Mid sem 2025
Biophysics(BIOP)

Total Marks:30

Time: 1 Hour

Section A

1. Which of the following best describes the FASTA format?
   A. A file format for storing protein structures
   B. A text-based format for representing nucleotide or peptide sequences
   C. A binary format used in protein alignment
   D. A compressed format for protein motifs

2. Which statement about water-mediated hydrogen bonds in protein folding is TRUE?
   A. They always destabilize folding
   B. They can stabilize transient intermediates
   C. They are weaker than direct hydrogen bonds and irrelevant
   D. They occur only in unfolded states

3. Proteins from thermophilic organisms are usually “harder” because:
   A. They have fewer hydrophobic residues
   B. They are shorter in sequence length
   C. They contain more stabilizing interactions
   D. They lack secondary structure

4. Which of the following correctly represents the hierarchical order in the CATH classification system?
   A. Fold → Architecture → Class → Topology → H-level
   B. Class → Topology → Architecture → Fold → H-level
   C. Class → Architecture → Topology → Fold families → H-level
   D. Architecture → Class → Fold → H-level → Topology

5. Which structural type would most likely occupy a φ ≈ –60°, ψ ≈ –45° region in a Ramachandran plot?
   A. Right-handed α-helix
   B. β-sheet
   C. Left-handed α-helix
   D. Random coil

6. Which statement is TRUE regarding the interplay of bonded and non-bonded interactions in protein folding?
   i. Bonded interactions determine long-range tertiary contacts
   ii. Non-bonded interactions only affect unfolded proteins
   iii. Bonded interactions define local geometry

iv. Non-bonded interactions guide folding and stabilization

(A) i&ii (B) i&iii (C) ii&iii (D) iii&iv

7. During transcription, RNA is synthesized in which direction?
   A. 3′ → 5′ along the RNA strand
   B. 5′ → 3′ along the RNA strand
   C. 3′ → 5′ along the DNA template
   D. Both B and C

8. Which of the following is not representing the stop codon?
   A. TAA
   B. TGC
   C. TAG
   D. TGA

10. Match the following algorithms with their applications in bioinformatics:

A. Smith Waterman algorithm	1. Multi-Chaperone system
B. Protein misfolding	2. Pairwise sequence alignment
C. Chou Fasman method	3. Protein secondary structure prediction
D. Protein folding	4. Baculovirus system

   A. A–1, B–2, C–3, D–4
   B. A–2, B–4, C–3, D–1
   C. A–3, B–4, C–1, D–2
   D. A–4, B–3, C–2, D–1

14. Keratin is a structural protein with a hierarchical organization. Which of the following correctly represents the order of assembly from the simplest to the most complex structure?

A. Protofilament → α-helix → coiled coil → filament
B. α-helix → coiled coil of two α-helices → protofilament → filament
C. Coiled coil of two α-helices → filament → protofilament → α-helix
D. α-helix → protofilament → filament → coiled coil

Section B

1. In a protein, valine is found buried inside the core, while serine is on the surface. Explain the chemical property (VAL & SER) responsible for this placement, and why/how this contributes to stability. **(3 mark)**

Mark	Focus Area	Essential Point to Be Made
1 Mark	Core Property Identification	The governing chemical principle is Polarity (or the Hydrophobic Effect). Valine is nonpolar/hydrophobic and Serine is polar/hydrophilic.
1 Mark	Placement Rationale	Valine is buried in the core to minimize unfavorable contact with the aqueous solvent, and Serine is placed on the surface to maximize favorable interaction (e.g., H-bonds) with water.
1 Mark	Contribution to Stability	This specific arrangement is stable because it collectively lowers the overall Gibbs Free Energy (ΔG) of the system by maximizing favorable (polar-water) and minimizing unfavorable (nonpolar-water) interactions.

2. A ligand binds to a protein and interacts with eight residues that are closely positioned in its quaternary structure.

a. Does this imply that these residues are also close in the protein's primary sequence? Justify your answer with structural reasoning. **(2 mark)**

Answer a: No/maybe, the residues interacting with the ligand in the protein's quaternary structure are not necessarily close in the primary sequence. (1 marks)
Protein Folding and Tertiary Structure: In a protein's primary sequence, residues can be far apart in terms of sequence numbering. However, during folding, these residues can come close in the three-dimensional (tertiary/Quaternary) structure due to the formation of secondary structures. (1 mark)

b. What is the primary command to select and highlight only the residues located within a 5 radius of the bound ligand (in Chimera)? **(1 mark)**

Answer b: **select :LIG z<5.0** (To select all the residues within 5A range of the ligand)

3. The evolution of proteins often results in functional diversity. Imagine two genes, initially identical, diverging over time to perform different, yet related, tasks in various organisms

(a) Define paralogs and orthologs, giving one biological example of each. **(2 mark)**

(a) Paralogs: Genes related by duplication within a genome; often evolve new functions. Example: Hemoglobin α and β chains in humans. Orthologs: Genes in different species that diverged after a speciation event; usually retain the same function. Example: Human and mouse insulin.

(b) If two proteins are homologous, but one performs glucose transport in humans and the other performs amino acid transport in humans, what relationship do they have? **(1 mark)**

(b) These are paralogs (gene duplication in the same organism, diverged functions).

(c) If two proteins perform glucose transport in humans and mice, what relationship do they have? **(1 mark)**

(c) These are orthologs (same function conserved across species after speciation).

Section - C

1. During molecular modeling of a newly designed enzyme, you notice that the folded protein structure shows several steric clashes in the hydrophobic core. Answer the following:

   (a) what happens to energy as interatomic distance (w.r.t LJ Potential) r→0? **(1 mark)**

   As r→0, the repulsive 1/r121/r^{12}1/r12 term dominates, and the energy rises steeply towards +∞, representing steric clashes.

   (b) Why are hydrophobic protein cores mainly stabilized by van der Waals interactions?**(1 mark)**

   Hydrophobic cores rely on van der Waals interactions because nonpolar side chains cannot form hydrogen bonds or ionic interactions; instead, they are stabilized by many weak dispersion forces acting cooperatively.

   (c) What do you understand by ‘Clashes’? How do van der Waals radii help prevent steric clashes?**(2 marks)**

   Clashes - unfavorable interactions where atoms are too close together; close contacts.

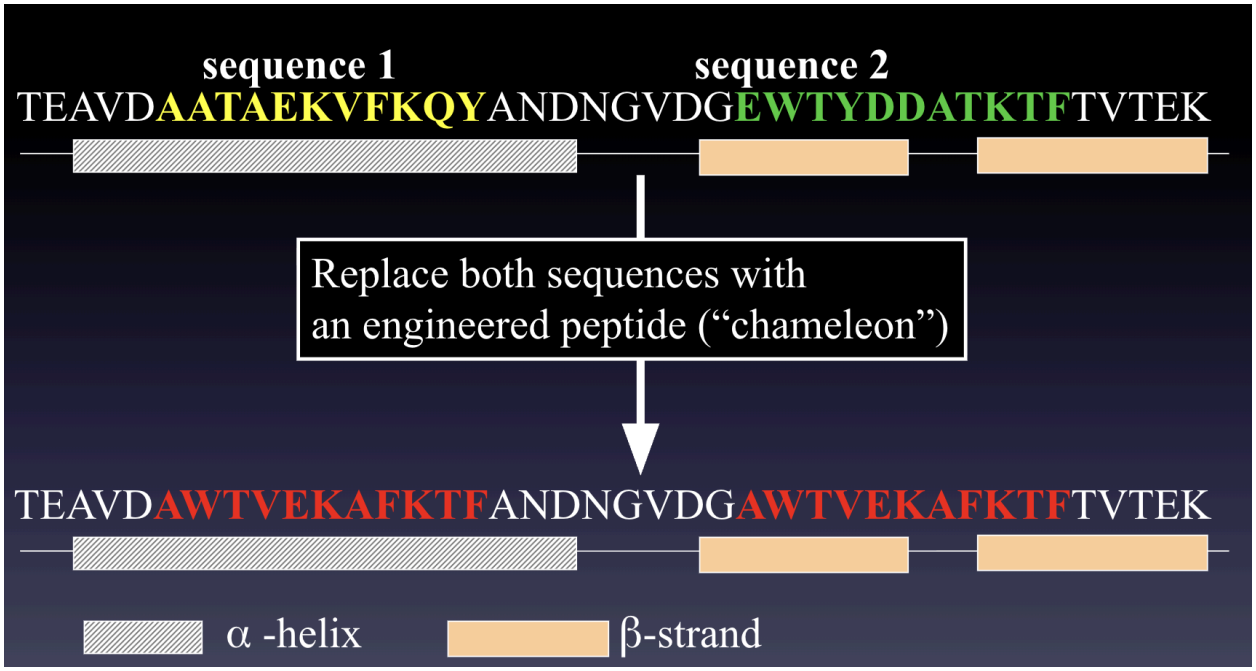
   Van der Waals radii represent the effective "size" of atoms. They define a minimum allowed distance between atoms, helping to avoid steric clashes.

   (d) Explain how the balance of Lennard–Jones attractive and repulsive forces determines protein packing density.**(1 mark)**

   The attractive ($1/r^6$) term pulls atoms together, while the repulsive ($1/r^{12}$) term pushes them apart at very short distances. The balance creates an equilibrium distance, which sets how tightly atoms can pack inside a protein.

2. A structural biology team is studying a small protein involved in cell signaling. Interestingly, a 10-residue stretch forms an α-helix when the protein is crystallized alone, but the same region forms a β-strand when bound to a partner protein. This conformational switch is thought to influence binding affinity and stability.
   a. What is this type of sequence in proteins called? Explain with an illustrative example **(3 mark)**

Answer: Such sequences are called chameleon sequences, stretches of amino acids that can adopt different secondary structures in different protein environments. (1 mark)



Illustrative example: (2 mark)

b. Why is it surprising in the context of secondary structure prediction?**(2 mark)**

Answer: This is unexpected because secondary structure prediction methods assume that the primary amino acid sequence alone determines secondary structure. (1 mark → For stating the basic assumption.)

Chameleon sequences challenge this assumption by showing that the same sequence can fold differently depending on environment and interactions. (1 mark → For explaining why chameleon sequences are surprising)