

AMS Common Exam Part B, Computational Biology Track, June Exam 2006

DO THREE OUT OF SIX QUESTIONS ONLY

One question must be based on AMS 535 (questions 1-3) and one question must be based on AMS 533 (questions 4-6). The remaining question can be from either section.

Name:

Questions Based on AMS 535:

1. (a) List by name the five potential energy terms used in most classical Molecular Mechanics force fields.
 - i.
 - ii.
 - iii.
 - iv.
 - v.

- (b) Draw a graph illustrating the shape of the standard Lennard-Jones potential. Clearly label all portions of the graph including the axis. Indicate the attractive and repulsive regions and the most common values for the exponents.

2. Solvent (water) dramatically reduces the interaction energy between two species. Using the data below answer the following questions:

species	Molecular Mechanics Gas (MMgas) kcal/mol	Molecular Mechanics GBSA (MMwater) kcal/mol
ligand	-54.90	-142.21
receptor	-6594.60	-10037.69
complex	-6844.05	-10220.49

(a) Estimate the interaction energy (i.e. the binding energy) in kcal/mol between the ligand and receptor in the gas-phase

(b) Estimate the interaction energy (i.e. the binding energy) in kcal/mol between the ligand and receptor in the condensed-phase.

(c) Which type of interaction energy calculation most reflects what would occur in biological systems?

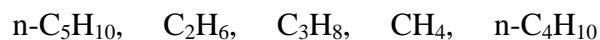
(d) Give a physics-based reason for the difference in the magnitude of the two computed binding energies

3. Answer the following questions. For drawings show and label all atom, put an "R" at points of attachment, and indicate stereochemistry when appropriate with hashed or wedged lines.

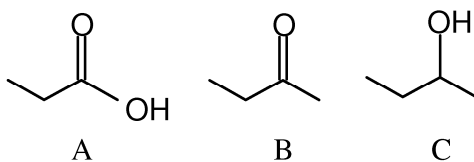
- (a) Partial atomic charges are not needed for Generalized Born calculations (True or False).
- (b) A successful docking calculation should yield a high RMSD between the most favorably scored binding mode found in the calculation and the experimental pose (True or False).
- (c) Disulfide bonds help stabilize proteins (True or False).
- (d) RMSD vs. time analysis of MD trajectories help researchers determine if simulations are _____ (fill in the blank).
- (e) Do Generalized Born simulation require periodic boundary conditions (Yes or No).
- (f) Draw a hydroxyl group
- (g) Draw a Et group
- (h) Draw a Me group
- (i) Draw a benzyl group
- (j) Write the major secondary structure elements under each protein in the following figure.



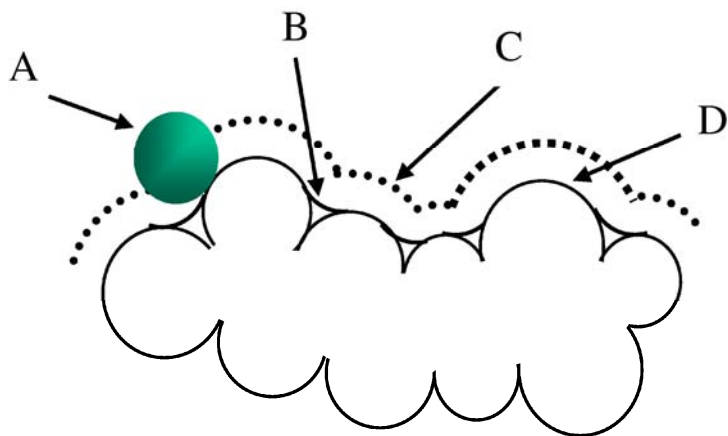
- (k) What are the four major groups of bio-molecules
- (l) Are polar side chains usually buried or unburied in folded proteins
- (m) Put the following five hydrocarbons in relative order of lowest to highest boiling point



- (n) Put the following three molecules in relative order of lowest to highest boiling point



- (o) Label what A thru B represent in the following diagram.



A =

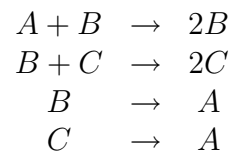
B =

C =

D =

Questions based on AMS 533:

4. Consider the following closed network of chemical reactions (assume standard kinetics):



- (a) Write the rate equation for each reaction.
- (b) Express the rate of change of all species in the network as a system of differential equations.
- (c) Find all steady states of the system.

5. The Singular Value Decomposition (SVD) plays a recurring role in many numerical applications.
- (a) Write the SVD of an arbitrary matrix, \mathbf{A} . Be sure to note any special properties of all matrices in the factorization.
 - (b) Explain how the SVD can be used to find the inverse of a singular (non-invertible), or near-singular, matrix.
 - (c) Explain how the SVD can be used to find a reduced-dimensionality approximation to \mathbf{A} .
 - (d) Explain the relationship between the SVD and principal component analysis (PCA).

6. Biochemical network models contain many parameters that must be estimated or fit to experimental data. Suggest and outline an algorithm to help understand parameter sensitivity in each of the following situations.
 - (a) A gene-regulatory network has been fit to experimental data, yielding 1000 sets of parameters with similar agreement to experiment. How might we understand which parameters are well-determined by the experiment, and which are less-well determined.
 - (b) A signal transduction network has been implemented with parameters estimated from biochemical data. Variation of the parameters within the allowed range results in two very different behaviors in response to a signal. How can we construct a method that will predict the behavior of the network given some new set of parameters (an initial step in understand the underlying mechanism of the difference)?