Genetics and Molecular Biology (BIO214) (Mid-Sem Examination) Year: 2024

Attempt Any Five (5) Questions Only.

Question 1: Explain the concepts of incomplete dominance, co-dominance, and dominant-recessive inheritance patterns. Provide an example for each, illustrating how the phenotype of the offspring differs in each case. Additionally, discuss how these patterns challenge the simple Mendelian view of inheritance and how they can lead to greater genetic diversity in populations.

1. Incomplete Dominance:

Incomplete dominance occurs when the phenotype of the heterozygote is an intermediate blend of the phenotypes of the two homozygotes. Neither allele is completely dominant over the other, resulting in a "mixing" effect in the offspring.

Example: Flower color in snapdragons is a classic example of incomplete dominance. If a plant with red flowers (RR) is crossed with a plant with white flowers (WW), the offspring (RW) will have pink flowers. The pink phenotype is a blend of red and white, showing that neither allele is completely dominant.

Genotype: RR (red), RW (pink), WW (white)
Phenotype: The heterozygote (RW) has a distinct intermediate color (pink).

2. Co-Dominance:

In co-dominance, both alleles are fully expressed in the heterozygote, and neither allele is dominant or recessive. The phenotype shows traits from both alleles simultaneously rather than blending them.

Example: The AB blood type in humans is an example of co-dominance. Individuals who inherit an A allele from one parent and a B allele from the other have blood type AB, where both the A and B antigens are equally expressed on the surface of their red blood cells.

Genotype: I^AI^A (type A), I^BI^B (type B), I^AI^B (type AB)
Phenotype: The heterozygote (I^AI^B) expresses both A and B antigens, demonstrating that both alleles are active and co-dominant.

3. Dominant-Recessive Inheritance:

In this classical Mendelian pattern, the dominant allele masks the effect of the recessive allele in the heterozygote. Only one dominant allele is needed to express the dominant phenotype, while the recessive phenotype appears only when an individual has two copies of the recessive allele.

Example: In pea plants, flower color is controlled by a dominant-recessive pattern. Purple flower color (P) is dominant over white (p). A plant with the genotype PP or Pp will have purple flowers, while only pp plants will have white flowers.

Genotype: PP (purple), Pp (purple), pp (white)
Phenotype: The heterozygote (Pp) exhibits the dominant trait (purple), and the recessive trait (white) is hidden unless both alleles are recessive (pp).

How These Patterns Challenge Mendelian Inheritance:
Mendel's laws of inheritance were based on the idea of simple dominance, where one allele is always dominant over the other.
Incomplete dominance shows that blending of traits can occur, unlike Mendel's principle of dominance, where the dominant trait completely masks the recessive one.
Co-dominance challenges Mendel's idea by demonstrating that both alleles can be fully expressed at the same time without blending.
Multiple alleles and polygenic inheritance (e.g., in co-dominant traits like blood type) show that more than two alleles can contribute to a phenotype, adding complexity beyond Mendel's two-allele system.

Contribution to Genetic Diversity:
These non-Mendelian patterns of inheritance contribute to greater genetic diversity within populations. Incomplete dominance and co-dominance increase phenotypic variety, creating new traits and combinations that enhance a population's adaptability. For instance, the existence of multiple blood types in humans (A, B, AB, O) is a result of co-dominance and the presence of multiple alleles, providing genetic diversity that can be advantageous in varying environments or disease resistance.

Question 2: Yuvraj Singh, a renowned cricketer, was diagnosed with lung cancer due to a somatic mutation in his cells, which did not affect his offspring. Using this case as a

starting point, explain the concept of mutations. Differentiate between somatic and germline mutations, highlighting how they impact individuals and inheritance. Additionally, describe the various types of mutations such as point mutations, insertions, deletions, and chromosomal mutations. How do these mutations contribute to diseases like cancer?

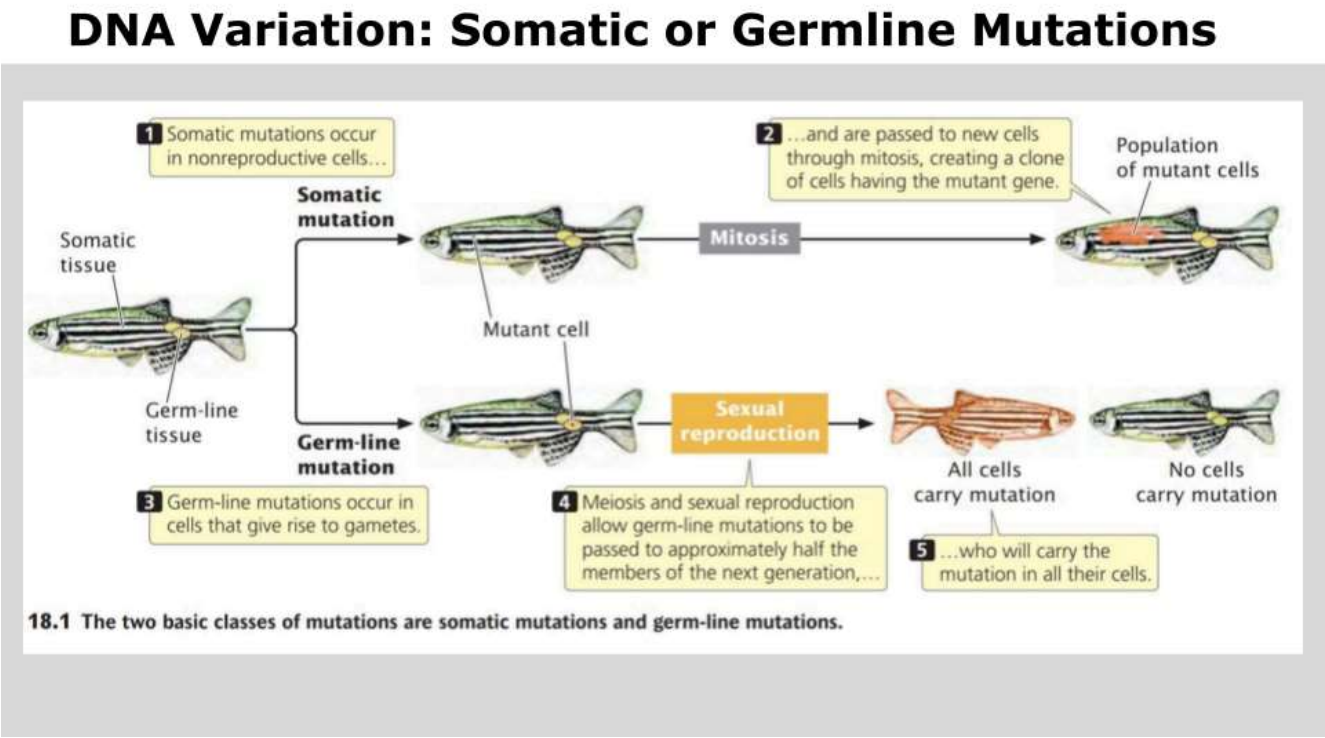
1. Somatic vs. Germline Mutations:

Somatic Mutations: These occur in non-reproductive cells and affect only the individual in whom they arise. They are not passed on to offspring. Yuvraj Singh's lung cancer resulted from a somatic mutation, meaning the mutation occurred in his lung cells and did not affect his germ cells (sperm). Somatic mutations can lead to conditions like cancer, where the mutated cells proliferate abnormally.

Impact: Affects only the individual and can lead to diseases like cancer if the mutation disrupts key cellular functions such as DNA repair or cell growth regulation.

Germline Mutations: These occur in the reproductive cells (sperm or egg) and can be passed on to offspring. Any mutation in the germline affects all cells in the offspring's body and may lead to hereditary conditions.

Impact: Can be inherited by the next generation and contribute to genetic disorders, such as cystic fibrosis or Huntington's disease.



18.1 The two basic classes of mutations are somatic mutations and germ-line mutations.

2. Types of Mutations:

Point Mutations: These involve a change in a single nucleotide in the DNA sequence. They can be further classified into:

Silent mutations: No effect on the protein due to redundancy in the genetic code.

Missense mutations: A change in one amino acid in the protein, which can alter its function.

Nonsense mutations: A point mutation that introduces a premature stop codon, leading to truncated, non-functional proteins.

Insertions: A few extra nucleotides are added into the DNA sequence, which can disrupt the reading frame of a gene (frameshift mutation), resulting in completely altered proteins.

Deletions: A loss of one or more nucleotides from the DNA sequence. Like insertions, deletions can cause frameshift mutations if the number of nucleotides deleted is not divisible by three.

Chromosomal Mutations: Larger changes that involve entire segments of chromosomes or even whole chromosomes, leading to major disruptions in genetic information. Types include:

Duplications: A portion of the chromosome is duplicated, leading to multiple copies of a gene.

Inversions: A segment of a chromosome is reversed end to end.

Translocations: Segments of chromosomes are rearranged, often leading to improper gene function.

3. Mutations and Cancer:

Mutations contribute to cancer by disrupting the normal regulation of cell growth and division. In cancer, somatic mutations typically affect genes involved in:

Oncogenes: These are genes that promote cell growth and division. Mutations can activate oncogenes inappropriately, leading to uncontrolled cell proliferation.

Tumor Suppressor Genes: These are genes that normally slow down cell division, repair DNA errors, or induce apoptosis (programmed cell death). Mutations that inactivate these genes allow cells to grow uncontrollably.

DNA Repair Genes: Mutations in genes that normally repair DNA damage can lead to an accumulation of mutations in other critical genes, driving the progression of cancer.

Question 3: During ISRO's Mars Orbiter Mission (MOM), a new organism has been discovered on Mars. As a scientist, you are tasked with identifying and characterizing the

nature of the nucleic acid in this organism. Considering all possibilities for the type of nucleic acid (DNA, RNA, or others), outline a detailed investigative approach.

Create a flowchart to demonstrate the following:

1. **Possible types of nucleic acids (DNA, RNA, or any unknown form),**
2. **Experimental methods to test for each type, explaining how to accept or reject each possibility,**
3. **Biochemical assays to measure the properties of the nucleic acid, such as its stability, composition, and replication mechanisms, with a focus on DNA properties.**

Answer: Possible types of nucleic acids: DNA (Single or Double stranded) and RNA (Single or Double stranded)

Experimental methods to test each type:

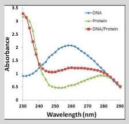
DNA : Physical and Chemical Properties

ABSORPTION

- The bases in DNA absorb ultraviolet light at the wavelength of 260 nm
  Most widely used method to measure DNA concentration in solution

NOTE: UV absorption indicates the order of the bases: less ordered means more absorption

1. Free bases absorb 1.60 units at 260 nm
2. Single stranded DNA absorb 1.37 units at 260 nm
3. Double stranded DNA absorb 1.00 units at 260 nm



DENSITY

- Measured by CsCl-density ultracentrifugation
- Density can be used to estimate G+C content
- Density studies show the existence of satellite DNA

$1\ OD_{260}$ unit = 1 mg/ml protein

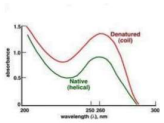
Purity of	Target A_{260}/A_{280} Ratio
DNA	1.8
RNA	2.0
Protein	0.6

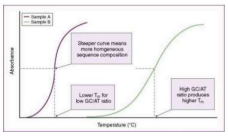
DNA : Physical and Chemical Properties

- **DENATURATION**: DNA is considered denatured when the double-stranded DNA molecule is converted into two single-stranded molecules
- This can be monitored by noting the increase in absorption of ultraviolet light

> **Temperature**

- As thermal energy increases, the frequency of hydrogen bonds breaking between the molecules increases. As temperature increases, the two molecules will separate into single-stranded molecules
- The Tm (melting temperature) of a DNA molecule is the temperature in which half the DNA molecules are denatures
- The Tm is used to estimate the G+C content of a DNA molecule
- G-C base pairs are held together by three hydrogen bonds (A-Ts by two) and it therefore takes more energy (higher temperatures) to separate molecules with high GC contents





DNA : Physical and Chemical Properties

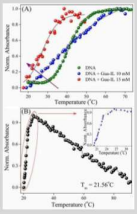
Hydrophobicity of solvent

- Substances that are hydrophobic tend to decrease the Tm of DNA molecules
- Hydrophobic substances will allow the bases in DNA to dissolve into the solvent
- Hence, the bases are not constricted to being stacked upon one another
- This will make it easier to disrupt the hydrogen bonding between DNA molecules
- Substances that are hydrophilic tend to increase the Tm of DNA molecules
- These will keep the bases of DNA stacked upon one another in the orientation that most favours hydrogen bonding between DNA strands.

pH

Acid

pHs lower then one result in the breakage of phosphodiester bonds between nucleotides and breakage of the N-glycosidic bond between the sugar and purine bases. pH of around 4 results in the selective breakage of N-glycosidic bonds between the sugar and purines. DNA treated this way is referred to a apurinic acid, since the purines have been removed



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DNA : Physical and Chemical Properties

- **pH**

Alkali

Base tends to change the polarity of groups involved in hydrogen bonds. Above pH 11.3, all hydrogen bonds are disrupted and the DNA is totally denatured DNA is resistant to hydrolysis to about pH 13. Unless it is apurinic, then it is hydrolyzed. RNA is hydrolyzed into ribonucleotides around pH 11.

Ionic strength

- The phosphates of the DNA sugar-phosphate backbones are negatively charged
- Like charges repel each other
- DNA in distilled water will spontaneously denature into single stranded DNA
- Salts that dissociate into ions will neutralize the charges of the phosphate groups
- Salts will stabilize the DNA double helix resulting in a higher Tm
- G+C content
- Variation

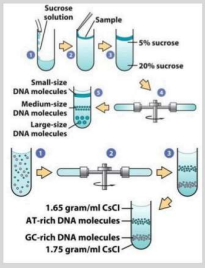
DNA : Physical and Chemical Properties

SOLUBILITY

- RNA is more soluble in aqueous solutions then DNA
- Ribose has a 2'-OH group where deoxyribose contains a 2'-H
- Hydroxyl groups are polar and dissolve in water better
- C-H is a non-polar bond and is therefore hydrophobic
- RNA is less stable than DNA
- The hydroxyl group on the 2' carbon of ribose is more reactive the hydrogen found in deoxyribose

Velocity sedimentation

- Sedimentation velocity is dependent upon two variables: density and shape
- The more dense the DNA the quicker it will sediment upon centrifugation
- Globular (more compact) molecules will sediment faster than linear molecules



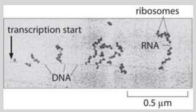
DNA : Physical and Chemical Properties

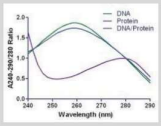
Electron microscopy

- The size of DNA molecules can be determined by electron microscopy
- The DNA is visualized on a grid of known size so that the size of the DNA molecule can be estimated

DNA CONCENTRATION

- Absorption
- DNA absorbs ultraviolet light at 260 nm
- The more DNA present, the higher the absorption
- DNA concentrations can be estimated by comparing its absorption to known concentrations of DNA
- DNA must be fairly pure, since many contaminating substances (e.g., proteins) also absorb around this wavelength





DNA : Physical and Chemical Properties

RENATURATION STUDIES

- DNA that has been denatured will often come back together when condition are met
- Renaturation occurs because of hydrogen bonds of complementary base pairs reforms
- Slowly lowering the temperature or adding ions to the solution may lead to renaturation
- ★ Renaturation rates are dependent on DNA concentration
- ★ The rate-limiting step in renaturation is the collision of complementary DNA molecules
- ★ The more molecules of complementary DNA molecules present, the faster they can find each other and renature

In eukaryotes, three major drops in absorbance occur in renaturation studies

- The first drop in absorption is when the highly repetitive DNA sequence renatures
- Since these are repeated so often, they are in the highest concentration
- The second drop in absorption occurs when the moderately repetitive DNA renatures
- Unique DNA sequences are the last to renature
- These are in the lowest concentration and take the longest time to find each other

Question 4: In humans, the ABO blood group system is determined by three alleles: I^A, I^B, and i, where I^A and I^B are co-dominant, and i is recessive. The Rh factor is determined by two alleles: Rh+ (dominant) and Rh− (recessive).

Given the following parental genotypes:

- **Parent 1: I^Ai, Rh^+Rh^-**
- **Parent 2: I^BI^B, Rh^-Rh^-**

1. **Calculate all possible genotypes and phenotypes of the offspring for both the ABO and Rh blood group systems.**
2. **What is the probability of the offspring having:**
    - **Blood group AB, Rh-positive?**
    - **Blood group O, Rh-negative?**
3. **Explain in detail the human ABO blood group at the genotype-phenotype level.**

1. Based on the ABO and Rh alleles that can be inherited from the parents, the following are the possible genotypes and phenotypes for their offspring:

ABO Genotype	ABO Phenotype	Rh Genotype	Rh Phenotype
IAIB	AB	Rh+Rh−	Rh-positive
IAIB	AB	Rh−Rh−	Rh-negative
IBi	B	Rh+Rh−	Rh-positive
IBi	B	Rh−Rh−	Rh-negative

2.

Blood Group AB, Rh-positive

For the offspring to have blood group AB, they must inherit the IA allele from Parent 1 and the IB allele from Parent 2:

- Probability of inheriting IA from Parent 1: 1/2
- Probability of inheriting IB from Parent 2: 1 (since both alleles are IB)

For the offspring to be Rh-positive, they must inherit the Rh+ allele from Parent 1 and the Rh− allele from Parent 2:

- Probability of inheriting Rh+ from Parent 1: 1/2
- Probability of inheriting Rh− from Parent 2: 1 (since both alleles are Rh−)

The probability of the offspring having blood group AB, Rh-positive is:

1/2 × 1 × 1/2 × 1 = 1/4 = **25%**

Blood Group O, Rh-negative

For the offspring to have blood group O, they must inherit two i alleles (ii). Since Parent 2 has no i allele (they are IBIB), it is impossible for the offspring to inherit two i alleles.

Thus, the probability of the offspring having blood group O, Rh-negative is **0%.**

3. The ABO blood group is determined by three alleles:

- I^A (A allele): Responsible for A antigens on red blood cells.

- I^B (B allele): Responsible for B antigens on red blood cells.
- i (O allele): Does not produce any antigen (recessive).

Alleles I^A and I^B are co-dominant, meaning if both are present, both A and B antigens will be expressed, resulting in blood type AB. The i allele is recessive, and it will only be expressed if a person inherits two i alleles (ii), which results in blood type O.

Phenotype (blood type)	Genotype	Antigen type
A	I^AI^A or I^Ai	A
B	I^BI^B or I^Bi	B
AB	I^AI^B	A and B
O	ii	None

Question 5: An explorer discovers a strange new plant species and sends some of the plant tissue to a geneticist to study. The geneticist isolates chromatin from the plant and examines it with an electron microscope. She observes what appears to be beads on a string. She then adds a small amount of nuclease, which cleaves the string into individual beads containing 280 bp of DNA. After digestion with more nuclease, a 120-bp fragment of DNA remains attached to a core of histone proteins. Analysis of the histone core reveals histones in the following proportions:

H1	12.5%
H2A	25%
H2B	25%
H3	0%
H4	25%
H7 (a new histone)	12.5%

Based on these observations, what conclusions could the geneticist make about the probable structure of the nucleosome in the chromatin of this plant?

Answer:

The 120 bp of DNA associated with the histone core is smaller than the 140 bp associated with typical nucleosomes. The new plant also is lacking histone H3. The new histone H7 apparently does not replace histone H3 in the nucleosome core because it is present in the same ratio as histone H1, or half of the ratios of nucleosomal core histones H2A, H2B, and H4. Finally, the 280 bp fragments with limited DNase digestion are larger than the 200 bp fragments seen with typical eukaryotic chromatin. These observations suggest a model in which the nucleosome core consists of just six histones, two each of H2A, H2B, and H4, explaining the lack of H3 and the smaller amount of DNA that is associated with the nucleosome core. The longer DNA per nucleosome can be explained in part by a molecule of H7 either in the spacer between nucleosomes or perhaps helping to cap nucleosomes in conjunction with H1.

Question 6: Describe Transformation, Transduction, and Conjugation. In addition to the text, please depict the underlying processes graphically.

1. **Transformation**: Transformation is a form of genetic recombination in which a DNA fragment from a dead, degraded bacterium enters a competent recipient bacterium and is exchanged for a piece of DNA of the recipient. Transformation usually involves only homologous recombination, a recombination of homologous DNA regions having nearly the same nucleotide sequences. Typically this involves similar bacterial strains or strains of the same bacterial species.
2. **Conjugation**: The transfer of genetic material through direct contact between bacterial cells, usually via a pilus.
3. **Transduction**: The transfer of bacterial genes by a virus (bacteriophage). During transduction bacteriophage, called a transducing particle, infects another bacterium, it injects the fragment of donor bacterial DNA it is carrying into the recipient where it can subsequently be exchanged for a piece of the recipient's DNA by homologous recombination.

Diagram: A well-labeled diagram should illustrate these three processes, highlighting how genetic material is transferred in each case.