END SEM: Fundamentals of Biology II **Max Marks: 25**

Short Answer Questions (Attempt any 3). Each question = 2 marks

1. Describe how epigenetic mechanisms provide a plausible explanation for phenotypic variation in genetically identical organisms (e.g., monozygotic twins).

Ans: Epigenetic mechanisms such as DNA methylation, histone modifications, and regulatory non-coding RNAs can change the level of gene expression without altering the DNA sequence. Although monozygotic twins have identical genomes, differences in their environments—diet, stress, infections, lifestyle—lead to distinct epigenetic marks over time. These differences cause certain genes to be turned on or off differently, producing measurable variation in traits, disease susceptibility, and aging patterns between genetically identical individuals.

2. What is the primary function of a plasmid vector in recombinant DNA technology?

Ans: A plasmid vector functions as a delivery vehicle that carries a desired DNA fragment into a host cell (often bacteria). It enables replication, maintenance, and sometimes expression of the inserted gene. Key features such as an origin of replication, selectable markers (e.g., antibiotic resistance), and a multiple cloning site allow the foreign DNA to be inserted, selected, amplified, and studied. Thus, plasmids are essential tools for gene cloning, protein expression, and genetic engineering.

3. Discuss one major technical challenge and one ethical consideration associated with the clinical use of CRISPR-Cas9 for human germline editing.

Ans: Technical challenge:
CRISPR-Cas9 may produce off-target mutations, meaning unintended cuts in the genome that can cause harmful genetic changes, developmental abnormalities, or mosaicism (not all cells carrying the edit). Ensuring precise and safe editing in all germline cells remains a major difficulty.

Ethical concern:
Germline edits are permanent and heritable, raising concerns about altering future generations without their consent. It risks creating designer babies, increasing social inequality, and introducing unpredictable effects into the human gene pool. There is also concern about misuse for non-medical enhancements.

4. Explain why a phylogenetic tree is considered a hypothesis, not a definitive fact. What kind of evidence can cause a tree to be revised?

Ans: A phylogenetic tree is a scientific hypothesis because it represents the best current interpretation of evolutionary relationships based on available evidence. It is not final or absolute. New data—such as more comprehensive DNA sequences, better molecular markers,

newly discovered fossils, or improved computational models—can reveal different branching patterns. Such evidence may change the tree's topology, showing that evolutionary relationships are continuously refined as science advances.

5. Discuss how the integration of genomics, bioinformatics, and synthetic biology could lead to a "personalized medicine" approach for treating a complex disease like cancer.

Ans: Genomics provides a detailed map of an individual's tumor mutations, copy-number changes, and gene expression profile, identifying unique molecular signatures. Bioinformatics analyzes these large datasets to find driver mutations, predict drug sensitivity, classify tumor subtypes, and discover therapeutic targets. Synthetic biology applies this information to design customized treatments, such as engineered immune cells (CAR-T), synthetic gene circuits that sense cancer cells, or personalized neoantigen vaccines. Together, these fields allow therapy to be tailored to the patient's unique genetic and molecular profile, improving treatment precision and reducing side effects.

Multiple Choice Questions. Each question = 2 marks; 50% Negative marking

Q1: **b)** Increase neural activity, potentially causing seizures or anxiety.
GABA-A is inhibitory; an antagonist blocks inhibition → net excitation.

Q2: **a)** Antigenic variation.
Changing surface proteins to avoid antibody recognition is antigenic variation.

Q3: **b)** The genetic regulatory toolkit for initiating eye development is evolutionarily ancient and shared.
Pax6 (eyeless) conservation indicates a shared developmental program, not independent origin.

Q4: **b)** 0.7
If $q^2 = 0.09 \rightarrow q = 0.3$, so $p = 1 - q = 0.7$.

Q5: **c)** Group organisms into clades.
Synapomorphies (shared derived traits) define clades in cladistics.

Long Questions (Attempt Any One)

Question 1: Describe the central dogma of molecular biology. Then, explain how modern concepts in epigenetics, recombinant DNA technology, and evolutionary developmental biology (EvoDevo) have expanded, challenged, or refined our

understanding of the relationship between genotype and phenotype. Use specific examples for each area.

Ans: **The** Central Dogma of Molecular Biology

The central dogma, proposed by Francis Crick, states that genetic information flows in one direction:

DNA → RNA → Protein

1. DNA replication: DNA copies itself.
2. Transcription: DNA is transcribed into RNA.
3. Translation: mRNA is translated into proteins, which perform most cellular functions and ultimately shape phenotype.

This model emphasizes that genotype (DNA sequence) determines phenotype (traits) mainly through protein production.

However, modern biology shows that this linear flow is far more flexible, regulated, and context-dependent.

2. How Modern Biology Has Expanded or Refined the Central Dogma

A. Epigenetics — Genotype is not the Whole Story

Epigenetics refers to *heritable changes in gene expression without altering the DNA sequence.*

Key mechanisms:

- DNA methylation (silences genes)
- Histone modifications (open or close chromatin)
- Non-coding RNAs (microRNA, lncRNA regulating translation)

How this refines the central dogma:
Epigenetics shows that *the same DNA sequence can produce different phenotypes* depending on epigenetic marks.

Example:

- Monozygotic twins share identical genomes but develop differences in appearance, disease susceptibility, and behavior due to different epigenetic patterns.

- X-chromosome inactivation: one X chromosome in females is silenced by methylation—same genotype, different expression.

- Nutrition and epigenetics: Dutch Hunger Winter showed famine in pregnant mothers caused DNA methylation changes in offspring → higher risk of metabolic disorders even decades later.

Conclusion:
Epigenetics demonstrates that phenotype is shaped by gene expression regulation, not just DNA sequence.

B. Recombinant DNA Technology — Genotype Can Be Artificially Rearranged

Recombinant DNA technology allows scientists to cut, paste, clone, and express genes across organisms.

Tools:

- Restriction enzymes

- Plasmid vectors

- PCR

- CRISPR-Cas9

How this expands the central dogma:
Recombinant DNA shows that genes are *modular and portable*. Phenotypes can be altered intentionally by modifying genotype.

Examples:

- Human insulin production: The human insulin gene is inserted into *E. coli*, which then produces human insulin protein. This proves that the same gene can give the same protein in a completely different organism.

- Transgenic plants (e.g., Bt cotton): Bacterial toxin genes inserted into plants → insect resistance.

- Gene therapy: Defective genes in humans can be replaced to restore normal phenotype (e.g., treatment of SCID by introducing ADA gene).

Conclusion:
Recombinant DNA shows that genotype-phenotype relationships are manipulable, and genetic information can function across species barriers.

C. Evolutionary Developmental Biology (EvoDevo) — Gene Regulation, Not Gene Number, Creates Diversity

EvoDevo studies how changes in developmental gene regulation drive evolution.

Key principles:

- Small changes in regulatory DNA (not coding DNA) can produce large phenotypic differences.

- Developmental toolkit genes (e.g., Hox genes, Pax6) are deeply conserved across animals.

How EvoDevo refines the central dogma:
It shows that phenotype evolves mainly through changes in when, where, and how genes are expressed, not through changes in the proteins themselves.

Examples:

- Pax6 gene controlling eye development in flies and mice:
  The mouse Pax6 gene can trigger eye formation in fruit flies.
  → Eye development across species relies on the same regulatory genes.

- Beak shape in Darwin's finches:
  Differences arise from variation in expression levels of developmental genes BMP4 and Calmodulin, not new genes.

- Insects vs. vertebrates: Different body plans arise from different *regulatory networks* acting on conserved genes.

Conclusion:
EvoDevo reveals that phenotype depends heavily on gene regulation during development, shifting focus from genes themselves to the regulatory architecture around them.

Question 2: Trace the flow of biological information and regulation from the cellular level to the organismal level. Your answer should integrate concepts from signal transduction, gene regulation (including epigenetic factors), endocrine function, and neural signaling. Use a specific physiological process (e.g., the body's response to low blood sugar) as a framework to illustrate these connections.

Ans: Tracing the Flow of Biological Information and Regulation from the Cellular to the Organismal Level

Biological information flows and regulatory mechanisms in organisms are organized hierarchically, from molecular signaling at the cellular level to integrated physiological responses at the organismal level. This integration ensures homeostasis and coordinated responses to environmental or internal stimuli. Let us illustrate this using the body's response to low blood sugar (hypoglycemia) as a framework.

1. Cellular Level: Sensing and Signal Transduction

At the cellular level, individual cells detect changes in their environment through specialized receptors. For instance, pancreatic α-cells in the islets of Langerhans monitor glucose levels in the blood. When blood glucose falls, these cells sense decreased intracellular glucose metabolism, leading to changes in ATP/ADP ratios.

- Signal transduction mechanisms:
    - The reduction in ATP-sensitive potassium channel activity causes cell membrane depolarization.
    - Depolarization triggers voltage-gated calcium channels to open, allowing calcium influx.
    - Elevated intracellular calcium acts as a second messenger, initiating the exocytosis of glucagon-containing vesicles.

Thus, a biochemical change inside a single cell is translated into a molecular signal—glucagon secretion—that can affect other cells in the body.

2. Gene Regulation and Epigenetic Modulation

Cells also adjust their longer-term responses through gene expression:

- Transcriptional regulation: In α-cells, transcription factors such as Foxa2 and MafB regulate the expression of glucagon in response to sustained low glucose levels.

- Epigenetic factors: DNA methylation and histone modifications can alter the accessibility of glucagon gene promoters, modulating how strongly α-cells respond to chronic changes in glucose.

- Feedback loops: Other cells, such as hepatocytes, respond to glucagon by activating genes encoding enzymes for glycogenolysis and gluconeogenesis, raising blood glucose levels. This involves transcription factors like CREB (cAMP response element-binding protein) activated by glucagon-mediated cAMP signaling.

Thus, intracellular regulatory networks ensure that transient and long-term cellular responses are appropriately tuned.

3. Endocrine Integration: Intercellular Communication

At the tissue and organ level, signal propagation involves endocrine signaling:

- Glucagon secreted from pancreatic α-cells acts as a hormone, traveling through the bloodstream to target tissues such as the liver.

- In the liver, glucagon binds to G protein-coupled receptors (GPCRs), activating the adenylate cyclase–cAMP–PKA signaling cascade, leading to phosphorylation of enzymes that catalyze glycogen breakdown and glucose release.

- This systemic hormone-mediated regulation exemplifies how cellular signals are amplified and coordinated across multiple tissues to maintain organismal homeostasis.

4. Neural Signaling: Rapid and Coordinated Control

Neural systems complement endocrine regulation by providing rapid feedback:

- Peripheral glucose sensors, such as those in the hepatic portal vein, send afferent signals to the hypothalamus via the autonomic nervous system.

- The hypothalamus integrates information from glucose sensors and orchestrates responses via the sympathetic nervous system:

    - Sympathetic nerves release norepinephrine to stimulate hepatic glycogenolysis.

    - Adrenal medulla secretes epinephrine, which also promotes glycogen breakdown and inhibits insulin release, enhancing blood glucose levels.

- Neural control allows moment-to-moment fine-tuning, ensuring glucose levels rise rapidly to meet immediate energy demands.

5. Organismal Response and Homeostasis

Finally, the integration of cellular, endocrine, and neural responses restores blood glucose levels:

- Immediate response: Neural signals trigger rapid glycogen breakdown and inhibit insulin secretion.
- Short-term response: Glucagon-mediated hepatic glucose release sustains blood sugar levels.
- Long-term adaptation: Gene regulatory mechanisms in the liver and α-cells adjust enzyme and hormone production for future glucose fluctuations.

This illustrates how molecular events (ion fluxes, signaling cascades, gene transcription) scale up to tissue, organ, and organismal responses, ensuring homeostasis.

Conclusion

The flow of biological information begins at the cellular level with signal detection and transduction, is modulated by gene regulation and epigenetic factors, is propagated across the body via endocrine and neural pathways, and culminates in coordinated physiological responses at the organismal level. The body's response to hypoglycemia demonstrates this hierarchical integration: from intracellular calcium signaling in α-cells, to glucagon secretion, to hepatic glucose production, and to neural feedback—all working together to maintain glucose homeostasis.