Exam Practice Questions and Solutions

CS 279, BIOE 279, BMDS 245, BIOPHYS 279, and CME 279

Fall 2026

Exam Details

The exam will be held on Thursday, December 10, 2026 from 12:15-3:15 PM (Location TBA). The exam will be closed-book, but you may consult one double-sided 8.5x11 page (or two single-sided pages) of notes.

Instructions

These are practice questions in the style of questions you might expect on the exam. Each question should be answerable in a few sentences (that is, you're not required to provide a great deal of detail). Depending on when you're reviewing this, some questions may be about topics to be covered in a future lecture.

Question 1: Why can template-based modeling often make reasonable predictions of protein structure even when the query protein and the template protein have significantly different sequences? (e.g. only 20% sequence identity)

Solution: Template-based modeling can make reasonable predictions of protein structures becausek during evolution, a protein's sequence tends to change more quickly than the overall structure of the protein. Even proteins with 15% sequence identity usually have similar structures.

Question 2: How do the energy functions used for molecular dynamics simulations differ from those used for ab initio protein structure prediction?

Solution: Molecular dynamics simulations use a molecular mechanics force field. This is a potential energy function — it specifies the energy of each precise arrangement of atoms, and therefore allows one to compute the force acting on each atom. Ab initio protein structure prediction generally uses an (approximate) free energy function, which specifies the energy associated with a set of atomic arrangements, and thus allows one to pose protein structure prediction as a minimization problem. Another acceptable solution is that energy functions used for molecular dynamics simulations are typically primarily physics-based, whereas energy functions used for ab initio protein structure prediction are typically primarily knowledge-based (derived from experimental data such as structures).

Question 3: We would like to estimate how tightly a particular drug candidate binds to a particular target protein.

(a) Provide a quantitative definition of binding affinity (i.e., "binding strength"). That is, what does it mean for one ligand to bind more tightly than another?

Solution: Ligand A binds with higher affinity than ligand B if A is bound to a target receptor/protein a larger fraction of the time, when A and B are at identical concentrations. Affinity can be defined either as a difference in free energy between the bound and unbound state of the ligand-protein system, or as the concentration of free ligand such that half the target molecules have a ligand bound and the other half do not.

(b) Suppose we have a single molecular dynamics simulation in which the drug candidate binds to the target and stays bound for the remainder of the simulation. Can we accurately estimate the binding affinity from that simulation? Why or why not?

Solution: No, you would need to see the ligand binding and unbinding many times in order to accurately estimate the fraction of time it will remain bound.

Question 4: X-ray crystallography and cryo-electron microscopy are both techniques for determining the structure of a molecule or molecular complex. Why is cryo-electron microscopy typically used for larger molecules or complexes than x-ray crystallography?

Solution: 1) It is generally harder to form crystals of larger molecules/complexes than of smaller ones; 2) In cryo-electron microscopy, it is usually harder to solve the computational reconstruction problem for smaller molecules, because smaller molecules tend to have more similar projections from different orientations.

Question 5: Discuss the trade-offs between a stochastic particle-based reaction-diffusion simulation versus a continuum approach (in which concentrations of each type of molecule are represented in each voxel).

Solution: The continuum approach is often faster, particularly for large numbers of molecules, but it's less accurate for small numbers of molecules.

Question 6: There is a very efficient algorithm for computing the Fourier Transform known as the Fast Fourier Transform (FFT). Describe how this algorithm is useful for one of the methods covered in this course.

Examples of Solutions:

- The FFT allows one to compute convolutions more efficiently. This is useful for filtering images, signals, etc.
- In x-ray crystallography, the FFT allows one to calculate efficiently the diffraction pattern associated with a hypothesized electron density.