BioPhysics - BIO361
Quiz2
25.11.24

Total marks :20
Time : 1hr

MCQ(1*10=10 marks)

1.The third law of thermodynamics states that:
a) The entropy of a system approaches zero as the temperature approaches zero.
b) The entropy of a system is always zero.
c) The entropy of a system depends on pressure and volume.
d) Absolute zero cannot be reached.

2.Which thermodynamic process involves a decrease in entropy?
a) Melting of ice
b) Expansion of a gas
c) Freezing of water
d) Mixing of two gases

3.Which of the following is the basic principle behind MD simulations?
a) Statistical mechanics
b) Newton's laws of motion
c) Quantum mechanics
d) Thermodynamic equilibrium

4.What type of boundary conditions is commonly used in MD simulations?
a) Fixed boundary conditions
b) Periodic boundary conditions
c) Reflective boundary conditions
d) Free boundary conditions

5. When might multi-template modeling fail to improve accuracy compared to single-template modeling?
a) When the templates have very high structural variability.
b) When the target-template alignment is perfect.
c) When the templates are from the same protein family.
d) When Modeller uses default optimization settings.

6. How does Modeller combine information from multiple templates?
a) By averaging all atomic coordinates from the templates.
b) By weighting the contribution of each template based on alignment quality.
c) By randomly selecting coordinates from one template.
d) By discarding templates with gaps in alignment.

7. What file specifies the simulation parameters for molecular dynamics in GROMACS?
A. topol.top
B. index.ndx

C. .mdp file
D. conf.gro

8. In a lysozyme-water GROMACS simulation, why is periodic boundary conditions (PBC) applied?
A. To reduce the system size
B. To simulate an infinite system by avoiding edge effects
C. To minimize the computational load
D. To increase the density of water molecules

9. Which analysis tool in GROMACS can be used to monitor the structural stability of lysozyme during the simulation?
A. gmx rms
B. gmx trjconv
C. gmx genion
D. gmx mdrun

10. What is the main role of adding counterions in a lysozyme-water GROMACS simulation?
A. To neutralize the system's overall charge
B. To stabilize the lysozyme structure
C. To increase the density of water molecules
D. To enhance the sampling rate of the simulation

Short answer type questions (2 * 5=10 marks)

1. How would you differentiate Free energy from energy? At low temperature, which term dominates?

Energy refers to the total capacity of a system to perform work, including kinetic and potential energy.
Free energy (e.g., Gibbs free energy) incorporates entropy and temperature to predict the spontaneity of a process. At low temperatures, the **enthalpy (energy-related term)** dominates over the entropy term because the contribution of entropy (TΔST\Delta STΔS) is scaled by temperature.

2. A process occurs at constant pressure, another occurs at constant volume. Which free energy will you use to calculate work in each case?

At **constant pressure**, use **Gibbs free energy** (G=H−TSG = H - TSG=H−TS).
At **constant volume**, use **Helmholtz free energy** (A=U−TSA = U - TSA=U−TS).

3. In multi-template modeling with Modeller, how does the software handle conflicting structural information between templates, and what factors influence the contribution of each template to the final model?

When multiple templates are used to build a model, there may be regions where the templates do not agree—such as different conformations of loops, variations in side-chain orientations, or even different backbone structures. These differences are called **conflicting structural information**.

For example:

- **Template A** might suggest that a loop region is extended, while

- **Template B** might indicate that the same loop is more compact.

Modeller addresses these conflicts by creating a **weighted average** of the structural information.

Modeller decides how much influence each template has on the final model based on the **following factors:**

a) Sequence Alignment Quality

- The alignment between the target sequence (what you want to model) and each template is crucial.
- If Template A aligns better (has higher sequence similarity) with the target in a specific region, it will be given **more weight** for that region.
- Conversely, if Template B aligns poorly in the same region, its contribution will be **reduced**.

b) Structural Compatibility

- Modeller checks if the structural features of the templates are physically realistic and consistent with the target.
- If a template's structure fits well with the rest of the model being built, it contributes more to the final structure.

c) Coverage

- Templates that cover specific parts of the target sequence are prioritized for those regions.
- For example, if Template A covers only the N-terminal, but Template B covers the entire protein, Template B will dominate for regions where Template A has no information.

d) Resolution of the Templates

- If a template is derived from a high-resolution experimental structure (e.g., 1.5 Å), it is considered more reliable than one with lower resolution (e.g., 3.0 Å).

Conflicting structural information can lead to errors or unrealistic models if not handled carefully. Modeller's method ensures:

- **Accuracy**: By prioritizing reliable templates, the final model closely resembles the actual structure of the target protein.
- **Consistency**: The generated model is physically realistic, avoiding sharp breaks or unnatural conformations.
- **Versatility**: Using multiple templates allows the software to handle complex proteins, especially when no single template covers all regions.

4. How can periodic boundary conditions (PBC) and the choice of the simulation box shape influence the accuracy of a lysozyme in water MD simulation using GROMACS?

PBC prevents edge effects by simulating an infinite system, reducing artifacts.

The **shape of the simulation box** (e.g., cubic, truncated octahedral) affects the number of water molecules required and the uniformity of solvation. Proper box shapes optimize computational efficiency while minimizing artificial interactions.

5. During an MD simulation of lysozyme in water using GROMACS, what key considerations should be made when selecting the force field and water model, and how can these choices impact the simulation results?

When selecting the force field, consider the compatibility with the protein (e.g., AMBER, CHARMM, or GROMOS) and its ability to accurately represent interatomic interactions for lysozyme. For the water model (e.g., TIP3P, SPC/E, or TIP4P), choose based on the force field's recommendations to ensure consistency and accuracy in simulating solvent effects.

The choice of force field affects protein dynamics, stability, and secondary structure retention, while the water model impacts solvation behavior, hydrogen bonding, and bulk properties like density and viscosity. Mismatched or inappropriate models can lead to artifacts, such as unrealistic folding or incorrect hydration shell formation.

The force field should accurately describe protein and water interactions (e.g., CHARMM, AMBER).

The water model (e.g., TIP3P, SPC/E) impacts solvation dynamics and stability.

A mismatch in force field and water model parameters can lead to artifacts in protein stability and dynamics. Selection must ensure compatibility and relevance to the system being studied.