Quiz-2
Computer-Aided Drug Design (CADD) BIO563

Total Marks: 20
Total Time: 1 Hour

Section A
MCQ (Choose the most appropriate answer for each question.)
(1*10=10 marks)

Question 1: Why is structure-based drug design often preferred when high-resolution receptor structures are available?
A) It avoids molecular modeling
B) It reduces lab experiments
C) It provides specific atomic-level interaction insights
D) It increases ligand weight

Question 2: Which of the following is *not* typically considered a feature in pharmacophore modeling?
A) Hydrogen bond acceptor
B) Aromatic ring
C) Energy minimization constant
D) Hydrophobic group

Question 3: In the context of CADD, why is Boltzmann's inversion significant in modeling energy functions?
A) It reduces the number of drug candidates
B) It translates observed atomic distances into probabilistic energy models
C) It accelerates protein synthesis
D) It blocks ligand interaction

Question 4: Which of the following is not the part of receptor preparation in docking?
A) Removal of H20
B) Removal of charges
C) Adding hydrogens
D) Adding Charges

Question 5: Which of the following is NOT a protein-ligand docking software?
A) GOLD
B) FLEXX
C) MOLFIT
D) GLIDE

Question 6: Autodock uses which type of searching algorithm ?
A) Stochastic
B) Systematic
C) Incremental
D) Deterministic

Question 7: The ensemble method will fail for ligand that:
A) Have rigid atoms

B) Lacks rigid atoms
C) Lacks ring system
D) Have flexible side chains

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

Question 8: Why are pharmacophore models important in virtual screening?

A) They define molecular weight limits for drug-like molecules
B) They identify key structural and functional features required for biological activity
C) They determine a molecule's solubility
D) They predict a molecule's metabolism

Question 9: Which type of interaction is primarily responsible for ligand specificity in molecular docking?

A) Hydrophobic interactions
B) Van der Waals forces
C) Electrostatic interactions
D) π-π stacking interactions

Question 10: How does water displacement in a binding pocket influence entropy during docking?

A) Removing ordered water molecules increases entropy and enhances binding affinity
B) Water displacement decreases entropy, leading to weaker ligand binding
C) Water molecules always stabilize ligand binding by decreasing entropy
D) The presence of water does not influence entropic contributions in docking

Section B
(Short Answer Questions)

(2*5=10 marks)

Question 1: While performing docking for a particular target and small molecule, you found that ligand is not binding at the correct active site. What can be the probable reasons for it?(Mention any 2)

1. Inaccurate grid size
2. Did not remove bound ligand
3. Did not add Hydrogens
4. Did not remove water

Question 2:In molecular docking, Monte Carlo-based search algorithms often produce different binding poses in each run. How do you explain this and how does it impact the reliability of the result?

Monte Carlo algorithm works by making random changes to a single ligand or a population of ligands. Novel Ligand is identified using predefined probabilistic models

Diverse Binding Poses: Since Monte Carlo searches different regions of the conformational space in each run, the resulting ligand poses can vary, leading to multiple plausible binding modes.

Energy Fluctuations: The binding affinity scores may differ between runs due to variations in sampled conformations, affecting the confidence in ranking docked poses.

Question 3: How can pharmacophore models be used in combination with molecular docking to improve hit identification in virtual screening pipelines?

Increases Accuracy: Pharmacophore filtering ensures that only relevant compounds are docked, improving hit enrichment.

Reduces False Positives: Docking helps eliminate false positives from pharmacophore screening by confirming ligand-protein interactions.
Handles Ligand Flexibility: Pharmacophore models account for conformational variations, while docking refines the best-bound conformation.
Improves Computational Efficiency: Screening millions of compounds using docking alone is computationally expensive—pharmacophore filtering reduces the dataset before docking.

Question 4: What are two major challenges or limitations of using ensemble docking in drug discovery?

1. Loss of information if conformations are guided only by the subsets of atoms in the molecule.
2. It will fail for ligands that lack internally rigid atoms.
3. The use of chemical matching and critical clusters is limited

Question 5: For screening a large molecule database which scoring function would you use and why?

I would use knowledge based scoring as :

1. Reproduces experimental structures rather than binding energies
2. Complex is modelled using comparatively simple atomic interaction pairs.
3. Computational simplicity
4. Number of atom-type interactions are defined depending on molecular environment.