. Three models were proposed: conservative, semi-conservative, and dispersive. The conservative model suggested that the two parental DNA strands stayed together after replication. The dispersive model suggested that the parental and daughter DNA were interspersed in both strands after replication. The semi-conservative model, proposed by Watson and Crick, suggested that each of the two strands of the parental DNA served as a template for new DNA to be synthesized.

The semi-conservative model was confirmed in 1958 by Matthew Meselson and Franklin Stahl using a clever experimental design involving isotopes of nitrogen. They demonstrated that all DNA molecules were of intermediate density after one round of replication, consistent with the semi-conservative model.

Table 1: Key Discoveries in the History of DNA Replication

Year	Discovery	Scientists

1869	Discovery of "nuclein" (later DNA)	Friedrich Miescher
1944	DNA is identified as the molecule of heredity	Oswald Avery, Colin MacLeod, Maclyn McCarty
1953	Double helix structure of DNA	James Watson, Francis Crick, Rosalind Franklin, Maurice Wilkins
1958	Semi-conservative model of DNA replication	Matthew Meselson, Franklin Stahl
1956	Discovery of DNA polymerase	Arthur Kornberg

5.3 Elucidation of the Mechanism of DNA Replication

The subsequent decades saw the elucidation of the detailed mechanisms of DNA replication. Arthur Kornberg discovered the first DNA polymerase, an enzyme that could synthesize DNA, in 1956. However, this enzyme, later named DNA polymerase I, could not initiate DNA synthesis, a puzzle that was solved with the discovery of RNA primers.

The discovery of the replication fork, where DNA replication occurs, and the realization that DNA replication is bidirectional were other significant milestones. The discovery of Okazaki fragments, short pieces of DNA synthesized on the lagging strand, and the discovery of DNA ligase, which joins these fragments together, further refined our understanding of DNA replication.

The discovery of the telomere, the end of the chromosome, and the enzyme telomerase, which extends the telomere, solved the end-replication problem, the inability of DNA polymerase to fully replicate the ends of linear DNA.

Conclusion

The history of DNA replication is a testament to the power of scientific inquiry and collaboration. It is a story of how a series of discoveries, often serendipitous, built upon each other to unravel the mysteries of life at the molecular level. Today, our understanding of DNA replication underpins much of modern

5.4 Prokaryotic DNA Replication

Prokaryotic DNA replication is a highly coordinated process that ensures the faithful duplication of the bacterial chromosome. Unlike eukaryotes, prokaryotes have a single circular chromosome, and replication begins at a single origin of replication and proceeds bidirectionally. This section will delve into the intricacies of this process.

The Replication Machinery

The replication machinery, or replisome, is a complex of proteins that carry out DNA replication. let's delve deeper into the components of the prokaryotic replisome and their roles in DNA replication.

i. DNA Helicase

DNA helicase is a motor protein that uses the energy from ATP hydrolysis to unwind the double-stranded DNA at the replication fork. This enzyme moves along the DNA in the 5' to 3' direction on the lagging strand, breaking the hydrogen bonds between the base pairs and generating two single-stranded DNA templates for replication. The unwinding of the DNA by helicase is the first step in the replication process.

ii. Single-Strand DNA Binding Proteins (SSBs)

Once the DNA strands are separated, they are prone to reannealing or forming secondary structures. Single-strand DNA binding proteins (SSBs) bind to the single-stranded DNA exposed by the helicase, stabilizing the single-stranded state and preventing the strands from reannealing. SSBs also protect the single-stranded DNA from degradation by nucleases.

iii. DNA Gyrase (Topoisomerase)

The unwinding of the DNA by helicase generates tension in the DNA molecule ahead of the replication fork, leading to supercoiling. DNA gyrase, a type of topoisomerase, relieves this supercoiling by introducing negative supercoils into the DNA. DNA gyrase achieves this by making a transient double-strand break in the DNA, passing another segment of the DNA through the break, and then resealing the break.

iv. DNA Primase

DNA polymerases, the enzymes that synthesize new DNA, cannot initiate DNA synthesis de novo. They require a primer with a free 3' hydroxyl group to which they can add nucleotides. DNA primase synthesizes a short RNA primer that provides this 3' hydroxyl group. The primer is synthesized in the 5' to 3' direction and is complementary to the DNA template.

v. DNA Polymerase III

DNA polymerase III is the main replicative enzyme in prokaryotes. It adds nucleotides to the 3' end of the RNA primer, synthesizing new DNA in the 5' to 3' direction. DNA polymerase III has a high processivity, meaning it can add many nucleotides to the primer before dissociating. This is due to its association with a sliding clamp protein that tethers it to the DNA.

vi. DNA Polymerase I

Once a segment of DNA has been synthesized, the RNA primer is no longer needed and must be removed. DNA polymerase I removes the RNA primers and replaces them with DNA. It has both polymerase activity, which allows it to add nucleotides, and exonuclease activity, which allows it to remove the RNA primers.

vii. DNA Ligase

The removal of the RNA primer and its replacement with DNA leaves a gap in the sugar-phosphate backbone of the DNA. DNA ligase seals this gap, creating a continuous DNA strand. DNA ligase achieves this by catalyzing the formation of a phosphodiester bond between the 3' hydroxyl group of one DNA fragment and the 5' phosphate group of the next DNA fragment.

Table 2:Key Components of the Prokaryotic Replisome

Component	**Function**
DNA Helicase	Unwinds the double-stranded DNA
Single-Strand DNA Binding Proteins (SSBs)	Bind to the single-stranded DNA to prevent reannealing
DNA Gyrase (Topoisomerase)	Relieves supercoiling ahead of the replication fork

DNA Primase	Synthesizes a short RNA primer
DNA Polymerase III	Main enzyme for DNA synthesis
DNA Polymerase I	Removes RNA primers and replaces them with DNA
DNA Ligase	Seals the gaps between the newly synthesized DNA fragments

The Process of Prokaryotic DNA Replication

Initiation

The initiation of DNA replication in prokaryotes begins at a specific sequence of DNA known as the origin of replication, or oriC in bacteria like E. coli. The oriC region is rich in adenine-thymine (AT) pairs, which are easier to separate than guanine-cytosine (GC) pairs due to fewer hydrogen bonds.

The initiation process starts with the binding of the initiator protein DnaA to the DnaA box sequences within the oriC region. DnaA is an ATPase, and its ATP-bound form has a high affinity for the DnaA box. The binding of multiple DnaA molecules to the oriC region leads to the formation of a DnaA-oriC complex, which causes the DNA to bend and leads to the separation of the strands in the AT-rich region.

Unwinding and Stabilization

Once the DNA strands are separated, DnaB helicase, with the help of DnaC, a helicase loader, is recruited to the replication origin. The helicase unwinds the DNA at the replication fork, breaking the hydrogen bonds between the base pairs and generating two single-stranded DNA templates for replication.

The single-stranded DNA binding proteins (SSBs) then bind to the single-stranded DNA to prevent the strands from reannealing and to protect them from degradation by nucleases. SSBs also help in removing secondary structures that may form within the single-stranded DNA.

Topoisomerases, such as DNA gyrase, relieve the supercoiling of the DNA ahead of the replication fork that results from the unwinding of the DNA. DNA gyrase introduces negative supercoils into the DNA, which helps in maintaining the underwound state of the DNA and facilitates the movement of the replication fork.

Primer Synthesis

The synthesis of a new DNA strand begins with the synthesis of a short RNA primer, a process carried out by the enzyme DnaG primase. The primase synthesizes a primer approximately 10 nucleotides long, providing a 3' hydroxyl group for the attachment of DNA nucleotides.

Elongation

The elongation of the new DNA strand is carried out by DNA polymerase III, the main replicative enzyme in prokaryotes. DNA polymerase III is a complex enzyme with multiple subunits that perform various functions, including nucleotide synthesis, proofreading, and interaction with other replication proteins.

DNA polymerase III adds nucleotides to the 3' end of the RNA primer, synthesizing new DNA in the 5' to 3' direction. The enzyme uses the original DNA strand as a template and follows the base pairing rules, adding a deoxyadenosine triphosphate (dATP) opposite a thymine (T), a deoxyguanosine triphosphate (dGTP) opposite a cytosine (C), and so on.

In the replication fork, there are two strands: the leading strand and the lagging strand. The leading strand is synthesized continuously in the 5' to 3' direction, the same direction as the movement of the replication fork. The lagging strand, on the other hand, is synthesized discontinuously in short fragments known as Okazaki fragments.

Each Okazaki fragment begins with an RNA primer, which is synthesized by the primase. DNA polymerase III then adds nucleotides to the primer, synthesizing the DNA in the 5' to 3' direction. Because the overall direction of synthesis is opposite to the movement of the replication fork, the lagging strand is synthesized in a series of steps, each involving the synthesis of a new primer and a new Okazaki fragment.

Primer Removal and Gap Filling

Once the Okazaki fragments have been synthesized, the RNA primers need to be removed and replaced with DNA. This is carried out by two enzymes: DNA polymerase I and DNA ligase.

DNA polymerase I has both polymerase and exonuclease activity. Its exonuclease activity allows it to remove the RNA primers, and its polymerase activity allows it to replace the primers with DNA. However, DNA polymerase I cannot join the newly synthesized DNA fragments together.

This is where DNA ligase comes in. DNA ligase seals the gaps between the Okazaki fragments, creating a continuous DNA strand. The result is a fully replicated DNA molecule.

Termination of Prokaryotic DNA Replication

The termination of DNA replication in prokaryotes, such as E. coli, occurs when the two replication forks meet at a specific region on the circular chromosome known as the termination region or ter region. This region is located approximately opposite the origin of replication (oriC) on the chromosome.

The ter region contains specific DNA sequences known as termination sequences or ter sites. In E. coli, there are ten ter sites, designated TerA to TerJ, which are oriented in two clusters that face in opposite directions. Each ter site can halt the progress of a replication fork, but only when it is moving in one direction.

The ability of the ter sites to halt replication is due to the binding of a protein known as the termination utilization substance (Tus). The Tus protein binds strongly to the ter sites and forms a Tus-ter complex that acts as a physical barrier to the replication fork.

The mechanism by which the Tus-ter complex blocks the replication fork is quite fascinating. The Tus protein has a specific binding pocket for the DNA helicase, the enzyme that unwinds the DNA at the replication fork. When the helicase encounters the Tus-ter complex, it binds to the Tus protein and is effectively "trapped," unable to move forward and unwind more DNA.

However, the Tus-ter complex is not a permanent block to replication. Under certain conditions, such as when the DNA is supercoiled, the Tus protein can change its conformation and release the helicase, allowing replication to continue. This ensures that replication can be completed even if the replication forks do not meet exactly at a ter site.

Once the replication forks meet and replication is complete, the two newly synthesized DNA molecules are separated. This process, known as decatenation, is carried out by topoisomerases, which can break and rejoin the DNA strands to untangle the DNA molecules.

The result is two identical copies of the bacterial chromosome, each containing one old (parental) strand and one new (daughter) strand, consistent with the semi-conservative model of DNA replication.

Understanding the termination of DNA replication is crucial for our knowledge of how cells duplicate their genetic material and ensure the faithful transmission of this material to daughter cells. Errors in this process can lead to genomic instability and disease, making this an important area of study in molecular biology.

Conclusion

Prokaryotic DNA replication is a complex and highly regulated process that ensures the accurate duplication of the bacterial chromosome. Understanding this process is fundamental to our knowledge of how life works at the molecular level. It also has important implications for biotechnology and medicine, including the development of antibiotics and the understanding of bacterial resistance.

5.5 Eukaryotic DNA Replication

Eukaryotic DNA replication is a complex process that involves multiple proteins and occurs within the context of chromatin. Unlike prokaryotes, eukaryotes have multiple linear chromosomes, and replication begins at multiple origins of replication along each chromosome. This section will explore the process of eukaryotic DNA replication in detail.

The Replication Machinery

The eukaryotic replication machinery, or replisome, shares many similarities with the prokaryotic replisome but also has some unique features. The key components of the eukaryotic replisome include:

i. Helicase

Helicase is a motor protein that uses the energy from ATP hydrolysis to unwind the double-stranded DNA at the replication fork. In eukaryotes, the primary helicase is the minichromosome maintenance (MCM) complex, a hexameric protein complex that forms a ring around the DNA. The MCM complex moves along the DNA in the 3' to 5' direction on the leading strand, breaking the hydrogen bonds between the base pairs and generating two single-stranded DNA templates for replication.

ii. Single-Strand DNA Binding Proteins (RPA)

Once the DNA strands are separated, they are prone to reannealing or forming secondary structures. Replication protein A (RPA) is a single-strand DNA binding protein in eukaryotes that binds to the single-stranded DNA exposed by the helicase, stabilizing the single-stranded state and preventing the strands from reannealing. RPA also protects the single-stranded DNA from degradation by nucleases.

iii. Topoisomerase

The unwinding of the DNA by helicase generates tension in the DNA molecule ahead of the replication fork, leading to supercoiling. Topoisomerases relieve this supercoiling by introducing breaks into the DNA. In eukaryotes, topoisomerase I makes single-strand breaks and topoisomerase II makes double-strand breaks, allowing the DNA to rotate and relieve the tension.

iv. Primase

DNA polymerases, the enzymes that synthesize new DNA, cannot initiate DNA synthesis de novo. They require a primer with a free 3' hydroxyl group to which they can add nucleotides. In eukaryotes, the primase is a part of a complex known as DNA polymerase α-primase. The primase synthesizes a short RNA primer that provides the 3' hydroxyl group, and then DNA polymerase α extends the primer with a short stretch of DNA.

v. DNA Polymerases

Eukaryotes have multiple DNA polymerases. DNA polymerase α initiates DNA synthesis by extending the RNA primer with a short stretch of DNA. DNA polymerase δ and ε then take over to synthesize the lagging and leading strands, respectively. DNA polymerase δ synthesizes the Okazaki fragments on the lagging strand, while DNA polymerase ε is thought to synthesize the leading strand.

vi. RNase H and FEN1

Once a segment of DNA has been synthesized, the RNA primer is no longer needed and must be removed. In eukaryotes, the RNA primers are removed by two enzymes: RNase H, which degrades the RNA part of the RNA-DNA hybrid, and flap endonuclease 1 (FEN1), which removes the remaining RNA and the associated DNA synthesized by DNA polymerase α.

vii. DNA Ligase I

The removal of the RNA primer and its replacement with DNA leaves a gap in the sugar-phosphate backbone of the DNA. DNA ligase I seals this gap, creating a continuous DNA strand. DNA ligase I achieves this by catalyzing the formation of a phosphodiester bond between the 3' hydroxyl group of one DNA fragment and the 5' phosphate group of the next DNA fragment.

Table 3:Table of Eukaryotic DNA polymerases:

Polymerase	**Function**	**Subunits**	**Processivity**	**Proofreading**
α (alpha)	Synthesizes a short RNA-DNA primer to initiate DNA replication	Four (POLA1, POLA2, PRIM1, PRIM2)	Low	No
δ (delta)	Main enzyme for lagging strand synthesis. Also involved in DNA repair, recombination, and replication of mitochondrial DNA	Four (POLD1, POLD2, POLD3, POLD4)	High (with PCNA)	Yes
ε (epsilon)	Main enzyme for leading strand synthesis	Four (POLE, POLE2, POLE3, POLE4)	High (with PCNA)	Yes
γ (gamma)	Replicates mitochondrial DNA	One (POLG) with accessory subunit (POLG2)	High	Yes
β (beta)	Involved in DNA repair, particularly base excision repair	One (POLB)	Low	No
ζ (zeta)	Involved in DNA repair and translesion DNA synthesis	Two (REV3L, MAD2L2)	Low	No
η (eta)	Involved in translesion synthesis past UV-induced pyrimidine dimers	One (POLH)	Low	No

ι (iota)	Involved in translesion synthesis	One (POLI)	Low	No
κ (kappa)	Involved in translesion synthesis	One (POLK)	Low	No
λ (lambda)	Involved in DNA repair and non-homologous end joining	One (POLL)	Low	Yes
μ (mu)	Involved in non-homologous end joining	One (POLM)	Low	No
θ (theta)	Involved in DNA repair	One (POLQ)	Low	No
ν (nu)	Function not well understood	One (POLN)	Low	No

Note: Processivity refers to the number of nucleotides added per binding event of the enzyme to the DNA. High processivity indicates that many nucleotides are added before the enzyme dissociates from the DNA. Proofreading refers to the ability of the enzyme to correct its own errors by removing misincorporated nucleotides.

The Process of Eukaryotic DNA Replication

Eukaryotic DNA replication is a complex process that ensures the accurate duplication of the genetic material in preparation for cell division. This process involves a multitude of proteins and enzymes, each playing a crucial role. Here, we will delve deeper into the process of eukaryotic DNA replication, discussing each step in detail.

Initiation

The initiation of eukaryotic DNA replication begins at multiple origins of replication along each chromosome. These origins are recognized and bound by the origin recognition complex (ORC), a six-protein complex that marks the site for the initiation of replication. The ORC recruits additional proteins, including cell division cycle 6 (Cdc6) and Cdt1, which in turn recruit the minichromosome maintenance (MCM) complex. The MCM complex is the helicase that will unwind the DNA at the replication fork.The assembly of the ORC, Cdc6, Cdt1, and the MCM complex onto the DNA forms the pre-replication complex (pre-RC). The formation of the pre-RC is tightly regulated and occurs during the late mitosis and early G1 phase of the cell cycle.The activation of the pre-RC marks the transition from the initiation phase to the elongation phase of DNA replication. This activation involves the recruitment of additional proteins and the modification of existing ones. Key among these is the activation of the MCM complex by the kinases Cdc7 and cyclin-dependent kinase (CDK).

Unwinding of DNA and Formation of the Replication Fork

The activated MCM complex unwinds the DNA, breaking the hydrogen bonds between the base pairs and generating two single-stranded DNA templates for replication. This unwinding of the DNA forms a replication bubble with two replication forks. Replication proceeds bidirectionally from each origin until the replication forks meet at a termination region.The unwinding of the DNA generates supercoiling ahead of the replication fork. This supercoiling is relieved by topoisomerases, which introduce transient breaks into the DNA to allow it to rotate and relieve the tension.The single-stranded DNA exposed by the MCM complex is bound by replication protein A (RPA), which prevents the DNA strands from reannealing and protects them from degradation.

Primer Synthesis

The synthesis of new DNA requires a primer with a free 3' hydroxyl group to which the DNA polymerase can add nucleotides. In eukaryotes, the primer is synthesized by the primase activity of DNA polymerase α. DNA polymerase α synthesizes a short RNA-DNA hybrid primer, typically with about 10 RNA nucleotides followed by 10-20 DNA nucleotides.

Elongation

The elongation phase of DNA replication involves the synthesis of new DNA by DNA polymerases δ and ε. These polymerases add nucleotides to the 3' end of the primer, synthesizing new DNA in the 5' to 3' direction.

On the leading strand, DNA synthesis is continuous. DNA polymerase ε synthesizes the leading strand by extending the RNA-DNA primer synthesized by DNA polymerase α.

On the lagging strand, DNA synthesis is discontinuous. DNA polymerase α synthesizes a new primer at several points along the strand. DNA polymerase δ then extends these primers, synthesizing the lagging strand in short fragments known as Okazaki fragments.

Primer Removal and Gap Filling

Once the Okazaki fragments have been synthesized, the RNA primers need to be removed and replaced with DNA. This is carried out by two enzymes: RNase H, which degrades the RNA part of the RNA-DNA hybrid, and flap endonuclease 1 (FEN1), which removes the remaining RNA and the associated DNA synthesized by DNA polymerase α. DNA polymerase δ or ε then fills in the gaps left by the removal of the primers.

Ligation

The removal of the RNA primer and its replacement with DNA leaves a gap in the sugar-phosphate backbone of the DNA. DNA ligase I seals this gap, creating a continuous DNA strand. DNA ligase I achieves this by catalyzing the formation of a phosphodiester bond between the 3' hydroxyl group of one DNA fragment and the 5' phosphate group of the next DNA fragment.

Termination of Replication

Replication continues until the replication forks meet at a termination region. The two newly synthesized DNA molecules are then separated, and any remaining supercoils are relaxed by topoisomerases. The result is two identical copies of each chromosome, each containing one old (parental) strand and one new (daughter) strand, consistent with the semi-conservative model of DNA replication.

Termination of DNA replication in eukaryotes is a complex process that is not as well understood as the initiation and elongation phases. However, several key features of this process have been elucidated.

Replication Fork Convergence

In eukaryotes, DNA replication begins at multiple origins of replication and proceeds bidirectionally from each origin, creating two replication forks. The termination of DNA replication occurs when two replication forks meet and converge. This is known as replication fork convergence or fork collision.When two replication forks meet, the replication machinery from each fork must be disassembled, and the newly synthesized DNA strands must be connected to form a continuous double-stranded DNA molecule. This involves the removal of the RNA primers, the filling in of the gaps left by the removal of the primers, and the ligation of the newly synthesized DNA fragments.

Removal of the Replication Machinery

The disassembly of the replication machinery is a complex process that is not fully understood.

However, it is known that this process involves several proteins, including the p97 ATPase and its cofactors.The p97 ATPase, also known as valosin-containing protein (VCP), is a protein that uses the energy from ATP hydrolysis to perform mechanical work. In the context of DNA replication, p97 is thought to remove the replication machinery from the DNA.The action of p97 is directed by its cofactors, which recognize specific substrates. In the case of DNA replication, one of these cofactors is the ubiquitin ligase TRAIP. TRAIP ubiquitinates the MCM complex, the helicase that unwinds the DNA at the replication fork, marking it for removal by p97.

Ligation of the Newly Synthesized DNA

The ligation of the newly synthesized DNA involves the removal of the RNA primers, the filling in of the gaps left by the removal of the primers, and the ligation of the newly synthesized DNA fragments.The RNA primers are removed by the combined action of RNase H, which degrades the RNA part of the RNA-DNA hybrid, and flap endonuclease 1 (FEN1), which removes the remaining RNA and the associated DNA synthesized by DNA polymerase α. DNA polymerase δ or ε then fills in the gaps left by the removal of the primers.

The final step in the termination of DNA replication is the ligation of the newly synthesized DNA fragments. This is carried out by DNA ligase I, which seals the gaps in the sugar-phosphate backbone of the DNA, creating a continuous DNA strand. DNA ligase I achieves this by catalyzing the formation of a phosphodiester bond between the 3' hydroxyl group of one DNA fragment and the 5' phosphate group of the next DNA fragment.

Replication of Telomeres

In eukaryotes, the ends of the linear chromosomes present a unique challenge for DNA replication. This is because the RNA primer that initiates the synthesis of the lagging strand leaves a gap at the end of the chromosome that cannot be filled in by the conventional replication machinery. This is known as the end-replication problem.

The end-replication problem is solved by the enzyme telomerase. Telomerase is a reverse transcriptase that carries its own RNA template. It extends the 3' end of the DNA, providing a template for the synthesis of the complementary strand and ensuring that no genetic material is lost during replication.

The action of telomerase is tightly regulated and is typically active only in certain cell types, such as stem cells and cancer cells. In most somatic cells, telomerase is inactive, and the telomeres shorten with each round of DNA replication, which is thought to contribute to cellular aging.

Regulation of Termination

The termination of DNA replication is tightly regulated to ensure the accurate duplication of the genetic material. This involves several checkpoint proteins, including the ataxia telangiectasia and Rad3-related protein (ATR) and the checkpoint kinase 1 (Chk1).

ATR and Chk1 are activated in response to replication stress, such as stalled replication forks or DNA damage. They coordinate the cellular response to replication stress, halting the cell cycle and promoting DNA repair to ensure the completion of DNA replication.

While our understanding of the termination of DNA replication in eukaryotes has advanced significantly in recent years, many aspects of this process remain to be elucidated. Future research in this area promises to shed light on the intricate mechanisms that ensure the accurate duplication of our genetic material.

Eukaryotic DNA replication is a complex and highly regulated process that ensures the accurate duplication of the eukaryotic genome. Understanding this process is fundamental to our knowledge of

how life works at the molecular level. It also has important implications for biotechnology and medicine, including the understanding of cancer and other diseases that result from errors in DNA replication.

Table 4:Key Checkpoints in Eukaryotic DNA Replication

Checkpoint	Function
G1/S Checkpoint	Monitors cell size, nutrients, growth factors, and DNA integrity before DNA replication
Intra-S Checkpoint	Monitors DNA integrity and halts cell cycle if DNA damage is detected during S phase
G2/M Checkpoint	Monitors DNA integrity and completion of DNA replication before mitosis

Key Differences Between Prokaryotic and Eukaryotic Replication

DNA replication is a fundamental process in all living organisms, ensuring that genetic information is accurately copied and passed on to the next generation. While the basic mechanism of DNA replication is conserved among prokaryotes and eukaryotes, there are several key differences due to the complexity and size of the eukaryotic genome, and the presence of a nucleus.

1. **Origin of Replication:** Prokaryotes typically have a single origin of replication, while eukaryotes have multiple origins of replication. This is because eukaryotic genomes are much larger and require multiple replication forks to ensure that DNA replication can be completed in a reasonable time.
2. **Replication Rate:** The rate of DNA replication is generally faster in prokaryotes than in eukaryotes. This is again due to the larger size of the eukaryotic genome.
3. **Replication Proteins:** While many of the proteins involved in DNA replication are conserved between prokaryotes and eukaryotes, there are some differences. For example, prokaryotes use DNA polymerase III for the bulk of DNA synthesis, while eukaryotes use multiple DNA polymerases, including DNA polymerases α, δ, and ε.
4. **Telomere Replication:** Eukaryotes have linear chromosomes that end in repetitive sequences called telomeres. Replication of the ends of linear chromosomes presents a challenge that is solved by the enzyme telomerase. Prokaryotes, with their circular chromosomes, do not have this issue.

Table 5:Comparative Account of Eukaryotic and Prokaryotic Replication

Feature	Prokaryotic Replication	Eukaryotic Replication
Origin of Replication	Single	Multiple
Replication Rate	Faster (approx. 1000 nucleotides per second)	Slower (approx. 50-100 nucleotides per second)
Replication	DNA Polymerase III is the main	Multiple DNA polymerases (α, δ, ε) for DNA

Proteins	enzyme for DNA synthesis	synthesis
Primer Removal	DNA Polymerase I	RNase H and FEN1
Strand Elongation	Continuous and discontinuous (Okazaki fragments on the lagging strand)	Continuous and discontinuous (Okazaki fragments on the lagging strand)
Telomere Replication	Not applicable (circular DNA)	Telomerase extends the ends of linear chromosomes
Complexity of Regulation	Less complex	More complex due to the cell cycle and multiple origins of replication

SAQ-

- Prokaryotic DNA replication is a highly coordinated process that ensures the faithful duplication of the bacterial chromosome.
- Eukaryotic DNA replication is a complex process that involves multiple proteins and occurs within the context of chromatin.
- The regulation ofDNA replication is crucial for maintaining the integrity of the genome and ensuring the proper timing and fidelity of replication.

5.6 Regulation of DNA Replication

The regulation of DNA replication is crucial for maintaining the integrity of the genome and ensuring the proper timing and fidelity of replication. This section will explore the various mechanisms that regulate DNA replication in both prokaryotes and eukaryotes.

Regulation in Prokaryotes

Regulation of DNA replication in prokaryotes is indeed a complex process that involves multiple steps and regulatory mechanisms. It is crucial to ensure that DNA replication is carried out accurately and efficiently, maintaining the integrity of the genetic material. Let's delve deeper into the regulatory mechanisms involved in prokaryotic DNA replication.

Control at Initiation

The initiation of DNA replication is the most critical point of regulation. In E. coli, the initiation of replication is controlled by the availability and activity of the DnaA protein. DnaA binds to the origin of replication (oriC) and promotes the unwinding of the DNA, marking the start of replication.

The activity of DnaAis regulated by several factors:

1. **ATP/ADP levels**: DnaA binds to ATP and ADP with equal affinity, but only the ATP-bound form can initiate replication. The ratio of ATP to ADP in the cell can therefore influence the initiation of replication.
2. **DnaA-ATP hydrolysis**: DnaA has an intrinsic ATPase activity, which is stimulated by the Hda protein and the DNA-loaded form of the beta clamp, a component of DNA polymerase III. This hydrolysis of DnaA-bound ATP after initiation helps prevent over-initiation.
3. **SeqA sequestration**: After initiation, the hemimethylated GATC sequences in the oriC region are bound by the SeqA protein. This sequestration of the oriC region prevents re-initiation until

the DNA methylation is restored.

4. **RimA and DiaA**: These proteins are positive regulators of DnaA. RimA helps maintain the ATP-bound form of DnaA, while DiaA stabilizes the DnaA-oriC complex.

Control During Elongation

The elongation phase of DNA replication is regulated to ensure the accuracy of DNA synthesis. DNA polymerase III, the main enzyme responsible for DNA synthesis, has a proofreading activity that can correct errors during replication.

Control at Termination

The termination of DNA replication is controlled by specific termination sequences (ter) and the Tus protein. The ter sequences are arranged in such a way that they allow passage of the replication fork in one direction but block it in the other. The Tus protein binds to these sequences and acts as a roadblock, stopping the progression of the replication fork.

Coordination with Cell Division

In bacteria, DNA replication is tightly coordinated with cell division. The Min system and the nucleoid occlusion system prevent cell division from occurring over the nucleoid, ensuring that cell division does not occur until DNA replication is complete.In summary, the regulation of DNA replication in prokaryotes involves a complex interplay of multiple factors and regulatory mechanisms. These mechanisms ensure that DNA replication is initiated only once per cell cycle and that it is carried out accurately and efficiently.

Regulation of DNA Replication in Eukaryotes

In eukaryotic organisms, the regulation of DNA replication is a multifaceted process, necessitated by the presence of multiple origins of replication and the intricacies of the eukaryotic cell cycle. This complexity ensures that the entire genome is accurately and efficiently replicated.

Initiation of Replication

The commencement of replication is governed by the assembly of the pre-replication complex (pre-RC) at the origin of replication. This complex is assembled during the G1 phase of the cell cycle and comprises the origin recognition complex (ORC), Cdc6, Cdt1, and the MCM helicase complex.The activation of the pre-RC is a tightly regulated process, controlled by two key kinases: CDK and DDK. CDK, or Cyclin-Dependent Kinase, is activated at the transition from the G1 phase to the S phase of the cell cycle. It phosphorylates several proteins within the pre-RC, priming them for the initiation of replication. Concurrently, DDK (Dbf4-Dependent Kinase) phosphorylates the MCM complex, which triggers its helicase activity, a crucial step for the unwinding of the DNA double helix.Once the pre-RC is activated, the replication process can commence. However, the formation of the pre-RC is a one-time event per cell cycle, which ensures that each segment of the DNA is replicated only once, preventing over-replication.

Checkpoints and DNA Damage Response

The regulation of DNA replication in eukaryotes also involves a series of checkpoints that monitor the integrity of the DNA and the progress of replication. These checkpoints can halt the replication process if they detect errors or damage to the DNA. This pause allows the activation of the DNA damage response, a series of repair mechanisms that rectify the damage before replication resumes.In eukaryotes, the primary checkpoints are the G1/S checkpoint, the intra-S checkpoint, and the G2/M checkpoint. These checkpoints are regulated by a variety of proteins, including the ATM and ATR kinases, the Chk1 and Chk2 kinases, and the p53 protein, all of which play crucial roles in maintaining

genomic stability.

Conclusion

The regulation of DNA replication is of paramount importance for maintaining the integrity of the genome and ensuring the proper timing and fidelity of replication. Disruptions or errors in the regulation of DNA replication can lead to genomic instability, which can, in turn, lead to diseases, including cancer. Therefore, understanding the complex regulatory mechanisms of DNA replication in eukaryotes is crucial for understanding and potentially treating these diseases.

Table 6:Regulation of DNA Replication in Prokaryotes

Strategy	**Description**
Initiation Control	The replication process begins at a specific point in the DNA molecule called the origin of replication. In prokaryotes, this is a sequence of DNA called the OriC. The initiation of replication is tightly controlled to ensure it only happens once per cell cycle.
DnaA Protein	DnaA is a protein that binds to the OriC and initiates the unwinding of the DNA double helix. The amount and activity of DnaA in the cell is a key factor in controlling the start of replication.
SeqA Protein	SeqA is a protein that binds to the newly replicated DNA and prevents re-initiation of replication. This ensures that each part of the DNA is only replicated once per cell cycle.
Dam Methylation	In E. coli, the OriC contains GATC sequences that are methylated by the Dam methylase enzyme. After replication, the new DNA strand is not immediately methylated, which helps to prevent re-initiation of replication.

Table 7:Regulation of DNA Replication in Eukaryotes

Strategy	**Description**
Multiple Origins of Replication	Eukaryotic DNA is much larger than prokaryotic DNA, so it has multiple origins of replication to allow the DNA to be replicated quickly.
Licensing Factors	Before replication can begin, the origin of replication must be 'licensed' by the binding of certain proteins. This ensures that replication only happens once per cell cycle.
Cyclin-dependent Kinases (CDKs)	CDKs are proteins that control the progression of the cell cycle. They prevent re-replication by inactivating the licensing factors after replication has started.
Checkpoints	The eukaryotic cell cycle has checkpoints that monitor the progress of replication and can halt the cell cycle if problems are detected. This helps to ensure the accuracy of replication.
Telomeres and Telomerase	The ends of eukaryotic chromosomes have special structures called telomeres, which are replicated by a special enzyme called telomerase. This helps to prevent the loss of genetic information during replication.

5.7 Summary

- Prokaryotic DNA replication is a highly coordinated process that ensures the faithful duplication of the bacterial chromosome. Unlike eukaryotes, prokaryotes have a single circular chromosome, and replication begins at a single origin of replication and proceeds bidirectionally. This section will delve into the intricacies of this process.
- Eukaryotic DNA replication is a complex process that involves multiple proteins and occurs within the context of chromatin. Unlike prokaryotes, eukaryotes have multiple linear chromosomes, and replication begins at multiple origins of replication along each chromosome. This section will explore the process of eukaryotic DNA replication in detail.
- The regulation of DNA replication is crucial for maintaining the integrity of the genome and ensuring the proper timing and fidelity of replication. This section will explore the various mechanisms that regulate DNA replication in both prokaryotes and eukaryotes.

5.8 Terminal Question

Question-1 Explain process of DNA replication.

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Question-2 Differentiate between Prokaryotes and Eukaryotes.

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Question-3 Regulation of DNA replication in Eukaryotes.

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Question-4 Regulation of DNA replication in Prokaryotes.

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5.9 Answer

SAQ-

- bacterial chromosome.
- Eukaryotic DNA replication
- regulation of DNA replication

5.10 Suggested books

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UNIT 6 : GENE TRANSCRIPTION AND RNA MODIFICATION

6.1 Introduction

Transcription is a process of formation of m-RNA from DNA. DNA acts as template on which m-RNA formation take place. The m-RNA which is form carries the genetic information needed to make proteins in a cell. It carries the information from DNA in the nucleus of the cell to the cytoplasm, where proteins are synthesized. Transcription takes place both in prokaryotes and eukaryotes cells.

Objective

After studying this unit you should be able to

- Understand transcription in prokaryotes
- Understand transcription in eukaryotes
- Understand RNA modification
- You will understand structure and function of t RNA,

6.2Transcription in prokaryotes

The process of formation of RNA from DNA sequence called as transcription. In this process in which DNA sequence is read by an RNA polymerase, which produces a complementary, antiparallel RNA strand called primary transcript.

According to central dogma of molecular biology, which was proposed by Crick 1956, DNA is the main component. The DNA is maintain in cell generation to generation by DNA replication process. The information coded in DNA is converted into RNA by the process called transcription and this RNA is changes into protein by mechanism called translation.

In 1975 Temin and Baltimore discovered reverse transcriptase enzyme in Rous Sarcoma virus which infect chicken. This reverse transcriptase enzyme converts RNA into DNA. This is called taminism

Transcription is copying of a complementary messenger RNA strands on a DNA strand. The DNA strands unwind and one of the two strands forms and m-RNA strand. Transcription requires

(1)Template : The two strand of DNA of which only one strand called the "sense" strand transcribe m-RNA.

(2)Activated precursors : The synthesis of m-RNA strand requires all four ribonucleoside triphosphate –ATP, GTP, UTP and CTP.

(3)Divalent metal ions : Mg^{++} or Mn^{++} are effective in transcription. *In vivo* synthesis requires Mg^{++}.

(4)RNA polymerase : The RNA polymerase (holoenzyme) consist of a core enzyme and sigma factors (σ). The core enzyme consist of 2 identical alpha (α) subunits and one chain of each of beta (β), beta dash (β'), omega (ω). The sigma factor (σ) help in the recognition of start signals on DNA molecule and direct RNA polymerase in selecting the initiation site (promoter). Once RNA synthesis is initiated and RNA molecule become 8 – 9 bases long, the (σ) factor dissociates from the holoenzyme and then the core enzyme bring about elongation of m-RNA. The β' subunit involve in binding of RNA polymerase to DNA. The β subunit of the core-enzyme is required for interaction with sigma factor.

The overall polymerization reaction can be writ as follow

$$nNTP + XTP \xrightarrow{\text{DNA, RNA-P}} (NMP)n\ XTP + nPP_1$$

(*In which XTP represents the first nucleotide at the 5' terminus of the RNA chain, NMP is a mononucleotide in the RNA. RNA-P is RNA polymerase, and PP_1 is the pyrophosphate released each time a nucleotide is added to the growing chain. The Mg^{++} is required for all nucleic acid polymerization reaction*)

The first step in the transcription is binding polymerase to a polymerase to a DNA molecule. The sigma (σ) subunit of RNA polymerase bind to the -35 sequences (recognition sequences) then it move along the DNA strand then bind to a the TATA box (-10 sequence) or binding site (Binding sequence TATAATG), then core enzyme of RNA polymerase come and complete the whole enzyme or holoenzyme. As the RNA polymerase bind to the binding site, the initiation site, which is near the binding site (6 or 7 base away), start the double helix to open to form the ***open promoter complex***.

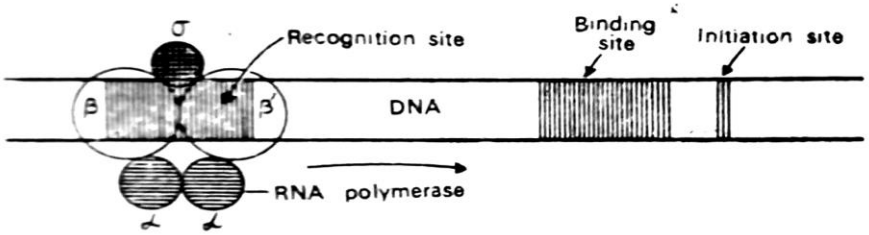
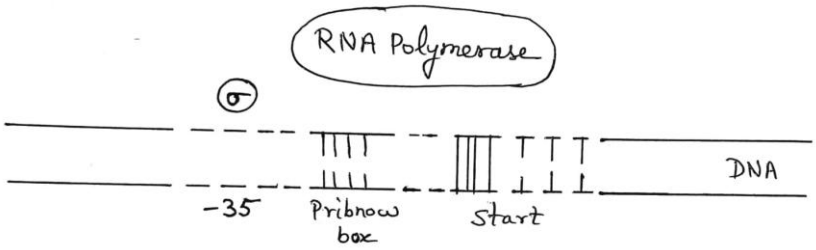


Fig: Recognition, binding and initiation sites on DNA

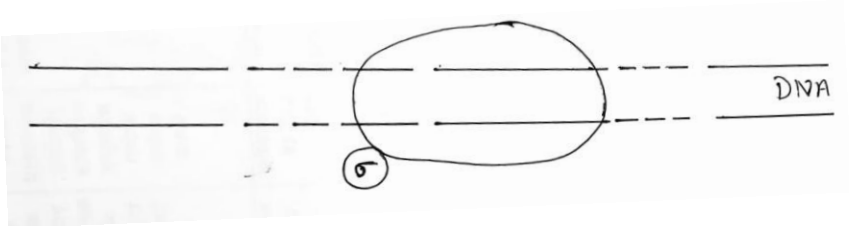
Once an open-promoter complex formed, RNA polymerase is ready to initiate RNA synthesis. RNA polymerase contains two nucleotide binding site, the initiation site and the elongation site. The initiation site binds only purine triphosphate ATP or GTP and one of these is the first nucleotide in the growing RNA chain. The first DNA base that is transcribed is usually Thymine (T). The initiating nucleoside triphosphate binds to the enzyme in the open-promoter complex and forms a hydrogen bond with the complementary DNA base. The elongation site is then filled with a nucleoside triphosphate that is selected strictly by its ability to form a hydrogen bond with the next base in the DNA strand. The two nucleotides are then joined together, the first base is released from the initiation site, and initiation is completed. The dinucleotide remains hydrogen bonded to the DNA. The elongation phase begins when the polymerase releases the base and then moves along the DNA chain. The RNA is synthesized in the 5' 3' direction from the single stranded region of the DNA template.

After addition of several nucleotides to the growing chain, RNA polymerase changes its structure and loses the sigma factor. Then elongation is carried out by the core-enzyme. The core-enzyme moves along the DNA, binding a nucleoside triphosphate that can pair with the next DNA base and opening the DNA helix as it moves, thus during elongation phase addition of 40 bases per second at 37^0C take place. The open region extends only over a few base pair that the DNA helix recloses just behind the enzyme. The newly synthesized RNA is released from its hydrogen bonds with the DNA as the helix reforms.

(A)Template binding



(B)Dissociation of σ (sigma) subunit form from -35sequence movement to pribnow box



(C)Establishment of open promoter complex

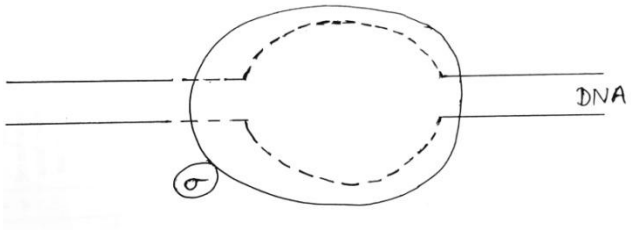


Fig : A model for the binding of RNA polymerase to a promoter to form an open promoter complex : PB = Pribnow box

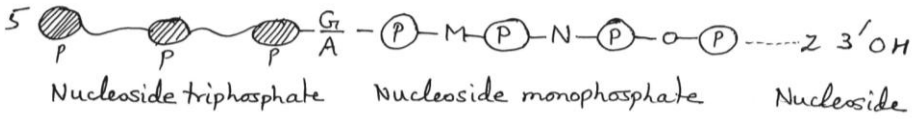
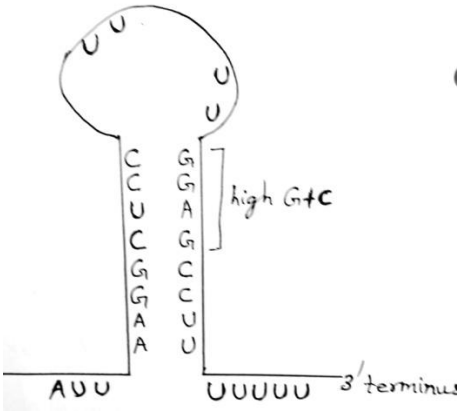


Fig : New formed RNA chain

Termination of RNA synthesis occurs at specific base sequences in the DNA molecule. The termination region consists of the following 3 important region (1) first there is an inverted repeat base sequence containing a central non-repeating segment, the sequences in one strand would be read like

A B C D E F —— XYZ —— F' E' D' C' B' A'

In which A and A', B and B' are complementary bases. This sequences is capable of infra strand base pairing forming "stem and loop" configuration in the transcript (RNA) and possibly in the DNA strands (2) The second region is near the loop end of the presumed stem and is a sequences having a G + C content. (3) A third region is a sequence of A T pairs that yields in the RNA a sequence of 6 to 8 (U) often followed by adenine.



There are 2 types of termination events. Those that depends only on the DNA base sequences and those that require the presence of termination protein called rho (ρ) discovered by J. Roberts 1969). According to Rho model RNA polymerase initiate the RNA chain and moves along the DNA template. The Nascent RNA elongation and the rho binding site become exposed. Rho moves along RNA from its binding site to RNA polymerase. This movement may be brought about by hydrolysis of ATP. Rho now come into contact with RNA polymerase. RNA & Rho dissociate from RNA polymerase. So Rho primary act a s a release factor and RNA polymerase is finally released.

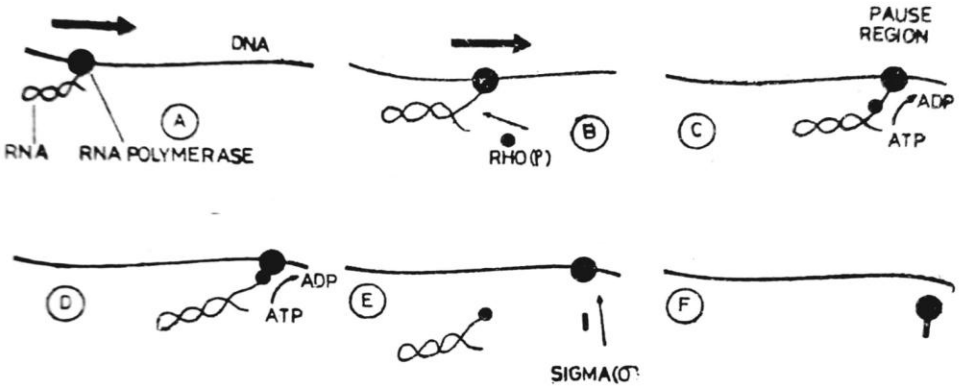


Fig : Richardson's (1978) model of RNA chain termination by rho factor

6.3 Transcription in eukaryotes

The transcription in Eukaryotes requires GTPs (general transcriptional factors) and RNA polymerase. The general transcriptional factors recognize the promoter and recruit RNA polymerase II to form pre initiation complex at promoter of protein coding genes. As they are required for transcription of all protein coding genes so called as general transcriptional factor. They have two important roles

They bind to RNA polymerase and recruit it to promoter on dsDNA to form (closed complex). They can carry out melting DNA to form open complex.

For protein coding genes, the GTF and RNA polymerase II bind to promoter elements in a particular order to produce the complete transcription initiation complex also known as pre initiation complex (PIC) because it is ready to begin transcription in Eukaryotes. The pre-initiation complex consists of GTFs + dsDNA + RNA Poly II. The RNA polymerase in Eukaryotes is classify as class A, B & C.

Class A polymerase : These are insensitive to amanitin and are localized in the nucleoli. They include enzyme A1 (RNA polymerase-I) and AII (I_B). A1 has been purified from calf thymus mouse myeloma and rat liver. RNA polymerase-I is involved in synthesis of r-RNA.

Class –B Polymerase are sensitive to low concentration of amanitin and are defined as RNA polymerase-II. They have purified from calf thymus, rat liver mouse myeloma and chick liver, among other tissue. It can be defined into three form BO(II_0), BI(II_A) and BII (a + b) IIb. These are located in nucleoplasmic. RNA polymerase –II involved in synthesis.

Class C Polymerase : These are sensitive to high concentration of amanitin and has classify into CI, CII, CIII a and CIII b form. RNA polymerase –III is involved in synthesis to t-RNA.

The general transcriptional factors (GTFs) are numbered for the RNA polymerase with which they work and are lettered to reflect their order of discovery. The GTF required for every gene transcribed by RNA polymerase II are designated by TF II. It is of various types

1) **TF II D :** TF IID is a multi subunit complex of more than 14 subunit. The component of TF II D that binds to the TATA box is called TBP (TATA binding protein). TBF is associated with 14 different factors called TATs. Some TAFs recognize other core promoter elements such as the inr, DPE & DCE. The TF II D is a critical factor in promoter recognition and pre initiation complex establishment. It is first factor to bind with promoter. The TAFs also interact with modifications on histone tails to start the transcription, also interact with activators. The TBP bind with TATA box also known as Goldsberg-Hogness box. The TBP has binding site for TATA which consist of beta sheets (DBD-DNA binding domain) and fit into minor groove of DNA and called unorthodox

recognition. So TBP is not sequence specific it associate with that part of DNA which can be easily melted. TBP has two phenylalanine amino acids which can cause bending in DNA, Bending is carried out at AT rich sequence which is easily to melt.

(2) **TF II A :** It bind to upstream of TBP/TF II D and recruit TF II B on BRE.

(3) **TF II B :** It has only one subunit, bind to BRE (B response elements) interact in major groove. TBP interact with TF IIB asymmetrically which make the transcription directional. The TF II B work like sigma factor in eukaryotes. It binds to BRE before TBP and inserts itself into RNA exit channel so lead to abortive initiation

(4) **TF II F :** It has 3 subunit, bind with the RNA polymerase II and recruit it to TBP –TATA + TF II A, TF II B complex to form a closed complex.

(5) **TF II E :** It consist of 2 subunit and recruits TF II H infront of RNA polymerase.

(6) **TF II H :** It is most complex and largest of all GTFs. It has 10 subunits of which 2 subunits has ATPase activity, one has kinase activity, one of has helicase activity. It acts as helicase during transcription and TCNER (Nucleotide excision repair). It binds to downstream of RNA polymerase II and melts DNA to carry out the transcription. Initial melting of DNA requires ATP hydrolysis in Eukaryotes.

The process of transcription of protein coding genes occur in 3 steps, initiation, elongation and termination

(1) Initiation : It occurs in three steps, closed complex formation, open complex formation and promoter escape.

Closed complex formation – In such case chromatin modifier converts heterochromatin into Euchromatin by methylation on histone and acetylation on histone chromatin remodelers make promoter available for the binding of GTFs. Activators associated with enhances or proximal promoter element may also help in transcription start. Firstly GTF, TF II D with TBP binds on TATA box non-specifically, it then recruits, TF II A to bind with it. TF IIA binds with RNA polymerase and recruit it on promoter by interacting with TF II D(TBP) + TF II A + TF II B ternary complex, load RNA polymerase on dsDNA. Then TF II E bind on downstream of the RNA polymerase, it further recruits TF II H. This is complex of dsDNA + RNA Polymerase + GTFs called as PIC (pre initiation complex) or closed complex.

Open complex formation and promoter escape

The initial melting and promoter escape require ATP hydrolysis. TF II H, which is helicase, ATPase and kinase carry out both these things for genes transcribed by RNA pol/III enzyme. TF II H adds phosphate on particular site on CTD tail which leads to conformational change in RNA polymerase. It results into melting of DNA & promoter escape.

(2)Elongation process : During elongation process CTD tail is phosphyalated by TF II H kinase. So many GTFs and mediator complex dissociate from the initiator complex. During elongation different processing occurs like capping, splicing occur in elongation & during in termination there is polyadenylation processes occur on synthesized RNA (m-RNA). For elongation four elongation factors are required for transcription of gene. These are pTEFb (protein transcription elongation factor) hSPT-5, TATSF1 and TF II S.

Capping – The process of capping at 5' end is essential to protect 5' end RNA from 5' ⟶ 3' exonuclease which cleave phosphodiester bond between 3' OH of one nucleotide and 5' phosphate of succeeding nucleotide. Once RNA polymerase II has made about 20 to 30 nucleotides of pre-mRNA, a capping enzyme add guanine nucleotide like 7-methylguanosine (m7G) to the 5' end. The capping is carried out by using three enzyme which produces unusual 5' 5' phosphodiester bond between

added 7 methyl guanine nucleotide and one nucleotide of m-RNA. The important enzymes are

⟶ **(a)*RNA triphosphatase* :** It removes gamma phosphate from 5' end of terminal purine i.e. ATP mostly.

(b)*Guanylyl transferase* (transfer GMP) – It use GTP and add GMP to beta phosphate of the terminal purine.

(c)*Methyl(GMP) transferase* : Methylation at N7 of base and 2' position of sugars is done to form 7 methyl guanosine mono phosphate

In the process of capping there is removal of gamma phosphate from first nucleotide at 5' end and addition of GMP on 5' beta phosphate by its 5' alpha phosphate → to from 5' → 5' phosphodiester bond. Once this linkage is made, the newly added guanine and the purine at the original 5' end of the m-RNA are further modified by the addition of methyl groups by methyltransferase. The resulting 5' cap structure subsequently recruits the ribosome to the mRNA for translation to begin guanine is then methylated at N7 position of guanine by methyl transferase.

(3)Termination : In eukaryotes three different RNA polymerases use different mechanism for termination. The RNA polymerase I require a termination factor like rho factor in bacteria. The RNA polymerase III ends transcription after transcribing a terminator sequence that produces a string of Us in the RNMA molecule, RNA polymerase III does not require that a hairpin structure precede the strings of Us.

Polyadenylation occurs uniquely on m-RNA 3' end. It leads to the termination of transcription. The polyadenylation occur after poly A site sequence being transcribe into RNA, trigger the transfer of polyadenylation enzymes to that RNA, leading to four events, cleavage of the message, addition of many adenine residues to its 3' end, degradation of RNA remaining associated with a 5' to 3' ribonuclease and subsequently termination of transcription.

Once Poly A site AAUAAA is transcribed into m-RNA, CPSF (cleavage and polyadenylation specificity factor) and CSTF (Cleavage stimulating factor) associated with the CTD tail of RNA Pol II binds m-RNA.

The protein coding genes do not have specific terminator sequences so for termination a number of models has been proposed of which torpedo model of termination is far good. According to Torpedo model polyadenylation in linked to termination, although exactly how is still not quite clear. Recently, however, an enzyme that degrades the second RNA as it emerges from the polymerase has been identified and this enzyme may itself trigger termination

Role of polyadenylation

- Increases the stability of mRNA because some poly A binding proteins bind to the poly a sequence.
- 3' → 5' exonuclease act on mRNA but before degradation many rounds of translation can be carried out PABII decide the rate of rate of activity of 3' → 5' exonuclease activity on mRNA and also stimulate the increase in the length of poly A tail.
- Translation on nascent mRNA is carried out till mRNA have 50Å.
- Poly A tail help in translation initiation.
- mRNA is not free in nucleus i.e. associated with the proteins like SR proteins, exon junction proteins, poly A proteins and cap binding proteins.
- These proteins are recognized by mRNA exporter proteins.

6.4 RNA modification

RNA modification means that RNA has to be edited so that there is change in the nucleotide sequence of RNA or RNA modification refers to the various chemical changes that occur to RNA molecules after they are synthesized. These modifications can affect the structure, function and stability of RNA molecule so that influencing gene expression, protein synthesis and cellular processes.

The some of the common RNA modification include

(1) Methylation : In methylation there is adding of a methyl group to the RNA base or sugar.

(2) Pseudouridylation : In this there is converting of uridine to pseudouridine.

(3) Editing : In this there is changing of individual nucleotides like adenosine to inosine.

(4) Capping : In such there is adding a modification guanine nucleotide to the 5' end.

(5) Polyadenylation : In this there is adding of a poly (A) tail to the 3' end.

(6) Splicing : When there is formation of RNA take place by DNA i.e. transcription, there is removal of intron and joining of exon take place.

(7) t-RNA modification : There are various changes to the t-RNA molecule take place. n

The t-RNA modification of RNA plays many crucial roles in

(a) Enhancing RNA stability

(b) Controlling cellular stress responses

(c) Regulation gene expression

(d) Influencing protein synthesis

(e) Modulation viral replication

RNA editing : It refers change in sequence of mature RNA after the transcription. It affects on localization, stability and product like protein. RNA editing is done in m-RNA, r-RNA, t-RNA etc. It occurs in eukaryotes, prokaryotes, plastid and mitochondria . In eukaryotes it is amin ly occurs in nucleus and rarely in cytosol. RNA editing in m-RNA is done to obtain large diversity in proteins by using modification or deletion of one or more bases.

This is done by two major ways

(1)Site specific deamination of cytosine and adenine

Deamination of cytosine into uracil

Cytidine deamination is tissue or site specific. The cytidine deamination occurs in intestine to carry out deamination of cytosine in m-RNA of ApoB100 to produce apoB48. Normally ORF of apo B100 contains 4564 codons. If entire ORF is translate it will produce longer protein of 4563 amino acids called ApoB100 as in liver. But in small intestine, the same gene, same mature m-RNA undergo post transcriptional site specific deamination of cytosine at codon number 2153 which converts codon CAA into UAA, which causes ORF is halfed so shorter protein (2152 amino acids) called as ApoB48 is synthesized in intestine.

(2) g RNA (guide RNA) mediate site specific insertion and deletion of uridine base.

Guide RNA mediated RNA editing occur mainly in mitochondria of the trypanosomes. Guide RNA is small RNA having 40 -80 nucleotide which has three regions transcribed in particular cell or condition.

(1) Anchor region toward 5' end to interact with the the m-RNA

(2) Specific region or editing region – where to add Us it is decided by forming mismatching with template

(3) Poly U at 3' end add Us

In such type, multiple Us are inserted into specific regions of m-RNA after transcription. These insertions can be so extensive that in an extreme case, they amount to as many as half the nucleotides of the mature m-RNA. The addition of Us to the message changes codon and reading frame, completely altering the meaning of the message.

6.5 Structure and function of t RNA

Introduction

t-RNAconstitute about 10 – 20 % of total RNA of the cell. The t-RNA is small RNA having molecular weight of about 25,000 to 30,000 and the sedimentation co-efficient is 3.8 S. It is made up of 75 – 93 nucleotides.

The main function of t-RNA is to carry amino acids to m-RNA during protein synthesis. Each amino acid is carried by a specific t-RNA. The t-RNA is synthesized on DNA template in the nucleus. Only 0.025% of DNA codes for t-RNA. Its synthesis takes place at the end of cleavage. After the synthesis of t-RNA on DNA template a ribonucleotide sequence (- CCA) is added at the 3' end. The t-RNA is single stranded loop. The 3' end always terminates with CCA sequence while 5' end terminate with adenine (A) or guanine. The t-RNA also contains many unusual bases.

Structure of t-RNA:

Robert Holley (1965) and his colleagues reported the complete nucleotide sequence of alanine t-RNA. There are several model of t-RNA has been proposed but clover leaf model of Holley has been widely accepted. According to clover leaf model the single polypeptide chain (primary structure) of t-RNA is folded itself to form 5 arms (secondary structure). As result of folding the 3' end and 5' end come nearer each other and form arm. Each arm consists of a stem and a loop. In the stem base pairing take place while in loop does not. The arms are named as acceptor stem, D arm, anticodon arm, variable arm and T Ψ C arm. The acceptor arm has stem but no loop. The variable arm may or may not have a stem.

The acceptor stem consists of 11 base pair of which 7 base are paired while 4 are unpaired. The 3'end will have CCA sequence and the amino acid will covalently attach to adenylic acid or A of CCA sequence during polypeptide synthesis. The 5' end will have Guanine or Adenine at the end. The D arm, consist of 15 – 18 nucleotide of which 3 – 4 are base pair form stem while 8 - 12 are unpaired bases form loop. The loop contains two variable region α and β on either side of two constant guanine residues. These region consist of 1 – 3 nucleotide mostly pyrimidine with a high proportion of dihydrouridine (DHU). The D loop helps in binding of amino acyl synthatase. The anticodon arm consists of 12 nucleotides of which 5 form base pairs and 7 are unpaired nucleotide forming loop. In the anticodon loop form the 3' end the third, fourth and fifth constitute the anticodon permits temporary complementary base pairing with codon on m-RNA.

On the 3' side of the anticodon is a hyper modified purine (H) while on the 5' side is U and pyrimidine (Y). The variable arm is of two types. In one type there is a loop containing 4 -5 bases but no stem. In other type, arm consist of 13 – 21 residue and both the stem and loop can be distinguished. The T Ψ C arm consist 12 nucleotide of which 5 base pair form stem and a loop is formed

by 7 nucleotides. The outer most of the 5 pairs of the stem is C - G. TheT Ψ C loop contains a constant sequence of T Ψ C. All the t-RNA a ribosome recognition site on the T Ψ C loop consisting of G –T -Ψ - C –R sequence.

The t-RNA contains unusual bases along with the usual bases. The unusual bases are important because they protect the t-RNA molecule against degraded RNAase. The protection is necessary because RNA is found floating freely in the cell. The unusual bases are methylguanine (Gme), dimethylguanine (GMe2), methylcytosine (Me), ribothymine (T), uridine(Ψ), dihydrouridine (DHU, H_2O), Ionsine (I), methylinosine (I Me, Me I)

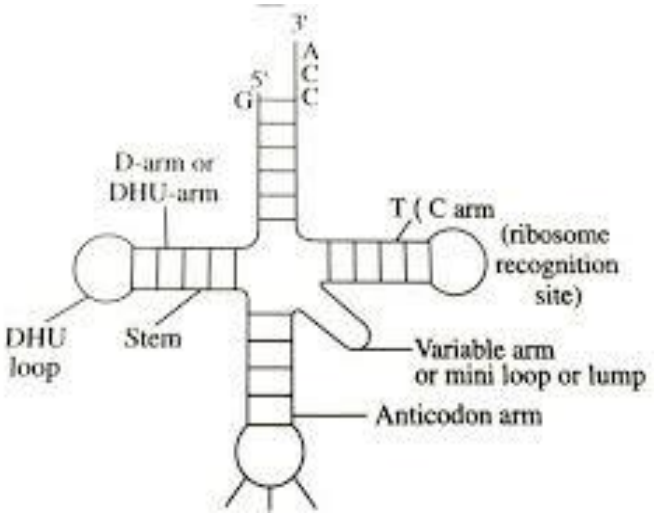


Fig : Clover leaf model t-RNA

Tertiary structure

The 3 dimensional structure of t-RNA was worked out by the help of X-ray crystallography study. A. klug the Nobel laureate of 1982 has contributed much to the 3 dimensional structure of t-RNA. The 3 dimensional structure (TDS) arises due to hydrogen bonding (i) between bases (ii) between bases and ribose- phosphate backbone (iii) between the back bone residues. S.H. Kim (1973) proposed a most acceptable 3 dimensional model of t-RNA i.e. phenylalanine t-RNA of yeast cells. According to Kim TDS of t-RNA takes a shape of letter "L" with a thickness of 20 Å - 25 Å with one limb is being formed by the acceptor stem and T Ψ C and other by D arm and the anticodon stem. The polynucleotide chain undergoes a sharp bending near residue at 9, 10, 11. The acceptor stem and T Ψ C stem are collinear. The D stem and the anticodon stem are not in the same straight line and their axes may deviation by 25^0. There are 10 base–base hydrogen bonding which maintain in two stacking domains corresponding to the two limb of the t-RNA molecule.

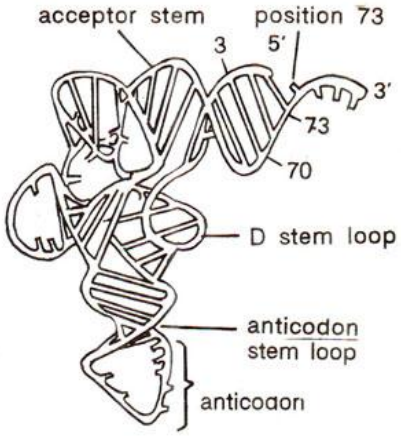


Fig : Three dimensional structure of t-RNA

Function of t RNA

- t-RNA plays an important role in protein synthesis.
- Aminoacylation of t-RNA is the first step in protein synthesis.
- It acts as an adapter molecule for linking amino acids to its specific codon present in mRNA.
- The t-RNA transfers the amino acid to the growing polypeptide chain in the ribosomes, which has three binding sites for t-RNA, namely A, P and E, which correspond to aminoacyl, peptidyl and exit, respectively.
- It acts as an adapter molecule for linking amino acids to its specific codon present in mRNA.
- t-RNA is specific to each amino acid and carries them during the translation process in the ribosomal subunits.
- This decoding of codons of mRNA by specific t-RNAs continues until the entire sequence for a polypeptide chain is translated

SAQ .

Complete the following sentences by inserting appropriate words in the blanks.

(i)The enzyme required for transcription is ----------

(ii)Sigma factor is a component of ----------

(iii)The anticodon is present in ----------.

(iv) RNA contains repeated units of -------

6.6 Summary

In this unit there is detailed study about transcription in prokaryotes. In this unit there is also detailed study about transcription in eukaryotes. This unit also contains RNA modification in very detailed manner.This unit also contains detailed study about structure and function of tRNA,

6.7 Terminal Question

Q1. Explain role of RNA polymerase in prokaryotes.

Q2. Explain the elongation process in transcription in eukaryotes.

Q3. Explain thestructure of t-RNA by Robert Holley.

6.8 Answers

SAQ (i) RNA polymerase

(ii)RNA polymerase

(iii) r RNA

(iv) Ribonucleotides

Terminal Question

Ans 1. The RNA polymerase (holoenzyme) consist of a core enzyme and sigma factors (σ). The core enzyme consist of 2 identical alpha (α) subunits and one chain of each of beta (β), beta dash (β'), omega (ω). The sigma factor (σ) help in the recognition of start signals on DNA molecule and direct RNA polymerase in selecting the initiation site (promoter). Once RNA synthesis is initiated and RNA molecule become 8 – 9 bases long, the (σ) factor dissociates from the holoenzyme and then the core enzyme bring about elongation of m-RNA. The β' subunit involve in binding of RNA polymerase to DNA. The β subunit of the core-enzyme is required for interaction with sigma factor.

The overall polymerization reaction can be writ as follow

$$nNTP + XTP \xrightarrow{\text{DNA, RNA-P}} (NMP)n\ XTP + nPP_1$$

(*In which XTP represents the first nucleotide at the 5' terminus of the RNA chain, NMP is a mononucleotide in the RNA. RNA-P is RNA polymerase, and PP_1 is the pyrophosphate released each time a nucleotide is added to the growing chain. The Mg^{++} is required for all nucleic acid polymerization reaction*)

Ans 2. During elongation process CTD tail is phosphyalated by TF II H kinase so many GTFs and mediator complex dissociate from the initiator complex. During elongation different processing occurs like capping, splicing occur in elongation & during in termination. There is polyadenylation processes occur on synthesized RNA (m-RNA). For elongation four elongation factors are required for transcription of gene. These are pTEFb (protein transcription elongation factor) hSPT-5, TATSF1 and TF II S.

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(a) ***RNA triphosphatase*** **:** It removes gamma phosphate from 5' end of terminal purine i.e. ATP mostly.

(b) ***Guanylyl transferase*** **(transfer GMP)** – It use GTP and add GMP to beta phosphate of the terminal purine.

(c) ***Methyl(GMP) transferase*** **:** Methylation at N7 of base and 2' position of sugars is done to form 7 methyl guanosine mono phosphate

Ans 3. Robert Holley (1965) and his colleagues reported the complete nucleotide sequence of alanine t-RNA. There are several model of t-RNA has been proposed but clover leaf model of Holley has been widely accepted. According to clover leaf model the single polypeptide chain (primary structure) of t-RNA is folded itself to form 5 arms (secondary structure). As result of folding the 3' end and 5' end come nearer each other and form arm. Each arm consists of a stem and a loop. In the stem

base pairing take place while in loop does not. The arms are named as acceptor stem, D arm, anticodon arm, variable arm and T Ψ C arm. The acceptor arm has stem but no loop. The variable arm may or may not have a stem.

The acceptor stem consists of 11 base pair of which 7 base are paired while 4 are unpaired. The 3'end will have CCA sequence and the amino acid will covalently attach to adenylic acid or A of CCA sequence during polypeptide synthesis. The 5' end will have Guanine or Adenine at the end. The D arm, consist of 15 – 18 nucleotide of which 3 – 4 are base pair form stem while 8 - 12 are unpaired bases form loop. The loop contains two variable region α and β on either side of two constant guanine residues. These region consist of 1 – 3 nucleotide mostly pyrimidine with a high proportion of dihydrouridine (DHU). The D loop helps in binding of amino acyl synthatase. The anticodon arm consists of 12 nucleotides of which 5 form base pairs and 7 are unpaired nucleotide forming loop. In the anticodon loop form the 3' end the third, fourth and fifth constitute the anticodon permits temporary complementary base pairing with codon on m-RNA.

On the 3' side of the anticodon is a hyper modified purine (H) while on the 5' side is U and pyrimidine (Y). The variable arm is of two types. In one type there is a loop containing 4 -5 bases but no stem. In other type, arm consist of 13 – 21 residue and both the stem and loop can be distinguished. The T Ψ C arm consist 12 nucleotide of which 5 base pair form stem and a loop is formed by 7 nucleotides. The outer most of the 5 pairs of the stem is C - G. TheT Ψ C loop contains a constant sequence of T Ψ C. All the t-RNA a ribosome recognition site on the T Ψ C loop consisting of G –T -Ψ - C –R sequence.

The t-RNA contains unusual bases along with the usual bases. The unusual bases are important because they protect the t-RNA molecule against degraded RNAase. The protection is necessary because RNA is found floating freely in the cell. The unusual bases are methylguanine (Gme), dimethylguanine (GMe2), methylcytosine (Me), ribothymine (T), uridine(Ψ), dihydrouridine (DHU, H_2O), Ionsine (I), methylinosine (I Me, Me I)

6.9 Suggested books

1. Alberts, B., Johnson, A., Lewis, J., Raff, M., Roberts, K., & Walter, P. (2014). Molecular biology of the cell (6th ed.). Garland Science.
2. Berg, J. M., Tymoczko, J. L., Gatto, G. J., & Stryer, L. (2022). Biochemistry (9th ed.). W. H. Freeman.
3. Darnell, J., Lodish, H., & Baltimore, D. (1990). Molecular cell biology (1st ed.). Scientific American Books.
4. Griffiths, A. J., Wessler, S. R., Lewontin, R. C., & Carroll, S. B. (2020). Introduction to genetic analysis (12th ed.). W. H. Freeman.
5. Lehninger, A. L., Nelson, D. L., & Cox, M. M. (2017). Lehninger principles of biochemistry (7th ed.). W. H. Freeman.
6. Lodish, H., Berk, A., Zipursky, S. L., Matsudaira, P., Baltimore, D., & Darnell, J. (2000). Molecular cell biology (4th ed.). W. H. Freeman.
7. Nelson, D. L., & Cox, M. M. (2017). Lehninger principles of biochemistry (7th ed.). W. H. Freeman.
8. Stryer, L. (1995). Biochemistry (4th ed.). W. H. Freeman.
9. Watson, J. D., Baker, T. A., Bell, S. P., Gann, A., Levine, M., & Losick, R. (2013). Molecular biology of the gene (7th ed.). Pearson.

UNIT 7 :TRANSLATION OF m-RNA

7.1 Introduction

Translation is the process by which m-RNA is responsible for coding of protein. The genetic information which is stored in DNA has to be transferred from one generation to other generation through the process of transcription and translation which is called as central dogma of molecular biology

Objective

After studying this unit you should be able to

- Understand the genetic basis of protein synthesis.
- Understand genetic code and relation of amino acids
- Understand ribosome structure & its functions
- You will understand the stages of translation

7.2 Genetic basis of protein synthesis

Genetic bases of protein synthesis involve the translation of genetic information encoded in DNA into a specific sequence of amino acids that take up a protein. This process involves three main steps.

(1) Replication : Formation of new DNA from old DNA

(2) Transcription : DNA is transcribed into m-RNA

(3) Translation : m-RNA is translated into a protein.

This entire process is called central dogma of molecular biology, which was proposed by Crick in 1956. So in the central dogma DNA is central molecule. The information in DNA nis converted into RNA irreversibly by process called as transcription. RNA is then copied into protein by translation irreversible. DNA is maintain in cell from generation to generation by replication.

In 1975 Temin and Baltimore discovered reverse transcriptase enzyme in Rous Sarcoma virus which infect chicken. This reverse transcriptase enzyme converts RNA into DNA. This is called taminism

Important genetic elements are

(i) ***Codon*** **:** Sequences of three nucvleotide (triplets in m-RNA that specify amino acids.

(ii) ***Genetic code*** **:** The set of rules mapping codon to amino acids (61 codons specify 20amino acid)

(iii) ***Start and stop codons*** **:** AUG (start) and UAA, UAG, UGA stop codons regulate translation initiation and termination.

(iv) ***Promoters*** **:** DNA regions that initiate transcription

(v) ***Operators*** **:** DNA regions that bnregulate gene expression.

Genetic bases of protein synthesis is important in study of

(a) Genetic therapy

(b) Gene Therpy

(c) Protein design

(d) Disease mechanisms

(e) Synthetic biology

7.3 Genetic code and amino acids

The genetic code is defined as the relationship between the sequence of bases in DNA/RNA and the sequence of amino acids in a polypeptide chain.

There are various views that how many bases can code a single amino acid. According to singlet code that each base can specify one amino acid. So for this only 4 out of 20 amino acid can code. According to doublet two bases would specific one amino acid so 16 (4 x 4) codon can code for 20 amino acid. The last triplet code was given by physicist Gamow in 1954. According to this 3 bases specific one amino acid, so 64 (4 x 4 x 4) codon are found which could codes for 20 amino acid. This was experimentally proved by Crick and co-worker in 1961. When they added or deleted single or double base pairs in aparticular region of DNA of T4 bacteriophages of *E. coli*, they found that bacteriophages cannot perform their normal function. But if there is addition or deletion of three bases pairs then it perform normal function. From this experiment they conclude that genetic code was triplet, because the addition of one or two base has disturbed the reading of codon. While the addition or deletion of third nucleotide causes proper reading of message.

Characteristic of Genetic code

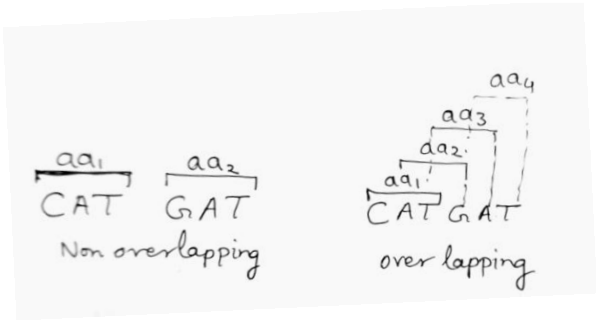
(1) The genetic is a triplet code : The nucleotides of m-RNA are arranged in a linear sequence of codons, each codon consisting of three successive nitrogenous bases i.e. the code is a triplet codon.

Codons in mRNA

First Base	Second Base								Third Base
	U		C		A		G		
	UUU	Phenylalanine	UCU	Serine	UAU	Tyrosine	UGU	Cysteine	U
U	UUC	Phenylalanine	UCC	Serine	UAC	Tyrosine	UGC	Cysteine	C
	UUA	Leucine	UCA	Serine	UAA	Stop	UGA	Stop	A
	UUG	Leucine	UCG	Serine	UAG	Stop	UGG	Tryptophan	G
	CUU	Leucine	CCU	Proline	CAU	Histidine	CGU	Arginine	U
C	CUC	Leucine	CCC	Proline	CAC	Histidine	CGC	Arginine	C
	CUA	Leucine	CCA	Proline	CAA	Glutamine	CGA	Arginine	A
	CUG	Leucine	CCG	Proline	CAG	Glutamine	CGG	Arginine	G
	AUU	Isoleucine	ACU	Threonine	AAU	Asparagine	AGU	Serine	U
A	AUC	Isoleucine	ACC	Threonine	AAC	Asparagine	AGC	Serine	C
	AUA	Isoleucine	ACA	Threonine	AAA	Lysine	AGA	Arginine	A
	AUG	Methionine or start	ACG	Threonine	AAG	Lysine	AGG	Arginine	G
	GUU	Valine	GCU	Alanine	GAU	Aspartic Acid	GGU	Glycine	U
G	GUC	Valine	GCC	Alanine	GAC	Aspartic Acid	GGC	Glycine	C
	GUA	Valine	GCA	Alanine	GAA	Glutamic Acid	GGA	Glycine	A
	GUG	Valine	GCG	Alanine	GAG	Glutamic Acid	GGG	Glycine	G

Fig : Genetic code is triplet code

(2) The code is non-overlapping: The DNA is along chain of nucleotides, it could be read either in an overlapping or non-overlapping manner. So the genetic code could be overlapping or non-overlapping. If the reading is done by non-overlapping the 6 nucleotide would code for 2 amino acid, while in the overlapping it will code for 4 amino acid.



In the non-lapping code each letter is read only while in the overlapping code it would be read three time. By the gene mutation studies it has been shown that code is the non-over lapping type. Recently it has also been shown that in bacteriophage ϕ x 174 there is possibility of overlapping of genes and codons.

(3) The code is comma less : The genetic code is comma less, which mean that no codon is reserved for punctuations. It means that after one amino acid is coded, the second amino acid will be automatically coded by the next three letters and that no letters are wasted as the punctuation mark.

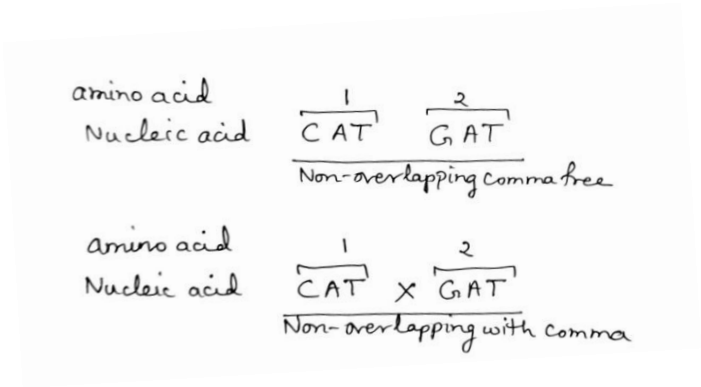


Fig : Two form of genetic code

(A) Genetic code without comma

(B) Genetic code with comma

(4) The code has polarity : The code is always read in a fixed direction i.e. in the 5' ⟶ 3' direction i.e. codon has polarity. It is apparent that if the code is read in opposite direction, it would specify two different proteins, since the codon would have reversed base sequence.

Codon	UUG	AUC	GUC	UCG	CCA	ACA	AGG
Polypeptide ⟶	Leu	Ile	Val	Ser	Pro	Thr	Arg
	Val	Leu	Leu	Ala	Thr	Thr	Gly ⟵

(5) Codons and Anticodon : The m-RNA is read in a polar manner 5' ⟶ 3' direction. But anticodon is written in the 3' ⟶ 5' direction, so as to bring about an easier correlation between the bases of the codon and anticodon. The anticodon of AUG is written as 3' UAC 5' or UAC. This indicates the codon & anticodon pairing is antiparallel.

Base number	**1 2 3**
Codon (m-RNA)	5' A U G 3'
Anticodon (t-RNA)	3' U A C 5'
Base number	**3 2 1**

(6) The code is degenerate : When more than one codon specify the same amino acid is called degeneracy of the code. Except for methionine and tryptophan, which have single codon.

Amino acid	**No of codon**
(1) Tryptophan, Methionine	**1**
(2) Phenylalanine, Tyrosine, Histidine, Glutamine, Asparagine, Lysine, Aspartic acid, glutamic acid, Cysteine	**2**
(3) Isoleucine	**3**
(4) Valine, Proline, Threonine, Alanine, Glycine	**4**
(5) Leucine, Arginine, Serine	**6**

The code degeneracy is basically of two types : partial and complete. The partial degeneracy occurs when first two nucleotides are identical, but the third (i.e. 3' base) nucleotide of the degenerate

codon differ e.g. CUU and CUC code for leucine. The complete degenerate occurs when any of the four bases can take third position and still code for the same amino acid (e.g. UCU, UCC, UCA and UCG codes for serine). Degeneracy of genetic code has certain biological advantages. Degeneracy provides a mechanism of minimizing mutational lethality.

(7) Initiation Codon : In most organism AUG codon is the start or initiation codon i.e. the polypeptide chain start either with methionine (Eukaryotes) or N-*formyl* methionine (Prokarytes). The methionine or N-formyl methionine t-RNA specifically binds to the initiation site of m-RNA containing the AUG initiation codon. In rare cases GUG also serves as the initiation codon e.g. bacterial protein synthesis. Normally GUG codes for valine, but when normal AUG codon is lost by deletion, only the GUG is used as initiation codon.

(8) Termination codon : The 3 codons UAA, UAG, UGA are the chain termination codon. They do not code for any of the amino acids so they are also called nonsense codon.

The UAG was the first termination codon to be discovered by Sidney Brenner (1965). It was named amber after a graduate student named Bernstein (= German word for amber) and amber means brownish (yellow) who helped in the discovery of a class of mutation Apparently to give uniformity the other two termination codons were also named after color such as Ochre for UAA and opal or umber for UGA (Ochre means yellow red or pale yellow, opal means milky white and umber mean brown)

Termination codons do not code for any amino acids and hence cause termination and release of polypeptide chains No t-RNA species has anticodons complementary to the termination codons. Termination codon are not read by any t-RNA molecule but read by some specific protein called release factors. In prokaryotes there are three release factor RF-1, RF-2 and RF-3. RF-1 recognize UAA and UAG while RF-2 recognizes UAA and UGA. RF-3 stimulates RF-1 and RF-2. In eukaryotes a single release factors (RF) recognizes all three termination codon.

(9) The code is universal : The genetic code is valid for all organism ranging from bacteria to man. Such universality of the codon was demonstration by Marshall, Caskey and Nirenberg (1967) who found that *E.coli* (bacterium), Xenopus *laevis* (amphibian) and guinea pig (mammal) amino acyl t-RNA use almost the same code.

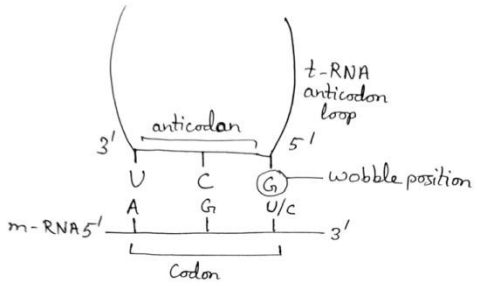
Nirenberg has also stated that the genetic code may have developed 3 billion years ago with the first bacteria and it has changed very little throughout the evolution of living organism.

Wobble Hypothesis

To explain the possible cause of degeneracy of codon, Cricks (1966) proposed the wobble hypothesis, since there are 61 codons specifying amino acids, so the cell should contain 61 different t-RNA molecules each with a different anticodon. But the number of t-RNA molecule was found much less than 61. Thus explain that anticodons of some t-RNAs read more than one codon on m-RNA.

According to wobble hypothesis only the first two positions of a triplet codon on m-RNA have a precise pairing with the bases of the t-RNA anticodon. The pairing of the third position bases of codon may not clear (ambiguous) and varies according to the nucleotide present in this position. Thus a single t-RNA type is able to recognize two or more this position. Thus a single t-RNA type is able to recognize two or more codons differing only in the third base. The anticodon UCG of serine t-RNA recognizes two codons AGC and AGU. The bonding between UCG and AGC follows the usual Watson Crick pairing pattern. In UCG and AGU pairing, hydrogen bonding takes place between G and U. This is a difference from the usual Watson Crick pairing mechanism where G pairs with C and A with U. Such interaction between the third bases is referred to as "***Wobble pairing***".

m-RNA codon	**5' AGC 3'**	**5' AGU' 3'**
t-RNA anticodon	**3' UCG 5'**	**3' UCG 5'**



Thus Crick's wobble hypothesis states that the bases at 5' end of the anticodon is not spatially confined as the other two bases allowing it to form hydrogen bonds with any of several bases located at the 3' end of a codon.

7.4 Ribosome structure and assembly

In 1955 Palade discovered small dense granules in the cytoplasm. He called it as Palade's granules, which were later called as ribosome. So ribosomes are small dense rounded and granular particles. They contain ribonucleo-protein. They occur either freely in the matrix of the mitochondria, chloroplast and cytoplasm or remain attached with the membrane of the endoplasmic reticulum and nucleus.

The ribosome occurs in both prokaryotic and eukaryotic cells. In the cell in which active protein synthesis take place, the ribosomes remain attached with the membranes of the endoplasmic reticulum. The cells where such active synthesis takes places are pancreatic cells, hepatic cell, osteoblasts, serous cells of submaxillary gland, chief cells of glandular stomach, thyroid cells and mammary gland cells.

Shape : The shape of ribosome are spherical. The ribosomes of prokaryotes are smaller in size than eukaryotes. In prokaryotes they are 150 Å and in eukaryotes they are 250 Å in diameter.

Number : The number of ribosomes is directly related to the RNA content of the cell. In rabbits reticulocytes, they are 1 X 10^5 per cell. One mm of liver contains 2 x 10^{13} ribosomes. In *E. coli* they are about 20,000 to 30,000 ribosome per cell.

Structure of RNA

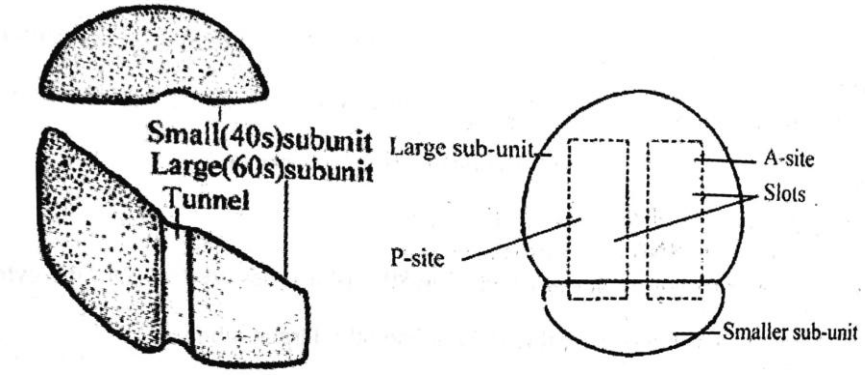


Fig : Ultra structure of RNA

The ribosomes are generally spherical in shape but they are flattened at the poles. Such shape is described as oblate spheroid. Due to a cleft in the ribosome, each ribosome has two subunits, the large

subunit and small subunit. The large subunit forms a dome shape and smaller subunit forms the capto cover it.

The ribosome is associated with the membrane of the cell organelles by the larger subunit and a cleft separates the two subunits in such a case runs parallels to the membrane.

The low concentration of Mg^{++} (.001M) in the cytoplasm plays an important role in the cohesion of ribosomes. If the Mg^{++} concentration is increased ten times, two ribosomes combine to form a dimer. If the Mg^{++} concentration is lowered, a single ribosome gets dissociated into subunits, a dome and a cap.

Types of Ribosomes

The ribosomes are of two types 70S and 80S.

(1) 70S Ribosomes : The 70S ribosome are relatively smaller than 80S. They are found in prokaryotes example bacteria, Blue green algae and *E.coli*. The 70S ribosome consists of two subunits a small cap of 30S and large dome of 50S subunit. The length of 70S ribosome is 290Å and the width is 210Å. The cleft between the two subunits is deeper as compared to the 80S ribosome. The 30S subunit contains 21 different proteins and 16S r RNA. The 50S subunit contains 34 proteins and 5S and 23S r RNA. Some proteins are identical in both subunits. The RNA : Protein ratio in the 70S is 2:1.

(2) 80S Ribosome : 80 S ribosome are larger than 70 S ribosome. The 80S ribosomes are found in the cytoplasm of eukaryotes. The 80S ribosome has 40S smaller subunit and 60S larger subunit.

The length of the 80S ribosome is 300 to 400 Å and its width is 200 to 240 Å. The cleft between the two subunits is superficial. The 40S small subunit contains 33 proteins and 16S and 18S r RNA. The 60S large subunit contains 49 proteins and 25S, 29S, 5.8S and 5S r RNA. The RNA : Protein ratio in the 80 S ribosome is 1 : 1.

Function of Ribosomes

(1) The ribosome plays important role in the protein synthesis. It is the assembly shop where amino acids are linked to produce proteins. During protein synthesis two subunits join together on the m-RNA. So in this way many ribosomes are attached to the mRNA to form polyribosomes.

(2) The ribosomes are chemically composed of RNA and proteins. The ribosomal RNA (r RNA) plays a central role in the process of protein synthesis. The ribosomal protein enhances the catalytic function of the r RNA.

(3) The mRNA passing through the ribosome is produced from nucleases. Similarly newly synthesized polypeptide chains are protected from protease.

7.5 Stages of translation

In translation the genetic information present in mRNA directs the order of specific amino acids to form a polypeptide or protein. The stages of translation process consists of following steps

(1) Activation of amino-acids

(2) Transfer of the activated amino-acid to t-RNA

(3) Initiation of polypeptide chain synthesis

(4) Chain elongation

(5) Chain termination

(1) Activation of amino-acids : There are 20 amino acids used in protein synthesis which are activated by ATP in the presences of specific activating enzyme (E) called amino acyl synthetase to form amino acyl adenylates (aaa) also called amino acyl AMP. The pyrophosphates are released.

$$AA + ATP + E \longrightarrow \underbrace{E.\ aa - AM\ P}_{\text{Amino –acyl adenylate enzyme complex}} + PPi$$

(2) Transfer of the activated amino-acid to t RNA : The activated amino acid is transferred to a specific t-RNA with release of AMP and activating enzyme

$$E.\ aa - AMP + E + t\text{-}RNA \longrightarrow \underbrace{aa - t\text{-}RNA}_{\text{Amino acyl t-RNA}} + AMP + E$$

The amino acyl t-RNA moves towards the site of protein synthesis i.e. ribosomes with m-RNA. The attachment of the amino-acid to its t-RNA is the only step in protein synthesis in which the identity of amino acid (i.e. R group) plays a part. This was shown by Chaperville (1962).

(3) Initiation of polypeptide chain synthesis : For initiation require the ribosome subunits, m-RNA, an energy source (GTP), activated amino acids attached to t-RNA (aa-t-RNA) and initiation factor (IF). These factors are called IF-1, IF-2, and IF-3 in prokaryotes and eIF-2, eIF-2', eIF-$2a_1$, eIF$2a_2$, eIF-$2a_3$ and eIF-3 in Eukaryotes.

First the 30S ribosomal subunit attaches to m-RNA to form an m-RNA-30S complex. The process requires IF-3 and Mg^{++}. The starting amino acid is methionine (Met) in Eukaryotes and N-*formyl* methionine (f-Met) in prokaryotes. The amino acid-t-RNA complex (f-Met-t-RNA) attaches to the initiation codon, AUG on m-RNA through its anticodon UAC to form the 30S initiation complex. This process requires initiation factors IF-2 and IF-1 as well as GTP. Since the protein synthesis begins at an AUG start codon, there are many AUG sequence. To identify a particular AUG sequence, in prokaryotic m-RNA a particular base sequence- AGGAGGU called ribosome binding site is present containing 8 to 13 nucleotides. This site is also called *shine-Dalgarno* sequence and occurs near the AUG codon used for initiation purpose and base pairs with a complementary sequence near the 3' terminus of the 16S-r-RNA molecule of the ribosome. The t-RNA $^{f\text{-}Met}$ charged with the first amino acid (N-*formyl* methionine) binds to the 30S subunit at the P site at three ribonucleotides. After that the larger subunit (50S) joins to the 30S initiation complex to form the complete initiation complex (70S). The energy for this union is supplied by the hydrolysis of a molecule of GTP.

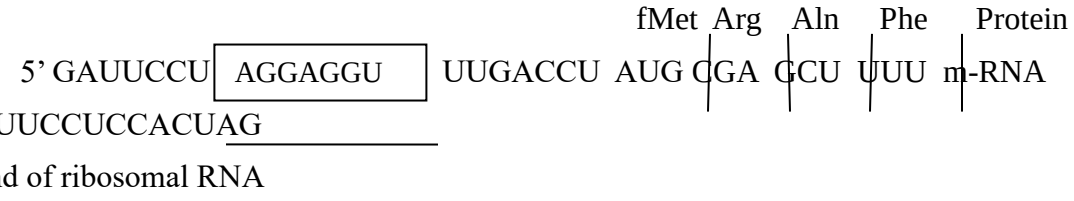


Fig : Shine –Dalgarno sequence

The larger ribosomal submit has two binding site for t-RNA, an A or acceptor site and a P or peptidyl site. F Met-t-RNA binds to the P site.

(4)Chain elongation : Elongation of the polypeptide chain requires elongation factors (EF). These are Ef-Tu, EF-Ts and EF-G in prokaryotes and EF-1 and EF-2 in eukaryotes. Now the second amino acid t-RNA complex (aa_2-t-RNA) occupies the A site. There is enzymatic recognition of internal codons. This process requires EF-Tu, GTP and Mg^{++}. Now there is a formation of peptide bond between the carboxyl group of the first amino acid with the amino group of the second amino acid.

This causes a formation of a dipeptide whose carboxyl end is still bonded to the second t-RNA, whose amino end is free. This reaction is catalyzed by an enzyme associated with 50S subunit and called peptidyl transferase. The energy for peptide bond formation is come from by the dissolution of the amino acyl bond between the first amino acid and its carrier. The first amino acid is removed from its attachment to its t-RNA and transferred to the free $–NH_2$ terminus of the second amino acid. The first amino acid is placed on the top of the second.

The aa_2–t-RNA complex moves from the A site to the P site. This process is called translocation and requires EF-G, GTP and Mg^{++}. Translocation involves movement of the ribosome relative to m-RNA in ~~the 5~~ 3' direction. The t-RNA molecule f-Met is unload from the ribosome. The third amino acid t-RNA complex (aa_3-t-RNA) now occupies the vacant P site.

(5) Chain termination : Chain elongation continue until a termination codon (UAA, UAG or UGA) reaches the ribosomes. The chain is then terminated and released from the ribosome. This process requires releasing factors (RF-1, RF-2 and RF-3) in prokaryotes and RF in Eukaryotes. The RF-1 identifies termination codons UAA and UAG while factor RF-2 recognizes codon UGA. The RF-3 stimulated the action of RF-1 & RF-2.

The termination codon provides signals to the ribosomes for the attachment of release factors. The release factor interacts with peptidyl transferase causing hydrolysis of the bond between t-RNA and the polypeptide chain and the chain is released from the ribosome. The hydrolysis of GTP results in the dissociation of the release factors from the ribosome. The t-RNA is also unloaded. The ribosomal subunit dissociates and m-RNA is released for break down to nucleotide. After that the polypeptide chain undergoes for processing for the removal of methionine or N-*formyl* methionine.

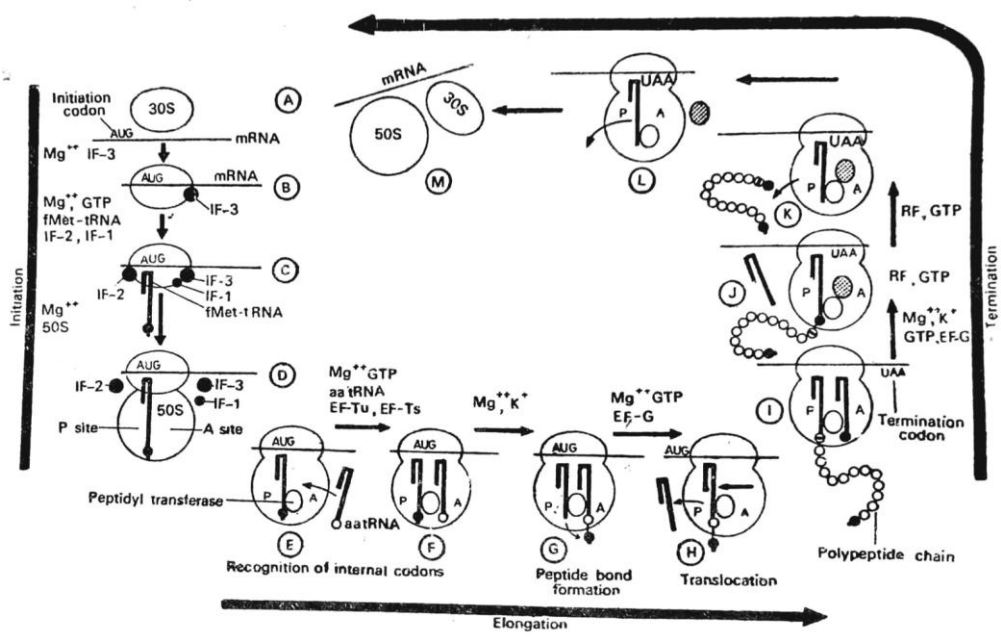


Fig : Outline of Translation

SAQs 1.

Complete the following sentences by inserting appropriate words in the blanks.

(i) The initiation codon in Eukaryotes ----------

(ii) ---------- proposed the wobble hypothesis,

(iii) Granular structure found attached with ER are ----------.

(iv) The ribosomes are meant for ----------

7.6 Summary

In this unit you will study about genetic basis of protein synthesis in very detailed manner. This unit also contains about genetic codes and its relation to amino acids and also hypothesis involve in genetic code. In this unit it also describes about ribosomes, its types and function of ribosomein very detailed manner. It also contain about stages involves in translation process in very detailed manner.

7.7 Terminal Question

Q1. Explain Genetic code.

Q2. Explain the Wobble Hypothesis .

Q3. Explain thetypes of Ribosomes.

7.8 Answers

SAQ 1 (i)AUG

(ii)Cricks (1966)

(iii) Ribosomes

(iv)Protein synthesis

Terminal Question

Ans 1. The genetic code is defined as the relationship between the sequence of bases in DNA/RNA and the sequence of amino acids in a polypeptide chain.

There are various views that how many bases can code a single amino acid. According to singlet code that each base can specify one amino acid. So for this only 4 out of 20 amino acid can code. According to doublet two bases would specific one amino acid so 16 (4 x 4) codon can code for 20 amino acid. The last triplet code was given by physicist Gamow in 1954. According to this 3 bases specific one amino acid, so 64 (4 x 4 x 4) codon are found which could codes for 20 amino acid. This was experimentally proved by Crick and co-worker in 1961. When they added or deleted single or double base pairs in aparticular region of DNA of T4 bacteriophages of *E. coli*, they found that bacteriophages cannot perform their normal function. But if there is addition or deletion of three bases pairs then it perform normal function. From this experiment they conclude that genetic code was triplet,

because the addition of one or two base has disturbed the reading of codon. While the addition or deletion of third nucleotide causes proper reading of message.

Ans 2. To explain the possible cause of degeneracy of codon, Cricks (1966) proposed the wobble hypothesis, since there are 61 codons specifying amino acids, so the cell should contain 61 different t-RNA molecules each with a different anticodon. But the number of t-RNA molecule was found much less than 61. Thus explain that anticodons of some t-RNAs read more than one codon on m-RNA.

According to wobble hypothesis only the first two positions of a triplet codon on m-RNA have a precise pairing with the bases of the t-RNA anticodon. The pairing of the third position bases of codon may not clear (ambiguous) and varies according to the nucleotide present in this position. Thus a single t-RNA type is able to recognize two or more this position. Thus a single t-RNA type is able to recognize two or more codons differing only in the third base. The anticodon UCG of serine t-RNA recognizes two codons AGC and AGU. The bonding between UCG and AGC follows the usual Watson Crick pairing pattern. In UCG and AGU pairing, hydrogen bonding takes place between G and U. This is a difference from the usual Watson Crick pairing mechanism where G pairs with C and A with U. Such interaction between the third bases is referred to as "***Wobble pairing***".

Ans 3. The ribosomes are of two types 70S and 80S.

(1)70S Ribosomes : The 70S ribosome are relatively smaller than 80S. They are found in prokaryotes example bacteria, Blue green algae and *E.coli*. The 70S ribosome consists of two subunits a small cap of 30S and large dome of 50S subunit. The length of 70S ribosome is 290Å and the width is 210Å. The cleft between the two subunits is deeper as compared to the 80S ribosome. The 30S subunit contains 21 different proteins and 16S r RNA. The 50S subunit contains 34 proteins and 5S and 23S r RNA. Some proteins are identical in both subunits. The RNA : Protein ratio in the 70S is 2:1.

(2)80S Ribosome : 80 S ribosome are larger than 70 S ribosome. The 80S ribosomes are found in the cytoplasm of eukaryotes. The 80S ribosome has 40S smaller subunit and 60S larger subunit.

The length of the 80S ribosome is 300 to 400 Å and its width is 200 to 240 Å. The cleft between the two subunits is superficial. The 40S small subunit contains 33 proteins and 16S and 18S r RNA. The 60S large subunit contains 49 proteins and 25S, 29S, 5.8S and 5S r RNA. The RNA : Protein ratio in the 80 S ribosome is 1 : 1.

7.9 Suggested books

1. Alberts, B., Johnson, A., Lewis, J., Raff, M., Roberts, K., & Walter, P. (2014). Molecular biology of the cell (6th ed.). Garland Science.
2. Berg, J. M., Tymoczko, J. L., Gatto, G. J., & Stryer, L. (2022). Biochemistry (9th ed.). W. H. Freeman.
3. Darnell, J., Lodish, H., & Baltimore, D. (1990). Molecular cell biology (1st ed.). Scientific American Books.
4. Griffiths, A. J., Wessler, S. R., Lewontin, R. C., & Carroll, S. B. (2020). Introduction to genetic analysis (12th ed.). W. H. Freeman.
5. Lehninger, A. L., Nelson, D. L., & Cox, M. M. (2017). Lehninger principles of biochemistry (7th ed.). W. H. Freeman.
6. Lodish, H., Berk, A., Zipursky, S. L., Matsudaira, P., Baltimore, D., & Darnell, J. (2000). Molecular cell biology (4th ed.). W. H. Freeman.
7. Nelson, D. L., & Cox, M. M. (2017). Lehninger principles of biochemistry (7th ed.). W. H. Freeman.

8. Stryer, L. (1995). Biochemistry (4th ed.). W. H. Freeman.
9. Watson, J. D., Baker, T. A., Bell, S. P., Gann, A., Levine, M., & Losick, R. (2013). Molecular biology of the gene (7th ed.). Pearson.

UNIT 8 : GENE REGULATION

8.1 Introduction

Gene regulation was first study in bacteria as mutants were available and easy manipulation in genes of bacteria. Those mechanisms that increase or decrease expression of a given gene as the requirement for its product varies. There are various stages at which expression of a gene can be regulated. Genes can be regulated at number of point such as genomic level, transcriptional level, m-RNA processing, post transcriptional level or transcriptional level.

Objective

After studying this unit you should be able to

- Understand the basics of transcriptional regulation
- Understand the Lac operon- model and regulation
- Understand Trp operon- model and regulation
- You will understand Translational and post-translational regulations

8.2Overview of transcriptional regulation

The gene is a sequence of DNA which can be transcribed into RNA or protein i.e. functional product. Gene expression is the formation of functional product from the gene. So the conversion of genotypes into phenotype is called as gene expression. In gene expression process information in DNA is converted into RNA by the transcription. This mRNA is read by ribosomes to produce protein by mean of translation, then by using some covalent modifications done on the protein called post translation modification active protein is obtained and this protein will decided the particular characters of an organism.

The organisms have thousands of genes responsible for the different functions, some are responsible for metabolism, some are for stress, chemo taxis, protection etc. In higher organism behaviour is also controlled by genes. Development of organism or differentiation process depends on the differential gene regulation.

Gene regulation can be describe as changing gene expression as per the requirement of cell. The regulation is of two types i.e. gene can be up regulated (increase in expression level i.e. increase in amount of final functional product) or down regulated (decrease in expression level). If we consider the protein coding genes, amount of active protein can be increased by increasing transcription making more

mRNA to undergo translation, increase in protein synthesis and decrease in degradation etc.

There are two types of genes in organism based on extent of gene regulation in them

(1)Regulatory gene

(2)Housekeeping gene

Gene whose activity is controlled in response to the needs of a cell or organism are called regulated genes. All organisms also have large number of genes whose products are essential to the normal functioning of a growing and dividing cell, no matter what the conditions are. These genes are always active in growing cells and are known as constitutive genes or housekeeping genes for example genes that code for the enzymes needed for protein synthesis and glucose metabolism. So it is noted that all the genes are regulated on some level. The gene regulation may be positive (activator mediator) or negative (repressor mediator). The positive regulation is a regulation where gene expression is stimulated by using activators. The negative regulation is the regulation where gene expression is inhibited by repressors. Positive and negative regulations occur in bacteria and eukaryotes, however negative control is more important in bacteria where as eukaryotes are more likely to use positive control mechanism. Because bacterial promoters are strong as compare to eukaryotes.

8.3 Lac operon- model and regulation

The concept of gene regulation in bacteria or prokaryotes comes from the studies on lac operon of *E.coli* by Jacob and Monad (1961). There studies and other investigation have established that in prokaryotes the gene is regulated at a transcription level. They explain the regulatory mechanism of expression or action of regulated gene at transcriptional level. Jacob forward a hypothesis called " O**peron hypothesis**".

Lac Operon of *E. coli*: The lac operon (lactose) of the bacteria *E. coli* has been well studied. It has a small segment of a circular DNA molecule which constitute genetic material of the bacterium. It has follows genes.

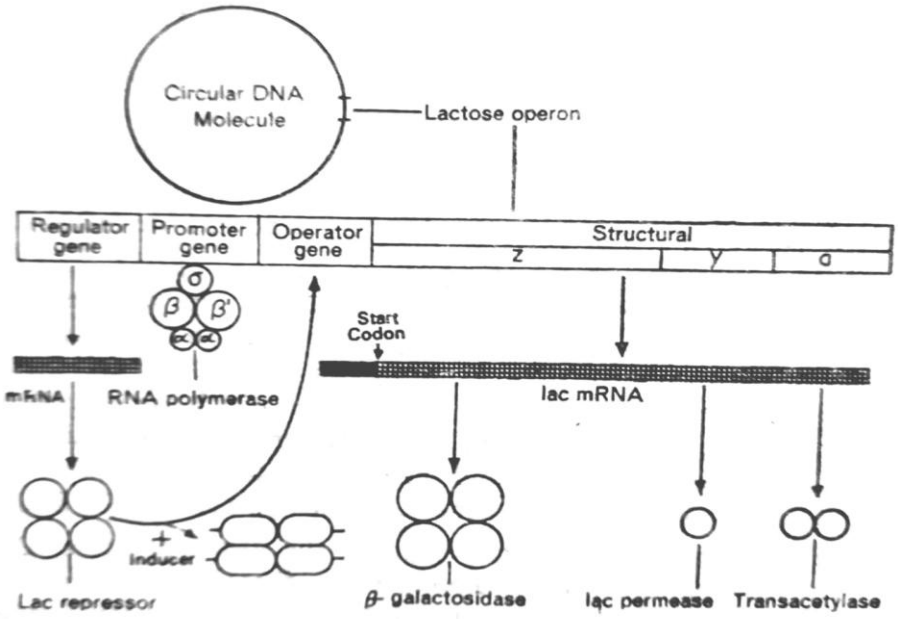


Fig : The lac operon of *E.coli*

(i) Structure gene : It has 3 structural gene z, y, a which transcribe one long polycistronic mRNA (when one gene (cistron) codes for a single m-RNA it is said monocistronic while if several

adjacent cistron may transcribe mRNA molecule it is said polycistronic or polygenic mRNA). The **Z** gene (3063 bp) codes for enzyme β-galactosidase which hydrolysis lactose into glucose and galactose. The **Y** gene (800 bp) codes for β-galactosidase permease which is present in the cell of bacteria and help in uptake of lactose from the external medium to internal medium. The **A** gene (800bp) codes for β-galactosidase acetylase appears in small quantities upon lactose induction.

(ii) Operator gene : The operator gene is adjacent to the first structural gene and it control the activity of structural gene. If the product of regulator gene, repressor is bind to the operator gene and forming complex operator-repressor complex it will inhibit the activity of structure gene.

The lac operator of *E. coli* consist of 35 bp. The base pair shows palindromic sequences {The nucleotides of one strand go in one direction while an identical sequence of nucleotides goes in the opposite direction e.g. }

read →

A A T T G C A A T T

T T A A C G T T A A

← read

The basic function of the operator is that on binding the repressor it physically prevents RNA polymerase from forming in initiation complex. The RNA polymerase bind at promoter region, while the transcription of m-RNA begins in the operator gene. The fact is derived by complementary lac operator sequence is present at the begin of lac m-RNA. The segment of m-RNA transcribed by the bases of operator gene preceeds the start codon of lac m-RNA.

(iii) Promoter gene : The promoter gene is continuous with the operator gene. The complete nucleotide sequence of the control region of the lac operon of *E.coli* has been worked by Gilbert and Maxam 1973. This sequence extends from the termination codon (ACT on DNA = UGA on m-RNA) of the structural gene and includes the promoter and operator genes.

The promoter region contains a sequence of two fold symmetry (palindromic) which is present at CRP site. The CRP binds a protein called CRP (cyclic AMP receptor protein). This protein is essential for the binding of the enzyme RNA polymerase to the promoter. In *E. coli*.CRP combines with cyclic adenosine monophosphate (c-AMP) to form a CRP – cAMP complex. This combine binds to the promoter. The binding of CRP – cAMP complex to the promoter enhances RNA polymerase attachment to promoter and thus increases transcription and protein synthesis is known as positive control.

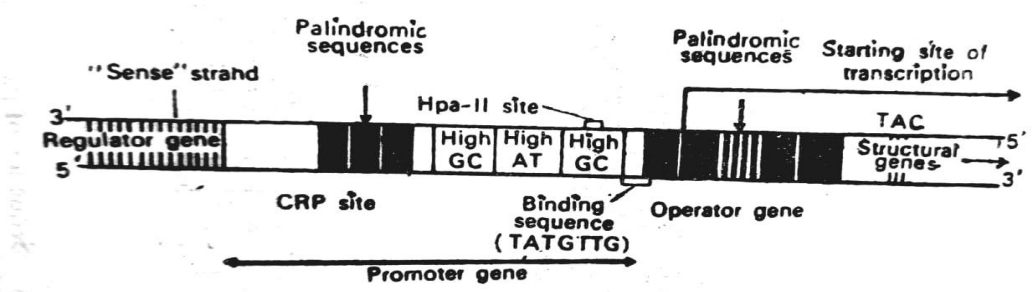


Fig : Part of the lac operon of E.coli. The vertical arrow s indicates the axis of two fold symmetry of the palindromic sequence. TAC is the initiation codon

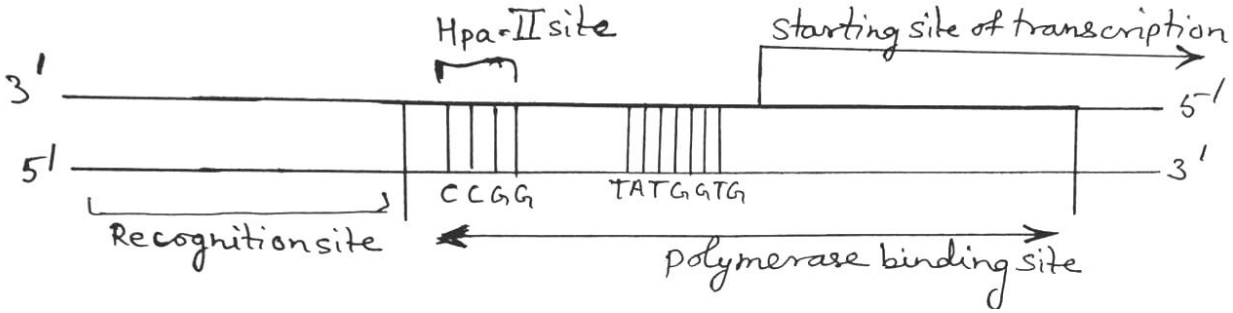


Fig: Diagram of *E.coli* promoter gene

According to Pribnow (1975) proposed that the promoter region has 3 site are as

(a) ***A recognition sequence*** : The recognition sequence is outside the polymerase binding site. The RNA polymerase first binds to DNA by forming a complex with the recognition sequence. It then binds with the binding sequence to produce the pre-initition complex.

(b) ***The binding sequence*** : The binding site consist of a sequence of seven bases. It never differs by more than two bases from the following sequence 5' T A T Pu A T G 3'.

(c) ***RNA initiation site*** : The start of m-RNA transcription take place on one of two bases near the binding sequence. In lac operon there is a overlapping of promoter and operator site. At least a part of the operator sequence appears in the polymerase binding site sequences.

(iv)Regulator gene : The regulator gene is present near the promoter gene. In lac operon regulator gene is composed of 12 - 15 nucleotide. It produce repressor protein consist of 4 subunit, each is of 40,000 daltons and has 347 amino acid residues.

The regulator gene synthesis a protein which may be an active repressor or an inactive repressor (apo-repressor). In inducible system the active repressor bind to the operator gene and unable the structural gene to transcribe m-RNA. If inducer (e.g. Lactose) is present then the repressor will bind to inducer and form inducer-repressor complex and the repressor will undergoes a conformational change which make it inactive and cannot bind to the operator gene and hence structure gene synthesize protein.

In repressible system the repressor protein formed by the regulator gene is inactive i.e. apo-repressor and does not block operator and hence structural gene synthesize protein. The repressor is activated by the presence of a co-repressor and the repressor-co-repressor complex bind to operator gene and hence no protein synthesize.

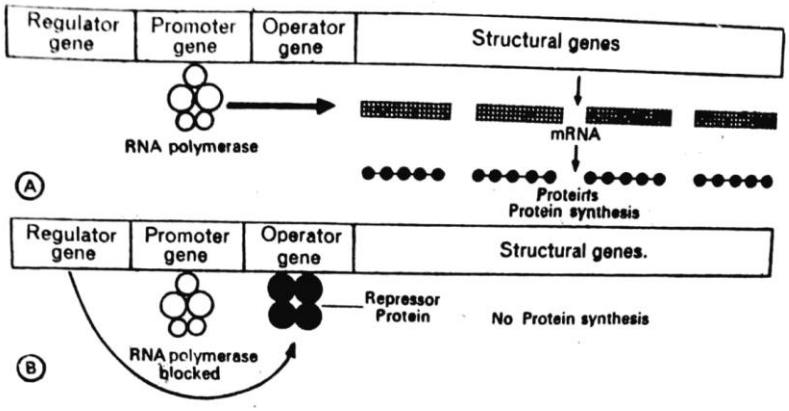


Fig : Promoter gene

(A) Binding of RNA polymerase to promoter gene. RNA polymerase moves along the structural gene catalyzing synthesis of proteins.

(B)Repressor protein formed by the regulatory gene binds to the operator gene. Movement of RNA polymerase is blocked, and hence no protein synthesis take place.

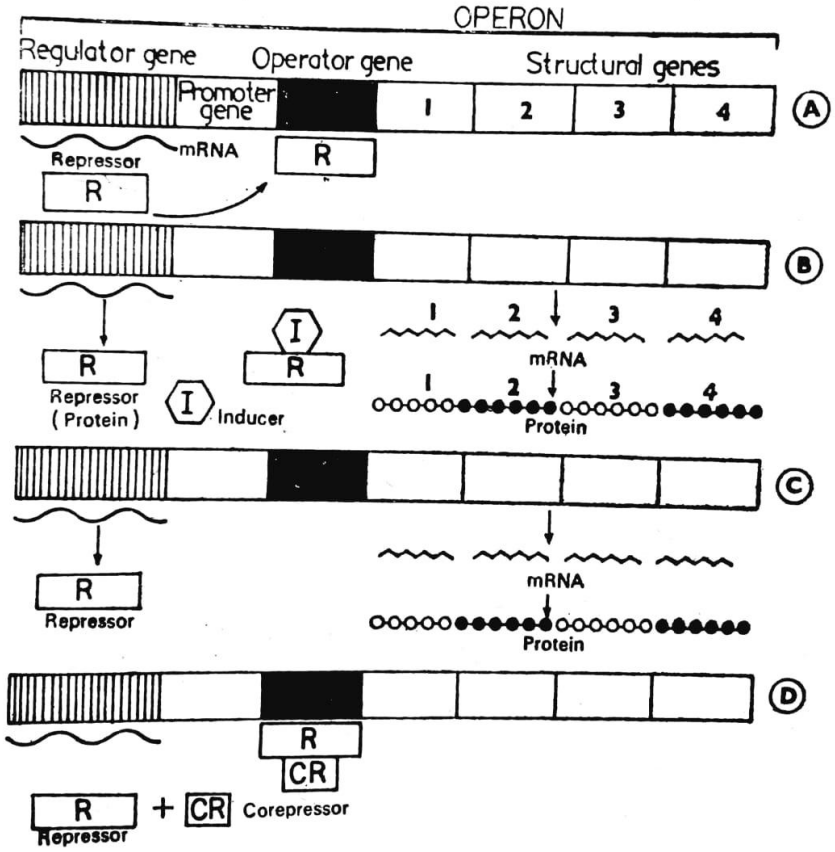


Fig : Regulation of protein synthesis

(A)Inducible system, inducer absent

(B)Inducible system, inducer present

(C)Repressible system, co-repressor absent

(D)Repressible system, co-repressor present

Inducible & Repressible system

In *E.coli* there is an enzyme β-galactosidase which is responsible for the hydrolysis of lactose into glucose and galactose

$$\text{Lactose} \xrightarrow{\beta\text{-galactosidase}} \text{glucose} + \text{galactose}$$

If β-galactosidase is not supplied externally to *E. coli* cells. The presence of β-galactosidase in *E. coli* is not found (hardly detectable) but as soon as lactose added the production of enzyme β-galactosidase is greatly increased as much as 10,000 time. If the quantity of substrate (lactose) is removed then production of β-galactosidase enzyme quantity fall down very quickly as the substrate is removed. Such enzyme whose synthesis can be induce by adding the substrate are known as inducible enzyme and genetic system responsible for the synthesis of such an enzyme are known as "**Inducible**

System".

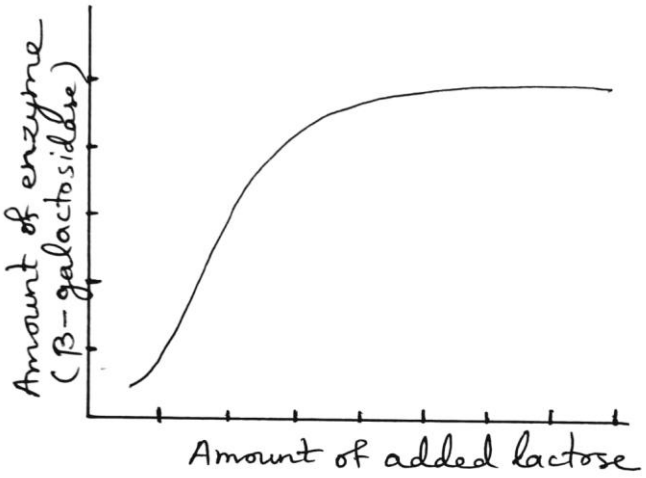


Fig : Induction of β-galactosidase enzyme by Lactose

In repressible the case is reverse where there is no amino acid are supplied from outside. *E. coli* can synthesize all the enzyme needed for synthesis of different amino acids. However if a particular amino acid like histidine is added, production of histidine synthesizing enzyme will fall down. In such a system the addition of end product of a biosynthetic pathway will check synthesis of the enzyme needed for its biosynthesis such enzyme whose synthesis can be checked by adding end product are known as repressible enzyme and these genetic system would be known as "**Repressible systems"**.

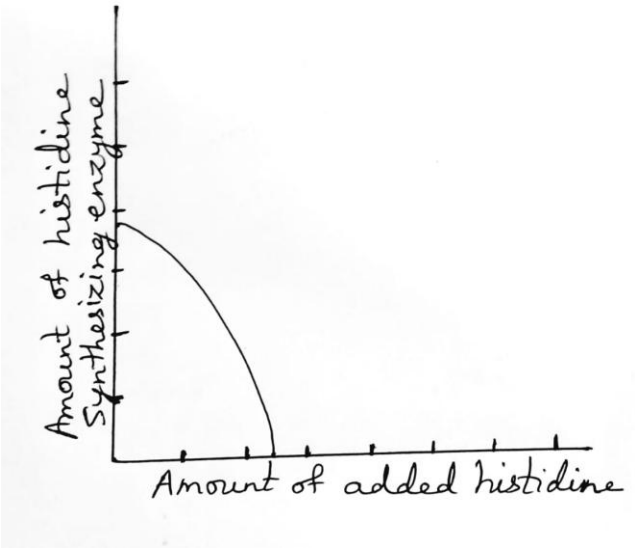


Fig : Repression of histidine synthesis enzyme by histidine

The Induction is characteristic of catabolic or degraded pathway. Repression is characteristic of anabolic or biosynthetic pathway.

8.4 Trp operon- model and regulation

Trp or tryptophan operon is a type of repressible operon. In tryptophan operon the repressor initially becomes inactive and in presence of effector it become active and repress the operon. Trp operon consists of Trp promoter followed by operator. The operator is followed by leader sequence and leader

sequence is followed by structural gene. The structural gene consist of 5 structural genes for four enzymes involved in tryptophan biosynthesis are kept under the single promoter. It is present in many bacteria but firstly it was studies in *E.coli*. It is first repressible operon to be discovered. The five enzymes and there gene are as follows.

- Anthranilate Synthase - Trp E
- Anthranilate phosporibosyl transferase – Trp D
- Phosphoribosyl anthranilate isomerase and indole 3 glycerol p synthase - Trp F + Trp C
- Tryptophan Synthase B subunit - Trp B
- Tryptophan Synthase A subunit - Trp A

The following step involve in synthesis of tryptophan

Chorismate

↓ *Anthranilate synthase* (trpE/trp G)

Anthranilate

↓ *Anthranilate phosphoribosyl tranferase* (trpD)

N-(5'Phosphoribosyl)- anthranilate

↓ *Phosphoribosyl-anthranilate isomerase* (trp F)

1-(o – carboxyphenylamino-1-deoxyribulose 5-phospahte

↓ *Indoleglycerol phosphate synthase* (trp C)

Indole 3 –glycerol phosphate

↓ *Tryptophan synthase* (trpA/trp B)

L-Tryptophan

It has repressor called as Trp R encoded by another gene having its own promoter. The repressor is continuously produced in inactive form so can't bind on operator to stop expression in absence of tryptophan but in presence of tryptophan (co-repressor) it get activated and repress the transcription.

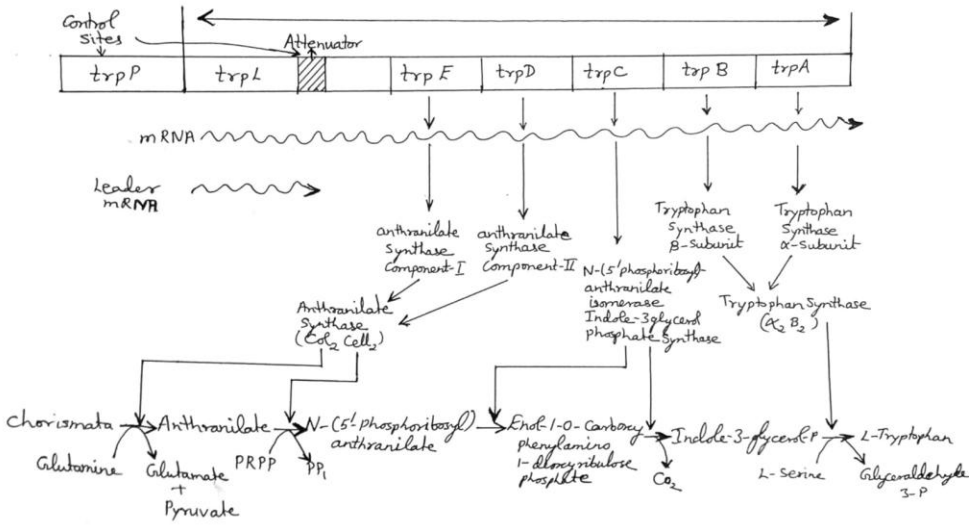


Figure 19 Fig : Trp operon- model

Trp operon is regulated by two mechanisms

(1)Repression

(2)Attenuation

(1)Repression : In the absence of tryptophan, Trp operon is on/ expressing. In this condition trp repressor is in inactive form, as it requires a co-repressor for activation like complex enzyme called apo-repressor. If tryptophan is present above the threshold amount it act as co-repressor and interact with apo-repressor to activate it. Active repressor binds on operator and repress the operon. In order to completely repress, then another mechanism can be adopted i.e. Attenuation. **(2)Attenuation :** Attenuation is done by leader sequence present between operator and first structural gene trp E. The length of leader sequence consists of 162 base pair. The leader sequence has four regions. Region 1, Region 2, Region 3 & Region 4. The region 1 has ribosome binding site followed by start codon, it has two trp codon (codon No. 10 & codon No. 11). The region 4 is followed by poly AAAAAA. There is stop codon in region 2. There are around 14 codons between start and stop codon.

In tryptophan starvation condition RNA polymerase bind on promoter and start the transcription as it transcribe the RBS and start site. When RNA polymerase is transcribing the region 1 ribosome get assemble on the RBS and start the translation from the region 1. When it translate the region 1 at a same time RNA polymerase is transcribing the region 3. If tryptophan is absent then charged t-RNA for trp also absent. Ribosome get arrested on the trp codon i.e. 10 and 11 codons in region one. So 2^{nd} region form base pairing with the region 3^{rd}, when there is arrest in translation. Transcription remain continue and RNA polymerase transcribe the operon, Such loop between 2 and 3 region is called antiterminator loop. When antiterminator loop is formed complete operon is transcribe by RNA polymerase to produce one mature 5 cistron containing mRNA. Structural genes have their own RBA for translation on upstream of start codon.

8.5 Translational and post-translational regulations

Translation is a process in which nucleotide sequence in mRNA is converted into the sequence of amino acids. It is more complex as compared to replication and transcription because in this the information from nucleotide sequence is converted into amino acid sequence and amino acids and nucleotides don't show complementary binding. So amino acids must attach to a specific adapter molecule that is capable of directly interacting with and recognizing the three nucleotide long coding units of the mRNA. Translation is one of the most conserved and highly energetic processes among all. Around 80% of the total energy of cell used for translation. Translation process is explained by Crick by its two hypothesis.

(1)Messenger hypothesis : Crick proposed that an RNA molecule forms as a complementaryRNA or mRNA, then travel from the nucleus to the cytoplasm, where it serves as an informational sequence of codons. Each codon consists of three consecutive nucleotides and different codons encode particular amino acids. Thus the mRNA sequence determines the ordered sequence of amino acids in a polypeptide chain, which is built by the ribosome.

(2)Adapter hypothesis : According to Crick that there must be an adapter molecule that can both bind a specific amino acid and recognize a specific sequence of nucleotides. He proposed that this recognition function occurs because the adaptor molecule contains an anticodon complementary to the codon in the mRNA. He envisioned such adapters as molecules with two regions, one serving the binding function and other serving the recognition function. In due course, such adapter molecules were found, they are known as t-RNA. Each t-RNA recognizes a specific codon in the mRNA and simultaneously carries the specific amino acid corresponding to that codon.

In Eukaryotes translation occur in cytoplasm i.e. either in cytosol or on rough endoplasmic reticulum

membrane. In prokaryotes all the m RNA are translated in cytosol on free ribosome.

Post-translational regulations : Transcriptional regulation is the means by which a cell regulates the conversion of DNA to RNA. A single gene can be regulated in a range of ways, from altering the number of copies of RNA that are transcribed to the temporal control of when the gene is transcribed. This control allows the cell or organism to respond to a variety of intra and extra cellular signals and thus mount a response. Some examples of this include producing the mRNA that encode enzymes to adopt a change in a food source, producing the gene products involved in cell cycle specific activities and producing the gene products responsible for cellular differentiation in multicellular eukaryotes.

The post translation regulation refers to the control of the levels of active protein. It is performed either by means of reversible events i.e. post translation modification or by mean of irreversible events i.e. proteolysis.

Post translation modification : There are some enzymatic covalent modification done on side chains of amino acids or N, C terminus proteins after protein synthesis called as post translation modifications. Generally these modifications are done on serine, Threonine, tyrosine side chain hydroxyl group, acidic side chains of Asp & Glu, Amine side chain of Arg, Lys. Thiol side chain of Cys, imidazole side chain of His, rarely on amine side chain of a Asn and methionine side chain also act as modification site.

The post translational modifications are determined by mass spectrometry, eastern blotting, western blotting etc. The following are the important steps involved in post translation modification in prokaryotes

(1) Deformylation and proteolytic cleavage : In prokaryotes Nascent proteins have N formyl methionine on N terminus. In bacteria deformylase enzyme remove formyl group from methionine. This methionine is cleaved by amino peptidase.

(2) Protein folding : Synthesized protein is in secondary structure which depend on the amino acid sequence in protein. In ribosome protein exit tunnel only alpha helices structure can be formed. 3D structure of protein depend on the interaction of amino acids in proteins with environment i.e. folding of protein is hydrophobicity driven spontaneous process.

Some proteins called chaperons or chaperonins assist the protein folding of unfolded proteins. Most of the chaperons belong to the class called HSPs (heat shock protein). They are ubiquitous. The HSPs are synthesized continuously but their amount increases in stress condition. Chaperones are recruited to protein exit channel by some ribosome large subunit protein to carry out proper folding of protein. Chaperones are of two types chaperonin and chaperones.

(a) *Chaperonin* : Bacterial chaperonins are present in cytosol of prokaryotes and in eukaryotes in mitochondria and chloroplast, nucleus etc. They create the supra-molecular machinery which maintains microenvironment for protein folding by using ATP hydrolysis. They are of two types i.e. group I and group II chaperonin.

Group I chaperonins are present in bacteria and organelles of endosymbiotic origin like mitochondria and chloroplast. It is group I chaperonin it assist protein folding by using ATPase energy source. In bacteria it consists of GroEL forming drug like structure by two rings placed on each other. Each ring is made up of 7 subunit and GroEs (7 subunit lead on GroEL drum like structure).

(b) *Chaperones* : These are proteins which assist in protein folding. They occur in almost all cells. They use ATP as sources of energy for assisting protein folding. The HSP70 is well studied chaperone. In bacteria Hsp70 act as chaperone but it is activated by co-chaperone called HSP40 by increasing the rate of ATP consumption. They act as Adenine exchange factor.

(3) Acylation : The most common modification on protein is addition of fatty acid chain or

hydrophobic chain. Mainly for protein targeting on membrane. It occurs in eukaryotes and bacteria also. Depending on the chain length acylations are of various types like Acetylation, Mristylation farnysylation, palmitylation.

In acetylation addition of two carbon acyl chain on N-terminus of protein or on amino group of lysine. It is co-translation or post translation modification. In Mristylation, farnysylation, palmitylation type of acylations lead to formation of lipid anchored proteins. Here one of the above group is transferred to the cytosolic proteins to anchor them in membrane.

(4) Glycosylation: It is co-translational or post translational modification to form glycoproteins. It occurs mainly in secretory proteins. Mainly glycol part present on extracellular side of membrane or secretory proteins. Glycosylation is of 2 types, N linked or O linked glycosylation. N linked occurs in endoplasmic reticulum and Golgi body and O linked occur in golgi body and cytoplasm. The main function of glycosylation is

- To reduce protein density
- To protect protein from protease
- For quality control of protein folding
- It provides antigenicity of protein
- They are required for cell interaction

(5) Phosphorylation : Phosphorylation is post translational modification by kinase enzyme. The phosphate donor is ATP and for removal of phosphate there is need of phospatase. It is regulatory event. Phosphorylation occur on side chain of Tyr, Ser, Thr, His (two component system) Asp (P type of pump). Phosphorylation on protein can activate the protein or inactivate the protein.

(6) Proteolytic cleavage : It is found both in bacteria and eukaryotes. In eukaryotes it occurs in either vesicle, cytosol or even outside the cell. The regulatory role i.e. irreversible type of regulation so proteins are produced in inactive form having signal peptide in them called as proprotein or preproprotein, if require further proteolytic cleavage than removal of signal peptide like preproinsulin. The proteolytic cleavage is for irreversible activation of some enzyme like zymogen/proprotein into active protein.

(7) Methylaition : It has regulatory role like histone methylation on lysine or Arginine. It leads to conversion of euchromatin or heterochromatin. Methylation also occurs on DNA.

(8) Sumolyation : Small ubiquitin like Modifier (SUMO) protein of 97 aa addition on the target. It is involved in proteins stability, cytosolic protein transport, transcriptional regulation and protein localization.

(9) Gamma carboxylation : Most of the coagulation proteins are gamma carboxylated by gamma carboxylase enzyme on glutamic acid. Gamma carboxylase enzyme requires Vit K as co-enzyme.

(10) Polyubiquitination : It is the addition of multiple Ub protein on target protein. Ubiquitin is 76 amino acid small proteins. It is required for controlled degradation of protein which either mis-folded or non functional. After half life of proteins such proteins are degraded in controlled manner by two ways like lysosome mediate degradation i.e. by autophagy mechanism.

8.6 Summary

In this unit you will study about overviews of transcriptional regulation. You will also study about Lac operon- model and regulation in very detailed manner. You will also study about Trp operon-

model and regulation in very detailed manner. This unit also contains translational and post-translational regulations in very detailed manner.

SAQs 1.

Complete the following sentences by inserting appropriate words in the blanks.

(i)In both prokaryotes and eukaryotes cells, the synthesis of protein chains is initiated with

---

(ii)Transcription in eukaryotes is initiated when ---------- is present

(iii)Lac operon is example of ----------.

(iv)Which operon is anabolic ----------

8.7 Terminal Question

Q1. Explain Inducible & Repressible system in *Ecoli.*

Q2. Explain the Trp or tryptophan operon

Q3. Explain thetranslation.

8.8 Answers

SAQ 1 (i)Methionine

(ii)RNA polymerase

(iii) Both positive and negative regulation

(iv)Trp operon

Terminal Question

Ans 1.

In *E.coli* there is an enzyme β-galactosidase which is responsible for the hydrolysis of lactose into glucose and galactose

$$\text{Lactose} \xrightarrow{\beta\text{-galactosidase}} \text{glucose} + \text{galactose}$$

If β-galactosidase is not supplied externally to *E. coli* cells. The presence of β-galactosidase in *E. coli* is not found (hardly detectable) but as soon as lactose added the production of enzyme β-galactosidase is greatly increased as much as 10,000 time. If the quantity of substrate (lactose) is removed then production of β-galactosidase enzyme quantity fall down very quickly as the substrate is removed. Such enzyme whose synthesis can be induce by adding the substrate are known as inducible enzyme and genetic system responsible for the synthesis of such an enzyme are known as "**Inducible System**".

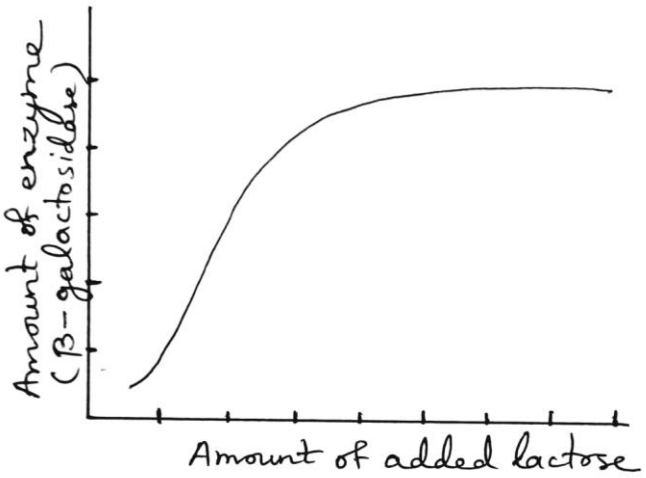


Fig : Induction of β-galactosidase enzyme by Lactose

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Ans 2.

Trp or tryptophan operon is a type of repressible operon. In tryptophan operon the repressor initially becomes inactive and in presence of effector it become active and repress the operon. Trp operon consists of Trp promoter followed by operator. The operator is followed by leader sequence and leader sequence is followed by structural gene. The structural gene consist of 5 structural genes for four enzymes involved in tryptophan biosynthesis are kept under the single promoter. It is present in many bacteria but firstly it was studies in *E.coli*. It is first repressible operon to be discovered. The five enzymes and there gene are as follows.

- Anthranilate Synthase - Trp E
- Anthranilate phosporibosyl transferase – Trp D

- Phosphoribosyl anthranilate isomerase and indole 3 glycerol p synthase - Trp F + Trp C
- Tryptophan Synthase B subunit - Trp B
- Tryptophan Synthase A subunit - Trp A

The following step involve in synthesis of tryptophan

Chorismate

Anthranilate synthase (trpE/trp G)

Anthranilate

Anthranilate phosphoribosyl tranferase (trpD)

N-(5'Phosphoribosyl)- anthranilate

Phosphoribosyl-anthranilate isomerase (trp F)

1-(o – carboxyphenylamino-1-deoxyribulose 5-phospahte

Indoleglycerol phosphate synthase (trp C)

Indole 3 –glycerol phosphate

Tryptophan synthase (trpA/trp B)

L-Tryptophan

Ans 3.

Translation is a process in which nucleotide sequence in mRNA is converted into the sequence of amino acids. It is more complex as compared to replication and transcription because in this the information from nucleotide sequence is converted into amino acid sequence and amino acids and nucleotides don't show complementary binding. So amino acids must attach to a specific adapter molecule that is capable of directly interacting with and recognizing the three nucleotide long coding units of the mRNA. Translation is one of the most conserved and highly energetic processes among all. Around 80% of the total energy of cell used for translation. Translation process is explained by Crick by its two hypothesis.

(1) Messenger hypothesis : Crick proposed that an RNA molecule forms as a complementaryRNA or mRNA, then travel from the nucleus to the cytoplasm, where it serves as an informational sequence of codons. Each codon consists of three consecutive nucleotides and different codons encode particular amino acids. Thus the mRNA sequence determines the ordered sequence of amino acids in a polypeptide chain, which is built by the ribosome.

(2) Adapter hypothesis : According to Crick that there must be an adapter molecule that can both bind a specific amino acid and recognize a specific sequence of nucleotides. He proposed that this recognition function occurs because the adaptor molecule contains an anticodon complementary to the codon in the mRNA. He envisioned such adapters as molecules with two regions, one serving the binding function and other serving the recognition function. In due course, such adapter molecules were found, they are known as t-RNA. Each t-RNA recognizes a specific codon in the mRNA and simultaneously carries the specific amino acid corresponding to that codon.

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Unit 9 : Origin of Life

9.1 Introduction

The origin of life on Earth has long captivated our collective imagination, igniting a burning curiosity that spans across the vast tapestry of human history. This profound enigma has enthralled scientists, philosophers, and scholars alike, each seeking to unravel the secrets of our genesis that have remained shrouded in the mists of time. As our understanding of the early Earth, its chemistry, and the intricate tapestry of biological processes have evolved, so too has the kaleidoscope of theories that endeavor to illuminate the mystery of how life first began. In this chapter, we embark on a captivating odyssey, delving into the depths of this alluring enigma and exploring the myriad of perspectives that have shaped our understanding of the origins of life.

Our journey commences with an examination of the early concepts and theories of the origin of life, venturing back through the annals of history to the dawn of human civilization. From the ancient cosmologies of the East and West to the epoch-making insights of luminaries like Aristotle, Avicenna, and Paracelsus, the early theories on the genesis of life offer a fascinating glimpse into the intellectual and cultural landscape of the past. These nascent ideas, though often shrouded in myth and allegory, laid the foundation for the development of a systematic and rigorous approach to the study of the origins of life.

As we traverse the historical narrative, we arrive at the modern concept of the origin of life—a vista shaped by the scientific revolution and the rapid advances in knowledge that have transformed our understanding of the natural world. Building upon the foundations laid by their predecessors, visionaries like Aleksandr Oparin, J.B.S. Haldane, and others have proposed groundbreaking theories that seek to explain the emergence of life through the lens of chemistry, geology, and biology. Through their pioneering work, we glimpse the intricate dance of molecules, elements, and forces that have given birth to the miraculous phenomenon we call life.

Our odyssey through the enigma of life's genesis brings us to the groundbreaking experiments of Stanley Miller. These monumental studies, conducted in the 1950s, provided the first empirical evidence that the essential building blocks of life could form spontaneously under the conditions thought to have been present on the early Earth. Miller's experiments marked a watershed moment in the history of science, unveiling a tantalizing clue in the search for the origins of life and inspiring generations of researchers to follow in his footsteps.

Finally, we conclude our journey with an overview of the compelling evidence in favor of organic evolution, which has emerged from a multitude of scientific disciplines over the past century

and a half. From the awe-inspiring fossil record that chronicles the ancient history of life on Earth to the intricate genetic code that underpins the functioning of all living organisms, the evidence in support of the idea that life has evolved over time is both diverse and powerful. This wealth of evidence not only deepens our understanding of the processes that have shaped the history of life on our planet but also offers a tantalizing glimpse into the broader principles that govern the emergence and evolution of living systems across the cosmos.

In this chapter, I invite you to join me on a captivating odyssey through the enigmatic world of life's origins, exploring the myriad perspectives, theories, and discoveries that have shaped our understanding of this profound mystery. As we delve into the depths of this alluring enigma, we hope to ignite your curiosity and inspire you to seek your own path in the timeless quest for the genesis of life.

Objectives

After studying this unit, you will be able to know-

- Early concepts of theories
- Modern Concept of the Origin of Life
- Evidences in Favour of Organic Evaluation
- Molecular Biology and Genetics

9.2 Early concepts of theories

The search for understanding the origin of life has been a central quest for human civilizations throughout history. From early mythologies to philosophical inquiries, various cultures from the East and the West have proposed explanations for how life began. In this expanded section, we will examine the early concepts and theories about the origin of life from ancient civilizations, including those in Greece, China, India, Mesopotamia, and the Americas. We will explore the contributions of individual philosophers and the approximate timelines associated with their ideas.

- Ancient Greek Theories

In ancient Greece, several prominent philosophers proposed theories about the origin of life. These theories focused on the roles of natural elements and the emergence of life from non-living matter.

Figure 20:Aristotle

a. Anaximander (610-546 BCE): Anaximander, a pre-Socratic philosopher, proposed that life originated from a primordial substance called the "apeiron," which he described as infinite, eternal, and ageless. He believed that the first living creatures were born in water and then moved to dry land as they evolved.

b. Empedocles (490-430 BCE): Empedocles, another pre-Socratic philosopher, theorized that life emerged from the combination of the four classical elements: earth, air, fire, and water. He suggested that these elements were brought together by two forces: love, which attracted the elements, and strife, which separated them. According to Empedocles, living creatures were initially formed from various combinations of these elements and then evolved through natural selection.

c. Aristotle (384-322 BCE): Aristotle, one of the most influential philosophers in Western thought, supported the concept of spontaneous generation. He believed that life could arise from non-living matter under certain conditions, such as the presence of warmth and moisture. Aristotle also introduced the concept of the "scala naturae" or "Great Chain of Being," which organized living organisms into a

hierarchy based on their complexity and perceived perfection.

- Ancient Chinese Theories

Ancient Chinese thinkers also developed their own ideas about the origin of life, often influenced by their cultural and religious beliefs.

a. Fu Xi (Mythical Figure, Approx. 2900 BCE): Fu Xi is a legendary figure in Chinese mythology who is often credited with creating humanity. According to the myth, Fu Xi and his sister Nuwa molded the first humans from clay and infused them with life.

b. Taoist Philosophy (Approx. 6th Century BCE): In Taoist philosophy, the concept of the "Tao" or "the Way" represents the natural order of the universe. Taoists believe that life emerged spontaneously from the Tao as a result of the interactions between the opposing forces of Yin and Yang. This idea shares similarities with the concept of spontaneous generation found in other civilizations.

- **Ancient Indian Theories**

The ancient Indian civilization, with its rich tapestry of religious, philosophical, and scientific traditions, has produced numerous theories about the origin of life. Many of these theories are intertwined with religious texts and philosophical beliefs, offering intriguing insights into the Indian understanding of the cosmos and the genesis of life.

a. Hindu Creation Myths (Approx. 1500-500 BCE)- Hindu creation myths, found in sacred texts such as the Rigveda, the Upanishads, and the Puranas, offer diverse accounts of the universe's creation and the emergence of life. These narratives are steeped in symbolism and allegory, reflecting the complexity and richness of the Hindu tradition.

i. Creation by Brahma

In one prominent Hindu creation myth, the universe and all life within it are created by the god Brahma, who is often depicted as the creator in the Hindu trinity (Trimurti), alongside Vishnu, the preserver, and Shiva, the destroyer. According to this account, Brahma creates living beings either from his own body or through the power of his mind.

In some versions of the myth, Brahma splits himself into two halves, male and female, to create the first man, Manu, and the first woman, Shatarupa. This act of self-division allows for the genesis of life and the propagation of all living beings. The Puranas, a collection of ancient Indian texts, describe how Brahma creates various life forms, including animals, plants, and humans, and assigns them their respective duties and roles in the cosmic order.

Figure 21: Vishnu Within the Cosmic Egg,19th century Pahari style painting

ii. Hiranyagarbha: The Cosmic Egg

Another Hindu creation myth revolves around the concept of Hiranyagarbha, the cosmic egg or the golden womb. According to this myth, before the universe came into existence, there was only a vast, undifferentiated expanse of water. From this primordial chaos, the cosmic egg emerged, containing the seed of all life and the potential for the creation of the universe.

The cosmic egg, which is sometimes equated with the god Brahma or the supreme being, is said to have floated on the primordial waters for a thousand years before it broke open, releasing the various elements and life forms that would eventually give rise to the universe as we know it. In this version of the myth, the creation of life is an organic process, with the universe

and its inhabitants emerging from a common source.

The Hindu creation myths, with their intricate symbolism and allegorical narratives, offer a unique window into the ancient Indian understanding of the cosmos and the origins of life. While these myths may not align with modern scientific theories, they provide valuable insights into the cultural, religious, and philosophical traditions that have shaped Indian thought and worldview for millennia.

b. Jainism (Approx. 6th Century BCE): Jainism, an ancient Indian religion, teaches that the universe is eternal and uncreated, with life and matter existing in a cycle of creation and destruction. According to Jain beliefs, life exists in various forms throughout the universe, and the soul is eternal, passing through countless cyclesof birth, death, and rebirth. Jainism rejects the idea of a creator deity and instead emphasizes the importance of individual spiritual development and the natural processes governing the universe.

c. Buddhist Philosophy (Approx. 6th-5th Century BCE): Buddhism, another ancient Indian religion, posits that the universe undergoes infinite cycles of creation, preservation, and destruction. Life is seen as a product of dependent origination, a process in which phenomena arise in dependence upon other phenomena. This concept extends to the origin of life, suggesting that living beings emerge through the complex interplay of various conditions and causes.

- ## Mesopotamian Creation Myths

In ancient Mesopotamia, various creation myths were developed to explain the origin of life, often centered around the actions of powerful deities.

a. Sumerian Creation Myths (Approx. 3000-2000 BCE): In Sumerian mythology, the universe was created by the gods An (heaven) and Ki (earth). The first humans were believed to have been fashioned from clay by the goddess Nammu and given life by the god Enki. These early humans were created to serve the gods and maintain order in the world.

b. Babylonian Creation Myth (Enuma Elish, Approx. 1800-1100 BCE): The Babylonian creation myth, known as the Enuma Elish, tells the story of the god Marduk's victory over the primordial sea goddess Tiamat. After defeating Tiamat, Marduk used her body to create the heavens and the earth. He then created humanity from the blood of another slain god, Kingu, to serve the gods and maintain the cosmic order.

- ## Mesoamerican and Andean Creation Myths

The civilizations of Mesoamerica and the Andes also developed their own unique creation myths, reflecting their distinct cultural and religious beliefs.

a. Maya Creation Myth (Popol Vuh, Approx. 2000 BCE - 1500 CE): The Maya civilization's creation myth, as recounted in the Popol Vuh, describes the gods Kukulkan and Tepeu creating the world and its inhabitants. The first attempts at creating humans were unsuccessful, resulting in animals and other imperfect beings. Finally, the gods created humans from maize dough, giving rise to the first true humans who were capable of worshiping the gods.

b. Inca Creation Myth (Approx. 1200-1533 CE): According to Inca mythology, the god Viracocha emerged from the waters of Lake Titicaca and created the sun, the moon, the stars, and the first humans. These early humans were made of stone, but Viracocha later created a new generation of humans from clay. He then breathed life into them, providing them with the knowledge and skills necessary to build a great civilization.

In summary, throughout human history, various civilizations have grappled with the question of the origin of life. Early concepts and theories often centered around the actions of gods or supernatural

forces, as well as the emergence of life from non-living matter. Although these early ideas differed significantly in their details and cultural contexts, they all represent humanity's enduring fascination with understanding the origins of life and the natural world.

- **Christian Perspective: The Bible**

The Christian perspective on the origin of life is primarily based on the accounts in the Bible, particularly the Book of Genesis, which is shared by both Judaism and Christianity. According to the Genesis creation narrative, God created the world and everything in it, including life, in six days.

a. Creation of life (Approx. 1400-400 BCE): On the third day, God created vegetation, including plants and trees. On the fifth day, God created living creatures in the waters, as well as birds that fly in the sky. On the sixth day, God created land animals, and finally, human beings. According to the Bible, God created the first man, Adam, from the dust of the ground and breathed life into him, and later created the first woman, Eve, from one of Adam's ribs. There are various interpretations of the Genesis creation narrative among Christians. Some take the account as a literal description of events, while others view it as a symbolic or allegorical representation of the origins of life. Many Christians also seek to reconcile their faith with scientific theories, such as the Big Bang and evolution, by viewing these natural processes as the means through which God created the universe and life on Earth.

- **Islamic Perspective: The Quran**

The Islamic perspective on the origin of life is based on the teachings of the Quran, the holy book of Islam, which is believed to be the word of God as revealed to the Prophet Muhammad. The Quran contains numerous references to the creation of life and the natural world, emphasizing that all living beings were created by Allah, the one and only God.

a. Creation of life (Approx. 610-632 CE): The Quran teaches that Allah created everything in the universe, including the Earth and all living beings. In several verses, the Quran describes the creation of life as a gradual process, with the Earth initially being in a state of chaos before Allah shaped and organized it into its current form. The creation of human life is also described in the Quran, which states that Allah created the first human, Adam, from clay and then breathed life into him. Islamic scholars have offered various interpretations of the Quran's teachings on the origin of life. Some emphasize the divine nature of the creation process, while others seek to understand the Quran's teachings in light of scientific knowledge. Many Muslims accept the idea of evolution as a natural process guided by Allah, but maintain that the creation of human beings was a direct and unique act of divine intervention.

9.3 Modern Concept of the Origin of Life

The modern understanding of the origin of life has been shaped by numerous scientific discoveries and theories that have emerged over the last few centuries. Advances in fields such as biology, chemistry, geology, and astronomy have allowed us to explore the early conditions on Earth and develop hypotheses about how life may have arisen. In this expanded section, we will examine the key theories and scientists who have contributed to our current understanding of the origin of life. We will explore their ideas in chronological order, providing the scientist's name and the approximate timeline associated with their work.

- **Panspermia Hypothesis**

The panspermia hypothesis posits that life on Earth may have originated from extraterrestrial sources, with organic molecules or primitive life forms being transported through space via meteorites, comets, or other celestial bodies. This hypothesis suggests that the building blocks of life or even simple life forms may have formed elsewhere in the universe and subsequently arrived on Earth, where they

evolved into more complex organisms. We will explore the historical context, key proponents, and supporting evidence for the panspermia hypothesis in the following subsections.

a. Svante Arrhenius (1859-1927): The Swedish scientist Svante Arrhenius was one of the earliest proponents of the panspermia hypothesis. In 1903, he proposed the concept of "radiopanspermia," suggesting that microscopic spores containing the seeds of life could be ejected from a planet's surface and travel through space on radiation pressure. These spores could then land on another planet, giving rise to new life forms. Arrhenius believed that the pressure exerted by sunlight on these spores would be sufficient to propel them across vast distances in space, potentially allowing them to seed life on other planets.

b. Fred Hoyle (1915-2001) and Chandra Wickramasinghe (born 1939): British astronomer Sir Fred Hoyle and Sri Lankan mathematician and astrobiologist Chandra Wickramasinghe further developed the panspermia hypothesis in the 1970s and 1980s. They proposed that life could be seeded through the transport of complex organic molecules, such as amino acids and other biomolecules, on comets and meteorites. Hoyle and Wickramasinghe also suggested that life on Earth could have been influenced by the continuous influx of these extraterrestrial organic molecules, potentially contributing to the diversification of life and even the emergence of new species.

c. Supporting Evidence for Panspermia: Several lines of evidence support the panspermia hypothesis, although it remains a subject of ongoing debate among scientists. Some of the key findings that have lent credence to the hypothesis include:

- Detection of organic molecules in space: Astronomers have discovered complex organic molecules, such as amino acids, in meteorites and within interstellar dust clouds. This suggests that the building blocks of life can form in extraterrestrial environments and could potentially seed life on other planets.
- Resilience of microorganisms in extreme conditions: Some microorganisms, such as bacteria and tardigrades, can survive extreme conditions, including radiation, desiccation, and freezing temperatures. This raises the possibility that simple life forms could potentially survive the harsh conditions of space and interplanetary travel.
- Viability of microorganisms on meteorites: Laboratory experiments have shown that certain microorganisms can survive and even reproduce when attached to meteorite samples. This supports the idea that life could potentially hitchhike on celestial bodies and spread across the cosmos.
- Potential for panspermia in the solar system: The discovery of water ice on Mars, Europa (a moon of Jupiter), and Enceladus (a moon of Saturn) has fueled speculation that life may have emerged in these environments and could potentially be transported within our solar system through panspermia.

While the panspermia hypothesis offers a fascinating perspective on the origin of life, it is essential to note that it does not provide an explanation for how life initially formed in the universe. Instead, it addresses the possibility that life or the building blocks of life might have been transported across space, seeding life on Earth and potentially other planets. Further research and discoveries are required to fully understand the extent to which panspermia may have contributed to the origin and evolution of life on Earth.

- **Primordial Soup Theory**

The primordial soup theory suggests that life on Earth began in a "soup" of organic molecules, with the building blocks of life assembling spontaneously in the presence of an energy source. This theory proposes that the early Earth's environment provided the necessary conditions for simple organic compounds to combine and form more complex molecules, eventually leading to the emergence of the first living organisms. In the following subsections, we will discuss the key proponents of this theory and the main ideas behind the concept of the primordial soup.

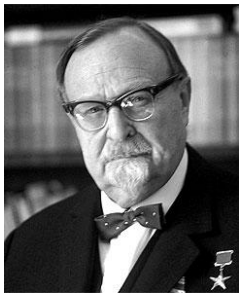


Figure 22: Alexander Ivanovich Oparin

a. Aleksandr Oparin (1894-1980) and J.B.S. Haldane (1892-1964): In the 1920s, Russian biochemist Aleksandr Oparin and British scientist J.B.S. Haldane independently proposed the idea that life may have originated in a "primordial soup" of organic molecules. They suggested that the early Earth's atmosphere and oceans contained a rich mixture of simple organic compounds, such as methane, ammonia, and water vapor, which could combine to form moreJ.B.S. Haldane complex molecules in the presence of an energy source like sunlight, heat, or lightning.

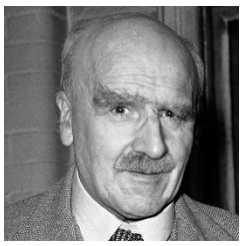


Figure23:J.B.S. Haldane

b. Key Ideas Behind the Primordial Soup Theory: Oparin and Haldane's primordial soup theory is based on several key ideas that describe how the building blocks of life could have formed and assembled under the conditions present on the early Earth:

- Reducing Atmosphere: The primordial soup theory assumes that the early Earth's atmosphere was reducing, meaning it contained little or no oxygen but was rich in hydrogen and other gases like methane and ammonia. In such an atmosphere, simple organic molecules could form spontaneously from inorganic precursors, providing the raw materials for more complex molecules.
- Energy Sources: The presence of energy sources, such as ultraviolet radiation from the Sun, heat from volcanic activity, or electrical discharges from lightning, would have been necessary to drive the chemical reactions that formed complex organic molecules from simpler precursors.
- Concentration and Assembly of Molecules: As organic molecules formed and accumulated in the early Earth's oceans, they would have been exposed to various environmental factors, such as evaporation, precipitation, and tidal processes. These processes could concentrate the organic molecules and promote their assembly into more complex structures, such as the formation of polymers from monomers.
- Emergence of the First Living Organisms: Over time, the continued formation and assembly of complex organic molecules could have given rise to the first living organisms. These primitive life forms would have been simple, self-replicating structures capable of evolving and adapting to their environment, eventually leading to the development of more complex and diverse life forms.

c. Experimental Evidence for the Primordial Soup Theory: The Miller-Urey experiments, conducted in the 1950s, provided the first experimental evidence in support of the primordial soup theory. These experiments demonstrated that a mixture of simple organic molecules could form spontaneously under simulated early Earth conditions, including amino acids, which are the building blocks of proteins. Since then, numerous other experiments have been conducted to explore the formation of organic molecules under various conditions, further supporting the idea that the building blocks of life could have originated spontaneously in the early Earth's environment.

In conclusion, the primordial soup theory offers a compelling explanation for the origin of life on Earth, suggesting that the building blocks of life could have formed spontaneously under the conditions present on the early Earth and assembled into the first living organisms. This theory has been supported by experimental evidence, such as the Miller-Urey experiments, and has laid the foundation for the field of prebiotic chemistry, which investigates the chemical processes that may have led to the emergence of life.

- ## Hydrothermal Vent Hypothesis

The hydrothermal vent hypothesis proposes that life began in the extreme conditions found in deep-sea hydrothermal vents, where high pressures, temperatures, and chemical gradients could have facilitated the formation of organic molecules.

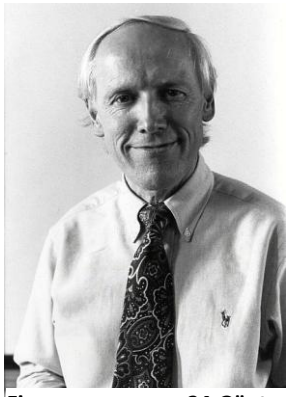


Figure 24:Günter Wächtershäuser

a. Günter Wächtershäuser (b. 1938): In the 1980s, German chemist Günter Wächtershäuser proposed the idea that life may have originated at hydrothermal vents on the ocean floor. These vents release hot, mineral-rich fluids that create unique chemical environments with the potential to support the formation and evolution of organic molecules. Wächtershäuser's hypothesis emphasizes the role of inorganic surfaces, such as iron-sulfur minerals, as catalysts for chemical reactions leading to the synthesis of complex organic molecules.

b. Michael J. Russell (b. 1944): Building on Wächtershäuser's work, British geochemist Michael J. Russell has further developed the hydrothermal vent hypothesis by focusing on alkaline vents. These vents emit fluids with high concentrations of hydrogen and other chemicals that could have provided the energy and building blocks necessary for the formation of organic molecules and the emergence of primitive cells.

- ## RNA World Hypothesis

The RNA world hypothesis posits that RNA molecules played a central role in the early stages of life, serving as both genetic material and catalysts for chemical reactions.

a. Carl Woese (1928-2012), Francis Crick (1916-2004), and Leslie Orgel (1927-2007): In the 1960s and 1970s, American microbiologist Carl Woese, British molecular biologist Francis Crick, and British chemist Leslie Orgel independently proposed the idea of an "RNA world." They suggested that, before the emergence of DNA and proteins, RNA molecules could have served as both the genetic material and as catalysts for essential biochemical reactions. This hypothesis is based on the discovery that RNA can store genetic information, catalyze chemical reactions, and self-replicate, making it a plausible candidate for the first self-replicating molecule.

b. Thomas Cech (b. 1947) and Sidney Altman (b. 1939): The RNA world hypothesis gained significant support in the 1980s when Thomas Cech and Sidney Altman independently discovered the catalytic properties of RNA molecules, known as ribozymes. Their work demonstrated that RNA could not only store genetic information but also facilitate chemical reactions, further supporting the idea that RNA played a critical role in the early stages of life.

- ## Clay Mineral Hypothesis

The clay mineral hypothesis suggests that clay minerals played a crucial role in the origin of life by providing a suitable surface for the assembly and replication of organic molecules.

a. A. Graham Cairns-Smith (1931-2016): In the 1960s, Scottish chemist A. Graham Cairns-Smith proposed the clay mineral hypothesis, which posits that clay minerals acted as templates for the

formation and replication of organic molecules. Clay minerals, such as montmorillonite, have unique properties that can promote the adsorption and concentration of organic molecules, as well as facilitate their polymerization and replication. Cairns-Smith's hypothesis suggests that these processes could have eventually led to the emergence of more complex molecules, such as RNA, and the first living cells.

- ## Lipid World Hypothesis

The lipid world hypothesis proposes that life originated with the spontaneous formation of lipid-based structures, such as micelles or vesicles, which provided a protected environment for the assembly and evolution of organic molecules.

a. David Deamer (b. 1939) and Jack Szostak (b. 1952): American biochemists David Deamer and Jack Szostak have been influential proponents of the lipid world hypothesis. They have conducted extensive research on the role of lipids in the formation of cell-like structures, demonstrating that fatty acids can spontaneously form micelles, vesicles, and other membrane-bound compartments. These lipid-based structures could have provided a stable environment for the assembly and evolution of organic molecules, ultimately leading to the emergence of the first living cells.

- ## Metabolism-First Hypothesis

The metabolism-first hypothesis emphasizes the role of simple metabolic processes in the origin of life, suggesting that life began with the emergence of self-sustaining chemical reactions that generated energy and organic molecules.

a. Harold Morowitz (1927-2016) and Robert Shapiro (1935-2011): American biophysicist Harold Morowitz and chemist Robert Shapiro were early proponents of the metabolism-first hypothesis. They argued that life could have originated from simple metabolic processes driven by geochemical energy sources, such as hydrothermal vents or volcanic activity. According to this hypothesis, the first living systems were networks of chemical reactions that generated energy and produced organic molecules, eventually leading to the emergence of more complex molecules, such as RNA or DNA, and the first cells.

In summary, the modern concept of the origin of life encompasses a diverse array of theories and hypotheses, each focusing on different aspects of the processes that may have led to the emergence of life on Earth. While no single theory has been universally accepted, the ongoing research and discoveries in fields such as biology, chemistry, geology, and astronomy continue to deepen our understanding of the complex and fascinating story of life's origins.

- ## Miller's Experiments

The Miller-Urey experiments, conducted by American chemists Stanley Miller and Harold Urey in the 1950s, were groundbreaking investigations into the potential for organic molecules to form under the conditions thought to be present on the early Earth. These experiments not only provided evidence in support of the primordial soup theory but also laid the foundation for the field of prebiotic chemistry. In this expanded section, we will examine the Miller-Urey experiments in detail, as well as related studies and their implications for our understanding of the origin of life. We will break this discussion into different sections, focusing on the historical context, the experiments themselves, subsequent research, and the broader impact of these studies on the scientific community.

- ## Historical Context

In the early 20th century, the primordial soup theory, proposed by Aleksandr Oparin and J.B.S. Haldane, posited that life on Earth began in a "soup" of organic molecules that formed spontaneously in the presence of an energy source. However, experimental evidence for this theory was lacking until the

landmark Miller-Urey experiments.

- **Miller-Urey Experiments**

a. Stanley Miller (1930-2007) and Harold Urey (18931981): In 1952, Stanley Miller, a graduate student at the University of Chicago, began working under the supervision of Harold Urey, a Nobel Prize-winning chemist. Together, they designed a series of experiments to investigate the possibility of organic molecule formation under conditions simulating those of the early Earth.

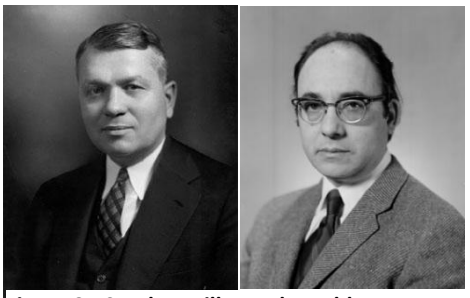


Figure 25:Stanley Miller andHarold Urey

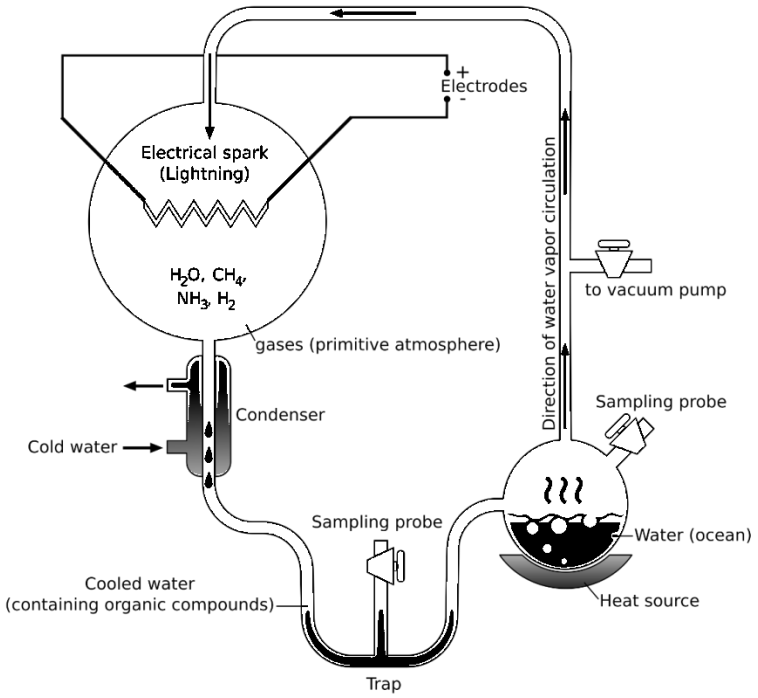


Figure 26: Miller-Urey experiment

b. Experimental Setup: Miller's experimental apparatus consisted of a closed system containing a mixture of water, methane, ammonia, and hydrogen, which was thought to represent the composition of the early Earth's atmosphere and oceans. The system included a flask containing water, representing the primordial ocean, and another flask filled with the gases, simulating the atmosphere. The gases were exposed to an electric discharge, simulating lightning, while the water was heated to create evaporation and condensation, mimicking the Earth's water cycle.

c. Results: After running the experiment for a week, Miller observed the formation of a variety of organic compounds, including amino acids, which are the building blocks of proteins. These results provided the first experimental evidence that the basic building blocks of life could form spontaneously under the conditions believed to be present on the early Earth.

- **Subsequent Research and Modifications**

Following the Miller-Urey experiments, numerous scientists have conducted related studies to further investigate the potential for organic molecule formation under various conditions and using different starting materials.

a. Alternate Gas Mixtures: Researchers have tested different gas mixtures to simulate various early Earth atmospheric compositions. Some of these experiments have demonstrated that organic molecules can form even in the presence of less reducing atmospheres, including those containing carbon dioxide and nitrogen.

b. Additional Energy Sources: In addition to electrical discharge, other energy sources have been explored in prebiotic chemistry experiments, such as ultraviolet radiation and high-energy particle bombardment. These studies have shown that a variety of energy sources can facilitate the formation of organic molecules under early Earth conditions.

c. Extraterrestrial Scenarios: Some researchers have conducted experiments simulating extraterrestrial environments, such as the surfaces of meteorites or icy moons, to explore the potential for organic molecule formation in these contexts. These studies have revealed the possibility that the building blocks of life could form in various extraterrestrial environments, lending support to the panspermia hypothesis.

- ## Broader Impact and Legacy

The Miller-Urey experiments and their successors have had a profound impact on the scientific community's understanding of the origin of life and the field of prebiotic chemistry.

a. Support for the Primordial Soup Theory: Miller's experiments provided the first experimental evidence in support of the primordial soup theory, demonstrating that the basic building blocks of life could form spontaneously under the conditions believed to be present on the early Earth. This lent credibility to the idea that life on Earth could have originated from simple organic molecules.

b. Emergence of Prebiotic Chemistry: The Miller-Urey experiments laid the groundwork for the field of prebiotic chemistry, which investigates the chemical processes that may have led to the formation of life's building blocks and the emergence of the first living organisms. Prebiotic chemistry has since become a multidisciplinary field, drawing on knowledge from chemistry, biology, geology, and astrophysics to explore the conditions and processes that could have given rise to life on Earth and possibly other planets.

c. Impact on Astrobiology and the Search for Extraterrestrial Life: Miller's experiments and subsequent research have also informed the field of astrobiology, which studies the potential for life elsewhere in the universe. By identifying the conditions and processes that can lead to the formation of organic molecules, scientists can better understand where to look for signs of extraterrestrial life and what biosignatures to search for in the search for life beyond Earth.

d. Ongoing Debates and Questions: While the Miller-Urey experiments and related studies have made significant contributions to our understanding of the origin of life, many questions and debates remain. For example, the precise conditions of the early Earth's atmosphere are still a topic of discussion, as are the specific processes that led to the transition from simple organic molecules to the first living cells. Nevertheless, the experiments conducted by Miller and Urey continue to inspire new research and inform our understanding of life's origins.

- ## The Role of Borosilicate Glass in Miller's Experiments

Recent research has shed new light on the significance of the materials used in the original Miller-Urey experiments, suggesting that the borosilicate glassware may have played a more important role in the formation of organic molecules than previously realized. In this section, we will explore these findings and discuss their implications for our understanding of the origin of life. Miller and Urey used borosilicate glassware in their experiments, a heat-resistant material commonly used in chemical laboratories. Although the choice of materials might have seemed incidental at the time, recent studies

have shown that the interaction between the glass and the simulated early Earth conditions may have been a crucial factor in the formation of organic molecules. A new study by Criado-Reyes et al. recreated the Miller-Urey experiments using three different setups: one with borosilicate glass flasks, one with Teflon flasks, and one with Teflon flasks containing pieces of borosilicate glass submerged in water. The results showed that far fewer organic compounds formed in the experiments using just the Teflon flasks, suggesting that the borosilicate glass played a significant role in the formation of organic molecules in the original experiments.

The researchers found that the corrosion of the borosilicate glass surface by the hot and caustic water in the experiments released silicon-dioxide molecules into the solution. This, in turn, acted as a catalyst, speeding up the chemical reactions between nitrogen, carbon, and hydrogen atoms, ultimately leading to the creation of organic molecules. Additionally, the corrosion on the glass surface formed millions of tiny pits, which could have served as microscale reaction chambers, further accelerating the formation of organic molecules. The findings of the Criado-Reyes study suggest that silicate-rich rocky surfaces, like those found on the early Earth, may have played a crucial role in the emergence of life. More than 90% of Earth's crust is composed of silicates, minerals primarily made up of silicon-dioxide. The weathering of silicate minerals by the corrosive primordial atmosphere and water may have provided the right conditions for the assembly of the first building blocks of life on our planet.

These results are consistent with the idea that the origin of life on Earth was facilitated by a combination of factors, including a reduced atmosphere, electrical storms, silicate-rich rocky surfaces, and liquid water. This new understanding of the role of borosilicate glass in the Miller-Urey experiments not only deepens our knowledge of the conditions that might have given rise to life on Earth but also provides a fresh perspective on the importance of the interactions between geological materials and the early Earth's atmosphere.

In conclusion, the Miller-Urey experiments represent a pivotal moment in the study of the origin of life, providing the first experimental evidence that organic molecules could form spontaneously under early Earth conditions. These experiments have since inspired countless related studies and have helped shape the fields of prebiotic chemistry and astrobiology. While many questions and debates about the origin of life persist, the legacy of Miller's experiments endures as a testament to the power of scientific inquiry and the potential for new discoveries to deepen our understanding of the natural world.

SAQ-

- …… a pre-Socratic philosopher, proposed that life originated from a primordial substance called the "apeiron," which he described as infinite, eternal, and ageless.
- In one prominent Hindu creation myth, the universe and all life within it are created by the god Brahma, who is often depicted as the creator in the ……(Trimurti), alongside Vishnu, the preserver, and Shiva, the destroyer.
- Brahma creates living beings either from his own body or through the …….
- Ancient Indian religion, posits that the universe undergoes infinite cycles of creation, …….
- The Islamic perspective on the origin of life is based on the ……, the holy book of Islam, which is believed to be the word of God as revealed to the Prophet Muhammad.

9.4 Evidences in Favour of Organic Evaluation

The study of organic evolution has attracted the attention and passion of countless scientists and researchers, who have sought to unravel the mysteries of life's development and diversification over time. Through their collective efforts, a wealth of evidence has been amassed, painting a complex and

fascinating picture of the evolutionary history of life on Earth. In this section, we will explore the major lines of evidence that support the theory of organic evolution, delving into the works of influential scientists and their contributions to our understanding of the natural world.

- **Fossil Record**

The fossil record serves as a window into the distant past, providing invaluable insights into the history of life on Earth. By studying fossils, scientists can reconstruct the evolutionary relationships between extinct and extant organisms, shedding light on the processes and events that have shaped the development of life over millions of years.

In the early 19th century, French naturalist Georges Cuvier pioneered the study of fossils, recognizing that the distinct layers of rock strata represented different time periods in Earth's history. Through his work, Cuvier demonstrated that many fossils belonged to species that no longer existed, providing the first evidence of extinction as a natural process.

Charles Darwin and Alfred Russel Wallace, who independently proposed the theory of evolution by natural selection in the mid-19th century, recognized the importance of the fossil record in supporting their ideas. They understood that, if their theory was correct, the fossil record should show a gradual progression of life forms, with transitional forms linking different groups of organisms. Subsequent discoveries, such as the famous "missing link" between reptiles and birds—Archaeopteryx—found in 1861, provided strong support for Darwin and Wallace's ideas.

Since then, the fossil record has continued to reveal countless transitional forms and intermediate species, highlighting the gradual and interconnected nature of the evolutionary process. For example, the discovery of numerous transitional fossils between fish and tetrapods in the late 20th and early 21st centuries has provided crucial insights into the evolutionary transition from water to land.

- **Comparative Anatomy and Embryology**

The study of comparative anatomy and embryology has long been a cornerstone of evolutionary biology, offering powerful evidence for the existence of common ancestry among diverse organisms. By examining the similarities and differences in the anatomical structures of various species, scientists can infer the evolutionary relationships between these organisms and reconstruct their shared history.

In the early 19th century, French biologist Étienne Geoffroy Saint-Hilaire was among the first to recognize the importance of comparative anatomy in the study of evolution. He observed that, despite their many differences, vertebrates shared a common anatomical plan, suggesting that they had evolved from a common ancestor. This idea was later supported by the work of Charles Darwin, who recognized the significance of these similarities as evidence for his theory of evolution by natural selection.

Embryology, the study of the development of organisms from fertilization to birth, has also provided compelling evidence for organic evolution. In the late 19th century, German biologist Ernst Haeckel proposed his "biogenetic law," which postulated that the development of an organism recapitulates its evolutionary history. Although Haeckel's law has since been revised and refined, the study of embryology has continued to yield important insights into the evolutionary relationships between organisms.

9.5 Molecular Biology and Genetics

The advent of molecular biology and genetics in the 20th century has revolutionized our understanding of the mechanisms and processes that underpin organic evolution. By comparing the genetic sequences of various species, scientists can uncover the underlying molecular basis of evolutionary relationships, providing powerful evidence for the existence of common ancestry among

living organisms.

In 1953, James Watson and Francis Crick discovered the structure of DNA, laying the foundation for our understanding of the genetic code that underpins all life on Earth. This groundbreaking discovery paved the way for the development of molecular biology and the study of the genetic basis of evolution.

In the 1960s, American biologist Emile Zuckerkandl and Austrian-born biochemist Linus Pauling pioneered the concept of the molecular clock, which uses the rate of genetic mutations to estimate the time at which two species diverged from a common ancestor. This innovative technique has since become an essential tool in the study of evolutionary relationships and the reconstruction of the tree of life.

The field of genomics, which emerged in the late 20th and early 21st centuries, has taken the study of molecular evolution to new heights. By comparing the complete genetic sequences of different organisms, scientists can uncover the detailed molecular signatures of evolutionary events, such as gene duplication, horizontal gene transfer, and the emergence of novel genetic elements.

One of the most compelling lines of evidence for organic evolution comes from the study of shared genetic traits, or "molecular homologies," among different species. For example, the conservation of certain genes, such as the homeobox (Hox) genes, which are responsible for the basic body plan in animals, suggests that these genes have been inherited from a common ancestor and have played a crucial role in the evolution of diverse life forms.

- **Biogeography**

Biogeography, the study of the distribution of species and ecosystems in geographic space and through geological time, offers important insights into the patterns and processes of organic evolution. By examining the geographic distribution of species, both extant and extinct, scientists can infer the historical events and environmental factors that have shaped the development of life on Earth.

Charles Darwin's observations of the unique fauna of the Galapagos Islands during his voyage on the HMS Beagle played a pivotal role in the development of his theory of evolution by natural selection. He noted that the animals on the islands were similar to those on the nearby South American mainland but had evolved distinct adaptations to their specific island environments. This observation led Darwin to propose that species evolve through a process of descent with modification from a common ancestor.

The study of biogeography has continued to provide compelling evidence for organic evolution. For example, the discovery of closely related species on different continents supports the theory of continental drift and the role of geographic isolation in the speciation process. Similarly, the presence of endemic species on remote oceanic islands, such as the Hawaiian honeycreepers, suggests that these organisms have evolved from a small number of ancestral colonizers through a process of adaptive radiation.

- **Coevolution and Symbiosis**

The study of coevolution and symbiosis has provided fascinating insights into the complex interrelationships between different species and the role of these interactions in shaping the course of organic evolution. Coevolution occurs when two or more species reciprocally affect each other's evolution through processes such as predator-prey interactions, competition, and mutualism.

One of the most famous examples of coevolution is the relationship between flowering plants and their pollinators, which has driven the diversification of both groups over millions of years. The intricate adaptations of plants and their pollinators, such as the long proboscis of the hawkmoth and the deep flowers of certain orchids, demonstrate the powerful role of coevolution in shaping the form and

function of living organisms.

Symbiosis, the close and long-term association between different species, can also play a crucial role in the evolution of novel traits and adaptations. For example, the endosymbiotic theory, first proposed by Russian botanist Konstantin Mereschkowski in 1905 and later developed by American biologist Lynn Margulis in the 1960s, posits that mitochondria and chloroplasts, the energy-producing organelles within eukaryotic cells, originated as free-living bacteria that were engulfed by a host cell. Over time, these symbiotic relationships became so essential that the host cell and the endosymbiont effectively merged into a single organism, giving rise to the complex eukaryotic cells that make up plants, animals, and fungi.

The study of coevolution and symbiosis has revealed the intricate web of relationships that connect the diverse tapestry of life on Earth, highlighting the dynamic interplay between species that has driven the process of organic evolution.

- **Experimental Evolution**

Experimental evolution, the study of evolutionary processes in controlled laboratory settings, provides direct evidence for the occurrence of organic evolution and the mechanisms that underpin it. By manipulating environmental conditions and observing the resulting changes in populations of organisms over multiple generations, scientists can gain valuable insights into the factors that shape the course of evolution.

One of the most famous examples of experimental evolution is the long-term evolution experiment conducted by American evolutionary biologist Richard Lenski. Since 1988, Lenski and his team have been tracking the evolution of 12 populations of Escherichia coli bacteria, observing the emergence of new traits and adaptations in response to changes in the laboratory environment. This groundbreaking study has provided a wealth of information on the molecular basis of adaptation, the dynamics of evolutionary change, and the repeatability of evolutionary trajectories.

Experimental evolution has also been used to study the evolution of multicellular organisms, such as fruit flies, yeast, and plants, as well as the evolution of complex traits, such as antibiotic resistance and cooperative behavior. These studies have not only provided direct evidence for the occurrence of organic evolution but have also helped to refine our understanding of the factors that drive evolutionary change.

In conclusion, the evidence in favor of organic evolution is diverse, encompassing a wide range of scientific disciplines and lines of inquiry. From the fossil record to molecular biology, comparative anatomy to biogeography, the study of organic evolution has yielded a wealth of insights into the processes and mechanisms that have shaped the development of life on Earth. As our understanding of these processes continues to grow, so too does our appreciation for the intricate tapestry of life and the remarkable journey of evolution that connects us all.

9.6 Summary

- Finally, we conclude our journey with an overview of the compelling evidence in favor of organic evolution, which has emerged from a multitude of scientific disciplines over the past century and a half.
- Anaximander (610-546 BCE): Anaximander, a pre-Socratic philosopher, proposed that life originated from a primordial substance called the "apeiron," which he described as infinite, eternal, and ageless.
- In one prominent Hindu creation myth, the universe and all life within it are created by the god

Brahma, who is often depicted as the creator in the Hindu trinity (Trimurti), alongside Vishnu, the preserver, and Shiva, the destroyer. According to this account, Brahma creates living beings either from his own body or through the power of his mind.

- Buddhist Philosophy (Approx. 6th-5th Century BCE): Buddhism, another ancient Indian religion, posits that the universe undergoes infinite cycles of creation, preservation, and destruction.
- The Islamic perspective on the origin of life is based on the teachings of the Quran, the holy book of Islam, which is believed to be the word of God as revealed to the Prophet Muhammad.

9.7 Terminal Questions

Q.1 Explain the early concepts of theories.

Q.2 Write in details about the modern concept of the origin of life.

Q.3 Explain the evidences in favour of organic evaluation.

Q.4 Explain the molecular biology and genetics.

9.8 Answers

SAQ-

- Anaximander (610-546 BCE
- Hindu trinity
- power of his mind
- preservation, and destruction.
- teachings of the Quran

Suggested Books

1. Deamer, D. W. (2020). *Origin of Life: What Everyone Needs to Know®*. Oxford University Press.
2. Deamer, D. W., & Szostak, J. W. (2010). *The Origins of Life: A Subject Collection from Cold Spring Harbor Perspectives in Biology*. Cold Spring Harbor Laboratory Press.
3. Egel, R., Lankenau, D.-H., & Mulkidjanian, A. Y. (2011). *Origins of life: The primal self-*

organization. Springer Science & Business Media.

4. Fry, I. (2000). *The Emergence of Life on Earth: A Historical and Scientific Overview*. Rutgers University Press.
5. Kolb, V. M. (2014). *Astrobiology: An Evolutionary Approach*. CRC Press.
6. Luisi, P. L. (2016). *The Emergence of Life: From Chemical Origins to Synthetic Biology*. Cambridge University Press.
7. Luisi, P. L., & Chiarabelli, C. (2011). *Chemical Synthetic Biology*. John Wiley & Sons.
8. Smith, E., & Morowitz, H. J. (2016). *The Origin and Nature of Life on Earth: The Emergence of the Fourth Geosphere*. Cambridge University Press.
9. Spitzer, J. (2021). *How Molecular Forces and Rotating Planets Create Life: The Emergence and Evolution of Prokaryotic Cells*. MIT Press.
10. Zubay, G. (2000). *Origins of Life: On Earth and in the Cosmos*. Elsevier.

UNIT-10Lamarckism& Darwinism

10.1 Introduction

Lamarck (1744-1829). was the greatest of French evolution who for the first time suggested a complete theory of evolution. Osborn regards him the most preminent figure between Aristotle and Darwin. He published his ideas of evolution in greater detail in Philosophie Zoologique in 1809. Evolution simply means 'change'. Herbert Spencer (1857) first used the term evolution to refer to the development of more complex forms of life (plants and animals) from simpler and earlier forms. Evolution is the term used in a variety of fields, but when we talk of evolution of organisms, the plants and animals, it is called organic evolution.

Lamarckism, a theory of evolution based on the principle that physical changes in organisms during their lifetime—such as greater development of an organ or a part through increased use— could be transmitted to their offspring. Lamarckism was proposed by Jean-Baptiste de Monet Lamarck in the year 1809, He published Philosophie Zoologique, in which he described a two part mechanism by which change was gradually introduced into the species and passed down through generations.

Charles Darwin (1809-1882) was greatest naturalist and philosopher of 18th century. He studied geography of South America, and is usually regarded as one of the eminent scientists for propounding his theory of natural selection. He read Malthus's view on population which state that population increases in geometrical ratio whereas food in arithmetical ration. A.R. Wallace (1823-1913) a naturalist, who was exploring the Malaya Archipelago, also studied the same Malthus's ideas and both (**Darwin and Wallace)** on the advice of Lyell published a joint paper in 1858. These views were later on incorporated in the book "*Origin of Species*" by natural selection or the preservation of favored races in the struggle for life.

Objectives:-

After studying this unit, you will be able to know-

- theory of evaluation of Lamarckism and Darwinism
- analysis of Lamarck theory and Neo Darwinism theory
- Weismann's germ plasm theory

10.2 Lamarckian Theory

The complete theory of evolution given by **Lamarck** is in the form of four postulates or "laws".

- The internal forces of life tend to increase the size of an organism i.e. the whole body and also the different parts upto a limit determined by life itself.
- The formation of a new organ or a part in the body is the result of a need or want which has arisen and continues to be felt by the organism.
- The development of an organ and its power of action is directly proportional to its use; continuous use strengthening the organ while disuse having reverse effect.
- All the changes which organism acquire during their life time are transmitted to their off springs by the process of inheritance. *Inherited* is the most attractive and controversial law, now known as *"Lamarckian doctrine".*

Lamarck's theory played an essential role in evolution.

a) Role of Environmental Factors- Lamarck believed that various factors like soil, food, temperature etc. causing changes of environment act directly in case of plants while indirectly in case of animals (since they possess nervous system).

b) Effects of Needs or Physical Wants- Lamarck thought that change of habits may bring about the modification of organs. These changes also create new organs.

c) Use and disuse- The continuous use of organ makes them functional while disuse makes them undeveloped.

d) Competition- There is a sort of competition in nature not to overcrowd the earth. The stronger organism try to destroy the weaker ones. The smaller multiply faster while larger slowly, thus a balance is maintained.

e) Inheritance of acquired characters- The favorable structural changes gained by every individual due to use or disuse are passed on to its offsprings, which show continuous progression (useful) or retrogression (harmful) of the characters.

f) Cross-breeding- These various peculiarities produced in the organisms, always appear in successive generations (provided breeding is confined to such unions only). As a result crosses between individuals not acquiring these peculiarities, result in the disappearance of such characters acquired in particular circumstances.

g) Isolation- The separation of various generations bring about their different features which in the course of evolution become specialized into particular species.

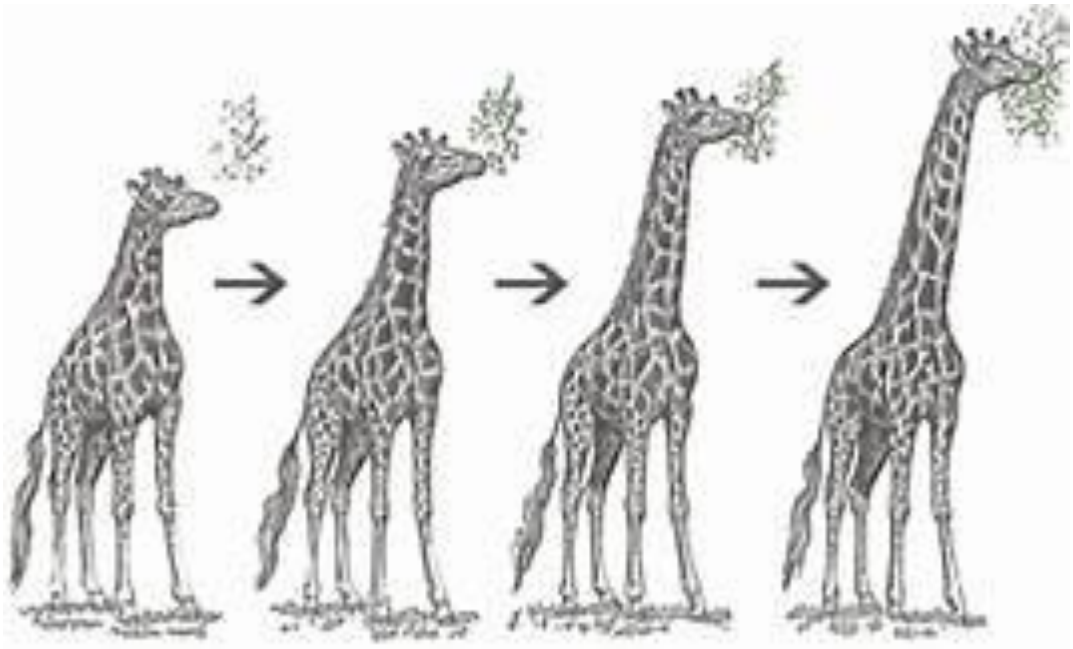


Diagram showing elongation of neck in giraffe to Lamarck

Examples used by Lamarck

Examples like Long neck of giraffe, Disappearance of limbs in snakes, Webbed feet of ducks, Blindness of moles, Flat Fishes, Flightless Birds, Retractile Claws of Carnivorous Mammals, Speed of Deer, Cave Dwellers

SAQ-1

1. Evolution cab be describe as ……..
2. Lamarck's theory of evolution is known as …….
3. Lamarck's theory published in ……..

10.3 ANALYSIS OF LAMARCK'S THEORY

First Law- The first law of Lamarck is merely the growth process of the organism with which we agree. The increase in size in living beings is common due to metabolic activities which are controlled by vital forces of life.

Second Law- This law of the development of an organ due to its need is unacceptable to the modern evolutionists. No body can believe that any organ can develop if we felt the need of its presence. It means that by simply wanting eyes on the back of head, they would develop.

Third Law- The principle of use and disuse of organs appears satisfactory and is supported by following evidences:

- A *black-smith* develops a large and strong biceps (muscles) due to his arm constantly in pounding his anvil. The continuous use of these muscles results in the strong and well developed biceps muscles of arm.
- *Snakes* have elongated body accompanied by loss of limbs. The continuous creeping through holes and crevices made limbs continuously useless for locomotion with the result that limbs become completely lost in snakes. There ancestors possess short limbs.
- The *flat fishes,* present at the bottom of sea where there is no sunlight, lead an inactive life lying on one side of the body. The eye of that side (lying towards bottom) migrated towards upper side and thus both eyes are on one side of the body. (Their larvae posses eyes on either side of the head).
- The continuous use of neck: by giraffe to catch high located fruits of desert tree caused the lengthening of its neck. This was due to continuous use of particular organ (neck) that enabled him to catch the food.

  Besides, there are other effects like *rudimentary eyes* in deep sea fishes due to disuse, vestigial organ in living animals due to disuse; claw in Carnivora; sensitive skin and tactile points on the ventral side of the body; callosities of palm in hard workers; webbed feet in swimming birds; etc., exemplifying Lamarckian theory.

Fourth Law- The transmission of acquired character is the most important principles usually termed as the *Lamarckian doctrine.* These acquired characters are hereditary or not i.e. whether any structural change induced in the body by the change in use or disuse or by a change in surrounding environment can affect the germ plasm in such a way that offspring will acquire these structural modifications or not is debatable.

10.4 Criticism of Lamarckism

The Lamarckian doctrine has been criticized very much. Followings are the main objections against the inheritance of acquired characters:

Criticism of Lamarckism: During the 1890s a revival of Lamarckian ideas became a strong component of the general upsurge in biological thought. Characteristically, the conditions and expressions of the revival varied from one country to another. Lamarck's theory was subject to severe criticism. Two scientists Cuvier and Weismann were great critics of Lamarck.

Some objections raised against Lamarckism are as follows:

If new organs were to develop in response to a new need, then man should have developed wings by now. Changes acquired during the lifetime of an organism cannot be inherited by the offspring. For example, if a man loses his arm in war, he does not produce children without an arm. According to August Weismann, somatic changes acquired during the lifetime of the organisms are non- heritable, whereas, changes in the germplasm or reproductive cells are inheritable by the offspring. Mendel's law of

inheritance also disproved Lamarck's theory.

- ***Mutilatian Experiments****:* Weismann was the main opponent of Lamarckian theory. He experimented on white mice by cutting their tails (mutilated) but their off-springs did not show any reduction of tail. He obtain 901 youngs from five (22) successive generations of mutilated parents but none of the offsprings showed vestigial tail. It means that acquired character (cut tail) was not inherited.
- **Loeb** produced artificial parthenogenesis in the sea urchin's egg with the help of chemical stimuli. Similar eggs were produced in corresponding environments in brine shrimp *Artemiasalina* but not of their generations showed acquired characters.
- **Boring** of ears and nostrils has been continued from centuries among human being but their offsprings do not show any trace of holes in ears and nostrils.

10.5 NEO-LAMARCKISM

Besides above, these are evidences which support that acquired characters are inherited from generation to generation. The category of evolutionists which support the Lamarckian doctrine of inheritance of acquired characters under the heading of neo-Lamarckians. Among the neo-Lamarckians, notable supporters are **Herbert Spencer, Eimer, Cope, Hyatt, Dall, Packard, etc.** Following are the evidences of transmission of the acquired characteristics:

(1) **F.B. Sumner** reared the white mice at 20^0C to 30^0C. He found that due to this high temperature they developed longer bodies, tail and hind feet. When these mice were bred at lower temperature their offspring showed their abnormal proportions of size.

(2) Lindsey subjected the cold blooded animals, warm blooded animals and plants to unusual environmental conditions. He saw that changes due to these conditions are transmitted to some extent in their offspring.

(3) Likewise it has been reported that when rough, non-type-specific forms of type II *pneumococci*(causing pneumonia) were exposed to the extracts of dead smooth type III *pneumococci*, the former changed into later smooth type III pneumococci.

(4) Various acquired diseases described by Brown-sequard are inherited from generation to generation. For example, *exophthalmia* was caused in parents by injuring the restiform body (in brain) with the result of protrusion of eye ball. This disease was later on inherited to the generations. The other diseases like *haematoma* and *dry gangrene* are produced (ear alternations) by injury to also the restiform body near the rib of calamus. Later these were found to be inherited.

(5) **McDougall** trained white rats to escape from a tank of water by certain route. These trained rats were mated and their offsprings in turn were taught the problem of escape. This was repeated for fourthy-four generations. He founded that there

was a marked and progressive decrease in the number of errors by white rats. These experiments were repeated by **Agar, Drummond** and **Tiegs** who obtained somewhat irregular result regarding the decrease and increase of errors.

(6) **Guyer and Smith** induced the hereditary changes in the eyes of fetuses (rabbit) by simply destroying the lens of living female with needle in situ. The anti-lens serum has been produced in the blood of these animals. These effects seem to be inherited in their generation. **Bagg and Hanson** and **Little** performed experiments of the radiation effects (by X-rays etc.) on mammalian germ cells which caused hereditable changes.

(7) **Griffith and Detlefson** recently performed the interesting experiments to prove the inheritance of acquired characters. They reared rats in cages placed on rotating tables for several months. Consequently they became adapted to the rotating condition to such an extent that when rotation was stopped they show signs of *nystagmus* (dizziness) and other physiological conditions. This condition was inherited for several generations.

10.6 Darwin's Natural Selection Theory

The idea of natural selection of very simple though its operation is highly complex and may be extremely subtle. In his monumental work, "origin of species" **Darwin** mentions the following factors for species formation by natural selection:

1. Over production (Prodigality).
2. Struggle for existence.
3. Survival of the fittest.
4. Variations under nature.
5. Species formation and natural selection.

(1) Over production (Prodigality).

The productivity of all living organism is far beyond the ultimate numbers which can possibly survive. The space and the available food supply, which these organism occupy remain the same while their quantity increases enormously i.e in geometric ratio. For example if elephant, who is the slowest breeder among mammals, is allowed to breed by a single pair at 30 years then upto 100 years of age it would produce about six young ones. **Darwin** calculated that this rate within 750 years there will be 19 milliones of descendants. Among fishes the number of eggs laid by them are enormouns e.g. about 20,000 in herrings, 6 millions in cod., 9 million in Turbot and 28 million in Ling. If all these eggs were to develop into adults them only one single species of fish would filt the entire ocean. Oyster lays about 60 million eggs, if the entire progeny survived and multiplied into grandsons then heaps of shells would be eight times the size of earth.

Huxley estimated that descendents of single green fly if all survived and

multiplied would at the end of one summer, weigh down the population of China, **Woodruff** described by his experiments on *Paramecia* the similar rate of overproduction.

All this indicates that every species of animals and plants have an extraordinary power of production and for controlling this overproductivity, there should be some efficient check. Darwin and Wallace both recognized this natural check and called it the *struggle for existence.*

2. Struggle for Existence

As a result of geometrical multiplication of individuals, the food and space become limited with the result that a struggle inevitably follows for existence. This struggle for existence may be between the individuals of the same species or different species or due to environmental factors. Consequently this is of three types.

(1) *Intraspecific Struggle:* Here strife of individuals occur within the same species. It is the most severe check of all, for each one's need are similar. Far example, in a forest, numerous young trees grow below the parent trees but only a few of them develop to maturity while most of them die or perish due to searcity of food, light and other means. The artificial lobster culture experiments have show that it is better to turn newly hatched youngs into sea rather than retaining them in aquarium, for they become *cannibalistic,* eating the weaker ones, which is the most worst type of competition.

(2) *Interspecific Struggle:* This struggle is more frequent occurring between the individuals of different species. Here one species may become food of other species. Mankind is very much concerned in the interspecific struggle. Every living form depends upon some other organisms for its food so none is exempted from this universal strife.

(3) *Extraspecific Struggle:* Third struggle is environmental in which excess of moisture, drought or heat, cold, earthquakes and volcanic eruptions play the main part. The interrelations of various organisms with these conditions are very intricate. The nature appears saying *"Thou art weighed in the balances and are found wanting."* Numerous organisms are reported to die due to these natural calamities, some times even floods take away many lives.

3. Survival of the Fittest

Due to these various struggles for existence only those individuals survive which are best fitted to new conditions of life and the least fit are the first to perish. These individuals show high selective value and in the course of time show various adaptive modifications to suit themselves in the changed conditions of life. The survival of the fittest is the result of *natural selecetion*, which enforces adaptations. For example, the *Tasmania Wolf* (Marsupial) which is confined only in Tasmania and became extinct from Australian mainland due to placental dog, the *dingo* which inhabits the mainland.

4. Variation under Nature

The fact that no two organisms or parts of the organisms are exactly alike, no matter how closely related, is a commonly observed phenomenon. It is the basic prerequisite and progressive factor for evolution because without variations, no change could occur and evolution would be impossible. Only those variations which can be inherited can take part in the evolution of species.

Darwin laid stress on variation which were *continuous and fortuitous.* They are generally *quantitative* rather than numerical variations. He observed that various useful variations are selected by individuals and thus evolution results. **Darwin** assumed variations as *axiomatic* without describing their real nature and origin in plants and animals.

5. Natural Selection and Species formation: In the course of long periods these best fitted and suitable individuals survive and become adjusted to nature. Nature being the super power, selects only those adapted organisms which become different species with the accumulation of variations. Species will differ widely from each other due to these variations which later on will acquire these suited changes.

10.7 Criticism (Objections) to the theory of Natural Selection (Darwinism)

Some of the objections which Darwin explained vaguely are the following:-

1. If species have descended as a result of *gradations* there should be innumerable *transitional stages* and the species should not be so well defined as we see them to be.
2. How natural selection can bring about characters of no use like the tail of *Giraffe* of trifling importance?
3. Whether the instincts are acquired and modified through natural selection or not?
4. How some species when crossed produce sterile offsprings whereas when varieties are crossed they produce fertile offsprings.
5. Darwin describe the survival of the fittest but not the arrival of fittest.
6. *Over- specialization* (some organs began to develop enormously in relation to size of body causing harm to individuals).
7. Degeneration of organs.
8. Artificial selection in plants and animals can never lead to definite or permaent specific variations.
9. How land animals could evolve from aquatic ones?
10. It appears somewhat absurd that variations tending in an infinitesimal degree should be preserved.

CRITERIA FOR DARWINISM (NATURAL SELECTION)

There are various aspects of natural selection theory which **Darwin** could not explain well. Some authors ask why has not the *Ostrich* acquired the power of flight? Why some animals have mental powers more developed whereas its development was advantages to all? Following are main reviews of natural selection theory:-

- Whenever **Darwin** felt the shortcomings of the selective factor he reconciled with the Lamarack principle of *use and disuse.*
- **Darwin** thought minute fluctuating variations as the principle factor for natural selection but they are mostly non-heritable. He considered *'sports'* and *saltation variations* as rare but they are frequent as we see today.
- **Darwin** believed that man could produce varieties and changed conditions hastened and stimulated variability thus formulating artificial selection ideas.
- According to **Darwin,** variations occurs in all structures and in all direction haphazardly. But we know that they occur along certain definite paths due to internal causes and thus natural selection has no value at all.
- It is inconceivable that the first, almost imperceptible variation could be of selective value. What would be the advantages of features in a bird when these were beginning to diverge from their reptilian ancestor? The mutation idea of **DeVries** can clear these obstacles.
- Origin of highly complex adaptations and co-adaptations whose effectiveness depends upon thee perfection can not be explained by natural selection. Such adaptations are electric organs of fishes and mimicry of *Kalima*. Evolution of land animals from aquatic ones can not be explained by natural selection.
- Natural selection does not explain the development of non-useful organs. If these useless characters which are sometimes quite large and prominent are independent of natural selection why do we need natural selection to explain adaptive factors. Darwin regarded them as cases of correlated variability.
- Why over-specialization occurs? *Irish elk* came to extinction due to over-specialization of size and horns far beyond the range of usefulness. Enormously overgrown and over-specialized *dinosaurs* became extinct, which natural selection is unable to explain.
- How structures became rudimentary? **Darwin** described that the first whale ancestors were handicapped by hind legs and that any decrease in size which would be enhanced by disuse will be advantageous. Why this reduction of limbs went on even in the subcutaneous part? Weismann explained them on the basis of *panmixia hypothesis.*
- Weismann's idea of all sufficiency has been criticized by the authors. Darwin was of

a different opinion. "I am convinced that natural selection has been the most important but not the exclusive means of modifications".

- It is objected that natural selection might explain the survival but not the arrival of fittest.
- Darwin dealt with the fluctuating variations which were mostly quantitative or plus or minus, whereas the differences between the species are qualitative. This is a serious objection and difficult to meet.
- Special objections are attributed to the subsidiary theory of sexual selection which involve passivity on the part of male, active choice on the part of female for more beautiful and attractive males. Such choice implies very high aesthetic powers in animals of relatively poor vision and mentality.
- Darwin did not recognize between somatic and germinal variations. He proposed pangenesis hypothesis in 1868 to explain the transmission of characters to generations which has been completely discarded,

PANGENESIS THEORY

Followings are the main points of pangenesis hypothesis:-

- All the somatic cells of the body not only multiply by cell division but also give off minute particles through their life called as gemmules which wander through the body.
- These gemmules later on are specially concentrated in the germ-cells in both sexes.
- Each germ cell is a minute replica of the parent's body and is capable of developing into the same kind of body even in minute detail.
- These gemmules are continuously produced at all stages of development.
- There is developed a sort of continuous competition in the germ cells between the original gemmules and new arrivals of gemmules.
- Sometimes certain gemmules might lie dormant for several generations and then develop bringing out in an individual its ancestral (atavistic) qualities.
- Thus according to this theory every somatic cell is a germ cell while the actual germ cells are the collection place for the germs of somatic cells. This theory has no basis at all and has been replaced by modern theory of germplasm put forward by Weismann.

SAQ-2

1. Who wrote the book Origin of species……
2. The concept of biological species was proposed by ……..
3. Analogous structure indicates ……..

10.8 Neo-Darwinism&Weismann's Germ Plasm Theory

- **Neo-Darwinism**

Since Darwin's natural selection theory there have been many researches and profound changes and likewise thetheory has been modified. These all supporters constitute Neo-Darwinians including Weismann, Mendel, DeVries etc. The following are the main recent experiments put forward to support the natural selection theory:-

- Weldon's experiments on shore crabs-Weldon experimented with the shore crabs of Plymouth-Sound which showed that as a result of changed climatic conditions natural selection produces an alteration in species by acting on minute variations as Darwin held. During demonstration of these experiments, the rate of flow of river water was slowed down by placing a large breakwater near the mouth of *Plymouth Sound*. With this slowing down of flow fine China-clay sediment settled more resulting in the death of numerous crabs of species *Carcinus maenas*.
- Cesnola's experiments with MantisCesnola tested the selective value of various colors of Mantis by fixing them on plants. Those colors which were harmonious with plants escaped while others of different colors were eaten up by birds.
- Poulton's and Sander's experiment with butterfly pupae many butterfly pupae of different color patterns were placed under the conditions favouring protective colors and other adverse. They concluded that protective coloration is a real survival factor.
- Davenport's experiments with chickens-A large number of variously tinted chickens for example black, gray, white barred etc. were allowed to wander free in fields. Most of them which were white and easily distinguishable were killed by enemies like hawks, kite etc. while others escaped due to conformity of colors with the surroundings.

- **WEISMANN'S GERM PLASM THEORY**

August Weismann (1834-1914):- was the neo-Darwinian who proposed 'germinal-selection' theory. He contended the continuity of germplasm as main criteria for inheritance of characters. All the heritable variations have their origin in germ cells and a new type of organisms arise only from changed type of germ cells. Thus this theory is in sharp contrast to Darwin's pangenesis theory, while the former is centrifugal and latter centripetal. The main points of his theory are following:-

1. Existence of Somatoplasm and Germplasm-Weis mann described that individual consists of two types of substances in its cells somatoplasm and germplasm. The somatoplasm plays no role in heredity, whereas protoplasm of the germ-cells, so called germ-plasm, is the actual vehicle of heredity.

2. Presence of Determinants-This theory supposes that there are minute complex structures situated in germ- plasm called as determinants. Each independently variable

part of organism is supposed to be represented in a germ cell by a minute physiological reproducing unit, determiner. They correspond to the so-called gemmules of Darwin's ideas. Each of the determinant is supposed to be responsible for the development of inherited feature.

3. Sub-units of Determinants Biophores-The determiners are rather complex structures which are made up of smaller units-biophores which in turn contain molecules. These control various characters in different capacities. Determiners are also grouped into units of a higher order "ids" each of which is complete in ancestral germ plasm.

4. Struggle among Determinants-There occurs a sort of struggle amongst determinants. With this, weaker deter- miner perish and only stronger ones play main part in speciation.

5. Continuity of germ plasm-According to this view germ plasm is immortal in that it is perpetuated from generation to generation through mitotic cell-division, each germ cell being the product of the division of previous germ cell. The soma looses its generalized characters and specializes in various ways.

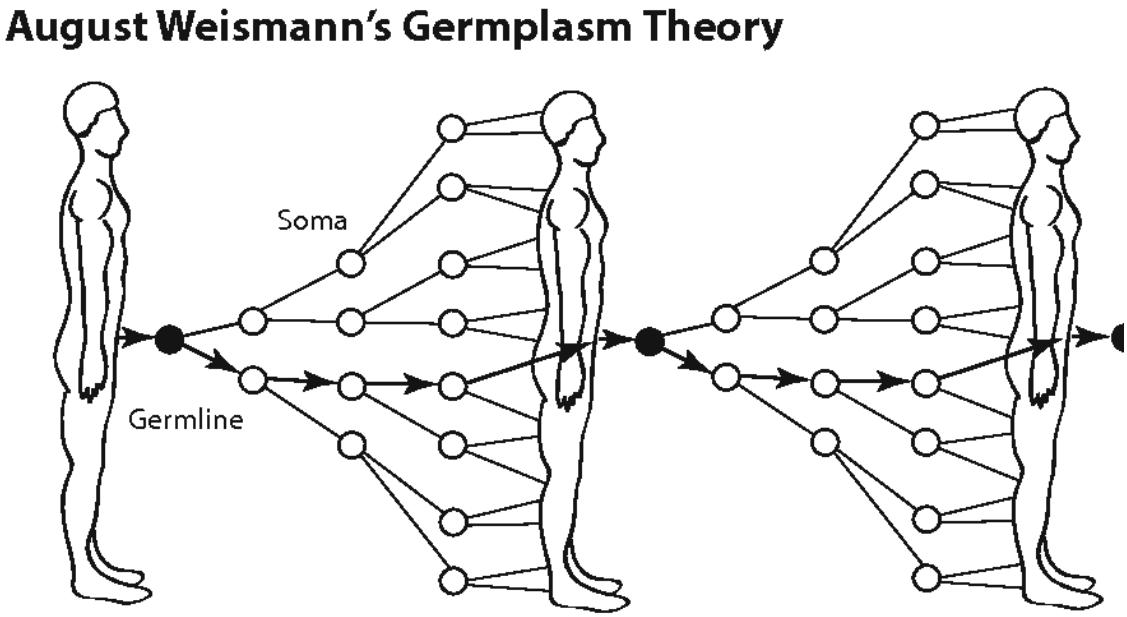
The following are objections to the germinal selection theory put forward by Weismann-

1. According to this theory there should be definite variations in particular directions

2. This theory does not imply about the constancy of species since biophores bring about rapid modifications causing changeability of species.

3. Well or ill nourished determinants may affect the organs but generally it is not so

4. There are no evidences that a struggle for existence is present between determinants as envisaged by theory.Thus Weismann's germs-plasm idea is the cornerstone of modern genetics which explained the inheritance of characters from generation to generation in a more plausible way



10.9 Summary

- Theories of organic evolution postulate that since life began on the earth it has been continuous and that later organisms have been derived from earlier forms by the inheritance of variations, either large or small, and induced either by the environment or by processes within the animals
- The term evolution refers to the development of more complex from of life from simpler or earlier forms.
- The Lamarckian theory mainly explained the inheritance of acquired characters and use and disuse of organs.
- The Darwinian theory consists of the principles such as over production, struggle for existence and survival of the fittest.
- Criticism of Lamarckism- The first proposition of the theory does not have any ground because there is novital force in organisms which increases their body parts.
- As regards the second proposition, the environment can affect the animal but it is doubtful that a new need forms new structures.
- The third proposition, the use and disuse of the organs is correct upto some extent.
- The fourth proposition regarding the inheritance of acquired characters is disputed.
- Mendel's Laws of Inheritance and Weismann's Theory of Continuity of Germplasm (1892)
- Discarded Lamarck's concept of inheritance of acquired character

10.10 Terminal Questions-

1. Describe in details Lamarckian theory.

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   …….....

2. Describe in details Darwin natural selection theory.

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3. Explain the Neo-Darwinism theory.

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4. Explain the Weismann's Germ Plasm theory.

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5. Explain the Objections to the theory of natural selection.

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Write shorts notes on

1. Analysis of Lamarck's theory

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……

……

2. Pangenesis theory

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10.11 Answer

SAQ-1

1. process of gradual adaptive changes in organism
2. inheritance of acquired characters
3. philosophic zoologique

SAQ-2

1. Charles Darwin
2. ernst mays
3. Convergent evaluation

10.12Reference

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UNIT-11Mutation

11.1 Introduction

In the previous unit of this course you learnt about Lamarckism and Darwinism. In this unit, we are going to study about different type of mutation, molecular basis of mutation. It is sole process generating new alleles; indeed by definition any change producing a new allele is called a mutation. Mutation is generally defined as a sudden change of a gene or chromosome from one form to another. It produces an alteration in the character under its control.

Objectives:-

After studying this unit you will be able to know-

- explain the different types of mutations
- explain the molecular basis of mutation
- discuss the causes of mutation
- explain the different types of mutagens

11.2 Origin of Mutation Theory

Mutations are one of the important factors that contribute to evolution, but only a few mutations silently take part in any evolutionary process. The new genetic variants give reproductive advantage to the organisms and by differential reproduction the new variants multiply in the population. Even harmful mutations can rapid evolutionary changes in the small population. The mutations which are being selected during evolution are mostly beneficial for survival of the organism but sometimes, harmful mutations can also integrate in gene pool of the population.

Mutations are alterations in the usual DNA sequence of an organism that result from the action of chemical and physical agents or due to errors of DNA replication. Once the mutation is introduced, the DNA sequence changes are made permanent by

DNA replication and are passed on to the daughter cells. Mutations are the basis of discontinuous variation in populations.

Darwin recognized two kinds of variations as the material for natural selection. These variations were mainly ever-present fluctuation (continuous) which played dominant role in species-formation. Besides, there were other discontinuous variations appearing occasionally in the generations which were termed as “sports” or “saltatory variations” or “mutations”. These sports occurred rarely and Darwin considered them of little importance.

In England, William Bateson collected large number of species showing discontinuous variations in contrast to continuous variations which Darwin termed fluctuating. Hungo De Vries (a well known Dutch Botanist) in Holland gave much importance to these discontinuous variations (sports or saltatory variations) and described that new species arise not by the accumulation of minute fluctuating variations through natural selection but by these suddenly appeared salutatory variations (mutations).

Mutagens create damage to DNA by disrupting the normal replication and genetic repair mechanisms. Some specific actions of mutagens include: **Alkylation: -** the addition of alkyl groups to bases, leading to increases in DNA mutations.

Oxidation: - the production of free radicals causes lesion formation in DNA. **Amination: -** the addition of an amine group leading to the development of precancerous and cancerous cells

In healthy individuals under normal conditions, DNA is built by adding nucleotides to the 3' ends of DNA strands. There are at least fifteen different forms of DNA polymerase that facilitate this process by performing replication, repair, and proofreading of DNA. When exposed to a mutagen, errors in DNA replication occur.

Mostly, it has been restricted to processes that result in alterations of gene contents rather than observable chromosomal changes. There are several types of mutations broadly classified on the basis of causative agents, observable phenotypes, gene products or alterations in molecular functions. Let us study about various types of mutations in detail.

11.3 Causes o f Mutations

- The cause of chromosomal aberrations may be environmental changes such as sudden lowering of temperature during germ cell cycle-Bates.
- H. J. Muller in 1926 has succeeded in producing mutations in *Drosophila* by exposing them to X-rays. But X-rays are not found in nature.
- Radium emanations and cosmic rays in nature might be the cause for mutation.

Mutations occur for various reasons, and they play a significant role in the process of evolution.

There are two primary causes of mutations

A. Many mutations that are relevant to evolution are considered “naturally-occurring”. When cell division starts, it must replicate its DNA to produce a new cell. However, this replication process is not always perfectly accurate.

B. During DNA replication, leading to changes in the DNA sequence. These changes, even if small, are referred to as mutations. These naturally occurring mutations introduce genetic diversity within a population, which can be crucial for evolutionary processes.

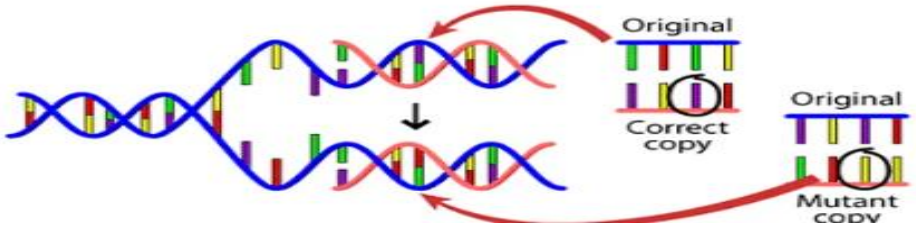


Fig:Causes of Mutations

Source: https://adpcollege.ac.in/online/attendence/classnotes/files/1589181737.pdf

- Mutations can also be induced by external factors such as exposure to specific chemicals or radiation. These external agents can cause DNA damage by breaking the DNA strands.
- Importantly, this **DNA damage is not limited to human-made sources;** natural and pristine environments. When cells attempt to repair this damage, they may not always restore the DNA to its original state accurately, resulting in mutations.
- The mutations caused by external influences can be more pronounced and potentially have greater impacts on the genetic makeup of an organism or population.

11.4 Types of Mutation

Mutations can be classified into the following types on the basis of the nature, stage of development etc

1. SOMATIC MUTATIONS

Somatic mutations occur in the somatic or vegetative cells of the organisms.

De Vries observed in Oenothera lamarkiana were somatic mutations. This type of mutation is not inherited and disappears with the death of the organisms.

The extent of phenotypic effect depends upon whether the mutation is dominant or recessive (dominant mutations generally have a greater effect).

The extent of the phenotypic effect depends upon whether it occurs early or late in development (early arising mutations have a greater effect).

Certain kinds of cancer like lung cancer, skin cancer, testicular cancer etc are the example of somatic mutation caused by certain chemicals (mutagens).

2. GERMINAL MUTATION

This type of mutation takes place in the germ cells. Mutations may be transmitted to progeny. When the mutation takes place in the gamete, it is called gametic mutation and when it takes place in the zygote, it is called zygotic mutation. It can be inherited from one generation to the other.

Dominant mutations are seen in the first generation after the mutation occurs.

If the female gamete containing an X- linked mutation is fertilized, the males will show the mutant phenotype.

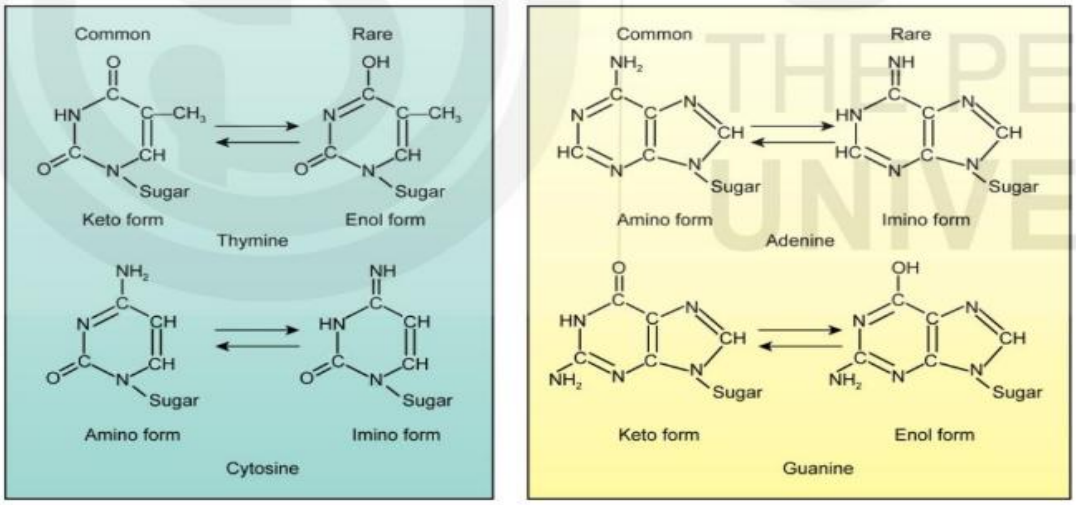
Recessive mutations will only be seen upon the chance mating with an individual carrying the recessive allele too, thus, the recessive mutation may remain hidden for many generations.

3. SPONTANEOUS MUTATION

The mutations that arise in the absence of any known mutagen treatment are called **spontaneous mutation**. The spontaneous mutations account for the "background rate" of mutation and are presumably the ultimate source of natural genetic variation that is seen in populations. For example, in bacteriophage and bacteria, spontaneous mutations inactivate gene function.

The bases in DNA can appear in one of several forms in equilibrium, called **tautomers,** which are isomers that differ in the positions of their atoms and in the bondsbetween the atoms. The imino and enol forms of the bases are rare, whereasamino and keto form of purine and pyrimidine bases respectively, are normally present in DNA. The rare tautomer of one standard base mispairs with the existing base on the alternate strand and result in a mutation in the next round of DNA replication.

Spontaneous mutation takes place naturally without any obvious cause. The appearance of a white-eyed male Drosophila during the culture of wild types by Morgan is a classical example of spontaneous mutation. Such mutation leads towards evolution.



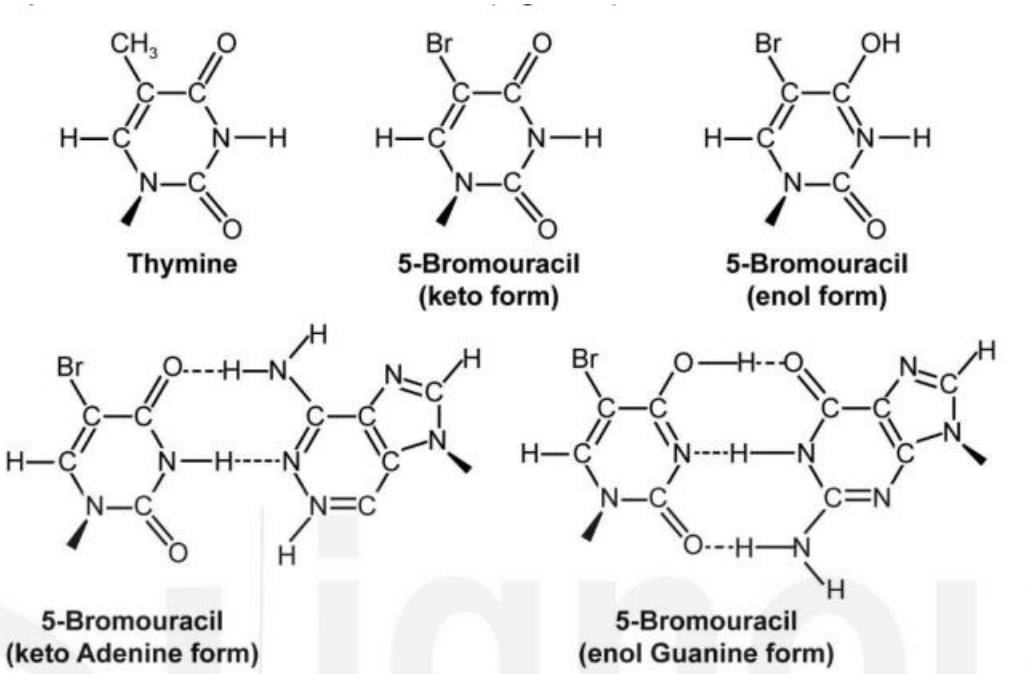
4. INDUCED MUTATION

Induced mutation was first produced in Drosophila with the help of X-ray by T.H. Muller in 1927. The mutations arising after treatment with certain compounds or exposure to environmental agents that increase the rate of mutations are called induced mutation.

There are several categories among induced mutations based on effects or effectors of mutations. Those substances, which mimic the normal nitrogenous bases, gets incorporated into DNA occasionally in place of normal bases, are called base analogs. These analogs have pairing properties like those of normal bases but cause incorrect nucleotides to be inserted opposite them in replication and causing anomalies in the genetic sequence that affect DNA replication and transcription of genes and produce mutations.

For example, 5-bromouracil (5-BU) is an analog of thymine that can pair with

either adenine or guanine, hence affecting base pairing during DNA replication, which leads to mutations.



It is possible to induce mutation by applying artificial means. The artificial agent which causes mutations is called mutagens or mutagenic agents. Many of such mutagens are known among which X-rays, ultra violet rays, radium are, heat, temperatures etc. Some chemicals like mustard gas, peroxides, colchicines, formaldehyde, coaltar, dimethyl sulphate, etc. These mutagens interact directly with the DNA and after the structure of individual nucleotides. Some mutagens work in a different way and cause serious physical distortions in the DNA which block DNA replication or transcription.

5. BIOCHEMICAL MUTATION

Mutations which affect specific biochemical processes is called biochemical mutation such mutation inhibits this ability of an organism to synthesize essential materials like the vitamins and enzymes. This inhibition may be total or partial. In partial inhibition, there is a partial blockage in the step of the synthetic processes. The alkaptonuria and phenylketonuria are the well known disease caused due to biochemical mutation. These are a type of metabolic errors and are recessive mutations.

6. LETHAL MUTATION

Sometimes mutations become lethal. They cause loss or alteration of a function during embryogenesis. Most of the biochemical mutations are lethal.

11.5 Molecular basis of mutations

Genes are made up of a segment of DNA at a specific locus on a chromosome having specific base sequence. The DNA molecule can be damaged and ultimately mutated by chemical mutagens, radiations, ultraviolet light and alkylation. Mutations involve alterations of the DNA sequence which include substitution or addition or deletions of one or more bases.

Change in hereditary material is called mutation and hence a permanent alteration of a base pair or a few base pairs in the DNA molecule takes place Alternation of a single base pair is called point mutation or gene mutation.

When heritable alterations occur in a very small segment of DNA molecule, i.e., a single nucleotide or nucleotide pair, then this type of mutations are called **"point mutations".**

DNA is composed of a lengthy sequence of smaller units joined together. **There are four fundamental types of units:** A,T,G and C which stand for adenine, thymine, guanine and cytosine, respectively. DNA is composed of four bases carrying genetic informations and its two strands are complementary and carry equivalent information. Adenine (A) in one strand always pairs with thymine (T) and cytosine (C) pairs with guanine (G).

The arrangement or sequence of these bases serves as the code. Different sections of DNA have different roles: some regulate the activation of genes, some have no known function, and some have functions. Other portions of DNA are genes, which carry the instructions for producing proteins. Proteins are long chains of amino acids and play a crucial role in constructing and maintaining an organism.

- **DNA that codes for proteins** can be divided into codons, which are sets of three bases. Each codon specifies either an amino acids or signals the termination of the protein. Codons are identified by the specific bases. For example "GCA" stands for guanine, cytosine, and adenine. Cellular machinery utilizes these instructions to create a string of corresponding amino acids, with one amino-acid corresponding to each group of three bases. For instance, the **'GCA"** codon corresponds to the manner; "**Stop"** codons indicate the conclusion of the newly formed protein.
- Substitution is a mutation where one base in swapped for another, essentially changing a single "Chemical letter." For instance, it could involve switching an A to a G in the DNA sequence.
- Alter a codon to encode a different amino acid, resulting in a minor change in the protein produced. An example is sickle cell anemia, caused by a substitution in the beta-hemoglobin gene, which changes a single amino acid in the resulting protein.
- Change a codon to one that still codes for the same amino acid, causing no impact on the protein. These are known as silent mutations.
- Convert an amino-acid-coding codon into a "**stop" codon.** Leading to an incomplete protein, this can have significant consequences, as the incomplete protein likely won't function properly.

Common example of gene mutation

Morgan began study of the evolution of the fruitfly. He bred one pair of flies for several generations and got thousands of individuals amongst which he found a white eyed male

fly while the typical colour of the eye is red. He crossed it with red eyed female and got all red eyed. Individuals in F, generation. But when F, males and females were interbred, he found 3/4th individuals with red eyes and 1/4th with white eyes-(3:1 ratio of F, mono hydrid cross) Hence this white eyed condition is due to a change in one gene for eye colour from dominant to recessive state. The white eye condition is a recessive character. Not long after he found another fly having yellow body colour instead of grey colour. It is also due to a change in another body colour gene. It was also inherited in the same manner as white eye character. In this way he discovered over three thousand different mutants in one species. There were other mutations which caused changes in physiology of the individual. Some of which resulted in the death of the fly i. e. lethal mutations. All these mutations are caused due to a change in a single gene. Gene mutations have now been found in a large number of plants and animals and their hereditary behavior was like that of Drosophila. According to Mendel all gene mutations are inherited. Some mutations are dominant, some recessive and some intermediate (a new condition in between old and new appears in F1 generation. Polydactylism in man is also a gene mutation resulted in some ancestor and appeared after some generations in an individual.

Effects of Point Mutations

Type	**Description**	**Example**	**Effect**
Silent	mutated codon codes for the same amino acid	CAA (glutamine) → CAG (glutamine)	None
Missense	mutated codon codes for a different amino acid	CAA (glutamine) → CCA (proline)	Variable
Nonsense	mutated codon is a premature stop codon	CAA (glutamine) → UAA (stop)usually	serious

Point mutations include changes that occur at specific sites in genes. These changes may be due to inaccurate replication of DNA caused by internal, natural or chemical factors.

Point mutations include the following:

A. Base pair substitution mutations.

B. Frame-shift mutations.

Base Pair Substitution Mutations:- Point mutation may be involve base substitution by replacement of base or alteration of base. This takes place by insertion or deletion of one or more bases from the DNA sequence.

A. Transition: A mutation due to substitution of a purine by anotherpurine or a pyramidine in a polynucleotide chain is called transition.

Transition may be caused by

a). Tautomerization,

b).Deamination,

c). Base analogs

In other words transition is a change when a purine replaces a purine

(A G) or a pyrimidine replaces a pyrimidine (A G).

B. Transversion: A mutation due to substitutions of a purine by apyrimidine or pyrimidine for a purine in a polynucleotide chain in calledtransversion.Transversion involves change where a purine base is replaced by apyrimidine bae or vico versa.

Transversion is caused by the following ways:

a). Depurination, b). Alkylating agent.

These types of mutations alter codon. The altered codon may code for adifferent amino acid and change property of protein. The effect may be seen inaltered phenotype which in turn changes the property of the protein.

Frame Shift Mutation

A mutation by the addition or deletion of a single nucleotide or multiplenucleotides (other than three) which lead to shift in reading frame ofDNA in a gene is called frame shift mutation.Acridine dyes have been shown to cause deletion or insertion of a single basepair. Acridine dye (e.g. 5-amino acridine) intercalate between two adjacentpurines which change the gap between the nucleotide from 3.4 A° to 6.8A°. Inthis change, during DNA replication either a base is inserted or deleted whichleads to frame shift mutations.

CHROMOSOME MUTATION:-

Chromosome mutation, where segments of chromosomes, whole chromosomes, or entire sets of chromosomes change. Mutations due to changes in the whole set of chromosome, are called chromosomal mutations It resulted in important changes in bodily characters. It is common in plants and some animals and appears to be a cause of a new species. Polyploidy (doubling of chromosome number in species) is an important factor for evolution (production of new)

Chromosome mutations or gross mutations are alterations in the structure and number of chromosomes. In this case a segment of chromosome may get lost (deficiency or deletion) or “read” twice at replication (duplication). The normal gene sequence may be altered due to the exchange of sections between two or more non homologous chromosomes section, reversing the liner order of genes in that part (inversion). It is following types:

- **Deletions:**

These involve the loss of a portion of DNA sequence. The amount of DNA lost

varies to great extent. Deletions can be as small as a single base. But in some cases it may be much larger or even the entire length of the gene sequence causing lethal effect. Deletions have been often associated with the development of abnormalities in animals as well as humans. Deficiencies in heterozygous state have led to may congenital disorders in man like myeloid leukemia and retinoblastoma.

- **Insertions:**

In this type, there is an addition or insertion of one or more nucleotides (bases) usually from another part of a chromosome Like deletion, the amount of base inserted may be one, two or even much larger.

- **Rearrangements:**

These mutations involve segments of DNA sequence within or outside a gene exchanging position with each other. For example, in inversion mutations, a portion of DNA sequence is excised (cut) and then reinserted at the same position but in the opposite direction i.e. a rotation of 180°.

Chromosomal mutations are involved in major alterations to gene sequences and so they have a serious effect on the encoded portion and are frequently associated with a mutant phenotype.

Changes in number of chromosomes:

1. **Euploidy**

- It involves the loss, orgain, of whole chromosome set the term euploidy (Gr.,eu=evenortrue;ploid=unit) designates genomes containing chromosomes that are multiples of some basic number (x).
- Euploids are those organisms which contain balanced set or sets of chromosomes in any number. The number of chromosomes in a basic set is called the monoploid number, Those euploid types whose number of sets is greater than two are called polyploid.
- Thus, 1x is monoploid, 2x is diploid; and the polyploid types are 3x (triploid), 4x (tetraploid), 5x (pentaploid), 6x (hexaploid) and so on.
- Mutation due to Euploidy refers to the state of having a chromosome number that is an exact multiple of a basic chromosome set. This means the number of chromosome sets is increased in euploidy.

Polyploidy

Addition of one or more sets of chromosomes.

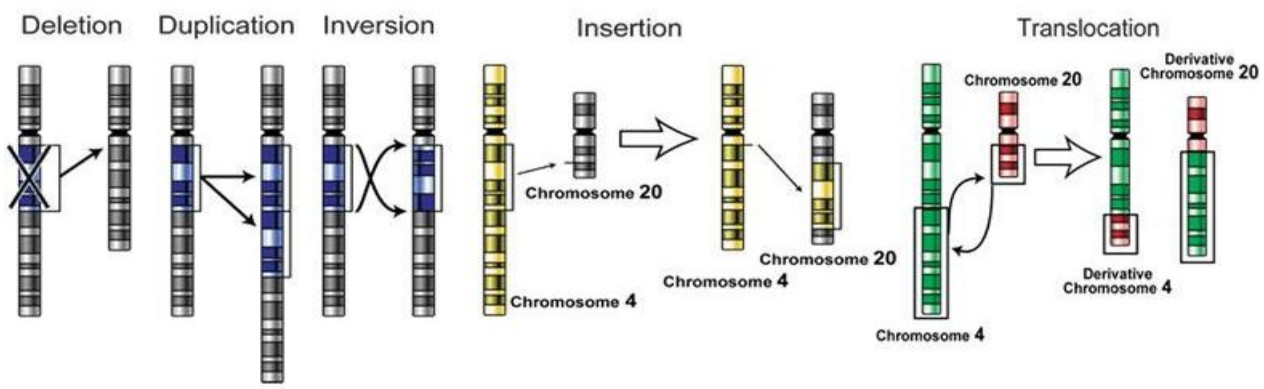


Fig: Types of Mutations

Source: https://adpcollege.ac.in/online/attendence/classnotes/files/1589181737.pdf

Some of the advantages of mutation theory are briefly mentioned below:

- The mutation theory is not intended to supplement the natural selection theory but to describe the importance of mutations in selective value of organisms.
- Mutations explain the occurrence of evolutionary changes within short period in contrast to natural selection which describes slow and continuous variations.
- Mutation theory also explains the absence of connecting links as no criteria against evolution but its possibility exist.
- This theory provides a great service to breeders.
- Occurrence of mutations in large and divergent directions remove the possibility of species disappearance by crossing etc.
- The differences between related species consist largely in differences of unimportant organs as explained by mutation theory.
- Since mutations appear fully formed from beginning there is no difficulty in explaining the incipient stages in the development of organs.

Objections to Mutation Theory

- It appears impossible to explain the discontinuity among individuals, by supposing that each member has appeared suddenly due to mutations.
- It is extremely hard to believe that mutations have provided sufficient opportunity for all specialized adaptations that exist in nature.
- Mutations cannot explain the presence of flightless birds on oceanic islands.

Radiations also cause mutation by forming ionized and excited molecules that can cause damage to cellular components and to DNA.

1. **Dominant mutations**

The mutations which have dominant phenotypic expression are called dominant mutations. For example, in manthe mutation disease aniridia (absence of iris of eyes) occurs due to a dominant mutant gene.

2. **Recessive mutations**

Most types of mutations are recessive in nature and so they are not expressed phenotypically immediately. The phenotypic effects of mutations of a recessive gene are seen only after one or more generations, when the mutant gene is able to recombine with another similar recessive gene.

3. **Isoalleles**

Some mutations alter the phenotype of an organism so slightly that they can be detected only by special techniques. Mutant genes that give slightly modified phenotypes are called isoalleles. They produce identical phenotypes in homozygous or heterozygous combinations.

11.6 Mutagenic Agent

Mutagenic term is defined as the ability to induce genetic changes in the DNA of an organism. There are many sources of mutagenic agents, including physical, chemical, and biological mechanisms. A **mutagen** refers to any agent found in an organism's environment capable of producing genetic mutations in DNA. Under normal circumstances, DNA replication occurs without the introduction of mutations or changes in the genetic code of an organism. This is due to the presence of DNA repair mechanisms such as base excision repair (BER), nucleotide excision repair (NER), and mismatch repair (MMR). In base excision repair, a damaged base is removed from the DNA during the G1 stage of the normal cell cycle. Nucleotide excision repair occurs during the G1 and G2 stages of the cell cycle and deletes lesions that form on nucleotide sequences in DNA. Even after the cell cycle is complete, mismatch repair can occur after replication to ensure that base pair matching is maintained within the DNA. Mutagens affect DNA by disrupting the normal repair mechanisms that typically detect the presence of errors in DNA production and replication. Moreover, mutagens cause regular human DNA polymerases to be replaced with Y-family polymerases that bypass the normal mechanisms of DNA proofreading and repair. While many mutations are considered harmful to organisms, mutations also represent the primary source of genetic diversity in populations and thus contribute to the process of evolution.

SAQ-

- Mutations can also be induced by external factors such as exposure to specific ……
- The ……which is caused due to loss or deletion of some portion (single nucleotide pair) in a triplet codon of a cistron or gene is called deletion

mutation.

- ……, viruses and bacteria that produce DNA damage resulting in cancer formation.

Types of Mutagens

Mutagens are often classified based on their origin and their effects upon DNA. There are three basic types of mutagens:

- Radiation mutagens
- Chemical mutagens
- Heat and Biological mutagens

Radiation mutagens:

The phenomenon of mutation and its role in biological evolution was realized long back. Its artificial production became possible only when Nobel Laureate H. J. Muller (1927) of Indiana University, USA, showed the development of mutants in *Drosophila* with the help of X-rays. His experiments also established the mutagenic property of high-energy radiations. All electromagnetic radiations have been proved to be mutagenic. Electromagnetic radiation is so-called, because it consists of waves of energy associated with electric and magnetic fields, resulting from the acceleration of an electric charge. Their mutation producing ability (mutagenecity) depends upon their energy which in turn, is inversely proportional to wavelength and directly proportional to the frequency. Greater the frequency, greater is the penetrating power and, hence, greater the mutagenecity.

Radiations are of two types, those capable of producing ions (electrically charged atoms or group or atoms) are called ionizing radiations, while those incapable of doing so, and are called unionizing ones.

(Physical mutagens include ultraviolet and gamma radiation. Both sources induce the creation of free radicals or molecules having unpaired electrons. These free radicals can then cause unintentional bonds to form between bases, such as covalent bonds between thymine molecules. The creation of the thymine dimer prevents the double helix from forming wherever this dimer exists in the nucleotide sequence.)

Chemical mutagens:

The majority of chemical mutagenes induce direct while others induce indirect mutagenesis. They cause additions, deletions and base substitution by various ways. These chemicals alter the sites of DNA. Some well known chemical mutagens are-

- **Nitrous Acid**

Nitrous acid acts directly on the bases of DNA. This acid replaces the amino (NH2) group of a base with a keto (=0) group. It can affect the bases of nucleotides or nucleic acids. The free amino acid groups are displaced by hydroxyl (-OH) groups. Hence,

Adenine, guanine and cytosine are converted into hypoxanthine, xanthine and uracil respectively by oxidative deamination The hypoxanthine and xanthine prefers to pair with cytosine while the uracil with adenine. The conversion of A to hypoxanthine causes a transition from an A-T to G-C base pair The conversion of uracil is the basis for transition of a C-G to an A-T pair.

- **Base Analogs**

A base analog is a substance that mimics the overall feature of a nucleotide Base analogs of DNA are substances having molecular structure similar to the normal bases of DNA. Transitional and transversional errors can also be caused by some chemicals like 5-bromouracil (BU) and 2-amino purine (AP) know an base analogs. BU in its normal keto form is the base analog of thymine and AP is the base analog of adenine, But both BU and AP can undergo tautomerism, the former from keto to the enol form and the latter from amino to imino.

- **Alkylating Agents**

Alkylating agents are the largest and most powerful group of chemical mutagens. Their modes of actions are direct as well as indirect the alkylating agents are commonly known as nitrogen and sulphur mustards. The best known alkylating agents are methyl and ethyl methane sulphonates (MMS and EMS).

- **Tautomerism**

In a normal DNA structure in organisms, purine base adenine (A) is linked topyrimidine base thymine (T) with two hydrogen bonds and purine baseguanine (G) is linked to pyrimidine base cytosine (C) with three hydrogenbands. Each nucleotide base can exist in alternate state. The shift from normalstate to alternate state is called tautomeric shift and molecules are termedtautomers e.g. existence of two tautomers are termed the keto and eno forms.Keto form is a stable form and eno form may revert back to keto form. Theexistence of unstable form in tautomers may lead to error of base incorporation during DNA replication.The rare bases can introduce mutations e.g. enol-thymine form in the parentDNA strand can introduce guanine in the complementary DNA chain. Furtherreplication of DNA will introduce cytosine in the complementary strand. It willlead to substitution of = AT base pair by ≡ CG base pair and new strand withmutated base will be synthesized. The type of isomerism in which a substance exists in two readily interconvertible different structures leading to dynamic equilibrium is known as tautomers or tautomerides. The four bases of DNA, two purines (adenine and guanine) and the rest pyrimidines (thymine and cytosine) undergo tautomerisin to cause both point and chromosomal mutations, sometimes useful and occasionally harmful.

- **Deamination**

Chemical substances such as nitrous acid, causes transitional mutation through the removal of the amino group (deamination) from adenine and cytosine. The removal of

amino group from adenine leads to the production of hypoxanthine. The hypoxanthine, later on transforms into ketotautomer which pairs with cytosine. Thus due to deamination transition of A-T pair into G-C pair takes place.

- **Heat and Biological mutagens**:

It was observed that the role of mutation in phage T4 increased surprisingly with even negligible rise in temperature. Both transitions and transversions are induced by heat treatment. Like HNO_2, the cytosine is usually deaminated to uracil, causing a GC to AT transition. Transversion from GC to CG is also induced by heat treatment.

Biological mutagens consist of bacteria and viruses capable of producing mutations in DNA. Human papillomavirus (HPV), for example, results in long-term infection in individuals unable to clear the virus from their bodies.

Beneficial mutations: — Have a positive effect on the organism in which they occur. They generally code for new versions of proteins that help organisms adapt to their environment. If they increase an organism's chances of surviving or reproducing, the mutations are likely to become more common over time. There are several well-known examples of beneficial mutations. Here are two such examples:

- Mutations have occurred in bacteria that allow the bacteria to survive in the presence of antibiotic drugs, leading to the evolution of antibiotic-resistant strains of bacteria.
- A unique mutation is found in people in Limone, a small town in Italy. The mutation protects them from developing atherosclerosis, which is the dangerous buildup of fatty materials in blood vessels despite a high-fat diet. The individual in which this mutation first appeared has even been identified and many of his descendants carry this gene.

Harmful Mutations:-A **genetic disorder** is a disease, syndrome, or other abnormal condition caused by a mutation in one or more genes, or by a chromosomal alteration. An example of a genetic disorder is cystic fibrosis. A mutation in a single gene causes the body to produce thick, sticky mucus that clogs the lungs and blocks ducts in digestive organs.

- **Cancer** is a disease in which cells grow out of control and form abnormal masses of cells (called tumors). It is generally caused by mutations in genes that regulate the cell cycle. Because of the mutations, cells with damaged DNA are allowed to divide without restriction.

Significance of Mutation: A sudden change in genetic character s known as a mutation. A mutation is the phenomenon of alterations in the DNA sequence or chromosomal arrangement. The mutation alters the genetic message carried by a gene. It results in the development of new characteristics that are capable of being inherited.

In the previous sections, different types of mutations have been discussed.

Mutations mostly produce detrimental effects. However, mutations can also be Beneficial in the following ways:

- Mutations produce genetic variations within genome which help in the evolutionary process in the organisms.
- Mutant organisms help in understanding the metabolic pathways in organisms.
- Plant breeders rely on the genetic variability in crop plants for their improvement. (e.g. improved variety, high yield, disease and pest resistance etc.).
- In humans, a specific 32bp deletion (CCR5- delta 32), a genetic mutation, leads to HIV resistance to homozygotes and delays AIDS onset in heterozygotes.
- Mutagenic action of Ionizing radiations have been used to create sterilized female insects to control and eradicate pests.

11.7 Summary

- Mutations can also be induced by external factors such as exposure to specific chemicals or radiation.
- The mutations which occur in the somatic or vegetative cells of the organisms are called somatic mutations.
- This type of mutation takes place in the germ cells. When the mutation takes place in the gamete, it is called gametic mutation
- Mutations which affect specific biochemical processes is called biochemical mutation.
- Mutation involving alteration of single base pair is called point mutation or gene mutation.
- The point mutation which is caused due to loss or deletion of some portion (single nucleotide pair) in a triplet codon of a cistron or gene is called deletion mutation.
- The point mutations which occur due to addition of one or more extra nucleotides to a gene or cistron are called insertion mutations.
- The mutations which arise from the insertion or deletion of individual nucleotides and cause the rest of the message downstream of the mutation to be read out of phase, are called **frameshift mutations.**

- A point mutation in which a nucleotide of a triplet is replaced by another nucleotide, is called substitution mutation
- The addition or deletion of a base or bases such that the coding sequence is shifted out of register. Note that addition or deletion of a multiple of three bases does not cause a frameshift. After the frameshift mutation is encountered, missense codons will be read upto the firsts top codon. Like nonsense mutations, frameshift mutation susually lead to complete inactivation of the gene.
- The mutations that arise in the absence of any known mutagen treatment are called spontaneous mutation.
- The mutations arising after treatment with certain compounds or exposure to environmental agents that increase the rate of mutations are called induced mutation.
- Physical mutagens: different forms of radiation that result in the production of free radical damage to DNA
- Chemical mutagens: compounds that create direct damage to bases, resulting in base pair mismatching and miscoded regions of DNA
- Biological mutagens: viruses and bacteria that produce DNA damage resulting in cancer formation.

11.8 Terminal Questions

1) Explain the Significant of mutation in evolution?

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2) What is importance of mutation?

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3) Define mutation. What are the various type of mutation?

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4) What is the molecular basis of mutation?

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5) Describe the point mutation?

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6) What are mutagens? Describe the various mutagens.

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7) Write short notes on:

a) Gross mutation

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b) Induced mutation

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c) Delition

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d) Transversion

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e) Fromshift mutation

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f) Chemical Mutation

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11.9 Answers

SAQ-

- chemicals or radiation
- point mutation
- Biological mutagens

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UNIT-12Isolation, Adaptation and Variation

12.1 Introduction

In the previous unit of this course you learnt about mutation theory. In this unit, we are going to study about isolation, adaption and variation. Isolation, Speciation and Variation is one of the most important factor for evolution. The division of a single population into two or more groups because of some barrier for interbreeding is called isolation. Isolation is one of the most important factor for evolution.In consequence of being separated from one another organisms (animals or plants) have developed different characteristics, due to which they have become separate species. Hence isolation is essential for the formation to new species. Speciation is the process by which new species are formed. Thus both isolation and speciation are inseparably associated with each other. Isolation is as important as Natural Selection of Darwin and it is one of the very important factors in organic evolution. Variation is the first fundamental factor for evolution It may be defined as the process whereby closely related organisms come to differ amongst themselves. There is a great variation in two organisms or parts of organisms two closely related beings. Without variation no change could occur and evolution would be impossible. It is the progressive factor for evolution. Variations are transferred to offsprings. Hence it is the basic prerequisite for evolution and with heredity, the evolution may be regarded as a undeniable fact.

But all the variations are not alike and also are not heritable. Hence only those variations which are heritable can take part in the evolution of a new species.

Objectives:-

After studying this unit you will be able to know-

- explain the different types of isolation and genetic basis of isolation
- explain the role of isolation in evolution
- discuss the different kinds of adaptation
- explain the different kinds of variation, sources and significance of variation

12.2 TYPES OF ISOLATION

Isolation is one of the most important factor for evolution.In consequence of being separated from one another organisms (animals or plants) have developed different characteristics, due to which they have become separate species. Hence isolation is essential for the formation to new species. There are so many ways in which free interbreeding maybe interfered and these are as follows:

1. Geographic isolation
2. Spatial isolation
3. Climatic isolation
4. Physical isolation
5. Biotic isolation
6. Reproductive isolation

1. **Geographic Isolation**-Moritz Wagner (1868) first made it clear that the geographical isolation was a factor in the formation of every species or race or tribe of animal or plant on the surface of the earth. The organisms are separated by geographical barriers, such as land masses in seas, bodies of water over the land, mountains etc. which causes the formation of new species or subspecies.
2. **Isolation due to sheer distance (Spatial Isolation)-**Sheer distance apart may also act as isolating factor for a species which occupies a great range of area which is unbroken by effective barriers. Its good example is Wrens of South America. Wrens are found all over the continent but the Wrens of one region differ from those of the other.
3. **Climatic Isolation**- Offen within the range of a species, occur distinct more or less abrupt climatic changes they may act as barriers for migration or individuals develop different adaptive changes so that they may thrive in those changed climatic conditions. Thus without the presence of any geographic barriers, a species split up to a northern and southern race or sub species which are genetically distinct, cannot thrive in the territory occupied by the other.
4. **Physical Isolation**-Physical differences in the environment, such as differences in water, soil, sunlight, elevation of land etc. also act as isolating factors for the formation of a sub species or races.
5. **Biotic Isolation-**Huxley believes that this is a special form of ecobiotic isolation (adaptation of animals to different modes of feeding), for example, the greater and lesser spotted wood peckers which differ in size, because of differences in the food taken. Huxley believes that with biological isolation the separation of new species is a gradual process. The above ecological isolation has been divided into three categories by Huxley, ecoclimatic isolation, ecotropic isolation and ecobiotic isolation.
6. **Reproductive Isolation-**The simplest type of reproductive isolation, is the changes in the copulatory organs due to mutation. Reproductive isolation is a change in the developmental rhythm (rate)of certain species. For example, the genus Cicada has probably split up into numerous species due to the genetic changes in the lengths of their life cycles. While there are only slight morphological differences among the species of Cicada there are marked differences in length of the larval periods. Hence interbreeding only takes place among those species that same development rhythm.

Role of Reproduction Isolation

Once new species arise from the parental species due to the effect of variation and natural selection, reproduction barriers prevent the two species from exchanging genes through reproduction. Thus two related species cannot mate with each other and remain distinct. Isolation means separation and reproduction isolation simply means that the two species are prevented from successful reproduction and kept genetically distinct from each other. Reproduction isolation operates in the following ways:

- **Ecological isolation and Seasonal isolation:** In ecological isolation the two species are unable to mate as they live in geographically different areas. Where as the seasonal isolation mating is prevented because the reproduction organs mature at different times.
- **Ethological (Behavioral) isolation and Mechanical isolation:** In ecological behavior isolation the songs in birds of two species or the coloration of two fishes are so different that female of one species is able to recognize only the male of its own species. Where as mechanical isolation the male and female organs for mating differ in different species and prevent their union.
- **Physiological isolation and Zygotic and developmental isolation:** The physiological isolation the sperms of one species are not able to survive in the female tract of another species. Where as, the zygotic and development isolation If all the above mechanisms fail and a "hybrid zygote" (zygote from mating of two different species) is formed, it dies after some time. If the hybrid zygote survives, it dies during development.
- **Hybrid sterility and F_2 breakdown:** In hybrid sterility, Mule, the offspring of a female horse and male donkey is a good example. It leads a normal life but is sterile and cannot reproduce. Where as F_2 breakdown in rare cases, all the above mechanisms fail and a hybrid (offspring of parents belonging to different species) is fertile, it can reproduce only for one generation.

12.3 Genetic Basis of Isolation and Role of Isolation in evaluation

- The **genetic isolate** is a population of organisms with little genetic mixing with other organisms within the same species due to geographic isolation or other factors that prevent reproduction.
- Genetic isolates form new species through an evolutionary process known as speciation. All modern species diversity is a product of genetic isolates and evolution.
- The current distribution of genetic differences and isolation within and among populations is also influenced by genetic processes, which can give significant input into evolution's basic principles.
- The resulting genetic diversity within a species' distribution range is frequently unequally distributed, and significant disparities can occur in the series of fields when population dispersion and isolation are critical for species survival.
- The interrelationship of genetic drift, gene flow and natural selection determines the level and dispersion of genetic differences between populations and among species assemblages.
- Geographic and natural elements may likewise add to these cycles and further impact species' advanced examples of hereditary variety, such as genetic differences that cause genetic isolation.
- Genetic variations are often unequally distributed over a species' geographic distribution, with differences between populations at the geographic center and the range's extremities.
- Significant gene flow occurs in core populations, resulting in genetic uniformity. In contrast, low gene flow, severe genetic drift, and diverse selection conditions occur in range periphery populations, enhancing genetic isolation and heterogeneity among people.
- Genetic differentiation resulting from genetic isolation occurs as significant alterations in genetic variations, such as fluctuations in allelic frequencies, that accumulate over time with geographic regional boundaries.
- Significant genetic diversity can be detected toward the limits of a species range, where population fragmentation and isolation are more likely to affect genetic processes.

- Fragmentation is the division of a large population into smaller, geographically separated habitats, resulting in genetic differences within and across groups. Regional splitting is produced by a variety of factors, including environmental processes that regularly change a species' indigenous distribution.
- Human-caused environmental changes such as deforestation and land degradation can result in rapid changes in a species' distribution, leading to population decrease, segmentation, and regional isolation.

❖ Prezygotic and Postzygotic forms of reproductive isolation

There are a few different ways organisms can be reproductively isolated from each other. These mechanisms generally fall into one of two categories: prezygotic and post-zygotic.

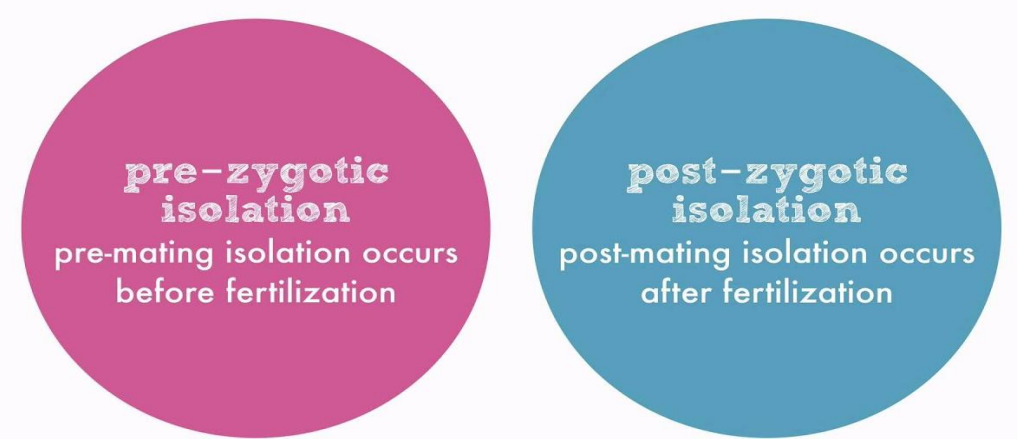
In **prezygotic** forms of reproductive isolation, organisms from different populations don't create a zygote. Or prezygotic isolates before the creation of the zygote the reasons for this vary widely. Sometimes, individuals from different populations prefer different habitats or mate during a different season. In these situations, individuals from different populations don't mate with each other because they are not in the same physical location or they are not ready to mate at the same time.

Sexual selection can also come into play, individuals from one population may not find the characteristics or courtship rituals of individuals from another population attractive enough to mate with them. Members of different populations may be mechanically or genetically unable to reproduce with each other—even if mating does occur, it will not lead to fertilization.

Postzygotic reproductive isolation means that hybrid offspring can occur between populations or species or postzygotic isolates after the creation of the zygote but these hybrid offspring don't survive to reproductive age. Mules, the offspring of a horse and a donkey—are a good example of a postzygotic barrier to reproduction. Though a horse and a donkey can mate and produce a mule, mules cannot successfully produce egg or sperm cells via meiosis because of their mismatched chromosomes. Therefore, they are sterile and can't produce their own offspring.

Genetic isolation form new species throw and evolutionary process known as speciation. **Speciation** is defined as the formation of one or more new descendant species from one ancestor species.

Natural selection, mutation, genetic drift, and gene flow (gene migration) all contribute to changes in allele frequencies. Collectively, these are referred to as the main **mechanisms of evolution**.



Prezygotic and Postzygotic isolation

Sources: https://www.google.com/imgres?imgurl=https://i.ytimg.com

SAQ-01

1. Isolation means …… and …….. isolation
2. Genetic isolates form new species through an evolutionary process known as ……..
3. ……. isolates before the creation of the zygote.
4. …….. isolates after the creation of the zygote

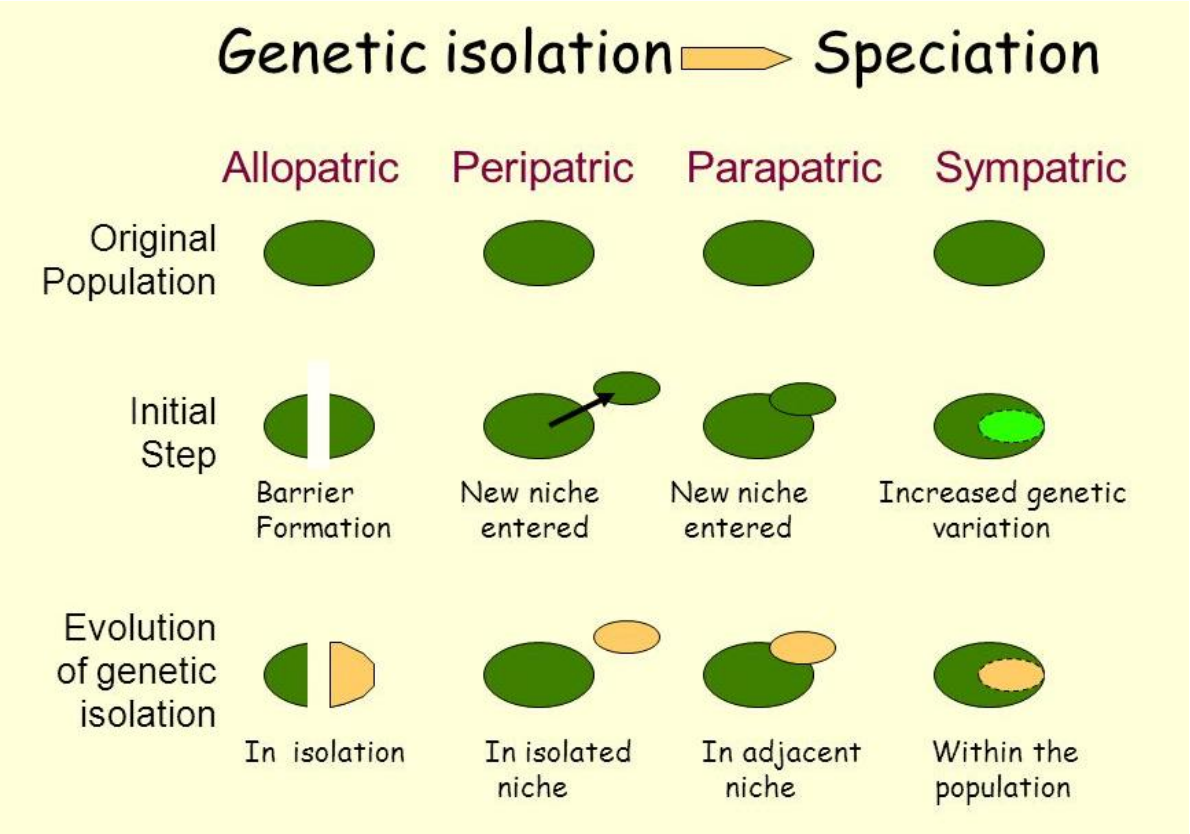
The different types of speciation are Sympatric, Allopatric speciation and Parapatric Speciation.

- **Sympatric speciation** occurs when populations of a species that share the same habitat become reproductively isolated from each other. This speciation phenomenon most commonly occurs through polyploidy, in which an offspring or group of offspring will be produced with twice the normal number of chromosomes. Where a normal individual has two copies **of** each chromosome (diploidy), these offspring may have four copies (tetraploidy).
- It's possible for reproductive isolation and subsequent speciation to occur without geographic isolation, too! This is called **sympatric speciation** (sympatric = "same homeland"). There are a few different ways sympatric speciation can happen.
- **Polyploidy**—having more than two full sets of chromosomes—is rare in animals. However, it is a fairly common source of sympatric speciation in plants.
- **Autopolyploidy** can occur when chromosomes don't separate properly during meiosis, producing gametes with an extra set (or sets) of chromosomes. A plant with these gametes couldn't produce viable offspring with other, normal gamete producing plants of its species. However, it could self-pollinate or produce viable offspring with plants whose gametes had the same number of (extra) chromosomes. This example is particularly interesting because it illustrates a situation in which speciation can occur over only a single generation!
- **Allopolyploidy** produces a hybrid organism with multiple sets of chromosomes by combining the gametes from two different species. If that hybrid organism produces a polyploid gamete that combines with a normal gamete from one of the parent species, viable fertile offspring may result if a full double set of chromosomes from each parent is formed. Wheat is an example of an allopolyploid organism humans have cultivated, crossing wheat (*Triticum*) with rye (*Secale cereale*).
- **Allopatric speciation**, the most common form of speciation, occurs when populations of a species become geographically isolated. When populations become separated, gene flow between them ceases. Over time, the populations may become genetically different in response to the natural selection imposed by their different environments.
- When populations become separated from each other by a geographic barrier, this leads to reproductive isolation. Geographic isolation can result from natural processes that range from gradual changes, such as erosion, to disasters, such as landslides or floods. Geographic isolation can also result from migration to a new location, especially when returning to the original location is impossible. Given enough time, this combination of geographic and reproductive isolation leads to allopatric speciation (allopatric = "in other homelands").
- **Parapatric speciation** is extremely rare. It occurs when populations are separated not by a geographical barrier, such as a body of water, but by an extreme change in habitat. While

populations in these areas may interbreed, they often develop distinct characteristics and lifestyles.

SAQ-2

1. It's possible for reproductive isolation and subsequent speciation to occur without geographic isolation, too! This is called …….
2. …… produces a hybrid organism with multiple sets of chromosomes by combining the gametes from two different species.
3. …….. the most common form of speciation, occurs when populations of a species become geographically isolated.



Sources: https://www.google.com/imgres?imgurl=https://i.ytimg.com

12.4 Different Kinds of Adaptation

The evolutionary theory, adaptation is the biological mechanism by which organisms adjust to new environments or to changes in their current environment.

Wallace believed that the evolution of organisms was connected in some way with adaptation of organisms to changing environmental conditions. In developing the theory of evolution by natural selection, Wallace and Darwin both went beyond simple adaptation by explaining how organisms adapt and evolve. The idea of natural selection is that traits that can be passed down allow organisms to adapt to the environment better than other organisms of the same species. This enables better survival and reproduction compared with other members of the species, leading to evolution.

Organisms can adapt to an environment in different ways. They can adapt biologically, meaning they alter body functions.

Scientists who studied adaptation prior to the development of evolutionary theory included

Georges Louis Leclerc Comte de Buffon. He was a French mathematician who believed that organisms changed over time by adapting to the environments of their geographical locations. Another French thinker, Jean Baptiste Lamarck, proposed that animals could adapt, pass on their adaptations to their offspring, and therefore evolve. The example he gave stated the ancestors of giraffes might have adapted to a shortage of food from short trees by stretching their necks to reach higher branches. In Lamarck's thinking, the offspring of a giraffe that stretched its neck would then inherit a slightly longer neck. Lamarck theorized that behaviors aquired in a giraffe's lifetime would affect its offspring. However, it was Darwin's concept of natural selection, wherein favorable traits like a long neck in giraffes suvived not because of aquired skills, but because only giraffes that had long enough necks to feed themselves survived long enough to reproduce. Natural selection, then, provides a more compelling mechanism for adaptation and evolution than Lamarck's theories.

Kinds of adaptations

Structurally adaptations may be morphological i. e. confined to the shape, size and external feature of the living organisms or anatomical in which visceral organs adapted according to its needs. These adaptations vary from individual to individual depending on the climatic conditions etc. According to **Matthew** they fall into following categories primarily on the basis of habits and habitats :

1. Terrestrial or ambulatory adaptations.
2. Cursorial adaptations
3. Fossorial and subterranean adaptations.
4. Scansorial adaptations (arboreal)
5. Volant adaptations
6. Aquatic adaptations
7. Other types namely rectigrade, amphibious etc.

1. Terrestrial (ambulatory) adaptations

These occur in ground-living forms like ruminants, primates etc. The bipedality or tetrapedality is the rule and limbs (feet) are pentadactyle. They are plantigrade type i. e.entire metatarsals of palm or sole rests on the ground. Neither wrist nor ankle is raised. Due to such adjustments these animals can with stand the weight of their body. The teeth are usually heterodont and thecodont type. Parental care is markedly significant as the young ones suck the milk from the mammary gland of their mother. In desert climatic conditions various morphological adaptations take place due to shortage of water and excessive heat. Some of these are following: -

- The skin is spiny and leathery to reduce evaporation of water. In Moloch (desert lizard) it is hygroscopic and absorbs water like blotting paper.
- Due to excessive heat and temperature eyes are protected by well-developed eye lids. Camel's nostrils are capable of being closed like eyelids. The ear opening is protected by fringes or scales or hairs. The chest is compressed.
- Most of reptiles are poisonous for self-defence. *Metachrosis* (change of colour) occurs most frequently for protection.

2. Cursorial adaptations:

These are also called speed adaptations as they are meant for fast locomotion. Various snakes, saurischians, flightless birds like *Emus, cassowaries, ostriches, rheas* etc. and mammals for example

bandicoots (*Peramelidae*), wolf, and rabbits (Leporidae), dogs (*Canidae*), cats and leopards (*Felidae*), horses (*Equidae*), deers (*Cervidae*) etc exhibit cursorial adaptations. They are characterised by following changes:

- **Streamlining of body contour-**The body contour is streamlined and moulded in such a way as to offer least resistance to medium. A race-horse with head and neck extended, ears thrown back and tense muscles of the body shows the beautiful contour for speedy cursorial mechanism. The thorax is compressed and ribs are flattened
- **Less development of fore limbs**-Among the propelling organs, the fore limbs are less developed as they may be concerned in food getting. Hind limbs being the main divers are modified.
- **Digiti gradation in foot-**The foot becomes digitigrade i. e running on the digits. The tarsals and metatarsals are raised from the ground. They are supported by muscular pads to sustain various shocks. Thus development of sole pads is an adaptation for the absorption of shock of impact in *Rhinoceros*. Digitigrade propulsion occurs in dinosaurs, birds and dogs.
- **Unguligrade mode of progression-**Another modification in ungulate (hoofed) mammals is the development of *unguligrade progression* i. e. walk on the modified nail or hoof. The distal toe bones (unguals) are depressed or flattened. In horses they reach highest degree of perfection. The modern camels have become secondarily digitigrade, foot being retrogressed as an adaptation due to desert sand.
- **Reduction of ulna and fibula-**In fore limbs ulna and in hind limbs fibula bones are greatly reduced as an adaptations for fast running. Clavicles tend to reduce.
- **6. Movements of limbs in one plane-**The limbs move only in one plane at the joints (except ball and socket joint of hip and shoulder). It is feasible to avoid interference between fore limbs and hind limbs during running as dog's hind limbs come forwards to fore limbs at high speed.
- **Lengthening of distalia of limbs**-Distal elements of foot and hand become lengthened for the pose of increasing the length of stride.
- **Bipedal changes-**In bipedal forms (e. g. man etc.). cursorial adaptations include reduction of fore limbs, shortening of neck and prevalence of mental precocity.

3. Fossorial and Subterranean adaptations:

Fossorial adaptations develop in the animals due to their digging habits. These animals live usually on the surface of the ground but occasionally go into earth. Subterranean adaptations are merely adjustments occurring in underground forms.

Fossorial creatures may dig either for their food or for retreat simply. Zoologically they are most primitive, defence- less and unambitious members of Animalia. The common examples of fossorial-types are *caecilians* among Amphibia, *sphenodon, uromastrix,* limbless lizards and desert snakes among Reptilia, *cliff swallow*, *starlet* sps. among birds, *Monotremes, Dasyurus, Notoryctes* Moles (Talpa), hedgehog (*Erinaceus*) etc. among mammals. They show following general adaptations in relations to their fossorial habits.

- **Spindle shaped body-**The body contour is spindle shaped or fusiform as to offer least resistance to subterrane- a passage. The greatest diameter of the body lies near the neck or shoulder. However legless forms, snakes, caecilians possess cylindrical body for burrowing.
- **Tapering of head-**The head tapers anteriorly to form a sort of snout for burrowing. In skull, expanded zygomatic or cheek arches are lacking with the result jaw musculature is feebly

developed.

- **Reduction of tail-**The tail is short or vestigial. In hedgehogs, woodchuck etc. It is short but in *wombat* etc. it is vestigial. In subterranean forms it serves as a tactile organ.
- **Loss of eyes:-**In actual fossorial animals, the eyes tend to become vestigial as they are of no use in dark habitat. Further more they may be injured during burrowing. In *Geomyidae* and *Bathyergidae* the eyes are small where as in marsupial mole (*Notoryctes*) they are functionless and in *Talpa* vestigial.
- **Disappearance of Pinnae-**The external ears also tend to disappear since they would be obstruction in burrowing. In *Geomyidae* external ears are small, in the ratel (*Mellivora*) they are minute; in the Bathyergidae (cape mole- rat) they are merely fringe of skin around aural aperture and in monotremes completely lacking.
- **Digging adaptations:-**For digging various changes occur. The snout is well developed in *Swine, Heterodon, Talpa,* etc. A prenasal bone develops at the tip of the nose cartilage in talpa. The incisor teeth and sometimes canines (swine) form fossorial organs being procumbent or forwardly directed. The fore limbs as well hind limbs are very short and stout, the formers are specially modified. The hand (fore- limbs) is broad and stout with long claws. The broadening of hand in mole and echidna occurs by the addition of another bone (*os falciforme*). The bones of fore limbs are very strong and bear prominent *tuberosities* for muscular attachment.

The *olecranon* process is specially large in fossorial forms. The shoulders are narrow and their sockets are near to each other. They are strengthened by clavicles and large T-shaped *episternum* as well paired coracoids. The ilium and ischium bones of pelvic girdle become elongated in the fore- and-aft direction and lie parallel to vertebral column instead of forming an angle. Furthermore, ilium is also fused through- out its entire length with the sacrum. The sacral vertebrae fuse and those of loin and neck also tend to ossify. Peculiar intercentral ossicles between lumbar vertebrae of mole, talpa and hedgehogs may be another adaptation in strengthening the vertebral column. All these skeletal modifications give the fossorial animal strength and rigidity during burrowing.

- **Hibernation:-**Hibernation or winter sleep is another feature of burrowing forms. It is device to tide over unfavorable climates by subterranean animals.

4. Scansorial Adaptations (Arboreal)

These adjustments have evolved in animals due to their climbing habits. The most remarkable examples are various namely fishes e. g. climbing perch (*Anabas scandens*) and mud skipper (*Periophthalamus barbarus*), among amphibians are tree frogs (Hyla sps.); among reptiles are geckoes, chameleon and tree snakes. The birds and mammals show predominantly arboreal adaptations. On the basis of bionomic classification (i. e. habitat) scansorial animals may be of three types.

(i) Wall and Rock climbers: These are not tree inhabiting but are well suited for climbing on the walls of houses and similar other rocky surfaces like geckos lizards, flying squirrels on rocks.

(ii) Terrestrio-arboreal forms-These include various carnivores, rodents, insectivores, insects etc. which are capable of climbing but still rest at home upon the ground beneath trees. Sometimes they form nests in the trees.

(iii) Arboreal forms-These are perfectly tree dwelling animals which make the trees their home. Occasionally such arboreal forms descend to the ground as some primates (gibbons). The arboreal forms fall into following categories

(a) Branch runners: Various squirrels lumurs, chameleonsetc. are included under this heading.

They live and move on the upper surface of the branches.

(b) Hanging of suspended Jorms- These include bats, sloths and flying lemus Galeopithecus etc. These animals are constituted in such a manner that they can not walk upon the branches but rest suspended by powerful claws of their limbs. Bats hang themselves by the claws of hind limbs and sloths by fore limb's claws.

(c) Brachiators: These are the animals swinging by the fore limbs. They show a very remarkable method of progression by means of the forelimbs, swinging with accuracy from tree to tree like apes etc.

Following are noteworthy climbing adaptations

- **Stoutness of body contour-**The body contour is stout, thorax is subcircular and ribs are much curved. In sloths ribs are numerous giving strength to the chest.
- **Toughness of Limb girdles**-Due to arboreal habits shoulder girdle (pectorals, is especially strong to support the weight of body.
- **Broadening of Ilium-**The ilium or hip bone of pelvic girdle become broadened out to support viscera.
- **Elongation of proximal limb segments-**In fore limbs proximal segments (i. e. humerus) become elongated especially in suspended and brachiating forms. These are generally plantigrade type.
- **Syndactyly and Zygodactyly in limbs-**The hind limbs (i. e. feet) are grasping type i. e. prehensile with oppo- sable digits or non-prehensile.

  (a) In non prehensile type claws are well developed besides spines and tubercles which help in climbing as in Canada tree-porcupine *Erethizon*.

  (b) Characteristic adhesive pads usually occur either on the tip of the digits or on the soles of feet as in tree-frogs, geckoes, Dendrohyrax etc.

  (c) In the prehensile or grasping type *syndactyly* (union of digits) is common. Such feet occur in marsupials and primates besides birds, reptiles etc. In marsupials hallux or great toe is offset so as to oppose fourth digit, the second and third are bound together in a common integumeat. In reptiles (e chamaeleons) syndactyly is marking in both fore and hind limbs. On the hand first three fingers are united together to form inner bundle and are opposed to outer bundle formed by the fusion of fourth and fifth finger.

Digital reduction-In arboreal forms there is tendency in the reduction of digits. In *Koala* second digit is lost and in tree sloths only two digits in hand and three in the foot are present,

Specialization of tail-The tail may be either prehensile (e. g. chamaeleon, monkey etc.), or non-prehensile, In the latter type climbing may be compensated by the presence of ectodermal spines or scales on the underneath of tail (e. g. flying squirrel. *Anomalous*).

Development of accessory organs-Due to scansorial habits various accessory climbing organs might be developed. These include spines and tubercles on the fore arm in some lemurs (*Hapalemur griseus*). In *Lemur catta* there is a specific climbing organ which is composed of a patch of hardened skin on the fore arm.

5. Volant Adaptations

These adaptations are concerned with the flight: This flight may be either passive or gliding type characterised by leaping (jumping) from a high point to low or true flight having the aerial flight like

birds etc.

A. Adaptations for gliding: - The gliding flight are per- formed by various lizards (flying *dragon-Draco volans*) fishes (e. g *Exocoetus* etc.); birds (*ostriches* etc.), mammals (lemurs) and amphibians (*Rhacophorus*). Following are noticeable adaptations met with in such forms:

(i) Development of patagia: The sustaining surface for the gliding is a fold or series of folds of the skin known as patagium. They may be supported by ribs as in Doraco volanes (flying dragon). It lies between fore limbs and hind limbs. Another example among reptiles is ptychozoon 'the flying or fringed gecko" in which lateral expansion of skin (patagium) extends along the side of neck, body, tail and limbs and between toes. Flying snakes (Chrysopelea) also leap by the concave ventral side.

The *pterodactylls* of Mesozoic era were volant creatures to birds. They possessed true flight, patagia were extensions between limbs supported by ribs. Flying lemur (Galeopithecus volans) patagium extends from side of the neck to the tip of tail even including digits which are webbed as for aquatic life.

(ii) Enlargement and high insertion of pectoral fins

Among fishes (*Exocoetus* etc.) pectoral fins become enlarged in the form of parachutes and are highly inserted on the body. The lower lobe of tail is also invariably longer helping in leaping.

B. Adaptations for true flight-These include bats. Birds various insects (*Dragon flies* etc.) and some mammals (*Propithecus, flying squirrels* etc.). The modifications are following:-

(i) Development of feathers: Feathers are exoskeletal structures present in the birds. They have been called "nature's masterpiece". Structurally it consists of a basal quill or calamus and distal rachis or shalt. The rachis bears a series of lateral barbs which further consists of double row of barbules connected with each other by barbicels. The barbs, barbules and barbicels (hooklets) form a sort of net which help in flight.

(ii) Presence of wings: In birds fore limbs are modified into flight structures **wings**. In bat wing humerus is well developed: radius long and curved and ulna is vestigial. The pollex is free and clawed for crawling and climbing.

In *pterodactyl* wing radius and ulna are equal. The next segment consists of a heavy metacarpal bearing great wing finger and three small metacarpals. There is also a pteroid bone directed towards the shoulder and is supposed to support the anterior margin of a prepatagium.

The bird wing is the most specialized of all modern wings. The digits are reduced to three and these are fused together to help in flight. The digits are represented by one or two phalanges supporting the so- called *bastard quills*. In *Archaeornis* (reptilian bird) there occurred claw on each of three free fingers.

In insect wing, the membranous fold are lateral projections having nervures etc. They are attached by the chitinised plate with the thorax and help in violent flight.

(iii) Pneumatization of bones: The bones are hollow and air filled containing many air cavities. These add buoyancy during flight.

(iv) Occurrence of flight muscles and keeled sternum In birds specific flight muscles are developed which connect wings with limb bones. The sternum or breast bone is well developed and bears a median keel or carina for attachment of pectoral muscles (flight muscles).

(v) Development of air sacs: They act as air reservoir during respiration and are buoyant.

6. Aquatic adaptations

Such changes have occurred in animals due to their aquatic habitats i. e, water is their home. These adaptations may be primary originating in fishes and permanently water living forms or secondary in such animals which have changed their habitats. Primary Aquatic adaptations-These occur in fishes which had never terrestrial ancestry and thus adapted to water medium. The main changes are -

- The compression of head, body and tail into a stream- lined form. Head is sub conical.
- Development of fins (paired and unpaired) which help in locomotion.
- Occurrence of ctenidia respiration as gills are well suited for gaseous exchange in water.
- Presence of air bladder in advanced bony fishes as an accessory respiratory organ as well as hydrostatic organ.

B. Secondary Aquatic adaptations-These are lung- breathers mainly amphibious vertebrates Various amphibians; swamp river turtles. Nothos urs, phytosaurs, croco dites, many birds like Ichthyornis, ducks and geese etc. and mammals like Hippopotamus, Otter, Desmun etc. show dual habitats. The Galapagos lizards (*Amblyrhynchos*) are terrestrial by choice but aquatic from necessity since they live on rocky islands and by swimming eat the seaweeds. The body is strongly compressed and swimming tail is flattened. The over all adaptations are following

Enlargement of size Water borne animals are larger in size because in these creatures, energy which in terrestrial in form is exhausted in gravitational forces, is turned into growth force.

Modification of skull: The cranium is shortened but becomes wider: facial portion is turned into rostrum (porpoises, Ichthyosaurs) and zygomatic arch is reduced (cetacea).

Shortening of neck: The neck shows fused cervical vertebrae in whales whereas loss of mobility in tail-driven types.

Simplification of vertebrae: In general vertebrae tend to be simple in secondarily aquatic forms.

Lightness of bones: The bones in aquatic forms are light and spongy. In whales their interstices are filled with oil.

(vii) ***Occurrence of laocmotory paddles (fins):***There Occur fleshy fin like expansions of the body wall in whales and ichthyosaurs which help in propulsion. In Plesiosaurs and turtles, oar propulsion occurs by fin-like limbs but in whales, sirenians etc. tail propulsion takes place as hind limbs be- come disappeared. Further more limbs (feet) are webbed and paddles become differentiated in which entire limb skeleton is enclosed in skin having no divisions into toes and fingers.

(viii) Disappearance of hairs, skin glands etc.: Skin is naked and hairs are usually absent. For the compensation of hair loss in mammals a fatty layer is formed below skin (blubber). Sweat or oil glands disappear as they have nothing to do with the aquatic mode of life.

7. Other types

These may include parasitic adaptations characteristic of various invertebrates. Besides, rectigrade adaptations are meant to sustain great weight of heavy body. Such forms are gigantic and consequently their limbs are modified. The deep sea adaptations are also merely aquatic adaptations.

12.5 Kind of Variation, Sources and Significance of variation

Variation: The differences that are found between the individuals of same species are called Variation. It is very difficult to find out two individuals exactly similar in the nature. It may be harmful, useless and useful. Harmful or useless variations make individuals unfit for struggle for existence, whereas the useful variations are quite significant and make organisms fit in the nature. Such variations are transmitted to the next generation so that the progenies are more suited.

KINDS OF VARIATIONS

Variations may be grouped under three pairs of contrasting types:-

1. Germinal or acquired
2. Continuous or discontinuous
3. Determinate or indeterminate

1. Germinal variations (Blastogenic)-They are intrinsic (originate inside the body) and have no external influence on the origin of germinal variations.

Germinal variations arise in the germ cells. It is either due to recombinations of genes, forming new groups, or due to mutations. Mutations radically change the gene complex causing germinal variation. Mutation may occur at any time i. e. from embryonic life till the death of the organism. Germinal variations are heritable i. e. handed over from generation to generation by heredity.

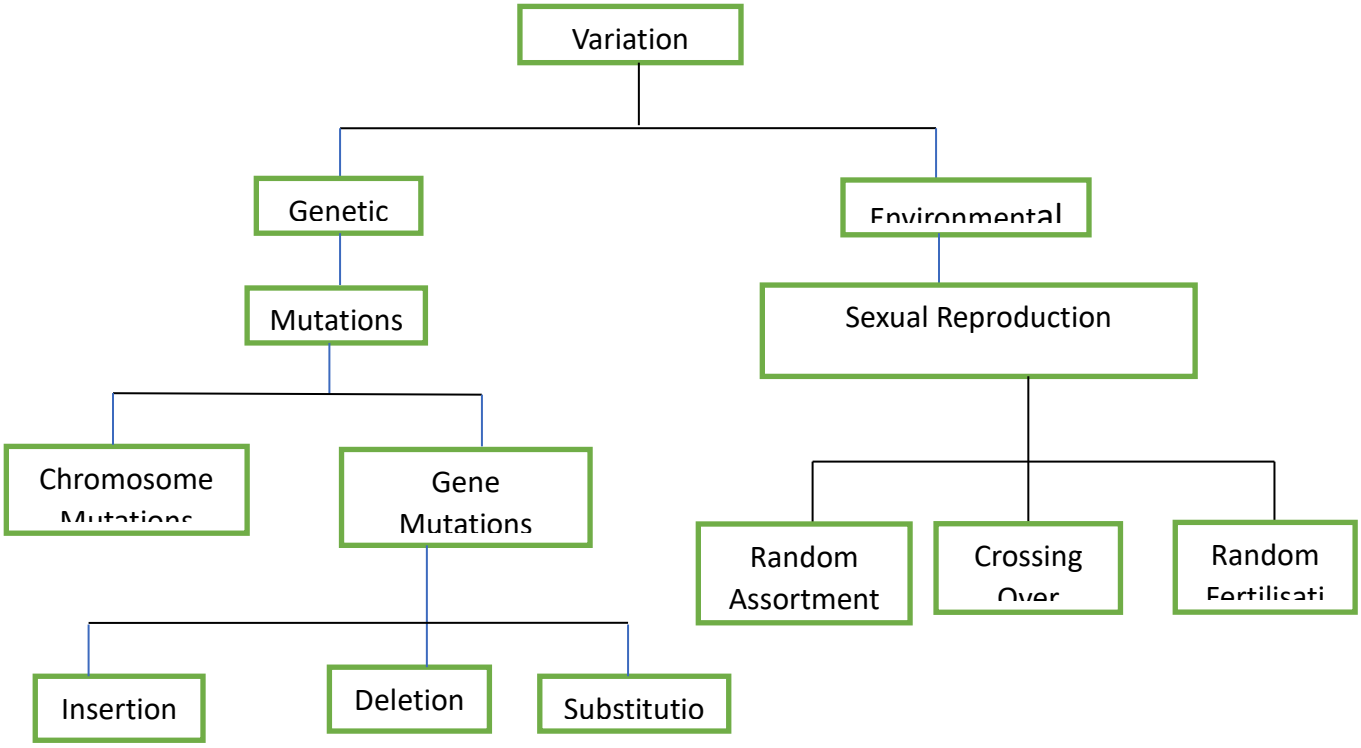
Examples-Occasional occurrence of supernumerary (exceeding the usual number) digits in man, domestic cat, the horse and other forms. It is not due to accident or due to external influence. These are occasionally inherited through several generations.

The variations that affect the germinal or reproductive cells only are called germinal variations. These are inherited from parents to their off-springs. Hence, these variations are very important for the evolution. The possible cause of such variations are mainly due to recombination and mutations. Recombination occurs due to reshuffling of parental genes which results in organisms with new genetic combination. Due to the mutation, structural changes in DNA or chromosomes occur resulting into change in phenotype.

2. Acquired variations (Somatogenic)-They are also called somatic variations or modifications These are due to external (extrinsic) influences. These are imposed upon the organism during its life time The somatic or acquired variations are not in herited from paraent to the offsprings. The variations that affect only the somatic cells are called somatic variations. These are not inherited from parents to the off-springs. These variations are acquired by theorganisms during their life time and are lost with death. Such variations are also called acquired variation. These variations are not important for the evolution point of view. The possible causes of such variations are:

1. Somatic variations:

- **Environmental factors:** The **environmental conditions** directly influence the form and functioning of animals, plants and micro-organisms. The various **abiotic and biotic factors** introduce changes, some of which proved to be adaptive in nature.
- **Use and disuse of organs:** According to **Lamarck,** continuous use of an organ makes it better develop, whereas continuous disuse causes reduction in size.
- **Conscious efforts:** Education, learning, training, nutrition and habit formation are examples of **somatic variations** due to conscious efforts.



2. **The long neck of giraffe, loss of eyes in cave-** dwellers, better development of muscles of right hand and right side of the chest of blacksmith etc. are all acquired changes due to functions.

3. **Indeterminate variations-**Those variations which occur in any conceivable direction are not governed by any law. These variations depends on chance only. They are fortuitous variations and may give a distinct advantage to its possessor in its successful fight for existence. Darwin's natural selection probably determines the variation to be selected. Variation of size in closely related organisms is an example of indeterminate variation.

4. **Determinate variations**-These variations occur in certain definite lines or directions usually in an adaptive direction. These variations are also called *orthogenetic.*

   These variations are controlled by some unknown influences or factors. Besides, there are meristic or numerical variations, which are variations in the number of the repeated parts of an organism (animal). For example star- fish are 5-rayed but meristic variations may give rise to 4-rayed or 6-rayed individuals. Cases of polydactylism (the development of extra digits) in hand or foot, is also an example of meristic variation. There are substantive variations which depend upon the structure-shape, size and colour of organism or its parts. For example the height of the individual, the shape of nose, ears and fingers, the colour of the eyes and hair. All these are subject to great variation. Some claim that determinate variations or variations in a certain definite directions, have no real existence. There is no such tendency to vary always in a given direction in successive generations. While others consider these variations as orthogenetic (variations in a definite line in successive generations), which are important for evolution.

5. **Continuous fluctuating variations-** These are small and indistinct variations. These fluctuate on the either side on the average condition. These are also described as the fluctuating variations or plus-minus variations. Since they are unstable and non-heritable, they do not have any role in evolution.

These affect the size, weight, shape, or color of an organism or its part. If the variations occurred very small and indistincting variations and these variations occurred accidentally (fortuitous) they are called Darwinian variations or fluctuations which are acted upon by natural selection.

Continuous variations are generally quantitative rather than numerical and the degree of change between successive generations is very small. The great mass of variations are continuous.

6. **Discontinuous variations**- These are large and sudden which deviate to a great extent from the normal and appear as totally new. These are also described as mutations.Since they are stable and heritable, they play important role in origin and evolution of species. These are mostly large and sudden rare. They are also known, the sports or monstrosities or saltations (Lat. saltare-to leap) or mutations. In this case new and more or less conspicuous characters appear suddenly and spontaneously without any obvious reason.

   Examples-Variations from the standard number of digits in vertebrates. In man, six, seven or even eight fingers in the hand have been observed.

CAUSES OF VARIATIONS

Causes of acquired variations-The acquired variations in an organism are caused due to external influence, in its life time. The influence of abundance or scarcity of food, which determines the stature of the animal, the influence of heat, cold, omnipresent enemies or absence of unreasonable conditions are causes of these variations.

The acquired variations have no concern with the evolution because they are not inherited and are only for individual, not for the race.

Cause of germinal variations-These variations are important for evolution, since they are inherited. The cause or causes of variations are of fundamental importance for evolution.

The causes of germinal variations may be:

1. Every organism has the inherent tendency.
2. No two organisms have the same shape and structure, however, they are closely related to each other.
3. Biparental parentage (amphimixis) is also a cause of variation.

   The germ plasm which is handed over to the next generation is partly derived from both the parents (male and female) It is a highly complex material, consisting of chromosomes. In man, there are 46 chromosomes. During the process of maturation of the ova and spermatozoa, the number is reduced to half i. e. 23. In fertilization process the number of chromosomes in an egg become once more 46. Hence in this way new combinations take place due to which variations in the offsprings appear.
4. They also occur in higher animals due to parthenogenesis, in which the ova, without the intervention of spermatozoa, develop e. g. in bees, plant lice etc.

   Hence, the variations in the offsprings appear due to biparental parentage and also by the third cause (single parentage).
5. Mutations also cause the modifications in the germinal constitution.
6. External influences, such as X-rays also cause the modifications in the germ plasm.

SOURCES OF VARIATION

- Environmental conditions influence the organisms and bring many variations. The heat or cold,

presence or absence of vegetation, scarcity of food, presence or absence of enemies, climatic conditions all effect individuals and bring about variation.

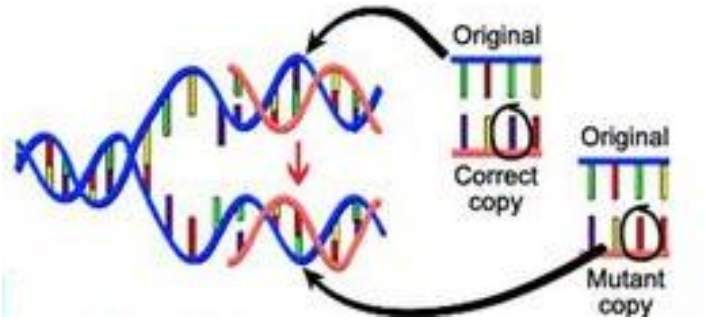
- Endocrine gland secrets hormone which influence the development and differentiation of various physical and mental characters & cause somatogenic and blastogenic variations.
- Genetic or blastogenic variations are also caused by changes in genetic material by gene mutations-change in structure and composition of genes
- Chromosomal Aberrations - Change in structure of chromosomes genetic variation is the difference in DNA among individuals or differences between populations among the same Species
- The multiple sources of genetic variation include mutation and genetic recombination.
- Genetic variation can also be indentified by examining, variation at the level of enzymes using the process of protein electrophoresis
- Genetic variation is caused by variation in order of bases in the nucleotides in genes.
- New technology now allows scientists to directly sequence DNA, which has identified even more genetic variation than was previously detected by protein electrophoresis
- Furthermore, random fertilization also contributes to variation
- A high mutation rate caused by the lack of a proofreading mechanism appears to be a major source of the genetic variation that contributes to RNA virus evolution.
- Crossing over (genetic recombination) and random segregation during meiosis con result in the production of new alleles or new combinations of alleles. Genetic recombination also has been shown to play a key role in generating the genetic variation that underlies RNA virus evolution
- Genotype is the total sum of genetic determinants carried by a cell that is transmitted from generation to generation. Genotype is determined by the genetic information contained in the entire DNA content of the genome in the chromosome.
- Genes carry instructions that are used for building protein. Differences in DNA sequence or gene between individuals are also known as genetic variations, and each variation of a gene is called an allele.
- Genetic variation occurs in entire species, known as genetic diversity. Genetic variation is essential for the natural selection process because natural selection can only decrease or increase the allelic frequency already present in the population.
- Genetic variation plays an advantageous role in the population because it favors some individuals to adapt to the environment. Mutation, gene flow, sexual reproduction, random mating between organisms, random fertilization, and crossing over are the main cause of genetic variation. Genetic variation along with environmental variation causes phenotypic variation in a population. An example of phenotypic variation is the height of a plant.

Mutations, gene flow and sexual reproduction are three primary sources of genetic variation.

Mutation is a process which produces altered DNA sequence. Mutations are the result of changes in the nucleotide sequence of DNA. Mutations often result from random errors in DNA replication that result in the addition or loss of a nucleotide from DNA. Nucleotide addition causes an insertion mutation while loss results in a deletion mutation. Both insertion and deletion mutations result in a frameshift mutation - an alteration in the reading frame of the DNA. Another type of mutation

is a substitution mutation, in which one nucleotide is replaced by another. In substitution mutations, the reading frame is unaltered and a single codon, or group of three nucleotides, changes. This may mean a change in the resulting amino acid sequence and in the final protein produced.

It may be induced by radiations and chemical mutagens in the environment or insult from endogenous reactive oxygen species (ROS) or occur spontaneously due to endogenous factors (errors in chromosomal segregation, recombination, DNA replication and repair, and also spontaneous chemical damage to DNA). Mutations are inexorable. They may have adverse effects on organism's health and survival. Sometimes, they may have no obvious effects or rarely, they may be beneficial for the bearer.



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Gene Flow

Gene flow is the transfer of genes from one population to another and thus affects the allele frequency. The rate of gene flow is directly proportional to the mobility of an individual and is limited by geographical barriers which may be natural or man-made. Cross-species hybridization in plants to generate new and improved varieties and gene transfer from bacteria or virus to new hosts lead to genomic variations. Gene flow is the movement of individual organisms and genetic information into and out of a population. Birds leaving a mainland population to colonize an island, human migration, and pollen blowing in the wind are all examples of gene flow. This migration of genes is a major factor in genetic variation within species and between populations, both positive and negative. For example, organisms can carry new variants of genes into a population that confer resistance to disease.

Sexual Reproduction

Somatic cells divide and multiply by mitosis that produces daughter cells, identical to the parent cell, whereas during gamete formation, a species type of cell division, i.e. meiosis, results in newer combinations of parental genotypes by crossing over and independent assortment of homologous chromosomes thus generating unique genotypes. Followed by random fertilization. Sexually reproducing organisms are more diverse than the asexually reproducing ones.

Significance of variations

- Human-caused environmental changes such as deforestation and land degradation can result in rapid changes in a species' distribution, leading to population decrease, segmentation, and regional isolation.
- Variations form the basis of heredity.
- They constitute the raw material for evolution.
- They help in adaptation of organisms to the changed environment.
- Due to variations, useful variants of animals and plants are created.
- These provide each organism a distinct individual.

- These make individuals better suited for their survival in nature.

SAQ-3

1. The differences that are found between the individuals of same species are called ……...
2. The …….. in an organism are caused due to external influence, in its life time.
3. ……., …… and …….. are three primary sources of genetic variation.

12.6 Summary

- Genetic isolates form new species through an evolutionary process known as speciation. All modern species diversity is a product of genetic isolates and evolution.
- Genetic variations are often unequally distributed over a species' geographic distribution, with differences between populations at the geographic center and the range's extremities.
- Human-caused environmental changes such as deforestation and land degradation can result in rapid changes in a species' distribution, leading to population decrease, segmentation, and regional isolation.
- Natural selection, mutation, genetic drift, and gene flow (gene migration) all contribute to changes in allele frequencies. Collectively, these are referred to as the main **mechanisms of evolution**.
- Genetic isolation form new species throw and evolutionary process known as speciation.
- It's possible for reproductive isolation and subsequent speciation to occur without geographic isolation, too! This is called **sympatric speciation**
- **Allopolyploidy** produces a hybrid organism with multiple sets of chromosomes by combining the gametes from two different species.
- **Allopatric speciation**, the most common form of speciation, occurs when populations of a species become geographically isolated.
- The variations that affect the germinal or reproductive cells only are called germinal variations. These are inherited from parents to their off-springs. Hence, these variations are very important for the evolution. The possible cause of such variations are mainly due to recombination and mutations Recombination occurs due to reshuffling of parental genes which results in organisms with new genetic combination Due to the mutation, structural changes in DNA or chromosomes occur resulting into change in phenotype.

12.7 Terminal Questions

1. Describe in details Isolating mechanism.

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2. Describe in details Genetic basis of Isolation.

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3. Describe in details different kinds of variation and significance of variation.

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4. Describe in details role of Isolation in evaluation.

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5. Differentiate in Isolation, variation and Speciation.

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6. Write short Notes on

a) reproductive isolation

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b) different kinds of adaption

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c) sources of variation

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d) biotic isolation

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e) sympatric speciation

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12.8 Answers

SAQ-01

1. separation, reproduction
2. speciation.
3. prezygotic
4. postzygotic

SAQ-2

1. sympatric speciation
2. Allopolyploidy
3. Allopatric speciation

SAQ-3

1. Variation.
2. acquired variations.
3. Mutations, gene flow and sexual reproduction

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Unit-13 Evolution of Human

Structure

13.1 Introduction

From the dust of ancient stars, we are forged. Carbon, hydrogen, nitrogen, and oxygen - the building blocks of life - are the same elements that make up the stars in the sky. These elements have journeyed across the cosmos, from one generation of stars to another, before finally coming together to create us. We are not just made of stardust; we are the embodiment of the universe's long and fascinating history. Within the very fabric of our being lies an epic narrative that spans billions of years, encompassing the birth and death of stars, the formation of galaxies, and the emergence of life itself. As we gaze up at the night sky, we are not merely observers of a vast and distant expanse; we are, in a very real sense, the cosmos made conscious.

The evolution of humans is a tale unlike any other. From single-celled organisms to complex beings with the ability to ponder the meaning of life itself, our journey has been marked by a relentless drive to survive and thrive. We have transcended the limitations of our ancestors, developing the capacity to think, communicate, and manipulate the world around us in ways that no other species can. Our very existence is a testament to the power of evolution, a force that has shaped and molded life on Earth for billions of years.

But how did we come to be the thinking, talking, and walking beings we are today? How did the remnants of an ancient star give rise to a species capable of exploring the cosmos and contemplating its own existence? These questions have captivated scientists, philosophers, and curious minds for centuries, and the search for answers has led us on a journey of discovery that spans the disciplines of biology, anthropology, archaeology, and more.

As we embark on this journey, it is important to remember that the story of human evolution is not a linear narrative with a clear beginning, middle, and end. Rather, it is a complex web of interrelated events, processes, and adaptations that have unfolded over the course of millions of years. There are still many gaps in our understanding, and new discoveries are continually reshaping our view of our own origins. Nevertheless, the story that has emerged thus far is a captivating and awe-inspiring one, filled with triumphs, setbacks, and surprises at every turn.

Our journey began some 4.6 billion years ago, with the formation of the Earth itself. In the early days of our planet's history, the conditions for life as we know it was far from ideal. The young Earth was a hot, chaotic, and inhospitable place, bombarded by meteorites and bathed in radiation from the newly formed Sun. Yet, against all odds, life managed to gain a foothold in this harsh environment,

taking advantage of the abundant resources and energy provided by the young planet.

The first life forms on Earth were simple, single-celled organisms, not unlike the bacteria and archaea that still inhabit our world today. Over time, these microscopic pioneers evolved, diversifying into a dizzying array of forms and functions.

As these early life forms adapted to their surroundings, they gave rise to a stunning array of complexity and diversity. From the depths of the ocean to the highest mountaintops, life began to spread and flourish, colonizing every corner of our planet.

Approximately 3.5 billion years ago, a remarkable event occurred that would forever change the course of life on Earth: the emergence of photosynthesis. This process allowed certain organisms to capture the energy of sunlight and convert it into chemical energy, providing a virtually limitless source of fuel for growth and reproduction. With the advent of photosynthesis, the stage was set for an explosion of life, and the first hints of the intricate ecosystems that we know today began to take shape.

Fast forward to around 800 million years ago, when another milestone in the history of life occurred: the appearance of multicellular organisms. These complex life forms were composed of multiple cells, each with its own specialized function, working together in a coordinated fashion to ensure the survival and reproduction of the whole organism. This innovation opened the door to an entirely new realm of possibilities for life on Earth, paving the way for the development of plants, animals, and, eventually, humans.

As the eons passed, life continued to evolve and diversify, giving rise to a stunning array of forms and functions. Some 540 million years ago, during a period known as the Cambrian explosion, the pace of evolution accelerated dramatically, resulting in the appearance of most major animal groups that exist today. This rapid burst of evolutionary innovation laid the foundation for the complex and diverse ecosystems that now cover our planet.

It is within this grand tapestry of life that our own story begins, some 7 million years ago, when a group of primates in Africa took the first tentative steps toward becoming human. These early ancestors, known as hominids, were still very much ape-like in appearance and behavior, but they possessed one key trait that set them on a path toward humanity: the ability to walk upright on two legs. This seemingly simple adaptation would prove to be a game-changer, as it allowed our ancestors to free their hands for other tasks, such as carrying food and using tools, which in turn would drive the evolution of our brains and the development of our culture.

Over the next several million years, our hominid ancestors continued to evolve, giving rise to a number of different species, each with its own unique set of adaptations and behaviors. Some, like the robust australopithecines, were built for a life of brute strength and physical endurance, while others, like the early members of the Homo genus, were characterized by their larger brains and more refined tool use.

As our ancestors continued to evolve and diversify, they began to spread out across the African continent, encountering new environments and challenges along the way. These challenges, in turn, drove the development of new adaptations and behaviors, as well as the emergence of new species. Among these new species was Homo erectus, a hominid that first appeared around 1.9 million years ago and would go on to become one of the most successful and long-lived members of our lineage.

Homo erectus was a true pioneer, venturing beyond the borders of Africa and into the wider world. Armed with an advanced toolkit and a newfound mastery of fire, these early humans were able to colonize a wide range of habitats, from the savannas of Africa to the forests of Asia and the grasslands of Europe. Along the way, they encountered other hominid species, such as the Neanderthals and the

Denisovans, with whom they interacted and, in some cases, interbred.

The story of human evolution is a tale of constant change and adaptation, a never-ending struggle to survive and thrive in an ever-changing world. As our ancestors faced new challenges, they developed new skills and strategies, gradually accumulating the knowledge and abilities that would one day give rise to our own species, *Homo sapiens*.

Around 300,000 years ago, the first members of our own species emerged in Africa, marking the beginning of a new chapter in the story of human evolution. *Homo sapiens*were distinguished by their larger brains, more sophisticated tools, and advanced cultural practices, all of which enabled them to thrive in a wide range of environments and eventually outcompete their hominid relatives.

As *Homo sapiens* spread across the African continent, they began to encounter other hominid species, such as the Neanderthals and the Denisovans. These encounters were marked by both competition and cooperation, as well as the exchange of genes through interbreeding. The legacy of these ancient encounters can still be seen in our own DNA today, as many modern humans carry small amounts of Neanderthal and Denisovan ancestry.

As our species continued to evolve and adapt, we developed new technologies and cultural practices that enabled us to harness the resources of our environment more efficiently and effectively. The development of agriculture, for example, marked a major turning point in human history, allowing for the growth of complex societies and the rise of civilization.

With the advent of civilization, the pace of human evolution accelerated, driven by a complex interplay of cultural and genetic factors. New challenges and opportunities emerged, such as the need to cooperate and communicate on a large scale, which in turn drove the development of new cognitive abilities and social behaviors.

As we spread across the globe, our species continued to diversify, giving rise to the many different populations and cultures that exist today. From the Arctic to the tropics, humans have adapted to a wide range of environments, each with its own unique set of challenges and opportunities.

In the relatively short span of our existence, *Homo sapiens* have come to dominate the planet, shaping the world around us in profound and lasting ways. We have harnessed the forces of nature, built great cities, and explored the far reaches of our solar system. And yet, despite all of our achievements, we remain a product of our evolutionary history, a species forged from the dust of ancient stars.

As we look to the future, we must remember that the story of human evolution is far from over. Our species will continue to change and adapt, driven by the same forces that have shaped our past. The challenges we face today, such as climate change, disease, and technological disruption, will undoubtedly leave their mark on our genetic and cultural heritage, shaping the course of our evolution for generations to come.

In conclusion, the story of human evolution is a remarkable testament to the power of life, a saga of adaptation and innovation that spans billions of years and countless generations. From the humble beginnings of single-celled organisms to the complex beings we are today, the story of our species is written in the stars and in our DNA. As we continue to unravel the mysteries of our past and look toward the future, we stand as living proof of the universe's capacity for creativity and change. Our journey is far from over, and the next chapter of human evolution remains to be written. But one thing is certain: as long as we continue to survive and thrive, the legacy of our ancient stardust ancestors will live on in each and every one of us.

Objectives:

After studying this unit you will be able to know-

- Discuss the Ancestral apes and fossil human
- Origin and races of modern human
- Explain the distribution of human diversity and colonization.

13.2 Ancestral Apes and Fossil Humans: The First Steps of Our Journey

Ancestral Apes: Our Distant Cousins

Millions of years ago, a group of primates known as the hominoids branched off from other primates, embarking on a unique and fascinating evolutionary journey. These hominoids included apes, such as gorillas, chimpanzees, bonobos, and orangutans, each of which played a critical role in shaping the trajectory of our lineage. It is from these apes that our lineage eventually diverged, leading to the rise of hominids, our direct ancestors. The first hominids are believed to have emerged around 7 million years ago, marking the beginning of a transformative era in the history of life on Earth.

The story of our ancestral apes is one of remarkable adaptability, resilience, and innovation. Confronted with a rapidly changing environment, these primates evolved a suite of traits that allowed them to thrive in diverse habitats, from the dense tropical forests to the open savannas. Among these traits was bipedalism, the ability to walk on two legs, which would prove to be a significant advantage in the African savannas. This ability to walk upright freed their hands, allowing them to carry food, use tools, and perform other tasks that would contribute to their survival.

As we delve into the rich tapestry of our ancestral apes, we find a diverse cast of characters, each with their own unique adaptations that played a crucial role in shaping our evolutionary path. The earliest hominoids, such as Proconsul, retained many monkey-like characteristics, including a flexible limb structure that allowed them to move adeptly through their arboreal environment. These early hominoids inhabited the forests of Africa and Asia, where they foraged for fruits, leaves, and other plant-based foods.

Over time, the hominoids began to diversify, giving rise to a variety of ape species with distinct adaptations and lifestyles. For example, the more advanced apes like Sivapithecus, which showed a striking resemblance to modern orangutans, were highly adapted to life in the trees, with long arms, hook-like hands, and a highly mobile shoulder joint that allowed them to swing effortlessly from branch to branch.

Another key player in our ancestral ape story is the genus Dryopithecus, which lived around 12 to 13 million years ago in Europe and Asia. These apes exhibited several traits that foreshadowed the emergence of the hominids, including a more human-like dental structure and a reduced reliance on arboreal locomotion. Dryopithecus provides an important link between the early hominoids and the later apes that would give rise to our own lineage.

The African apes, including gorillas, chimpanzees, and bonobos, represent our closest living relatives, sharing between 95% and 99% of their DNA with humans. The split between the human lineage and that of our closest relatives, the chimpanzees and bonobos, is thought to have occurred around 6 to 7 million years ago, setting the stage for the emergence of the first hominids.

In addition to their genetic similarity, our ancestral apes shared a number of behavioral traits that would lay the groundwork for the development of human culture and society. These apes exhibited complex social structures, cooperative behavior, and rudimentary tool use, all of which would play a critical role in the survival and success of our early ancestors.

As we reflect on the diverse array of ancestral apes that contributed to our evolutionary heritage, we are reminded of the intricate web of adaptations, innovations, and relationships that have shaped our species. It is through the study of these distant cousins that we can begin to unravel the mysteries of our own origins, piecing together the intricate puzzle of our evolutionary past. From the earliest hominoids to the advanced apes that walked the path towards hominids, each species represents a unique chapter in the story of human evolution.

The transition from ape to hominid was marked by a series of critical adaptations that set the stage for the emergence of our own species. Among these adaptations were the development of a larger brain, which facilitated the growth of complex cognitive abilities, and the refinement of bipedalism, which allowed our ancestors to traverse the open savannas more efficiently.

The emergence of bipedalism, in particular, represents a major turning point in our evolutionary history, as it enabled our ancestors to exploit new ecological niches and access resources that were previously unattainable. By walking upright, early hominids were better equipped to scan their surroundings for potential predators, as well as to reach and gather food from the ground and low-hanging branches. Bipedalism also facilitated the development of more sophisticated tool use, as it freed the hands for manipulating objects and performing intricate tasks.

As we trace the lineage of our ancestral apes through time, we encounter a diverse array of hominid species, each of which contributed to the tapestry of our evolutionary history. These early hominids, including species such as Ardipithecusramidus, Australopithecus afarensis, and *Australopithecus africanus*, exhibited a mix of ape-like and human-like traits, reflecting their transitional status between our ape ancestors and the members of the Homo genus.

The study of our ancestral apes and early hominids has been greatly facilitated by the discovery and analysis of fossils, which provide invaluable insights into the lives and adaptations of these ancient species. The ongoing excavation and examination of these fossils have revolutionized our understanding of human evolution, revealing a complex and dynamic process that has shaped our species over millions of years.

In conclusion, the story of our ancestral apes is a tale of remarkable resilience, adaptability, and innovation, as these primates navigated the challenges of a rapidly changing world. By examining the diverse cast of characters that make up our evolutionary heritage, we gain not only a deeper understanding of our own origins but also a profound appreciation for the extraordinary journey that has led us to where we are today. From the first tentative steps of our distant ape cousins to the rise of the hominids and the eventual emergence of *Homo sapiens*, our story is one of continuous transformation and reinvention, a testament to the power and potential of life itself.

SAQ:1

a) Over time, the .....began to diversify, giving rise to a variety of ape species with distinct adaptations and lifestyles.

b) The study of our .....and early hominids has been greatly facilitated by the discovery and analysis of fossils, which provide invaluable insights into the lives and adaptations of these ancient species.

c) From the first tentative steps of our distant ape cousins to the rise of the hominids and the eventual emergence of .....,

Table 8:Evidences of Ancestral Apes

Scientific Name	Timeline (Years Ago)	Geological Time Scale	Year of Discovery	Place of Discovery	Scientists Involved	Key Findings	Other Details
Proconsul	17-23 million	Early Miocene	1909	Kenya, Uganda	Arthur Hopwood	Early hominoid; transition from monkey-like primates to advanced apes	Quadrupedal arboreal locomotion
Dryopithecus	11-12.5 million	Late Miocene	1856	France, Spain	Edouard Lartet	Traits foreshadowing hominids; link between early hominoids and later apes	Suspensory adaptations, frugivory
Sivapithecus	12.5-8.5 million	Late Miocene	1879	India, Pakistan	Hugh Falconer, ProbyCautley	Closely related to orangutans; arboreal locomotion adaptations	Dental similarities to orangutans
Oreopithecus	7-9 million	Late Miocene	1872	Italy	Paul Gervais	Unique adaptations for bipedalism and climbing	Fossilized in coal deposits
Ardipithecusramidus	4.4 million	Pliocene	1994	Ethiopia	Tim D. White, Yohannes Haile-Selassie, BerhaneAsfaw	Early hominid; mix of ape-like and human-like traits including bipedalism	Forest-dwelling, opposable big toe
Australopithecus afarensis	3.9-2.9 million	Pliocene	1974	Ethiopia, Tanzania	Donald Johanson, Tom Gray, Maurice Taieb	Early hominid; bipedalism; key evidence for human evolution	"Lucy" specimen
Australopithecus africanus	2.1-3.3 million	Pliocene	1924	South Africa	Raymond Dart	Early hominid; evidence for human evolution, development of bipedalism	Taung Child specimen
Sahelanthropustchadensis	6-7 million	Late Miocene	2001	Chad	Michel Brunet, Alain Beauvilain, FanoneGongdibe, MahamatAdoum	One of the earliest known hominids; human-chimpanzee lineage split	Possibly bipedal, small brain size

Fossil Humans: The Rich Tapestry of Our Ancestors

Fossil evidence has provided us with invaluable insights into the lives of our ancestors, illuminating the complex web of relationships and adaptations that have led to our emergence as a distinct species. As we journey back in time, we encounter numerous species that played a part in our evolutionary story, each with their own unique characteristics and contributions to our shared heritage.

The story of our fossil ancestors begins with the enigmatic *Sahelanthropustchadensis*, a species that lived around 7 million years ago and is considered by many to be the earliest hominid. This species, known from a single skull discovered in Chad, displayed a mix of ape-like and human-like features, hinting at the beginnings of our divergence from our ape cousins.

From there, the tapestry of our ancestry grows increasingly complex and diverse, as we encounter species such as *Ardipithecusramidus*, a 4.4-million-year-old hominid that exhibited both bipedalism and arboreal adaptations. This species, nicknamed "Ardi," provides crucial evidence for the early development of bipedalism in our lineage, as well as the transition from a primarily tree-dwelling existence to a more terrestrial lifestyle.

The Australopithecines, a group of hominids that lived between approximately 4 million and 2 million years ago, represent another key chapter in our evolutionary story. Among the most famous of these early hominids is Australopithecus afarensis, exemplified by the iconic fossil "Lucy," which has provided invaluable insights into the development of bipedalism and other key traits in our lineage. Other important Australopithecine species include *Australopithecus africanus*, which was first discovered by Raymond Dart in 1924, and Australopithecus sediba, a more recent discovery that has shed light on the transition from Australopithecines to the genus Homo.

The emergence of the Homo genus marks a significant milestone in our evolutionary journey, as these early humans began to exhibit traits and behaviors that would come to define our species. Homo habilis, which lived around 2.1 to 1.5 million years ago, is considered one of the first known tool users. This innovative adaptation allowed our ancestors to access new food resources and cope with the challenges of their environment more effectively.

Homo erectus, another pivotal species in our lineage, lived between approximately 1.9 million and 100,000 years ago. This early human was the first to harness the power of fire, a development that not only provided warmth and protection but also facilitated the cooking of food, which in turn may have contributed to the development of our large brains. Homo erectus was also the first hominid to venture out of Africa, with fossils discovered in locations as far afield as Indonesia and Georgia, demonstrating a capacity for long-distance migration and the occupation of diverse habitats.

As we continue our journey through the rich tapestry of our fossil ancestors, we encounter an array of fascinating species that have left their mark on our evolutionary story. Among these are the enigmatic Homo naledi, discovered in South Africa's Rising Star Cave, which exhibited a mix of primitive and modern features, and the robust Homo heidelbergensis, which lived around 700,000 to 200,000 years ago and is considered a possible common ancestor of both *Homo sapiens* and Neanderthals.

The Neanderthals, or Homo neanderthalensis, represent one of the most intriguing chapters in our evolutionary tale. These close relatives of modern humans lived in Europe and parts of Asia from around 400,000 to 40,000 years ago and are known for their distinctive physical features, such as their robust build and prominent brow ridges. Recent genetic evidence has revealed that Neanderthals interbred with our own species, *Homo sapiens*, leaving a lasting legacy in the DNA of many modern humans.

In addition to fossil evidence, molecular research has provided a wealth of information on the genetic relationships and interactions between our ancestors and other hominid species. The discovery of the Denisovans, a previously unknown hominid species that contributed to the genetic ancestry of some modern humans, has revolutionized our understanding of the complex interplay between species during the Pleistocene. This research has also revealed evidence of interbreeding between Neanderthals, Denisovans, and early *Homo sapiens*, highlighting the fluidity of our evolutionary story and the intricate web of connections that have shaped our species.

As we contemplate the myriad species that have played a part in our evolutionary journey, we are reminded that our own existence is the culmination of millions of years of adaptation, innovation, and survival against the odds. From the first tentative steps of our distant ape ancestors to the rise of the Homo genus and its myriad descendants, our story is one of continuous transformation and reinvention, a testament to the resilience and creativity of life itself.It is through the study of our fossil ancestors and the molecular evidence left behind in our DNA that we can begin to unravel the mysteries of our past, piecing together the intricate tapestry of our evolutionary heritage. As we continue to uncover new fossils and unlock the secrets of our genetic code, we gain not only a deeper understanding of our own origins but also a profound appreciation for the extraordinary journey that has led us to where we are today. This is the story of how we became who we are, written in the stars and in our DNA – a story that continues to unfold as we push the boundaries of knowledge and embark on new adventures in our quest to explore the cosmos and contemplate our place within it.

Table 9: A summary of significant events in human evolutionary history

Scientific Name	Timeline (Years Ago)	Geological Time Scale	Year of Discovery	Place of Discovery	Scientists Involved	Key Findings	Other Details
Sahelanthropustchadensis	~7 million	Late Miocene	2001	Chad	Michel Brunet, Alain Beauvilain, Patrick Vignaud	Oldest known hominid, likely bipedal, small brain, ape-like features	Nicknamed "Toumaï," meaning "hope of life" in Goran language
Orrorintugenensis	~6 million	Late Miocene	2000	Kenya	Brigitte Senut, Martin Pickford	Bipedal, smaller canines than apes, possibly an early ancestor of humans	Nicknamed "Millennium Man"
Ardipithecusramidus	~4.4 million	Pliocene	1994	Ethiopia	Tim White, BerhaneAsfaw, Gen Suwa	Bipedal, opposable toe for climbing, likely lived in woodland environments	Nicknamed "Ardi"
Australopithecus anamensis	~4.2 - 3.9 million	Pliocene	1995	Kenya, Ethiopia	Meave Leakey, Alan Walker, Richard Leakey	Bipedal, large canines, likely an ancestor of A. afarensis	Transitional species between Ardipithecus and Australopithec

							us
Australopithecus afarensis	~3.9 - 2.9 million	Pliocene	1974	Ethiopia, Tanzania	Donald Johanson, Maurice Taieb, Yves Coppens	Bipedal, ape-like brain, small canines, long arms, curved finger bones for climbing	"Lucy" is the most famous specimen; Laetoli footprints show bipedalism
Australopithecus africanus	~3.3 - 2.1 million	Pliocene	1924	South Africa	Raymond Dart, Robert Broom	Bipedal, human-like teeth, larger brain than A. afarensis, possibly an ancestor of Homo genus	Taung Child and Mrs. Ples are well-known specimens
Homo habilis	~2.4 - 1.4 million	Pleistocene	1960	Tanzania, Ethiopia, Kenya, South Africa	Louis Leakey, Mary Leakey, Jonathan Leakey	First member of the Homo genus, larger brain, smaller teeth, used stone tools	Often referred to as "handy man"
Homo erectus	~1.9 million - 110,000	Pleistocene	1891	Africa, Asia, Europe	Eugene Dubois, Richard Leakey, KamoyaKimeu	Larger brain, smaller teeth, sophisticated tools, first to leave Africa, controlled fire	Some debate about possible subspecies, such as H. ergaster in Africa
Homo heidelbergensis	~700,000 - 200,000	Middle Pleistocene	1907	Africa, Europe	Otto Schoetensack	Ancestor of both Neanderthals and modern humans, used tools, possibly built shelters	Named after the location of the first discovery, Heidelberg, Germany
Homo neanderthalensis	~400,000 - 40,000	Middle to Late Pleistocene	1856	Europe, Asia	Johann Carl Fuhlrott, Hermann Schaaffhausen	Large brain, powerful build, advanced tools, evidence of burial rituals and art	Interbred with modern humans; ~1-2% of non-African human DNA is Neanderthal in origin.

Table 10:Events that helped put together the Human Evolutionary story

Year	**Discovery/Finding**	**Type of Finding**	**Location**	**Scientists Involved**	**Importance/Impact**	**Other Details**
1856	Discovery of the first Neanderthal	Fossil	Neander Valley,	Johann Carl Fuhlrott, Hermann	First recognized evidence of a distinct hominid species that	The species was later named Homo

	fossil		Germany	Schaaffhausen	lived alongside early *Homo sapiens*	neanderthalensis
1868	Discovery of the first Cro-Magnon fossil	Fossil	Les Eyzies, France	Louis Lartet	First evidence of anatomically modern humans (*Homo sapiens*) in Europe	Cro-Magnons are considered the first early modern humans of the European Upper Paleolithic
1924	Discovery of the Taung Child (*Australopithecus africanus*)	Fossil	Taung, South Africa	Raymond Dart	First evidence of early hominid species in Africa, challenged the idea that human ancestors were large-brained	This finding shifted the focus of human origins research from Europe and Asia to Africa
1953	Discovery of the structure of DNA	Molecular	Cambridge, England	James Watson, Francis Crick	Foundation for understanding genetic inheritance and the molecular basis of evolution	This discovery led to a greater understanding of genetics and its role in human evolution
Year	**Discovery/Finding**	**Type of Finding**	**Location**	**Scientists Involved**	**Importance/Impact**	**Other Details**
1960	Discovery of Homo habilis fossils	Fossil	Olduvai Gorge, Tanzania	Louis Leakey, Mary Leakey, Jonathan Leakey	First evidence of the Homo genus, bridging the gap between Australopithecus and Homo erectus	Nicknamed "Handy Man" due to the association with stone tools
1974	Discovery of "Lucy" (*Australopithecus afarensis*)	Fossil	Hadar, Ethiopia	Donald Johanson, Tom Gray	Provided insight into bipedalism and other key evolutionary traits in early hominids	Lucy is one of the most complete and well-preserved hominid fossils ever discovered
1987	Mitochondrial Eve research	Molecular	United States	Allan Wilson, Rebecca Cann, Mark Stoneking	Demonstrated that all living humans share a common female ancestor in Africa ~200,000 years ago	This research was based on the analysis of mitochondrial DNA (mtDNA) in a worldwide sample of humans
1994	Discovery of Ardipithecusramidus fossils	Fossil	Aramis, Ethiopia	Tim White, BerhaneAsfaw, Gen Suwa	Revealed the earliest known hominid ancestor that exhibited both bipedalism and arboreal adaptations	Nicknamed "Ardi"
2000	Discovery of	Fossil	Tugen	Brigitte	Suggested a more	Nicknamed

	Orrorintugenensis fossils		Hills, Kenya	Senut, Martin Pickford	ancient origin for human bipedalism, challenged the human-Australopithecus link	"Millennium Man"
Year	**Discovery/Finding**	**Type of Finding**	**Location**	**Scientists Involved**	**Importance/Impact**	**Other Details**
2008	Evidence of Neanderthal and *Homo sapiens* interbreeding	Molecular	Max Planck Institute, Germany	Svante Pääbo	Demonstrated that modern non-African humans have Neanderthal DNA, indicating interbreeding	This finding has led to a greater understanding of the relationship between Neanderthals and modern humans
2010	Discovery of Denisovan hominid through DNA analysis	Molecular	Altai Mountains, Siberia	Svante Pääbo, Matthias Meyer, David Reich	Revealed a previously unknown hominid species that contributed to the genetic ancestry of some modern humans	Denisovans are known primarily through their DNA, with only a few physical fossils discovered
2013	Discovery of Homo naledi fossils	Fossil	Rising Star Cave, South Africa	Lee Berger, John Hawks	Provided evidence of a new Homo species with a mix of primitive and modern features, and possible intentional body disposal	The exact age of the fossils remains uncertain, but they may be as old as 335,000 - 236,000 years
2015	*Homo sapiens* fossils dated to 300,000 years ago	Fossil	Jebel Irhoud, Morocco	Jean-Jacques Hublin, Abdelouahed Ben-Ncer	Pushed back the origin of our species by 100,000 years, suggesting a more complex evolutionary timeline	This discovery has implications for the understanding of early *Homo sapiens* dispersal and development
2018	Evidence of interbreeding between Denisovans and Neanderthals	Molecular	Vindija Cave, Croatia	Viviane Slon, Svante Pääbo	Showed that not only did Neanderthals and Denisovans interbreed with *Homo sapiens*, but they also interbred with each other	The discovery highlights the complexity of interactions between hominid species during the Pleistocene

13.3 Origin of Modern Humans, Races of Modern Human

The Emergence of Modern Humans: A New Dawn in Evolution

The origin of modern humans, *Homo sapiens*, is a subject that has fascinated scientists and scholars alike for centuries. Piecing together the puzzle of our species' emergence is no small task. It involves sifting through the remnants of our ancestral past, buried deep within the layers of the Earth, and unlocking the secrets encoded within our DNA. The narrative that emerges from these fragments of

evidence is complex and nuanced, reflecting the many twists and turns of our evolutionary journey.

It's generally agreed that *Homo sapiens* first appeared in Africa around 300,000 years ago, based on fossil evidence from sites such as Jebel Irhoud in Morocco and OmoKibish in Ethiopia. These early *Homo sapiens* displayed a mix of modern and archaic traits, signaling the dawn of a new era in human evolution.

The anatomical characteristics that define our species – a globular braincase, a reduced brow ridge, a more prominent chin, and a generally lighter and more gracile skeleton – did not emerge all at once, but gradually over time. This suggests that the evolution of *Homo sapiens* was a process of cumulative change, shaped by a combination of genetic, environmental, and cultural factors.

However, the emergence of *Homo sapiens* was not just a story of physical evolution, but also of cognitive and cultural innovation. Archaeological evidence suggests that early *Homo sapiens* were capable of symbolic thought and complex behavioral practices, as evidenced by the presence of abstract and representational art, sophisticated stone tool technologies, and elaborate burial practices. This cognitive and cultural leap, often referred to as the "Human Revolution", set the stage for the rapid expansion and diversification of *Homo sapiens*.

One of the hallmarks of *Homo sapiens* is our remarkable diversity, reflected in the myriad of physical and cultural variations that exist among contemporary human populations. This diversity is the result of complex interactions between genetic, environmental, and cultural factors over the course of our evolutionary history.

Modern human diversity is often described in terms of "races" or "ethnic groups", but these classifications can be misleading. The concept of race has no firm biological basis, as the genetic variation within any given human population is typically greater than the variation between different populations. This suggests that human diversity is not neatly compartmentalized, but exists along a continuum.

While the concept of race has been largely discredited in scientific circles, the study of human genetic variation remains a vital tool for understanding our evolutionary history. Recent advances in genomics have allowed us to probe deeper into our genetic heritage, revealing patterns of migration, admixture, and selection that have shaped our species.

One of the most significant findings from genomic studies is the evidence of interbreeding between *Homo sapiens* and other hominins, such as Neanderthals and Denisovans. This interbreeding has left a lasting imprint on our genomes, with contemporary non-African populations carrying approximately 1-2% Neanderthal DNA and some Oceanic populations carrying up to 6% Denisovan DNA.

Such findings challenge the traditional "Out of Africa" model, which posited that *Homo sapiens* replaced other hominins without interbreeding. Instead, the evidence suggests a more complex scenario, involving both replacement and assimilation of other hominins by *Homo sapiens*.

Despite these complexities, it's clear that *Homo sapiens* were extraordinarily successful, expanding across the globe and adapting to a wide range of environments. This success can be attributed in part to our species' unparalleled capacity for cultural innovation, which allowed us to create complex social structures, develop new technologies, and exploit novel resources.

However, the rise of *Homo sapiens* was not without its consequences. As our species spread across the globe, other hominins disappeared, marking the end of millions of years of hominin diversity. The reasons for these extinctions are still a matter of debate, but likely involve a combination of competition, interbreeding, and environmental change.

Despite these losses, the legacy of these extinct hominins lives on in our genomes and in our collective memory. Their story is part of our story – a story that is still being written, as we continue to

explore the depths of our evolutionary past and chart the course of our future.Below is a table summarizing the key milestones in the emergence of modern humans, along with the geographical locations and timeframes associated with these events.

Table 11: Key milestones in the emergence of modern humans

Key Milestone	Approximate Timeframe (Years Ago)	Geographical Location	Notable Characteristics
Emergence of Homo sapiens	300,000 - 200,000	Africa (Ethiopia, Morocco)	Fully modern human anatomy; Increased brain size; Sophisticated tool use
First Human Migration out of Africa	70,000 - 60,000	Middle East, Asia, Europe	Genetic divergence leading to distinct populations
Arrival in Australia	65,000 - 45,000	Australia	Evidence of sea travel; Unique adaptations to environment
Arrival in Europe	45,000 - 35,000	Europe	Interactions with Neanderthals; Development of symbolic art and culture
Arrival in North America	26,000 - 18,000	North America	Migration across Bering Land Bridge; Diverse adaptations to various environments
Arrival in South America	15,000 - 12,000	South America	Migration through Central America; Diverse adaptations to various environments
Development of Agriculture	10,000 - 8,000	Middle East, Asia, Americas	Shift from hunter-gatherer lifestyle; Permanent settlements; Population growth

The Diversity of Modern Humans: A Tapestry of Variation

Diversity is one of the defining features of our species. Today, Homo sapiens inhabit nearly every corner of the globe, from the frozen landscapes of the Arctic to the scorching deserts of the Sahara, from the dense rainforests of the Amazon to the towering peaks of the Himalayas. This geographical spread has given rise to a remarkable range of physical and cultural variations, reflecting our species' remarkable ability to adapt and innovate.

Physical variations among modern humans include differences in skin color, hair type, body size, and facial features. These differences are largely the result of local adaptations to specific environmental conditions. For example, populations living near the equator tend to have darker skin, which provides protection against the harmful effects of ultraviolet radiation, while populations living in colder climates tend to have lighter skin, which facilitates the production of vitamin D in low sunlight conditions.

However, physical traits represent only a small fraction of our species' genetic diversity. The vast majority of human genetic variation is found within populations, not between them. This means that any two individuals from the same population are likely to be as genetically different from each other as they are from an individual from a different population. This pattern of genetic variation challenges the traditional concept of race and underscores the unity of our species.

At the same time, the study of human genetic variation provides valuable insights into our evolutionary history. By tracing the patterns of genetic variation across different human populations, scientists can reconstruct the routes of ancient human migrations, identify episodes of interbreeding with other hominins, and detect signals of natural selection.

One of the most significant findings from these genetic studies is the evidence of interbreeding between Homo sapiens and other hominins, such as Neanderthals and Denisovans. As we noted earlier, this interbreeding has left a lasting imprint on our genomes, with contemporary non-African populations carrying approximately 1-2% Neanderthal DNA and some Oceanic populations carrying up to 6% Denisovan DNA.

Another key finding is the evidence of recent positive selection in the human genome. These selection events are often associated with local adaptations to specific environmental challenges. For example, populations living at high altitudes in the Himalayas, Andes, and Ethiopian Highlands have adapted to low oxygen conditions through genetic changes that enhance oxygen transport and metabolism.

Cultural diversity is another hallmark of our species. As Homo sapiens spread across the globe, they encountered a wide range of environments, each with its unique challenges and opportunities. In response to these varying conditions, human groups developed a diverse array of cultural practices, including different languages, belief systems, social structures, and technological innovations.

The diversity of modern humans is not a static feature but a dynamic process, continually shaped by evolutionary forces, environmental pressures, and cultural innovations. As we look towards the future, this diversity will likely continue to evolve, influenced by the interconnected forces of globalization, technological advancement, and environmental change.

To better understand the diversity of modern humans, the following table provides an overview of some key physical and cultural variations observed among contemporary human populations, along with their possible adaptive significances.

Table 12: Physical and Cultural Variations in Modern Humans

Human Population	Key Physical Variations	Key Cultural Variations	Possible Adaptive Significance
Inuit	Short, stocky body; Layer of body fat; Cold-adapted hemoglobin	Hunting-based culture; Seasonal migrations	Adaptations to cold environments; Efficient oxygen utilization
Maasai	Tall, slender body	Pastoral lifestyle; Dairy-based diet	Dissipate heat in hot environments; Metabolic adaptations to dairy diet
Sherpa	Enhanced lung capacity and blood flow	Mountain-dwelling lifestyle; Yak herding	High-altitude adaptations; Enhanced oxygen utilization
Aboriginal Australians	Dark skin pigmentation; Wavy hair	Hunting and gathering; Oral storytelling traditions	Protection against UV radiation; Maintenance of cultural knowledge
Kalahari San	Light skin pigmentation; Epicanthic eye folds	Hunting and gathering; Trance healing practices	Adaptations to desert environments; Maintenance of health and well-being

In the next section, we will delve deeper into the topic of human races, exploring the historical origins, scientific validity, and contemporary implications of this controversial concept."

The Concept of Human Races: A Historical Perspective and Modern Interpretations

The concept of race has a long and fraught history in human societies. For centuries, people have sought to categorize and classify humans based on observable physical traits such as skin color, hair texture, and facial features. These classifications, often rooted in social, political, and economic contexts, have been used to justify systems of power, privilege, and inequality, with profound and lasting consequences.

Historically, racial classifications were based on the misguided belief that human diversity could be neatly divided into distinct and homogenous groups. This view, often referred to as racial essentialism, posited that each race possessed unique and immutable traits that determined its members' behaviors, abilities, and worth.

By the mid-20th century, however, the scientific consensus had begun to shift. Researchers realized that human genetic variation did not conform to the traditional concept of race. The vast majority of human genetic diversity, they found, was found within populations, not between them. Furthermore, the patterns of genetic variation were continuous, not discrete, reflecting the gradual nature of human evolution and migration.

In light of these findings, many scientists and scholars argue that race is a social construct, not a biological reality. While physical differences among humans exist, they say, these differences do not constitute distinct races. Rather, they represent the complex interplay of genetics, environment, and culture.

At the same time, the concept of race continues to hold social and cultural significance. Racial identities influence people's experiences, opportunities, and perspectives, shaping societal structures and interpersonal relationships. Moreover, the legacy of racial essentialism persists in many forms of systemic racism, highlighting the importance of addressing and dismantling racial biases and disparities.

Recent advances in genomics have added a new layer of complexity to the discussion of race. With the advent of personal genomics, individuals can now trace their ancestry and identify genetic variants associated with specific traits and diseases. These developments raise important questions about the use and interpretation of genetic information, the boundaries of racial and ethnic categories, and the implications for health care, identity, and society.

To facilitate a nuanced understanding of the concept of race, the following table provides an overview of the historical and contemporary views on race, as well as their scientific, social, and ethical implications.

Table 13: Concept of Race: Historical and Contemporary Views

Perspective	Views on Race	Scientific Validity	Social and Ethical Implications
19th Century Racial Science	Races as distinct biological categories; Hierarchy of races	No scientific validity; Humans are highly genetically diverse within populations	Used to justify slavery, colonization, and eugenics
Mid-20th Century Anthropology	Races as cultural constructs; Rejection of biological determinism	Partial validity; Genetic differences exist but do not correspond neatly to racial categories	Contributed to civil rights movements; Emphasized cultural diversity
Contemporary Genomics	Race as a rough proxy for ancestral geography; Emphasis on individual genetic ancestry	Partial validity; Genomic variation exists but is complex and continuous	Raises issues of privacy and consent; Can reinforce stereotypes if misinterpreted

The Advent of Genomics and Personal Ancestry

The turn of the 21st century saw a seismic shift in our understanding of human diversity with the advent of genomics, the study of the full set of genes, or the genome, in a species. Genomic technologies have allowed us to probe deeper into our genetic code, unlocking new insights into the story of our species. One of the most captivating applications of this science is in the field of personal ancestry.

By analyzing an individual's DNA, scientists can trace their lineage back through time, revealing the geographic locations where their ancestors lived, the populations they were part of, and the migratory routes they took. This information is often represented as a percentage breakdown of an individual's genetic ancestry, showing the proportion of their genome that can be traced back to different regions or populations.

It's worth noting, however, that these estimates are just that - estimates. They are based on complex statistical models and depend on the reference populations used in the analysis. As our understanding of human genetic diversity expands, and as more people have their genomes sequenced, these estimates will become more precise.

The rise of personal genomics has not only transformed our understanding of human ancestry but also raised important questions about identity, privacy, and ethics. As we grapple with these issues, it's essential to remember that while our genetic ancestry is part of who we are, it does not define us. Our identities are shaped by a myriad of factors, from our personal experiences and relationships to our cultural heritage and values.

Table 14: Advent of Genomics and Personal Ancestry: Key Milestones, Implications, and Ethical Considerations

Milestone	Year	Implications	Ethical Considerations
Completion of the Human Genome Project	2003	Unprecedented insights into human genetics; Basis for personal genomics	Privacy and consent; Potential for genetic discrimination
Launch of first direct-to-consumer genetic testing service	2007	Democratized access to genetic information; Enabled exploration of personal ancestry	Misinterpretation of results; Inadequate genetic counseling
First use of genetic genealogy in criminal investigation	2018	New tool for law enforcement; Identification of Golden State Killer	Privacy of genetic data; Potential for surveillance and discrimination

The Future of Human Evolution: Speculations and Possibilities

As we peer into the future, we can't help but wonder: what's next for Homo sapiens? Will we continue to evolve, and if so, how? These questions, while impossible to answer with certainty, offer a fascinating opportunity for speculation.

One possibility is that we will continue to evolve in response to our environment, just as we have for millions of years. For example, as our world becomes increasingly urbanized, we might see the evolution of traits that enhance our ability to thrive in densely populated environments.

Alternatively, we might take control of our own evolution through advances in genetic engineering. Technologies like CRISPR have already made it possible to edit the human genome, raising the prospect of designer babies and the eradication of genetic diseases.

Finally, our future evolution might be driven by factors beyond our planet. If we become a space-faring species, living and reproducing in extraterrestrial environments, we could see the evolution of traits that help us survive in low gravity or withstand high levels of radiation.

While these scenarios are speculative, they underscore the dynamic and unpredictable nature of

evolution. As we step into the future, the only certainty is that change is inevitable. But whatever comes our way, we can take comfort in the fact that we are the descendants of a long line of survivors, inheritors of a legacy of adaptability and resilience.

Table 15:Future of Human Evolution: Speculative Scenarios, Potential Drivers of Change, and Implications

Scenario	Potential Drivers of Change	Implications	Further Details
Genetic Engineering	Advances in genome editing technologies like CRISPR, increasing understanding of human genetics, rise of personalized medicine	Potential for 'designer babies'; Reduction or elimination of certain genetic diseases; Creation of new phenotypic diversity	Ethical issues around consent, equity, and 'playing god'; Risk of unforeseen consequences due to complexity of genetics
Climate Change	Global warming; Rising sea levels; Increasing climate variability and extreme weather events	Evolution of heat-tolerant and weather-resistant adaptations; Population displacement and changes in mating patterns; Possible increase in disease resistance	Ethical issues around climate justice and intergenerational equity; Potential for increased conflict over resources
Space Colonization	Advances in space travel and terraforming; Increasing interest from private companies and governmental organizations	Evolution of space-adapted humans; Creation of new selective pressures (e.g., reduced gravity, radiation); Genetic divergence between Earth-bound and space-bound humans	Ethical issues around planetary protection, exploitation of resources, and governance in space; Potential for cultural divergence alongside genetic divergence
Cybernetics and Artificial Intelligence	Advancements in machine learning, AI, and neural interfaces; Increasing integration of technology and biology	Creation of cybernetic organisms with enhanced capabilities; Changes in brain evolution due to integration with AI; Changes in social dynamics and mating patterns	Ethical issues around privacy, consent, and equity; Potential for new forms of discrimination based on cybernetic enhancements

Globalization and Urbanization	Increasing interconnectedness of human populations; Growth of mega-cities; Shifts towards digital and virtual interactions	Reduction in geographical barriers to mating, potentially increasing genetic diversity; Adaptations to urban environments and lifestyles (e.g., resistance to pollution)	Ethical issues around cultural preservation and urban equity; Mental health implications of urban lifestyles
Pandemics	Emergence of new pathogens; Increasing antibiotic resistance; Global travel and climate change facilitating pathogen spread	Selection for disease resistance; Possible changes in social behavior and mating patterns; Impact on population structures	Ethical issues around health equity and access to medical care; Potential for increased xenophobia and discrimination

Human Adaptation and the Influence on Modern Human Diversity

Our ancestors' journey out of Africa to colonize the world was no small feat, and it left an indelible imprint on our genomes. As they moved into different environments, they encountered new challenges, from frigid arctic climates to high-altitude Mountains. To survive and reproduce in these diverse settings, they evolved a variety of adaptations, many of which are still present in modern human populations.

These adaptations can be seen in a myriad of physical characteristics. Skin pigmentation, for example, varies widely among human populations, reflecting a balance between the need for sun protection and vitamin D synthesis. People in equatorial regions, where sunlight is most intense, tend to have darker skin, which provides protection against harmful ultraviolet radiation. Meanwhile, people in high-latitude regions, where sunlight is less abundant, tend to have lighter skin, which allows for sufficient vitamin D production.

Other adaptations are less visible but equally significant. Populations living at high altitudes, such as the Andean and Tibetan peoples, have unique physiological traits that enable them to withstand low oxygen levels. These include increased lung capacity, higher blood oxygen saturation, and greater blood vessel dilation, among others.

Furthermore, cultural practices have played a crucial role in human adaptation. Agriculture, for instance, has had a profound impact on our species. With the advent of farming, humans began to consume large amounts of starchy foods, leading to an increased copy number of the gene AMY1, which produces an enzyme that breaks down starch. Similarly, the domestication of cattle and the subsequent practice of dairy farming led to the spread of lactose tolerance among some populations.

These examples underscore the complexity and dynamism of human evolution. As our ancestors moved across the globe, they did not merely passively respond to their environments; they actively shaped them, inventing new ways of subsisting and coexisting. In doing so, they laid the foundation for the incredible diversity we see in humans today.

To capture the breadth and depth of human adaptation, the following table provides a detailed overview of key adaptations in various human populations, including their genetic basis, environmental context, and evolutionary significance.

Table 16: Key human adaptations: genetic basis, environmental context, and evolutionary

significance

Human Population	Key Adaptation	Genetic Basis	Environmental Context	Evolutionary Significance
People in Equatorial regions	Dark Skin Pigmentation	MC1R, SLC24A5 genes	High intensity sunlight	Protection against harmful ultraviolet radiation
People in High-Latitude regions	Light Skin Pigmentation	MC1R, SLC24A5 genes	Low intensity sunlight	Adequate Vitamin D synthesis
Andean and Tibetan people	High-altitude Adaptation	EPAS1, EGLN1 genes	Low oxygen levels	Enhanced oxygen utilization
Populations with agricultural ancestry	Increased starch digestion	AMY1 gene	High starch diet	Enhanced energy extraction
Populations with dairy farming ancestry	Lactose Tolerance	LCT gene	Dairy consumption	Nutrient extraction from dairy products

In conclusion, the evolution of modern humans is a rich and intricate tapestry woven with threads of genetics, environment, and culture. As we delve into the layers of this tapestry, we encounter a narrative of transformation, innovation, and resilience, reflecting our species' extraordinary capacity to adapt and thrive. From our humble beginnings in the heart of Africa to our present-day global dispersion, we have been, and continue to be, shaped by our interactions with the world around us. By understanding and appreciating our shared evolutionary history, we can better understand ourselves, each other, and the world we inhabit.

13.3 Distribution of Human Diversity and Colonization: The Great Human Journey

The story of human evolution is not just a story of physical and cognitive adaptations; it is also a story of how our species came to populate every corner of the planet. The distribution of human diversity and colonization is a testament to our species' ability to adapt and innovate, overcoming countless challenges as we spread out across the globe. This journey is a fascinating and complex tale, involving the interplay of cultural, environmental, and genetic factors that have shaped the human experience.

Out of Africa: The Cradle of Humankind

The story of human colonization and diversity begins in Africa, the birthplace of our species and the cradle of humankind. Africa is not only home to the earliest fossils of *Homo sapiens* but also the site of our most ancient genetic lineages, making it the most important region for understanding the origins and early evolution of our species. In this section, we will delve into the rich and complex history of human evolution in Africa, examining the various factors that drove our ancestors to venture out into the world and explore new frontiers.

The African Origin of Homo sapiens

Fossil evidence and genetic data strongly support the idea that modern humans originated in Africa, with the oldest *Homo sapiens* fossils dating back to around 300,000 years ago. These early anatomically modern humans, sometimes referred to as "archaic *Homo sapiens*," exhibited a mix of primitive and derived traits, reflecting a transitional stage in our evolutionary journey. For example, the OmoKibish and Herto specimens from Ethiopia, dating back to 195,000 and 160,000 years ago, respectively, display a mosaic of features, with some similarities to both earlier hominins and later *Homo sapiens*.

The African origin of our species is further supported by genetic evidence, with studies of mitochondrial DNA (mtDNA) and Y-chromosome data indicating that all living humans share a common African ancestry. The "mitochondrial Eve" and "Y-chromosomal Adam," theoretical common ancestors of all humans, are estimated to have lived in Africa around 200,000 and 300,000 years ago, respectively.

The Role of Climate Change in Human Evolution

One of the key factors that shaped the evolution of *Homo sapiens* in Africa was the fluctuating climate of the Pleistocene epoch, which was characterized by alternating periods of glaciation and interglaciation. These climatic changes had profound effects on the African landscape, leading to the expansion and contraction of forests, savannas, and other ecosystems. This dynamic environment likely played a crucial role in driving the adaptation and diversification of early *Homo sapiens* populations.

During periods of increased aridity, the once-continuous forests of Africa became fragmented, giving rise to isolated pockets of more open savanna habitats. This ecological transformation may have promoted the emergence of new adaptive strategies, such as the development of more sophisticated tools and weapons, the use of fire, and the exploitation of a broader range of food sources. These innovations would have allowed early *Homo sapiens* to exploit new niches and expand their range, setting the stage for the eventual colonization of the rest of the world.

The Expansion of Homo sapien Within Africa

The first major dispersal of *Homo sapiens* within Africa is thought to have occurred around 70,000 to 80,000 years ago, as populations expanded out of their ancestral homeland in East Africa and into new territories across the continent. This expansion was likely driven by a combination of factors, including population growth, technological innovations, and ecological changes.

One of the most significant developments during this time was the emergence of the so-called "Middle Stone Age" (MSA) toolkit, a suite of more advanced stone tools and weapons that represented a major leap forward in technological sophistication. The MSA toolkit included finely crafted points, blades, and scrapers, which allowed early *Homo sapiens* to process food more efficiently and exploit a broader range of resources. This technological revolution likely played a crucial role in facilitating the expansion of *Homo sapiens* across Africa, as well as their eventual migration out of the continent.

As *Homo sapiens* populations expanded within Africa, they encountered a diverse array of environments, from the dense forests of Central Africa to the arid deserts of the Sahara and the fertile river valleys of the Nile and Niger. These varied landscapes presented both challenges and opportunities, prompting the development of new adaptive strategies and cultural innovations. For example, early *Homo sapiens* in the Sahara adapted to the harsh desert environment by developing sophisticated water management techniques, while those in the Nile Valley relied on agriculture and animal husbandry to sustain their growing populations.

The Out-of-Africa Hypothesis: Leaving the Cradle

The Out-of-Africa hypothesis, which posits that modern humans originated in Africa and later migrated to other parts of the world, is supported by a wealth of genetic, archaeological, and paleoanthropological evidence. The first major wave of *Homo sapiens* migration out of Africa is thought to have occurred around 70,000 years ago, when a small group of early modern humans crossed the Bab-el-Mandeb Strait at the southern end of the Red Sea and entered the Arabian Peninsula.

From there, these pioneering explorers embarked on a remarkable journey of colonization that would ultimately lead them to every corner of the globe. They followed the coastal regions of South Asia, eventually reaching Southeast Asia and Australia by around 50,000 years ago. Another branch of this migration took those northwards into Europe and Central Asia, where they encountered and eventually replaced the Neanderthals and other archaic hominins that had previously inhabited these regions.

Timelines and Geographical Hotspots of Early *Homo sapiens* Dispersal

The following table provides a summary of the major timelines and geographical hotspots associated with the early dispersal of *Homo sapiens* within and outside of Africa.

Table 17: Timelines and Geographical Hotspots of Early Homo sapiens Dispersal

Time Period (Years Ago)	Geographical Hotspot	Key Events
300,000	East Africa	Emergence of archaic *Homo sapiens*
195,000	Ethiopia	OmoKibish specimen
160,000	Ethiopia	Herto specimen
70,000-80,000	East Africa	Expansion of *Homo sapiens* within Africa
70,000	Arabian Peninsula	First wave of migration out of Africa
60,000	South Asia	Coastal migration along the Indian Ocean
50,000	Southeast Asia	Arrival in Australia
45,000	Europe	Replacement of Neanderthals
40,000	Central Asia	Interbreeding with Denisovans

The Genetic Legacy of Early Human Migrations

The migrations of early *Homo sapiens* not only shaped the course of human history but also left a lasting imprint on our genetic makeup. As *Homo sapiens* populations dispersed across the globe, they encountered and interbred with other hominin species, such as Neanderthals and Denisovans. These interbreeding events have left traces of archaic hominin DNA in the genomes of modern humans, with some populations exhibiting higher levels of archaic ancestry than others.

For example, it is estimated that around 1-2% of the DNA of non-African populations is of Neanderthal origin, while some populations in Southeast Asia and Oceania have up to 5% Denisovan

DNA. These genetic remnants not only provide valuable insights into the complex history of human migrations but also have important implications for our understanding of human biology, as some of the genes we inherited from our archaic cousins may have played a role in shaping our immune systems, metabolisms, and other physiological traits.

The Great Human Migration: Colonizing the World

The story of human migration is a testament to our species' remarkable capacity for adaptation, innovation, and resilience. As *Homo sapiens* ventured out of Africa and into the wider world, they encountered a diverse array of environments, from the frozen landscapes of the Arctic to the lush rainforests of South America. Each new habitat presented unique challenges and opportunities, prompting the development of novel strategies and technologies that enabled our ancestors to thrive in even the most inhospitable corners of the globe. In this section, we will explore the various stages of the great human migration, tracing the intricate web of movements that ultimately led to the colonization of every habitable continent on Earth.

The Initial Dispersal of *Homo sapiens* Out of Africa

As previously mentioned in section 2.1, the first wave of *Homo sapiens* migration out of Africa is thought to have occurred around 70,000 years ago, with a small group of early modern humans crossing the Bab-el-Mandeb Strait at the southern end of the Red Sea and entering the Arabian Peninsula. This initial dispersal was likely driven by a combination of factors, including population pressure, resource scarcity, and climate fluctuations, which may have created "push" and "pull" factors that encouraged early *Homo sapiens* to venture into new territories.

From the Arabian Peninsula, these pioneering explorers embarked on a remarkable journey that would ultimately lead them to every corner of the globe. They followed the coastal regions of South Asia, eventually reaching Southeast Asia and Australia by around 50,000 years ago. Another branch of this migration took them northwards into Europe and Central Asia, where they encountered and eventually replaced the Neanderthals and other archaic hominins that had previously inhabited these regions.

The Colonization of Europe

The arrival of *Homo sapiens* in Europe marked a major turning point in the history of human migration, as it brought our species into direct contact with the Neanderthals, who had been the dominant hominins in the region for hundreds of thousands of years. The interactions between these two groups are the subject of ongoing scientific debate, with some evidence suggesting that there may have been instances of both conflict and cooperation.

Over time, *Homo sapiens* gradually replaced the Neanderthals in Europe, with the last known Neanderthal populations disappearing around 40,000 years ago. This replacement process is thought to have been driven by a combination of factors, including competition for resources, interbreeding, and the superior cultural and technological innovations of *Homo sapiens*, which allowed them to adapt more effectively to the changing climate and landscape of the Late Pleistocene.

The colonization of Europe also coincided with the development of the so-called "Upper Paleolithic" culture, which was characterized by a suite of more advanced tools, weapons, and artistic expressions, such as cave paintings, sculptures, and personal ornaments. These cultural innovations likely played a crucial role in facilitating the expansion of *Homo sapiens* across the continent, allowing them to exploit a wider range of resources and adapt to diverse environments.

SAQ:2

a) It's generally agreed that *Homo sapiens* first appeared in Africa around 300,000 years ago

b) One of the most significant findings from genomic studies is the evidence of interbreeding between *Homo sapiens* and other hominins, such as Neanderthals and Denisovans.

c) As previously mentioned in section 2.1, the first wave of *Homo sapiens* migration out of Africa is thought to have occurred around 70,000 years ago,

The Settlement of Asia and the Pacific

Parallel to the colonization of Europe, *Homo sapiens* populations were also expanding eastwards into Asia and the Pacific. By around 50,000 years ago, early modern humans had reached the Southeast Asian archipelago, where they encountered another archaic hominin species, the enigmatic Denisovans. Like the Neanderthals in Europe, the Denisovans were eventually replaced by *Homo sapiens*, although the precise nature and timing of this replacement process remain poorly understood.

From Southeast Asia, *Homo sapiens* continued their eastward expansion, reaching the island of Australia by around 50, 000 years ago. The settlement of Australia represented a major achievement in human migration, as it required the development of sophisticated maritime technologies and navigation skills, as well as the ability to adapt to a diverse array of environments, from arid deserts to tropical rainforests.

Meanwhile, in northern Asia, *Homo sapiens* populations were also expanding their range, eventually reaching Siberia and the Arctic by around 30,000 years ago. The colonization of these extreme environments required the development of specialized technologies and survival strategies, such as the use of tailored clothing, advanced hunting techniques, and the construction of insulated dwellings.

The Peopling of the Americas

One of the last major chapters in the story of human migration is the peopling of the Americas, which is thought to have occurred around 15,000 to 20,000 years ago. The most widely accepted model for the initial colonization of the Americas is the "Bering Land Bridge" hypothesis, which posits that early *Homo sapiens* populations migrated from Siberia to Alaska via a land bridge that existed between the two continents during the last ice age.

Once in the Americas, these early colonizers embarked on a rapid southward expansion, reaching the southern tip of South America within just a few thousand years. The speed and success of this migration can be attributed to a combination of factors, including the relatively unexploited resource base of the Americas, which provided ample opportunities for population growth, and the advanced cultural and technological capabilities of *Homo sapiens*, which allowed them to adapt quickly to the diverse environments they encountered.

Timelines and Geographical Hotspots of the Great Human Migration

The following table provides a summary of the major timelines and geographical hotspots associated with the great human migration, from the initial dispersal of *Homo sapiens* out of Africa to the colonization of the Americas.

Table 18: The major timelines and geographical hotspots associated with the great human migration

Time Period (Years Ago)	Geographical Hotspot	Key Events
70,000	Arabian Peninsula	First wave of migration out of Africa

60,000	South Asia	Coastal migration along the Indian Ocean
50,000	Southeast Asia	Arrival in Australia and encounter with Denisovans
45,000	Europe	Replacement of Neanderthals
30,000	Siberia and the Arctic	Adaptation to extreme environments
15,000-20,000	Bering Land Bridge	Initial colonization of the Americas
13,000-15,000	North and South America	Rapid southward expansion

The Legacy of the Great Human Migration: Diversity and Adaptation

The legacy of the great human migration can be seen in the incredible diversity of human populations, cultures, and languages that exist today. As *Homo sapiens* populations dispersed across the globe and adapted to new environments, they developed distinct genetic, morphological, and cultural traits that reflect their unique evolutionary histories and adaptive trajectories.

This rich tapestry of human diversity is a testament to our species' remarkable capacity for innovation and resilience, as well as our deep interconnectedness. By studying the patterns of human migration and the factors that shaped our evolution, we can gain valuable insights into the shared history that unites us all, as well as the challenges and opportunities that lie ahead as we continue to navigate the ever-changing landscape of the modern world.

The Last Frontier: The Americas and Oceania

The colonization of the Americas and Oceania represents the final chapters in the epic story of human migration, as *Homo sapiens* ventured into the last unexplored frontiers of the Earth. These regions, characterized by their vast distances, diverse environments, and unique ecological challenges, provided the stage for some of the most remarkable feats of human adaptation, innovation, and cultural development in history. In this section, we will delve into the fascinating story of how early humans colonized the Americas and Oceania, focusing on the key migrations, timelines, and geographical hotspots associated with these regions.

The Settlement of Oceania

The settlement of Oceania, which includes the islands of the Pacific Ocean, represents one of the most astonishing achievements in human history, as it required the development of sophisticated maritime technologies, navigation skills, and the ability to adapt to a wide array of island environments. The colonization of Oceania can be broadly divided into two major phases: the settlement of Near Oceania, which includes the islands of Melanesia, and the settlement of Remote Oceania, which encompasses the islands of Micronesia, Polynesia, and New Zealand.

The settlement of Near Oceania began around 50,000 years ago when early *Homo sapiens* populations from Southeast Asia ventured into the region using simple watercraft. Over the ensuing millennia, these early colonizers adapted to the diverse island ecosystems of Melanesia, developing unique cultural traditions, languages, and genetic profiles that reflect their long isolation from the rest of the world.

The colonization of Remote Oceania began around 3,500 years ago when the ancestors of the

modern Polynesians, known as the Lapita people, embarked on a remarkable series of long-distance voyages that would eventually lead them to the furthest reaches of the Pacific. Using advanced double-hulled canoes and sophisticated navigational techniques based on the stars, winds, and ocean currents, the Lapita people were able to traverse vast distances and colonize even the most remote islands of the Pacific, from the tiny atolls of Micronesia to the distant shores of Hawaii, Easter Island, and New Zealand.

The Peopling of the Americas

The peopling of the Americas, which took place between 15,000 and 20,000 years ago, represents another major milestone in the history of human migration. As mentioned in section 2.2, the most widely accepted model for the initial colonization of the Americas is the "Bering Land Bridge" hypothesis, which posits that early *Homo sapiens* populations migrated from Siberia to Alaska via a land bridge that existed between the two continents during the last ice age.

Once in the Americas, these early colonizers embarked on a rapid southward expansion, reaching the southern tip of South America within just a few thousand years. The speed and success of this migration can be attributed to a combination of factors, including the relatively unexploited resource base of the Americas, which provided ample opportunities for population growth, and the advanced cultural and technological capabilities of *Homo sapiens*, which allowed them to adapt quickly to the diverse environments they encountered.

Timelines and Geographical Hotspots of the Settlement of the Americas and Oceania

The following table provides a summary of the major timelines and geographical hotspots associated with the settlement of the Americas and Oceania.

Table 19: Major timelines and geographical hotspots associated with the settlement of the Americas and Oceania.

Time Period (Years Ago)	Geographical Hotspot	Key Events
50,000	Near Oceania	Settlement of Melanesia
3,500	Remote Oceania	Settlement of Micronesia, Polynesia, and New Zealand
20,000-15,000	Bering Land Bridge	Initial colonization of the Americas
15,000-13,000	North America	Southward expansion through North America
14,000-12,000	South America	Rapid southward expansion

The Legacy of the Settlement of the Americas and Oceania: Diversity and Adaptation

The colonization of the Americas and Oceania gave rise to a myriad of diverse cultures, languages, and genetic profiles, reflecting the unique adaptive trajectories of the various human populations that settled these regions. From the complex societies of the Andean highlands to the seafaring cultures of the Polynesian islands, the inhabitants of the Americas and Oceania developed distinctive cultural practices, technologies, and belief systems that allowed them to thrive in a wide range of environments.

One of the most striking aspects of the settlement of the Americas and Oceania is the remarkable

degree of human adaptation that it entailed. In the Americas, early *Homo sapiens* populations had to contend with diverse environments, from the arctic tundra of Alaska to the tropical rainforests of the Amazon, as well as a host of novel ecological challenges, such as the megafauna that once roamed the continent. Similarly, in Oceania, early settlers had to adapt to the unique island ecosystems of the Pacific, which often required the development of innovative agricultural, fishing, and navigation techniques.

The legacy of the settlement of the Americas and Oceania can be seen in the rich tapestry of human diversity that characterizes these regions today, as well as the enduring cultural traditions that continue to shape the lives of their inhabitants. By studying the patterns of migration, adaptation, and cultural development in the Americas and Oceania, we can gain valuable insights into the deep historical connections that link these regions to the wider story of human evolution and the ongoing process of globalization that continues to shape the modern world.

The Impact of Colonization on Human Diversity

As our ancestors ventured forth from Africa, colonizing new lands and encountering new environments, they left a lasting impact on the genetic, cultural, and linguistic diversity of the human species. In this section, we will explore how the process of colonization shaped the complex tapestry of human diversity that we observe today, examining the interplay between migration, adaptation, and cultural innovation in shaping the demographic and genetic landscape of our species.

Genetic Diversity and the Role of Migration

The migration of human populations across the globe has played a critical role in shaping the patterns of genetic diversity that we observe today. As groups of people settled in different regions, they were exposed to a variety of environmental pressures, such as differences in climate, altitude, and diet, which in turn influenced their genetic makeup. Over time, these populations accumulated novel genetic variants through mutation and genetic drift, leading to the emergence of distinct genetic profiles that reflect their unique adaptive trajectories.

Table 20: Genetic Diversity Index of Human Population

Continent	Genetic Diversity Index	Key Genetic Features
Africa	High	Greatest genetic diversity; ancestral population
Europe	Moderate	Reduced genetic diversity; influence of Neanderthals
Asia	Moderate to High	Regional genetic diversity; influence of Denisovans
Americas	Low	Recent colonization; bottleneck events
Oceania	Moderate	Regional genetic diversity; influence of Austronesian expansion

One of the most striking aspects of human genetic diversity is the correlation between genetic distance and geographic distance. This pattern, known as isolation by distance, reflects the fact that populations that are geographically closer to one another tend to be more genetically similar than populations that are farther apart. This pattern arises due to the fact that migration and gene flow tend to occur more frequently between neighboring populations, leading to a gradual decrease in genetic diversity with increasing distance from the source population.

Cultural Diversity and the Role of Adaptation

The process of colonization has also had a profound impact on the cultural diversity of the human species. As populations migrated to new environments, they were forced to adapt to a variety of ecological challenges, such as differences in climate, resource availability, and the presence of other human and non-human populations. These pressures, in turn, drove the development of innovative cultural practices, technologies, and social structures that allowed these populations to survive and reproduce in their new habitats.

One of the most striking aspects of human cultural diversity is the sheer number of distinct languages, belief systems, and social practices that have emerged across the globe. This diversity reflects the fact that cultural adaptation is a highly flexible and context-dependent process, allowing human populations to develop a wide range of solutions to the ecological challenges that they faced. In many cases, these cultural innovations served to reinforce the genetic adaptations that characterized these populations, creating a complex feedback loop between biology and culture that further shaped the patterns of human diversity.

Table 21: Cultural diversity across continents

Continent/Region	Language Families	Key Cultural Features
Africa	Over 50	Diverse linguistic, cultural, and social practices
Europe	6	Indo-European language family; shared cultural history
Asia	Over 20	Diverse linguistic, cultural, and social practices
Americas	Over 30	Diverse linguistic, cultural, and social practices
Oceania	2	Austronesian and Papuan languages; unique island cultures

The Legacy of Human Colonization: Diversity and Globalization

In conclusion, the process of human colonization has left an indelible mark on the genetic, cultural, and linguistic diversity of our species. The long and arduous journey of our ancestors, from the earliest days in Africa to the far reaches of the globe, has given rise to an astonishing array of human societies, each with its own unique blend of adaptations, innovations, and historical trajectories.

Today, the legacy of human colonization can be seen in the remarkable diversity of peoples, languages, and cultures that populate the planet. However, as we move further into the 21st century, the forces of globalization and modernization are rapidly reshaping the demographic and cultural landscape of our species. In many cases, these forces are leading to the erosion of traditional boundaries, as people, ideas, and technologies flow more freely across the globe, fostering new forms of cultural and genetic exchange.

As we look to the future, it is essential that we strive to understand and appreciate the complex interplay between colonization, adaptation, and cultural innovation that has shaped our species. By doing so, we can gain a greater appreciation for the richness and diversity of the human experience, and work together to build a more inclusive and sustainable future for all.

Table 22:Timeline and Geographical Hotspots of Human Colonization

Time Period (Years Ago)	Geographical Hotspot	Key Events and Features
70,000-50,000	Africa	Modern humans (*Homo sapiens*) emerge; migration out of Africa begins
50,000-40,000	Asia, Europe	Expansion into Asia and Europe; encounters with Neanderthals and Denisovans
40,000-30,000	Europe	Upper Paleolithic Revolution; development of advanced tools, art, and symbolic culture
30,000-20,000	Asia	Spread of modern humans throughout Asia; development of diverse regional cultures
20,000-15,000	Americas	First human migration into the Americas via Beringia; rapid colonization of North and South America
4,000-2,500	Oceania	Austronesian expansion into Oceania; colonization of remote Pacific islands

As we have seen, the story of human colonization is a rich and complex tapestry, woven from the threads of countless individual journeys and encounters. From our earliest beginnings in Africa to our rapid expansion across the globe, the process of colonization has left an indelible mark on the genetic, cultural, and linguistic diversity of our species. In the face of ongoing challenges posed by globalization and modernization, it is essential that we continue to celebrate and safeguard the unique legacy of human diversity, working together to build a more inclusive and sustainable future for all.

The Future of Human Diversity and Colonization

As we look to the future, it is clear that the forces shaping human diversity and colonization are continuing to evolve in profound and sometimes unpredictable ways. Globalization, technological advancements, and changes in the natural environment are all influencing the complex web of interactions that drive our species' ongoing journey. In this final section of the chapter, we will explore some of the key trends and challenges that lie ahead, and consider how they might impact the future of human diversity and colonization. In doing so, we will draw on the latest scientific research, as well as insights from anthropology, demography, and other fields.

One of the most significant trends shaping the future of human diversity is the increasing interconnectedness of our world. As people, ideas, and technologies flow more freely across the globe, traditional barriers to interaction are breaking down, and new forms of cultural and genetic exchange are emerging. This process has the potential to both enrich and erode human diversity, as new connections and hybridizations give rise to novel cultural forms, while at the same time, some traditional practices and languages are lost.

Another important trend is the ongoing development and diffusion of new technologies. Advances in fields such as biotechnology, artificial intelligence, and communications have the potential to dramatically reshape the way we live, work, and interact with one another. As we grapple with the implications of these new technologies, we must consider how they might impact human diversity, as

well as our ability to colonize and adapt to new environments.

Climate change is another critical factor that will shape the future of human diversity and colonization. As the earth's climate continues to change, it will have far-reaching impacts on ecosystems, resources, and human populations. In some cases, these changes may lead to the displacement of entire communities or even the extinction of certain cultural groups. On the other hand, changing environmental conditions may also open up new opportunities for human colonization and adaptation, as people find new ways to survive and thrive in a rapidly changing world.

As we contemplate the future of human diversity and colonization, it is crucial that we develop a deeper understanding of the complex interactions between these various forces. To that end, the following table highlights some of the key trends, challenges, and opportunities that are likely to shape the coming decades:

Table 23: Trends, challenges, and opportunities

Key Trend/Challenge	Implications for Human Diversity and Colonization
Globalization	Increased interconnectedness, cultural and genetic exchange, erosion of traditional practices and languages, emergence of new cultural forms
Technological advancements	Impacts on social, economic, and cultural structures, potential for new forms of colonization (e.g., space exploration), ethical considerations surrounding biotechnology and AI
Climate change	Displacement of communities, extinction of cultural groups, changes in ecosystems and resources, new opportunities for colonization and adaptation
Population growth and migration	Shifts in demographic patterns, urbanization, impacts on cultural and linguistic diversity, challenges related to integration and social cohesion
Geopolitical dynamics	Conflicts over resources and territory, impacts on migration and colonization patterns, influence on cultural and linguistic diversity

In conclusion, the future of human diversity and colonization is both exciting and uncertain. As we face unprecedented challenges and opportunities, we must continue to explore the complex interplay between the forces that have shaped our species' past and those that will define its future. By doing so, we can gain a deeper appreciation for the richness and diversity of the human experience and work together to build a more inclusive and sustainable future for all. With the knowledge and insights gained from the study of human evolution, we are better equipped to navigate the complexities of the modern world and to ensure the preservation and celebration of our collective heritage.

As we strive to protect and promote human diversity in the face of these challenges, there are several key areas where concerted effort and collaboration will be essential. These include the preservation of endangered languages and cultural practices, the fostering of intercultural dialogue and understanding, and the development of policies and strategies to promote social cohesion and integration in an increasingly interconnected world.

Moreover, we must also consider the potential impact of new technologies on human diversity and colonization. For instance, advances in genomics and gene editing techniques may offer new insights into our genetic heritage and the history of human migration, while also raising ethical questions

about the manipulation of human genes and the potential consequences for future generations. Similarly, developments in space exploration could open up entirely new frontiers for human colonization, challenging our understanding of what it means to be human and forcing us to confront questions about the limits and responsibilities of our species.

In this dynamic and rapidly changing landscape, the study of human evolution provides a vital foundation for understanding the complex interplay of forces that have shaped our species and will continue to shape its future. By examining our past, we can gain valuable insights into the patterns and processes that have driven human diversity and colonization, and use this knowledge to inform our decisions and actions in the present.

Ultimately, the future of human diversity and colonization will be shaped by the choices we make as a global community. Will we embrace the opportunities presented by globalization and new technologies to promote greater understanding and cooperation, or will we allow these forces to exacerbate existing divisions and inequalities? Will we rise to the challenge of climate change and find new ways to adapt and thrive in a changing world, or will we fail to act, with devastating consequences for vulnerable populations and ecosystems?

The answers to these questions will depend on our ability to learn from the past, adapt to the present, and plan for the future. As we move forward into the unknown, it is essential that we continue to study and celebrate the rich tapestry of human diversity and colonization, using the lessons of our evolutionary journey to guide us in the pursuit of a more inclusive, sustainable, and just world.

13.5 Summary

In conclusion, the story of our ancestral apes is a tale of remarkable resilience, adaptability, and innovation, as these primates navigated the challenges of a rapidly changing world. By examining the diverse cast of characters that make up our evolutionary heritage, we gain not only a deeper understanding of our own origins but also a profound appreciation for the extraordinary journey that has led us to where we are today. From the first tentative steps of our distant ape cousins to the rise of the hominids and the eventual emergence of *Homo sapiens*, our story is one of continuous transformation and reinvention, a testament to the power and potential of life itself.

In conclusion, the evolution of modern humans is a rich and intricate tapestry woven with threads of genetics, environment, and culture. As we delve into the layers of this tapestry, we encounter a narrative of transformation, innovation, and resilience, reflecting our species' extraordinary capacity to adapt and thrive. From our humble beginnings in the heart of Africa to our present-day global dispersion, we have been, and continue to be, shaped by our interactions with the world around us. By understanding and appreciating our shared evolutionary history, we can better understand ourselves, each other, and the world we inhabit.

The colonization of Europe also coincided with the development of the so-called "Upper Paleolithic" culture, which was characterized by a suite of more advanced tools, weapons, and artistic expressions, such as cave paintings, sculptures, and personal ornaments. These cultural innovations likely played a crucial role in facilitating the expansion of *Homo sapiens* across the continent, allowing them to exploit a wider range of resources and adapt to diverse environments.

13.6 Terminal Questions

Q.1 How are humans and monkeys related?

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Q.2 What is common ancestor between human and apes?

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Q.3 Did humans evolve from monkeys? Human evolution explained.

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Q.4 Describe in details origin of modern human.

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Q.5 Write shorts notes on

a) Colonization

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b) Races of modern human

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c) Fossil human

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13.7 Answers

a) hominoids

b) ancestral apes

c) *Homo sapiens*

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