Biophysics - BIO361
Rubric Mid-Semester Exam

Total Marks : 30

Duration: 1h

Part1- Multiple Choice Questions

Total marks - 15*1=15 marks

Each Question is for one mark. No negative marking. Attempt all questions.

Correct answers are in BOLD letters.

1. What is the energy of hydrogen bond in water and in proteins?
   a) 1.2cal/mole,5cal/mol
   b) 2.5cal/mole,2kcal/mole
   c) 3.2kcal/mol,5kcal/mol
   d) 4.5kcal/mole,2kcal/mole

2. Who took the first X-ray diffraction images of DNA:
   a) Raymond and Gosling
   b) Rosalind and Franklin
   c) Watson and Crick
   d) Rosalind and Gosling

3. In a DNA molecule, what is the kind of bond between Sugar and Base, Sugar and Phosphate, between nucleotides:
   a) Phosphodiester Bond , Glycosidic Bond , Hydrogen Bond
   b) Hydrogen Bond, Phosphodiester Bond , Phosphoester Bond
   c) Phosphoester Bond , Phosphodiester Bond , Hydrogen Bond
   d) Glycosidic Bond , Phosphoester Bond , Hydrogen Bond

4. Which of the following statements is not correct?
   a) DNA contains thymine, while RNA contains uracil as one of its bases.
   b) Both DNA and RNA are double-stranded molecules.
   c) DNA is found exclusively in the nucleus, while RNA can be found throughout the cell.
   d) DNA is more stable and less prone to mutations compared to RNA.

5. If there is a RNA of 24 bases, what are the number of unique sequences it can have?
   a) 4^24
   b) 2^24
   c) (4^24) * 2
   d) None of the above

1 mark for either (a) or (d)

6. Which of the following are aromatic amino acids ?
   a) Phenylalanine, Serine,Cysteine
   b) Phenylalanine, Threonine, Tryptophan
   c) Phenylalanine, Tryptophan,Tyrosine
   d) Phenylalanine, Methionine, Cysteine

7. Which of the following phenomena results in the partial double-bond character of the peptide bond?
   a) Electronegativity
   b) Stearic hindrance
   c) Resonance
   d) Both Electronegativity and Stearic Hindrance

8. What is the significance of the E-value in protein sequence alignment?
   a) It is a measure of the significance of the alignment between the target protein and the template proteinll5
   b) It is a measure of the activity of the target protein and template protein.
   c) It is a measure of the size of the target protein and template protein.
   d) Options B and C are correct.

9. What are the start codon and stop codons of a protein?
   a) AUG and UAA
   b) AUG and UAG
   c) GAA and UGU
   d) Both A and B

10. In the CATH classification system, what does the term "homologous superfamily" refer to?
   a) Proteins with similar functions but different structures.
   b) Proteins with similar sequences and structures.
   c) Proteins sharing a common evolutionary ancestor and structural fold.
   d) Proteins with unrelated functions and structures.

11. DNA is devoid of oxygen atom from which of its following component?
   a) Sugar
   b) Phosphate
   c) Base
   d) All of the above

12. What do Purines contain?
   a) Adenine
   b) Alanine
   c) Cytosine

d) Thiamine

13. Right-handed alpha-helix allowed region is present in which of the following quadrants of Ramachandran plot?

a) Fourth quadrant
b) Second quadrant
c) First quadrant
d) Third quadrant

14. Which of the following amino acids is NOT chiral, and does it possess any unique characteristics?

a) Alanine
b) Glycine
c) Leucine
d) Aspartic acid

15. Which statement is untrue regarding the Sequence Alignment Step in homology modeling?

a) Once the structure with the highest sequence similarity is identified as a template, the full-length sequences of the template and target proteins need to be realigned using refined alignment algorithms to obtain optimal alignment.
b) The realignment is the most critical step in homology modeling.
c) The realignment directly influences the quality of the final model.
d) Errors made in the alignment step can be corrected in the following modeling steps.

Part 2 - Short Answer-type Questions (3 marks each)

Total marks - 5*3 = 15 marks
Answer any five questions.

1. Describe the significance of a Ramachandran plot in the context of protein structure analysis. Provide an example of a typical region in a Ramachandran plot and explain what it represents with a diagram.

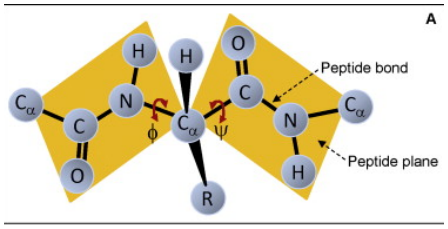
The plot displays the distribution of the backbone **dihedral** angles phi (ϕ) and psi (ψ) of amino acid residues in a protein. The phi angle is the angle of right-handed rotation around N-CA bond. The psi angle is the angle of right-handed rotation around CA-C bond (show in figure below).

These angles describe the orientation of the peptide bond between two adjacent amino acids in the protein backbone.

The purpose of the Ramachandran plot is to identify the regions of the plot where the backbone dihedral angles of a protein are located. Regions that correspond to allowed combinations of phi

and psi angles are considered favorable for protein structure, while regions with disallowed combinations are considered unfavorable.

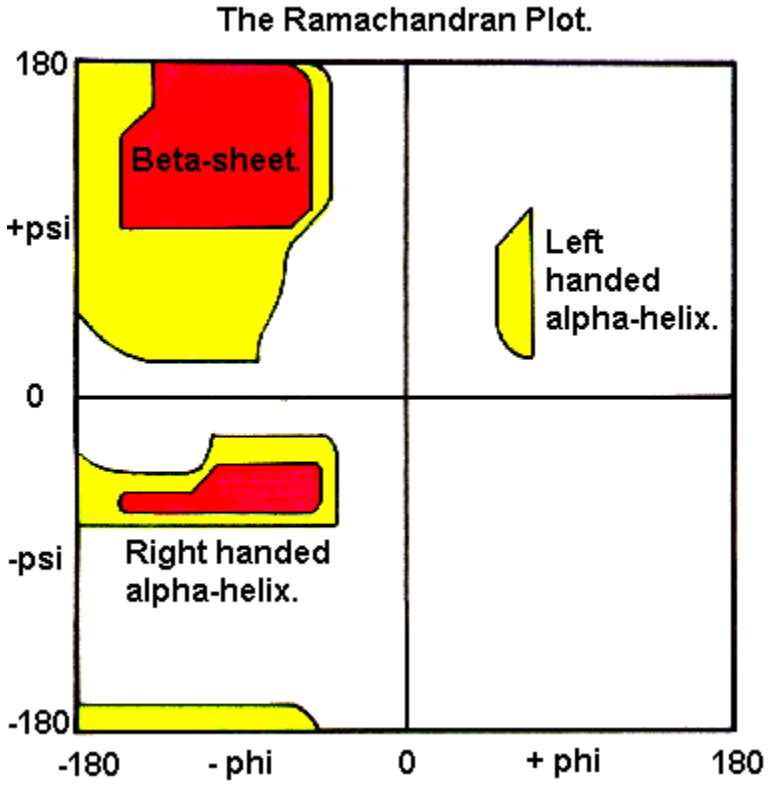
By examining the distribution of the backbone dihedral angles in a protein structure, scientists can evaluate the overall quality of the structure and identify potential errors in the model.



The phi angle is the angle of right-handed rotation around N-CA bond. The psi angle is the angle of right-handed rotation around CA-C bond

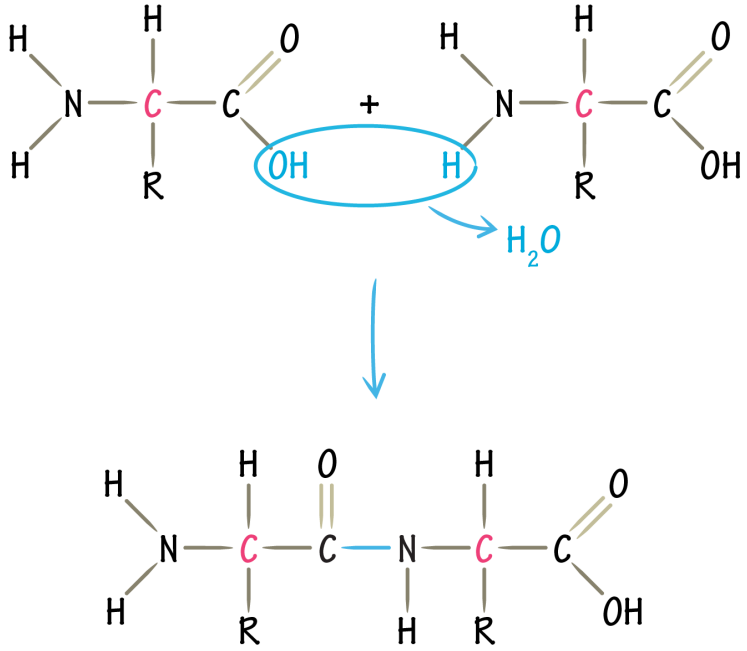
Ramachandran plot

Plot between Ramchnadran angles phi (horizontal axis) and psi (vertical axis)
White region- Sterically disallowed regions except Glycine (no side chains)
Red regions- Allowed regions, namely- Alpha Helix and Beta Sheet.
Yellow Areas- Outer limits (Generously allowed)



2. Describe the relation between sequence, structure, and function. Diagrammatically represent peptide bond formation. Which amino acid isomer is more found in nature?
The relationship between sequence, structure, and function is fundamental in the context of biomolecules, particularly proteins. Proteins are composed of amino acid sequences, and the specific arrangement of these amino acids dictates the three-dimensional structure of the protein, which, in turn, determines its biological function. Eg. the formation of active sites in proteins

Representation of peptide bond



Trans or L isomer.

3. How are proteins classified according to their structure, write a few points about properties of each.
Four levels of protein structure:
Primary structure: Linear sequence of amino acids that make up the protein chain. The primary structure is the simplest form of protein structure and is determined by the DNA sequence that encodes the protein.
Secondary structure: It is the way the protein chain folds into two basic shapes: alpha helices and beta sheets. These shapes are stabilized by hydrogen bonds between amino acids. The secondary structure of a protein can have a significant impact on its function and stability.
Tertiary structure: The tertiary structure of a protein is the three-dimensional shape that the protein takes on due to the interactions between its amino acids. These interactions can include hydrogen bonds, ionic bonds, van der Waals forces, and hydrophobic interactions. It determines the protein's active site, which is the region that binds to other molecules and catalyzes chemical reactions.

In some cases, a protein may have a quaternary structure, which is the way multiple protein chains come together to form a functional unit. The quaternary structure can be thought of as a higher-order structure than the tertiary structure.
OR

The CATH (Class, Architecture, Topology, Homology) protein structure classification system consists of four major levels of classification:
Class: The first level of classification is based on the secondary structure composition of proteins. Proteins are divided into four main classes: alpha, beta, alpha-beta, and few secondary structures.
Architecture: The second level of classification is based on the overall shape and arrangement of secondary structure elements in the protein. E.g. alpha-helical or beta-sheet structure, or a combination of both.
Topology: The third level of classification is based on the connectivity of secondary structure elements within the protein.
Homology: The fourth level of classification is based on sequence similarity and evolutionary relationships between proteins. Proteins with similar sequences and structures are grouped together into families and superfamilies based on their evolutionary relationships, even if they have different functions.

OR

1.Fibrous proteins:

- Insoluble,strong highly regular
- Often forms aggregates
- Lots of hydrogen bonds

2. Globular proteins:

- Water soluble, less regular
- complex folds
- Peptide chain interacts with itself, other domains and cofactors

3. Membrane proteins

- Found in oily lipid environment
- Attached to cellular membrane
- Often channels and transporters

4. What is Anfinsen's dogma, and how does it relate to Levinthal's paradox?

According to Levinthal's paradox, if a protein were to explore all possible conformations sequentially, it would take an impossibly long time to fold, even for small proteins.

Anfinsen's dogma helps to solve this paradox by suggesting that the folding process is not random, but rather is guided by the protein's primary sequence. It says that a protein sequence has the tendency to form a structure that has the least free energy. This means that the protein will fold into its native conformation in a relatively short amount of time, bypassing the need to explore all possible conformations. Anfinsen's dogma provides a framework for understanding how proteins fold into their functional conformations, and it has been supported by numerous experimental studies.

5. What factors should be considered when selecting a template for homology modeling using Modeller?

In the pairwise sequence alignments aided bydatabase search techniques such as FASTA and BLAST one with **high Sequence identity (> 80%)**, **lower E-value (more significant the sequence)**,**less or no missing residues** and **better resolution** should be considered.

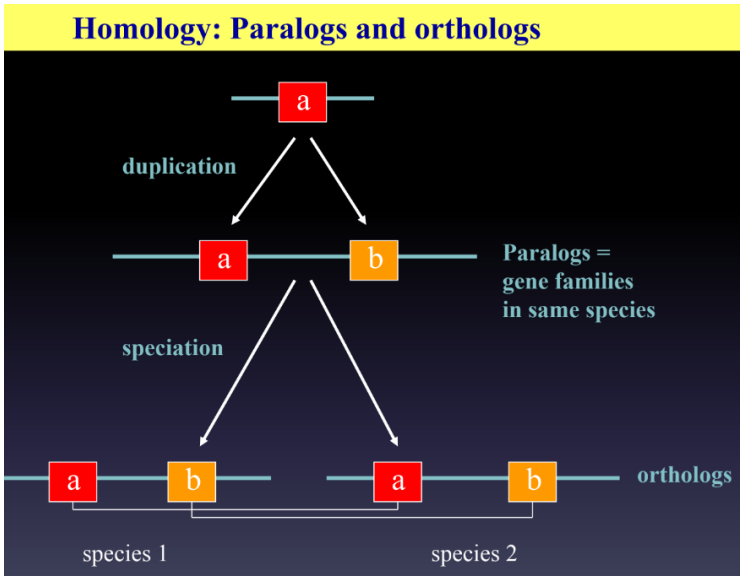
6. Explain the difference between

a) **Homologs and Paralogs**

A homologous gene (or homolog) is a gene inherited in two species by a common ancestor. Homology between protein or DNA sequences is defined in terms of shared ancestry.

Orthologs, or orthologous genes, are genes in different species that originated by vertical descent from a single gene of the last common ancestor. For instance, the plant Flu regulatory protein is present both in *Arabidopsis* (multicellular higher plant) and *Chlamydomonas* (single cell green algae)

Homologous sequences are paralogous if they were separated by a gene duplication event: if a gene in an organism is duplicated to occupy two different positions in the same genome, then the two copies are paralogous. Paralogous genes often belong to the same species, but this is not necessary. For example, the hemoglobin gene of humans and the myoglobin gene of chimpanzees are paralogs.



b) Bonded and Non-bonded interactions

Bonded interactions involve covalent bonds between atoms, It involves the sharing of electrons between atoms and are typically strong. Examples of bonded interactions include covalent bonds within molecules like H2O (water), where oxygen (O) and hydrogen (H) atoms share electrons to form stable bonds.

Non-bonded interactions, on the other hand, do not involve the sharing of electrons or the formation of covalent bonds. Weaker forces of attraction or repulsion between atoms or molecules that do not result in chemical bonding. Non-bonded interactions can be categorized into two main types: (i) Van der Waals Interactions (ii)Electrostatic Interactions

c) Sequence similarity and Sequence Identity

Sequence Similarity: Sequence similarity measures the degree of resemblance or likeness between two sequences based on the presence of similar amino acids or other components in corresponding positions.

Sequence Identity: It measures the exact match or identity between two sequences, considering only those positions where the amino acids are the same.