Quiz2 2025
Biophysics(BIOP)
(6. Nov.25)

Total Marks:20
Time: 45 min

Section-A (MCQ 1*10 Marks)

1. During NVT equilibration, which quantity is kept constant?

A. **Number of particles, volume, and temperature**
B. Number of particles, pressure, and temperature
C. Volume, pressure, and energy
D. Temperature, pressure, and density

2. Which of the following thermostats is *commonly used* in GROMACS?
A. Parrinello–Rahman
B. Berendsen
C. Nose–Hoover
D. **Both (b) and (c)**

3. Which command is used to compute RMSD in GROMACS?
A. **gmx rms**
B. gmx gyrate
C. gmx rmsd
D. gmx energy

4. The success of homology modelling relies primarily on the principle that:
A. Protein structure is more conserved than protein sequence during evolution
B. Protein sequence is more conserved than structure during evolution
C. Sequence and structure evolve independently
D. Sequence similarity implies identical function

5. Protein folding leads to a decrease in conformational entropy because:
A. The protein adopts many flexible conformations
B. The number of accessible microstates decreases
C. The solvent entropy decreases
D. The energy of the system increases

6. During protein folding, which thermodynamic quantity primarily drives the process despite an apparent decrease in conformational entropy of the protein chain?
A. Increase in enthalpy due to hydrogen bonds
B. Decrease in Gibbs free energy due to hydrophobic effect
C. Increase in conformational entropy of backbone
D. Increase in heat capacity of the solvent

7. Increasing temperature affects the Boltzmann distribution for protein conformations by:

A. Sharpening the distribution
B. Flattening the distribution
C. Increasing energy differences
D. Making all conformations equally probable

8. In molecular dynamics simulations, the Helmholtz free energy is more relevant than Gibbs free energy because:

A. Simulations are typically carried out at constant pressure
B. Volume fluctuations are negligible
C. Solvent compressibility is infinite
D. The system is adiabatic

9. Mixing two different amino acids in water increases entropy because:

A. The amino acids form more covalent bonds
B. The number of accessible microstates increases
C. Their mass changes
D. Hydrogen bonding is eliminated

10. When a charged side chain moves from solvent to protein core, the free energy change is usually:

A. Favorable ($\Delta G < 0$)
B. Unfavorable ($\Delta G > 0$)
C. Zero
D. Undefined

Short Answer Type (2 marks each)

1. **A protein in solution can adopt many unfolded conformations but only a few folded states. Explain how entropy contributes to protein folding being thermodynamically unfavorable at high temperatures.**

Folding decreases entropy

When a protein folds:

$$\Delta S = S_{folded} - S_{unfolded} < 0$$

This entropy loss is unfavorable, and contributes a positive (unfavorable) term to the Gibbs free energy:

$$\Delta G = \Delta H - T\Delta S$$

Because *ΔS is negative*, the term $-T\Delta S$ is positive, making folding less favorable. Increasing temperature magnifies the entropic penalty.

As temperature rises:

−TΔS becomes more positive, −TΔS becomes more positive because T is larger and ΔS is still negative.

Thus, high temperature amplifies the unfavorable entropy cost of ordering the protein chain.

2. **What is the difference between the SPC and TIP3P water models used in GROMACS?**
   SPC (Simple Point Charge): 3-site model optimized for MD with rigid geometry.
   TIP3P (Transferable Intermolecular Potential 3-Point): Similar but parameterized for different force fields (e.g., CHARMM/AMBER).
   Choice depends on the force field being used.

3. **How does the Verlet cutoff scheme improve performance in GROMACS?**
   It utilizes a neighbor list buffer region to predict atom movement, thereby avoiding frequent neighbor list updates and improving computational efficiency without compromising accuracy.

4. **Two protein conformations differ in energy by 5 kJ mol⁻¹. Which conformation is more populated at 300 K? Explain without calculation.**
   According to the Boltzmann distribution, the probability of a molecule occupying a state of energy *E* is proportional to $e^{-E/(k_B T)}$.
   Since the exponential factor decreases with increasing energy, the conformation with 5 kJ mol⁻¹ lower energy will have a higher Boltzmann weight and therefore a larger population at equilibrium.

5. **You are building a homology model for a newly sequenced protein (~310 amino acids). You find the following possible template structures:**

Template	Sequence Identity	Coverage (Aligned Length)	Resolution (Å)	Organism Similarity	Known Function Match
A	28%	98%	1.8 Å	Same organism	Function unknown
B	42%	85%	2.5 Å	Different organism	Known same enzymatic function
C	55%	60%	3.2 Å	Same organism	Known same biological nhb bb bgbgpathway
D	33%	100%	1.2 Å	Distant organism	Active site mutated (not conserved)

Which template would you select for homology modeling and why?

Template B or C should be selected because it has moderate sequence identity (~40%+) and functional similarity, ensuring correct fold and accurate active-site geometry.
Although its resolution is not the highest, functionally relevant templates are most reliable for modeling catalytic / binding regions, which is crucial for meaningful biological interpretation.