BIOSC 1540 - Computational Biology

CADD Quiz

Apr 9, 2024

50 points

Please read the following instructions carefully before beginning your assessment.

- **Time limit:** You have 75 minutes to complete and turn in this assessment.
- **Open note:** You may use notes for this assessment with the following restrictions.
  - You must hand-write notes on paper or digitally using a tablet and stylus and print them.
  - You may have up to one 8.5 $\times$ 11 in. sheets of paper.
  - All notes must be your work; sharing notes is strictly prohibited.
  - Your name must be clearly written on the first page.
- **No digital devices:** No digital devices are allowed during the assessment.
- **Submission requirements:** You must submit all your notes with the completed assessment.
- **No calculators:** Calculators are not permitted.

I agree to the above instructions. I affirm that I will not give or receive any unauthorized help on this assessment and that all work will be my own. Your assessment will only be graded if you write your name, sign, and put your student ID below.

_____ _____

Name Signature

_____

Student ID

Problem 1

Which of the following is not a primary goal of the drug discovery phase? (3 points)

(A) Identifying novel drug targets.

(B) Optimizing lead compounds for improved efficacy and safety.

(C) Conducting clinical trials to assess drug safety and efficacy.

(D) Screening for potential lead compounds.

Problem 2

Which of the following computational techniques is used for identifying potential binding sites on a target? (3 points)

(A) Molecular docking.

(B) De novo drug design.

(C) Molecular dynamics.

(D) Pocket detection.

Problem 3

Choose one or more answers that could complete this sentence: “Entropy is proportional to” (3 points)

(A) the number of macrostates.

(B) disorder.

(C) energy dispersal.

(D) the number of microstates.

Problem 4

True or False? Coevolution can be used to predict 3D protein structures from amino acid sequences without any templates/contact maps in AlphaFold2. (2 points)

(A) True

(B) False

Problem 5

In a scenario with limited structural information for a target, which virtual screening approach would be most suitable for identifying potential lead compounds? (1 points)

(A) Structure-based virtual screening.

(B) Ligand-based virtual screening.

(C) Combination of structure- and ligand-based approaches.

(D) None of the above.

Problem 6

True or False? We can observe large-scale protein folding in standard molecular dynamics simulations. (1 points)

(A) True

(B) False

Problem 7

A researcher is designing a new drug to target a specific protein. Which strategy will most likely improve the drug's selectivity for the target protein over other related proteins? (2 points)

(A) Increasing the drug's hydrophobicity.

(B) Decreasing the drug's size.

(C) Increasing functional groups that interact with non-conserved residues.

(D) Increasing the drug's conformational flexibility.

Problem 8

Which protein structure would be best suited for starting molecular dynamics simulations involving protein-ligand binding? (2 points)

(A) 1.1 Å X-ray crystallographic structure with 92% completeness

(B) 1.8 Å X-ray crystallographic structure with disorder in the active site.

(C) 2.7 Å cryo-EM structure with a local resolution of 1.5 Å in the region of interest.

(D) 2.1 Å X-ray crystallographic structure with 99% completeness.

Problem 9

Select all of the following statements that incorrectly describe the role of water molecules in protein-ligand binding. (4 points)

(A) Displacement of ordered water molecules from a hydrophobic binding site can enhance binding affinity by increasing entropy.

(B) Displacement of ordered water molecules from a hydrophilic binding site can enhance binding affinity by increasing entropy.

(C) Water molecules can form bridging hydrogen bonds between the protein and ligand, stabilizing the complex and enhancing binding affinity.

(D) Water molecules can compete with the ligand for hydrogen bonding interactions with the protein, potentially reducing binding affinity.

(E) Water molecules can fill voids in the binding site, preventing the collapse of the protein structure.

Problem 10

The binding of a particular ligand to a protein is driven primarily by a favorable change in entropy. Which of the following is the most likely explanation for this observation? (2 points)

(A) The ligand forms numerous hydrogen bonds with the protein upon binding.

(B) The ligand displaces ordered water molecules from a hydrophobic binding site.

(C) The ligand induces a conformational change in the protein that increases its flexibility.

(D) The ligand binds to multiple sites on the protein simultaneously.

Problem 11

Which file format is most commonly used for storing initial protein structure coordinates? (1 points)

(A) mol2

(B) pdb

(C) sdr

(D) xyz

Problem 12

What is the purpose of adding hydrogen atoms to a protein structure before an MD simulation? (2 points)

(A) To make the protein more stable.

(B) To make the protein more flexible.

(C) To satisfy valency and charge.

(D) To increase the protein's size.

Problem 13

Describe how AlphaFold2 computes pLDDT scores and how to interpret them. (3 points)

Problem 14

Explain these intermolecular forces in your own words: electrostatic, dipole-dipole, and dispersion. You may draw diagrams to supplement your response. (5 points)

Problem 15

What is the definition of binding equilibrium regarding forward and reverse binding rates? (3 points)

Problem 16

Is the solvation of a hydrophobic molecule mainly driven by enthalpy, entropy, or both? Justify your answer with a molecular explanation. (3 points)

Problem 17

Explain two ways we could efficiently generate small-molecule conformations using computational methods. (1 points)

Problem 18

List the main energy components of a typical force field used in molecular mechanics and why we need them for molecular dynamics. (3 points)

Problem 19

Explain the concept of bond stretching and how it is represented in a force field. How would the parameter(s) change between a single, double, and triple bonds? (3 points)

Problem 20

Discuss the potential biases that are present in AlphaFold2's training data and how these biases could influence the model's performance on diverse protein families. (3 points)