BioPhysics - BIO361
EndSem
10.12.24

Total marks :30
Time : 2hr

MCQ(1*20=20 marks)

1. Which among the following are acidic amino acids

1. **Glutamate and Aspartate**
2. Lysine and Arginine
3. Threonine and Serine
4. Tryptophan and Proline

2. Which prediction tool integrates multiple methods for a consensus prediction?

A. PSI-Pred
B. **PREDATOR**
C. **JPRED**
D. ZPRED

3. Which of the following time scales corresponds to *local motions* in biological molecules?

A. **10^{-15} to 10^{-1} seconds**
B. 10^{-9} to 1 second
C. 10^{-7} to 10^{4} seconds
D. None of the above

4. What type of motions are classified as rigid body motions in molecular systems?

A. Helix-coil transitions
B. Folding and unfolding
C. Atomic fluctuations
D. Domain motions and subunit motions

5. Which of the following shapes can be used for simulation boxes with PBC in GROMACS?

A. Octahedron
B. Pyramid
C. Circular
D. All of the above

6. What is the purpose of the "equilibration" phase in a GROMACS simulation?

a) To calculate the potential energy of the system

b) To adjust the simulation temperature and pressure
c) To visualize the trajectory
d) To generate the final simulation report

7. When using UCSF Chimera, which of the following file formats is typically used to import molecular structure data?

A. FASTA
B. PDB
C. BED
D. VCF

8. How does the folding of a protein reduce its free energy while maintaining a balance between enthalpy and entropy?

A. Folding decreases enthalpy by breaking covalent bonds and increases entropy by restricting motion of side chains.
B. Folding minimizes free energy by maximizing enthalpy and decreasing entropy entirely.
C. Folding stabilizes the protein by maximizing favorable enthalpic interactions and offsetting the entropic loss of the polypeptide chain with solvent entropy gains.
D. Folding increases free energy by introducing entropic penalties due to loss of conformational flexibility.

9. How does the hydrophobic effect drive protein folding?

A. By forming covalent bonds between hydrophobic residues, stabilizing the protein structure.
B. By increasing the entropy of the protein itself while decreasing the entropy of the solvent.
C. By minimizing the exposure of hydrophobic residues to water, increasing the entropy of surrounding water molecules.
D. By facilitating ionic interactions between hydrophobic residues and polar solvents.

10. Why is the transition state in protein folding critical for understanding the folding pathway?

A. It represents the point of lowest energy in the folding landscape.
B. It corresponds to the most stable intermediate in the folding process.
C. It is the highest-energy barrier that separates the unfolded state from the folded state.
D. It is the final conformation a protein adopts during folding.

1. In the Ramachandran plot, the region corresponding to left-handed helices is found in the **_top-right_/first**_____ quadrant.
2. The ____**peptide**_____ bond in the protein backbone restricts rotation, giving rise to specific dihedral angles.

3. Proteins are most stable when secondary structures form ___**intramolecular**_____ hydrogen bonds, minimizing free energy.
4. H-bonds are found between the individual chains of Beta-sheet.(True/**False**)
5. Non-bonded interactions are typically calculated using _____**LJ**____ and ___**Coulomb**_____ potentials in molecular simulations.
6. The basic assumption in homology modeling is that proteins with similar ___**residues/aminoacids/sequence**_____ have similar structures.
7. __**PDB**_____ is the structure database, whereas, **Uniprot**_____ is a sequence database.
8. While analyzing homology based constraints,___**Distance**____ and _____**Angle**__ between aligned positions should be similar.
9. In helical transmembrane proteins there is abundance of __**positively charged**_____ amino acid residues in the cytoplasmic side.
10. The entropy of an isolated system not in equilibrium will decrease over time.(True/**False**)

Short answer type questions (2 * 10=20 marks)

1. **What happens to entropy when gas expands into the vacuum?What is the relationship between entropy and Gibbs free energy?**

When a gas expands into a vacuum (free expansion), **entropy increases**. This occurs because the gas particles distribute themselves over a larger volume, increasing the number of possible microstates (configurations the particles can occupy). Since entropy (SSS) is a measure of disorder or randomness, and randomness increases in a vacuum, the entropy rises.

Mathematically, for an ideal gas expanding into a vacuum:

$$\Delta S = nR \ln \left(\frac{V_f}{V_i} \right)$$

Where:

- n is the number of moles of gas.
- R is the gas constant.
- Vf and Vi are the final and initial volumes, respectively.

Here, Vf>V, so ΔS>0,

No heat (q=0) or work (w=0) is exchanged in free expansion, but the system's entropy increases due to the larger available phase space in the vacuum.

Relationship between entropy and Gibbs free energy

In a vacuum, the relationship between entropy and Gibbs free energy remains consistent with the equation:

$G=H-TS$

Where:

- G is Gibbs free energy,
- H is enthalpy,
- T is temperature,
- S is entropy.

When gas expands into a vacuum:

- **Entropy (S) increases**, as discussed above.
- **Enthalpy (H) remains unchanged**, because no heat is exchanged and no external pressure does work.
- The change in Gibbs free energy (ΔG\Delta GΔG) depends solely on the entropy term.

For an ideal gas expanding into a vacuum, Gdecreases due to the TS term:

$\Delta G=-T\Delta S$
Since $\Delta S>0$, $\Delta G<0$, meaning the process is spontaneous. The vacuum provides no resistance, and the increase in entropy drives the expansion.

2. **Why are cis conformations almost never observed in peptide bonds?**

Cis conformations in peptide bonds are rare because of **steric hindrance**. In the cis conformation, the side chains (R groups) of adjacent amino acids are positioned on the same side of the peptide bond, causing steric clashes that make this conformation energetically unfavorable.

The trans conformation, in contrast, minimizes steric hindrance as the side chains are on opposite sides of the bond, making it far more stable. The exception is **proline**, where the cis conformation is observed more frequently due to the ring structure of proline reducing the steric clash.

3. **Which ones are the most important degrees of freedom in proteins?**
   Translational, rotational, and vibrational motions are fundamental degrees of freedom in proteins that govern their dynamics and interactions. Translational

motion involves the entire protein moving through space, crucial for diffusion and molecular recognition. Rotational motion allows proteins or domains to reorient, enabling proper alignment during binding or catalysis. Vibrational motion includes high-frequency bond stretching and low-frequency collective motions, such as domain bending or pocket breathing, which are often linked to functional changes like ligand binding or allosteric regulation. Together, these motions facilitate exploration of the energy landscape, enabling proteins to adopt functional conformations and interact effectively with their environment.
OR

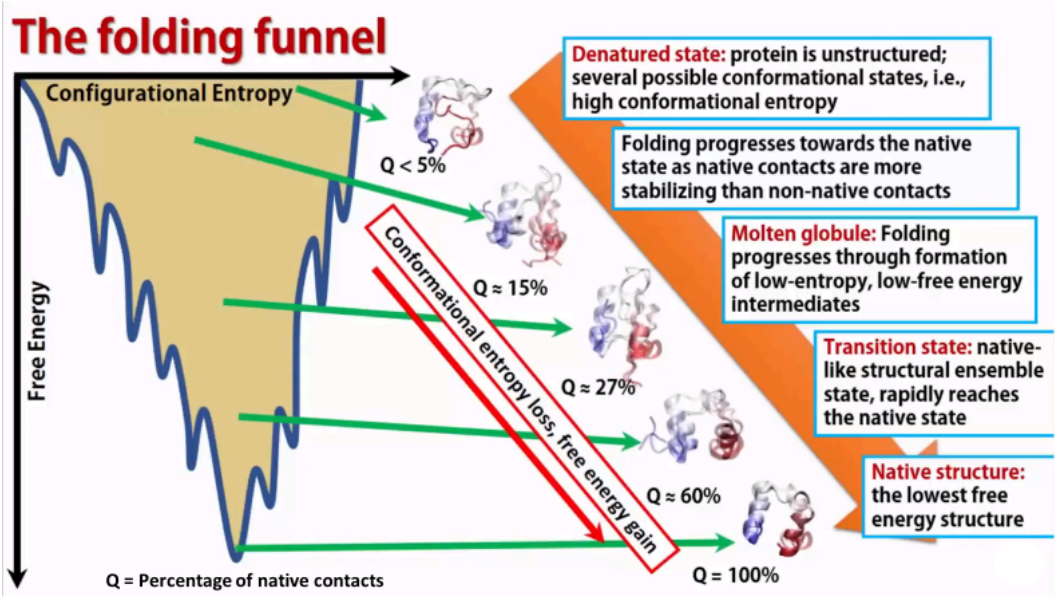
The most important degrees of freedom in proteins are related to the backbone torsion angles:

1. **Phi (ϕ\phiϕ)**: The angle around the bond between the nitrogen and alpha carbon.
2. **Psi (ψ\psiψ)**: The angle around the bond between the alpha carbon and the carbonyl carbon.
3. **Chi (χ\chiχ)**: The side-chain torsion angles.

These angles determine the protein's secondary and tertiary structures and play a critical role in protein folding and function.

4. **What are energy landscapes, how are their properties related to energy/entropy?**

Free energy landscape describes the energy of a system in terms of certain parameters, with respect to protein folding it will show the transition in energy as a protein goes from unfolded to most stably folded state.



When the protein tends to move from a denatured to a folded state, the percentage of native contacts increases, which reduces the entropy of the structure, making it energetically stable. decrease as it goes from the unfolded to the most stably folded state.

5. **How does hydrophobic effect play a role in maintaining the globular structure of the protein?**

The hydrophobic effect drives the burial of nonpolar (hydrophobic) side chains in the protein core, away from the aqueous environment. This minimizes the unfavorable entropy loss of water molecules, which would otherwise form ordered shells (clathrates) around hydrophobic groups. Instead, the protein folds in a way that:

- Hydrophobic residues cluster in the interior.
- Hydrophilic residues are exposed on the surface.

This segregation stabilizes the globular structure and is a key driving force in protein folding.

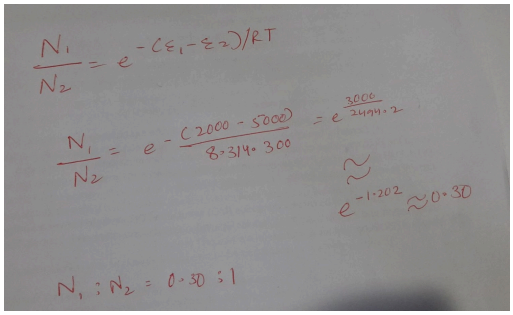
Quiz

1.(i)State the Boltzmann distribution formula and explain the significance of each term in the equation. (ii) Consider two energy levels, E1=2 kJ/mol and E2=5 kJ, in a system at T = 300K. Using the Boltzmann factor, calculate the ratio of the number of particles in these states (N1/N2). R=8.314 J/(mol.K).How does entropy change when more particles move to higher energy levels? Explain in terms of microstates.(1+2+2)

1. The Boltzmann distribution formula is:

$$P(E) \propto e^{-E/(k_B T)}$$

- $P(E)$: Probability of particles being in energy state E.
- E: Energy of the state.
- k_B: Boltzmann constant ($1.38 \times 10^{-23}\,\mathrm{J/K}$).
- T: Absolute temperature of the system.



As more particles occupy higher energy levels, the number of possible microstates increases, leading to a higher entropy.

2.State the principle of molecular dynamics (MD) simulations.Differentiate between Energy Minimization and Equilibration in Molecular Dynamics

Simulations, along with their significance. Why is a pbc important for a successful simulation? (1+3+1)

Molecular dynamics (MD) simulations involve solving Newton's equations of motion for a system of particles (atoms or molecules) to study their time-dependent behavior. By applying realistic force fields, MD provides insights into structural, dynamic, and thermodynamic properties at an atomic level.

Energy Minimization:

Purpose: The primary goal of energy minimization is to remove steric clashes and unfavorable interactions within the system. It ensures that the system starts at a stable state before the actual molecular dynamics simulation begins.

Role in Stabilizing the System: Energy minimization helps stabilize the system by eliminating unrealistic configurations and preparing it for the next stages of simulation. If this step is skipped, the simulation could start from an energetically unfavorable state, leading to incorrect results.

Temperature/Pressure Equilibration (Thermal and Baric Equilibration):

Purpose: After the system has been minimized energetically, temperature and pressure equilibration ensures that the system is at the correct temperature and pressure before production runs. This step adjusts the system to the desired thermodynamic conditions.

Role in Stabilizing the System: Temperature and pressure equilibration ensure that the system's internal degrees of freedom are properly distributed and that the system is in equilibrium with the environment (temperature and pressure). This step helps avoid unrealistic expansions or contractions of the system, ensuring the simulation is conducted under physically relevant conditions.

Pbc: Prevents artificial surface effects that could distort molecular interactions. Ensures that particles leaving one side of the simulation box re-enter from the opposite side, maintaining system density and continuity.