GMB QUIZ 1 RUBRICS (Total 50 Marks)
(ATTEMPT ANY 5)

Question 1: During DNA replication, the error rate before any proofreading or repair mechanisms is about 1 error per 100,000 nucleotides added. If a human genome consists of approximately 3 billion base pairs, calculate the expected number of initial replication errors in the entire genome before proofreading occurs. How might the presence of these errors affect genetic integrity, and what mechanisms mitigate this issue?

Solution:

Error Rate: Approximately 1 error per 100,000 nucleotides added or 1×10^{-5} errors per nucleotide

Human Genome Size: About 3 billion base pairs (or nucleotides) or 3×10^{9} base pairs

The expected number of initial replication errors can be calculated as follows:

Expected Errors = Total Nucleotides × Error Rate

Expected Errors= $3\times10^{9} \times 1\times10^{-5}$ = **30,000**

Impact on Genetic Integrity

The presence of these initial replication errors can significantly affect genetic integrity. Here are some potential impacts:

Mutations: Errors that are not corrected can lead to mutations, which may disrupt gene function or regulation.

Cancer Risk: Accumulation of mutations in critical genes (such as oncogenes and tumor suppressor genes) can increase the risk of cancer.

Genetic Diversity: While many mutations are neutral or harmful, some can contribute to genetic diversity and evolution. However, unchecked mutation rates can lead to deleterious effects on populations over time

Mechanisms to Mitigate Errors

Cells have evolved several mechanisms to minimize the impact of replication errors:

Proofreading by DNA Polymerases:

DNA polymerases have intrinsic proofreading activity that allows them to correct mistakes immediately after they occur during DNA synthesis. This significantly reduces the error rate from about 1×10^{-5} to around 1×10^{-7} or lower.

Mismatch Repair (MMR):

After DNA replication, MMR proteins scan the newly synthesized DNA for any remaining mismatches that escaped proofreading. They remove and replace incorrect bases, further lowering the mutation rate to approximately 1×10^{-9}

Question 2: Two different species have DNA with varying GC content: Species A has 40% GC content, and Species B has 60% GC content. Which species is likely to have a higher DNA melting temperature, and why? How does the GC content impact the structural stability of DNA under heat or chemical stress?

Solution:

Species B, with a 60% GC content, is likely to have a higher DNA melting temperature (Tm) compared to Species A, which has a 40% GC content. This difference is primarily due to the structural properties of the DNA bases and their interactions.

Reasons for Higher Melting Temperature in GC-Rich DNA

Hydrogen Bonds: GC pairs form three hydrogen bonds, while AT pairs only form two. This means that GC-rich DNA is inherently more stable due to the greater number of hydrogen bonds holding the strands together12.

Base Stacking Interactions: Beyond hydrogen bonding, the stability of DNA is also influenced by base stacking interactions. GC pairs have more favorable stacking energy than AT pairs, contributing to the overall stability of the double helix24.

Melting Temperature Calculation: The melting temperature can be estimated using formulas that incorporate GC content.

For example $Tm=70+(0.47\times GC)$

Applying this to Species A and B:

For Species A: $Tm = 70+(0.47\times 40)=70+18.8=88.8\ ^\circ C$

For Species B: $Tm = 70+(0.47\times 60)=70+28.2=98.2\ ^\circ C$

This calculation clearly indicates that Species B has a higher melting temperature.

Impact of GC Content on Structural Stability

Thermal Stability: Higher GC content enhances the thermal stability of DNA, making it less likely to denature under heat or chemical stress12. This stability is crucial for organisms that experience fluctuating temperatures in their environments.

Chemical Resistance: GC-rich regions are often more resistant to chemical agents that can cause DNA damage, further preserving genetic integrity3.

Biological Implications: The structural stability provided by higher GC content can influence various biological processes, including replication fidelity and gene expression regulation. It can also affect how DNA interacts with proteins involved in transcription and repair mechanisms.

Question 3: In a plant species, flower color is determined by a single gene with two alleles, where allele R (red) shows incomplete dominance over allele r (white). The heterozygous genotype Rr results in pink flowers. If two pink-flowered plants are crossed, calculate the expected phenotypic ratios of the offspring. Additionally, explain how this ratio differs from a typical Mendelian dominant-recessive pattern.

Solution:

1. Cross of Two Pink-Flowered Plants (Rr x Rr):

	R	r
R	RR (Red)	Rr (Pink)
r	Rr (Pink)	rr (White)

Expected Genotypic and Phenotypic Ratios:

Genotype ratio:

1 RR (Red)

2 Rr (Pink)

1 rr (White)

Phenotype ratio:

1 Red : 2 Pink : 1 White

Comparison to Mendelian Dominant-Recessive Pattern:

In a typical Mendelian dominant-recessive pattern, a cross between two heterozygous plants (e.g., Aa x Aa) would result in a 3:1 phenotypic ratio, where the dominant phenotype is expressed in 3 out of 4 offspring, and the recessive phenotype is expressed in 1 out of 4.

Key Differences:

1. Incomplete dominance leads to an intermediate phenotype (pink in this case) for the heterozygotes, resulting in a **1:2:1 ratio** rather than the **typical 3:1 ratio**.
2. In Mendelian dominance, heterozygotes express only the dominant phenotype, whereas in incomplete dominance, heterozygotes express a blended or intermediate phenotype.

Question 4: The ABO blood group system is determined by a single gene with three alleles: I^A, I^B, and i. The alleles I^A and I^B are codominant, while i is recessive. A child has blood type O, while one parent has blood type A and the other has blood type B.

a) What are the possible genotypes of the parents?

b) Explain how the child can inherit blood type O from these parents.

c) If this couple has another child, what is the probability that the child will have blood type AB?

Solution:

a) Possible Genotypes of the Parents

Parent with Blood Type A:

Possible genotypes: IAIA (homozygous) or IAi (heterozygous).

Parent with Blood Type B:

Possible genotypes: IBIB (homozygous) or IBi (heterozygous).

Given that the child has blood type O (genotype ii), both parents must carry the recessive allele (i). Therefore, the only possible genotypes for the parents are:

Parent A: I^Ai

Parent B: I^Bi

b) Inheritance of Blood Type O

For a child to have blood type O (genotype ii), they must inherit one i allele from each parent. Here's how this can occur with the identified genotypes:

Parent A (I^Ai) can pass down either:

I^A (resulting in blood type A)

i (resulting in blood type O)

Parent B (IBi) can pass down either:

I^B (resulting in blood type B)

i (resulting in blood type O)

The combinations from these parents can be represented as follows:

Parent A	**Parent B**	**Child's Genotype**
I^A	I^B	I^AI^B (AB)
I^A	i	I^Ai (A)
i	I^B	I^Bi (B)
i	i	ii (O)

for the child to have blood type O, **both parents must contribute an i allele.**

c) Probability of Having a Child with Blood Type AB

If this couple has another child, we can calculate the probability of that child having blood type AB. Using the previously established genotypes of the parents:

The probability of having a child with blood type AB is:

Probability=Number of AB outcomes= 1

Total outcomes=4

Probability=Total outcomes/Number of AB outcomes =¼ = 25%

Question 5: Mutations can occur at various levels of the genome, from a single nucleotide change to large chromosomal rearrangements. Consider the following types of mutations: point mutations (silent, missense, nonsense), frameshift mutations, and chromosomal inversions.

a) Describe how a missense mutation and a nonsense mutation can impact protein function differently.

b) Explain how a frameshift mutation might affect the reading frame of a gene and the resulting protein.

c) How might a chromosomal inversion affect gene expression, even if no genes are directly disrupted by the inversion?

Solution:

a) Impact of Missense and Nonsense Mutations on Protein Function

Missense Mutation: A missense mutation occurs when a single nucleotide change results in the substitution of one amino acid for another in the protein sequence. This can have varying effects on protein function, depending on the nature of the amino acid change:

Conservative Changes: If the substituted amino acid has similar properties to the original, the protein may retain much of its functionality.

Non-conservative Changes: If the substitution results in a significantly different amino acid (e.g., changing a hydrophobic residue to a polar one), it can alter the protein's structure, stability, or function, potentially leading to diseases such as sickle cell anemia.

Nonsense Mutation: A nonsense mutation occurs when a nucleotide change creates a premature stop codon in the protein-coding sequence. This leads to:

Truncated Proteins: The resulting protein is shorter and often nonfunctional because it lacks essential domains required for its activity.

Loss of Function: Nonsense mutations typically result in complete loss of function for the affected gene, which can lead to severe phenotypic consequences, such as genetic disorders like muscular dystrophy.

b) Effects of Frameshift Mutations on Reading Frame

A frameshift mutation occurs due to insertions or deletions of nucleotides that are not in multiples of three. This shifts the reading frame of the gene, leading to several consequences:

Altered Amino Acid Sequence: The entire downstream amino acid sequence is altered after the point of mutation. This can result in a completely different protein that may be nonfunctional.

Premature Stop Codons: The new reading frame may introduce premature stop codons, leading to truncated proteins that lack critical functional domains.

Loss of Function: Similar to nonsense mutations, frameshift mutations often result in proteins that cannot perform their intended biological functions.

Overall, frameshift mutations can have severe impacts on gene expression and protein function due to the extensive changes they cause in the translated product.

c) Effects of Chromosomal Inversions on Gene Expression

Chromosomal inversions involve the rearrangement of chromosome segments such that a portion of DNA is reversed within its chromosome. Even if no genes are directly disrupted by an inversion, several mechanisms can still affect gene expression:

Disruption of Regulatory Elements: Inversions may disrupt cis-regulatory elements (enhancers or silencers) located near inversion breakpoints. This can lead to altered transcription levels for genes that are not physically disrupted but are regulated by these elements.

Suppressed Recombination: Inversions reduce recombination rates within inverted regions during meiosis. This suppression can lead to the accumulation of mutations and changes in gene expression over generations.

Altered Gene Interactions: Inversions may bring together genes that were previously separated, allowing for new interactions between them that could enhance or suppress their expression.

Transcriptional Changes Across Breakpoints: Studies have shown that inversions can lead to widespread transcriptional changes across various genes, even those located outside the inversion region. This indicates that inversions can have extensive effects on gene expression profiles.

Question 1B: In an updated version of the Avery-MacLeod-McCarty experiment, a researcher is testing the role of various enzyme treatments on the ability of a heat-killed virulent bacterial extract to transform non-virulent bacteria. Mg^{2+} and Ca^{2+} ions are cofactors for DNAse activity. EDTA is a chelating agent used in DNA isolation which sequesters divalent cations. The researcher prepares extracts from heat-killed *Streptococcus pneumoniae* and treats them with the following conditions:

Condition A: Extract treated with DNase (which degrades DNA).
Condition B: Extract treated with RNase (which degrades RNA).
Condition C: Extract treated with protease (which degrades proteins).
Condition D: Extract with no enzyme treatment (control).
Condition E: Extract treated with DNase and EDTA
After treatment, each extract is mixed with non-virulent *S. pneumoniae* and the transformation of non-virulent bacteria into virulent strains is assessed by their ability to form colonies on selective media. Give reason for each case.

Solution:

Condition A: Extract treated with DNase (degrades DNA)
Expected outcome: No transformation.
Reason: DNase degrades DNA, which is the key transforming material. If DNA is destroyed, the non-virulent bacteria cannot acquire the genes responsible for virulence, preventing their transformation into virulent strains.

Condition B: Extract treated with RNase (degrades RNA)
Expected outcome: Transformation occurs.
Reason: RNA is not the genetic material responsible for transformation in this case. Degrading RNA does not impact the ability of the DNA (which carries the virulence genes) to transform the non-virulent bacteria.

Condition C: Extract treated with protease (degrades proteins)
Expected outcome: Transformation occurs.
Reason: Protein degradation does not affect the transforming ability because DNA is still intact. Therefore, the genetic material necessary for transformation remains available, allowing non-virulent bacteria to become virulent.

Condition D: Extract with no enzyme treatment (control)
Expected outcome: Transformation occurs.
Reason: Without any enzyme treatment, the DNA remains intact and can be taken up by the non-virulent bacteria, enabling them to acquire virulence and form colonies.

Condition E: Extract treated with DNase and EDTA (chelates divalent cations like Mg^{2+} and Ca^{2+})

Expected outcome: Transformation occurs.
Reason: EDTA sequesters Mg^{2+} and Ca^{2+} ions, which are essential cofactors for DNase activity. Without these ions, DNase cannot effectively degrade DNA, leaving the DNA intact and able to cause transformation of the non-virulent bacteria into virulent strains.

Question 3B: Quantifying DNA and Protein in Hershey and Chase Experiment
In the Hershey and Chase experiment, researchers labeled T2 bacteriophages with radioactive phosphorus-32 (^32P) to label the DNA and radioactive sulfur-35 (^35S) to label the protein coat. After the infection and separation steps, they quantified the amount of radioactive material inside the bacterial cells and outside in the protein coats. Suppose that after the experiment, they found that 80% of the total radioactivity was detected inside the bacterial cells, and 20% of the total radioactivity was detected in the protein coats. If the initial amount of ^32P-labeled DNA injected into the bacterial culture was 500 units of radioactivity, what would be the amount of radioactivity detected in the protein coats?

Solution:
Let the total radioactivity from both the DNA and protein coats combined be T. This includes the radioactivity found in both the DNA and protein.
Relating the 80% to the DNA:
Since 80% of the total radioactivity is found inside the bacterial cells (from the DNA), we can set up the equation:
(80/100) * T = 500
This tells us that 80% of the total radioactivity is equal to 500 units (since we are told the DNA radioactivity is 500 units).
Solve for the Total Radioactivity (T):
To find the total radioactivity (T), divide both sides of the equation by 0.80:
T = 500 / 0.80 = 625
So, the total radioactivity from both DNA and protein combined is 625 units.
Calculate the Radioactivity in the Protein Coats:
Since 20% of the total radioactivity is found in the protein coats, we calculate the radioactivity in the protein coats by taking 20% of the total radioactivity:
(20/100) * 625 = 125 units.
Therefore, the amount of radioactivity detected in the protein coats is 125 units.
Final Answer:
The radioactivity detected in the protein coats (labeled with ^35S) is 125 units.

Question 4B: Hydrogen Bonding in DNA

Describe the role of hydrogen bonding in maintaining the stability of the DNA double helix. How many hydrogen bonds are formed between an adenine (A) base and a thymine (T) base? How does this compare to the number of hydrogen bonds between a guanine (G) base and a cytosine (C) base?

Solution:

Hydrogen bonding plays a crucial role in maintaining the stability of the DNA double helix structure. In DNA, hydrogen bonds form between complementary base pairs, holding the two DNA strands together and providing structural stability. These bonds occur between the nitrogenous bases adenine (A) and thymine (T), as well as between guanine (G) and cytosine (C).

The number of hydrogen bonds between base pairs is as follows:

Adenine (A) - Thymine (T) Pair: Adenine and thymine form two hydrogen bonds. Adenine contains a hydrogen bond donor (NH2 group), and thymine has two hydrogen bond acceptors (carbonyl oxygen and methyl group), allowing for the formation of two hydrogen bonds between them.

Guanine (G) - Cytosine (C) Pair: Guanine and cytosine form three hydrogen bonds. Guanine contains three hydrogen bond donors (NH2 groups), and cytosine has three hydrogen bond acceptors (carbonyl oxygen and amino group), allowing for the formation of three hydrogen bonds between them.

The difference in the number of hydrogen bonds between the two base pairs (A-T and G-C) contributes significantly to the stability of the DNA double helix. The G-C pair forms one additional hydrogen bond compared to the A-T pair. This extra hydrogen bond enhances the strength of the G-C base pair interaction and contributes to the overall stability of the DNA molecule.

The hydrogen bonds between complementary base pairs help maintain the integrity of the double helix structure by preventing the strands from separating too quickly. They provide the necessary binding forces to keep the two strands together while allowing for the separation of the strands during processes like DNA replication and transcription. The specificity of hydrogen bonding between the base pairs also ensures accurate replication and transmission of genetic information.