

**MCB100A/Chem130**  
**MidTerm Exam 2**  
**April 4, 2013**

Name \_\_\_\_\_ Student ID \_\_\_\_\_

**True/False (2 points each).**

1. \_\_\_\_\_ The Boltzmann constant,  $k_bT$  sets the energy scale for observing energy microstates
2. \_\_\_\_\_ Atoms with favorable electronic configurations gain stability by forming covalent bonds
3. \_\_\_\_\_ Conformational entropy favors the folded state over the unfolded state
4. \_\_\_\_\_ QM potential energies are tractable for calculating the heat capacity of a protein
5. \_\_\_\_\_ The highest potential energy is the most probable energy state at constant NVT
6. \_\_\_\_\_ Statistical entropy can be applied to isothermal ideal gas expansion and ideal DNA pulling
7. \_\_\_\_\_ The natural log of multiplicity,  $\ln(W)$ , is not extensive
8. \_\_\_\_\_ The work done in an equilibrium process is less than work done in a non-equilibrium process
9. \_\_\_\_\_ Chemical potential for ideal gas is only dependent on entropy changes with molecule numbers
10. \_\_\_\_\_ The heat capacity at constant pressure is greater than the heat capacity at constant temperature
11. \_\_\_\_\_  $C_v$  is inversely proportional to the variance of the Gaussian distribution for energy at constant T
12. \_\_\_\_\_ The units of entropy are kJ/mol
13. \_\_\_\_\_ The Helmholtz free energy is available energy to do mechanical or chemical work
14. \_\_\_\_\_ The chemical potential,  $\mu$ , is the tendency of system to realize concentration changes.
15. \_\_\_\_\_ A reaction will go forward if the reaction quotient, Q is greater than equilibrium constant K
16. \_\_\_\_\_ Henderson-Hasselbach relates the pH to the acid dissociation constant  $K_a$
17. \_\_\_\_\_ The standard enthalpy and standard entropy are always independent of temperature, pressure
18. \_\_\_\_\_ The chemical potential is related to the mechanical (expansion) work of Gibbs free energy
19. \_\_\_\_\_ If protein A has a larger partition function than protein B then B has the higher heat capacity
20. \_\_\_\_\_ Temperature signifies how multiplicity of bath grows with energy

**Multiple Choice (5 points each).**

**21. Molecular interactions are classified as long-ranged when the power law exponent of  $r^{-n}$  is**

- (a)  $n < 3$  (b)  $n = 3$   
(c)  $n < 2$  (d)  $n > 4$

**22. What is the value of  $kT$**

- (a)  $\sim 2.5$  kJ/mol (b)  $\sim 210$  cm $^{-1}$   
(c)  $\sim 0.6$  kcal/mol (d) all of the above

**23. What is the probability of observing system with energy  $E_v$  at constant  $N, V, T$**

- (a)  $\exp(-\beta E_v^2)/Q$  (b)  $1/Q$   
(c)  $\exp(-\beta E_v)/Q$  (d) all of the above

**24. If a covalent bond vibrational excitation is  $\sim 25$ kJ/mole, is it significantly populated at 298K?**

- (a) yes (b) no  
(c) maybe (d) all of the above

**25. For an isolated system (constant  $N, V, E$ ) all energy microstates**

- (a) have different Boltzmann probabilities (b) are equally probable  
(c) have different multiplicities (d) all of the above

**26. Temperature signifies how multiplicity of bath (surroundings) grows with energy is embodied in**

- (a)  $(dE/dS)_{N,V}$  (b)  $(dW/dE)_{N,V}$   
(c)  $(dE/dT)_{N,V}$  (d) all of the above

**27. The condition for the multiplicity to be at an extremum or maximum for large  $N$  is**

- (a)  $dW/dN=0$  (b)  $d(\ln W)/dN=0$   
(c) both (a) and (b) (d) none of the above

**28. Which state function(s) predict spontaneous change?**

- (a)  $dS > 0$  (b)  $dA < 0$   
(c)  $dG < 0$  (d) all of the above

**29. Direction of spontaneous change is when  $dN$  particles move from regions of**

- (a) low chemical potential to high (b) equal chemical potential  
(c) high chemical potential to low (d) all of the above

**30. The extent of a chemical reaction with large and negative values of  $\Delta G^\circ$  correspond to**

- (a)  $K_{eq} \gg 1$  (b)  $K_{eq} \sim 1$   
(c)  $K_{eq} \ll 1$  (d) none of the above

**Short Problems (15 points each)**

**31. The basis of proton NMR is that the hydrogen atom has a magnetic moment, so that in a magnetic field it can populate two states: spin up ( $S\uparrow$ ) and spin down ( $S\downarrow$ ). The energy difference in a 300 MHz NMR spectrometer is  $3.5 \times 10^{-2}$  kJ/mol. For  $N=100$  hydrogen atoms and  $T = 300$  K**

**(a) Compute the relative population difference  $|N_{S\uparrow} - N_{S\downarrow}| / (N_{S\uparrow} + N_{S\downarrow})$**

**(b) How does the population difference change with increasing temperature?**

**32. Identify all relevant energetic interactions and their functional forms found for the following amino acid constituents:**

**(a) Intermolecular interaction between  $\text{CH}_4$  and  $\text{CH}_4$  (model for alanine-alanine)**

**(b) Intermolecular interaction between  $\text{NH}_3^+$  and  $\text{COO}^-$  (model for zwitter ionic termini)**

**Long Problems (25 points each)**

33. *E. coli* DNA polymerase introduces about 1 incorrect base in  $10^4$  internucleotide linkages during replication “*in vitro*”. However, “*in vivo*” the proofreading function of *E. coli* DNA polymerase is much better, making 1 mistake in  $10^8$  nucleotide polymerization events.

(a) If an average *E. coli* gene is  $\sim 100$  bases long, what is the probability of introducing an error per gene *in vitro*?

(b) What is the probability of introducing an error per gene *in vivo*?

(c) Given the large number of nucleotide polymerization events,  $N$ , in *E. Coli*, we will assume the number of errors,  $Err$ , is distributed according to a Gaussian distribution

$$P(Err) = \frac{1}{\sigma\sqrt{2\pi}} e^{-(Err - \langle Err \rangle)^2 / 2\sigma^2};$$

where  $\langle Err \rangle$  is the mean error and  $\sigma$  is the standard deviation. What is  $\langle Err \rangle$  and  $\sigma$  *in vivo* for  $10^8$  gene polymerization events? What is  $\langle Err \rangle$  and  $\sigma$  *in vitro* for  $10^8$  nucleotide polymerization events?

(d) What is the probability that the number of errors will be 1 standard deviation larger than the mean *in vivo*?

(e) What is the probability that the number of errors *in vivo* will be 5000 times smaller than the average number of errors *in vitro*?

34. The variation in the constant pressure heat capacity,  $C_P$ , of a protein as a function of temperature is known as the melting curve, as it measures the relative populations of the folded and unfolded proteins in water. We would like to use  $C_P$  measurements made along this curve to determine a single equation that gives the standard Gibbs free energy for unfolding,  $\Delta G_{unfold}^0(T)$ , at any temperature.

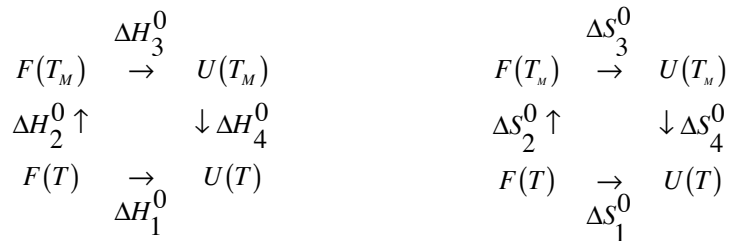
(a) Draw a typical heat capacity curve for a protein in water from 25C to 90C. Name 3 intramolecular energy interactions that break and therefore new energy levels that become populated as the protein goes from the folded to the unfolded state.

(b) Express  $\Delta G_{unfold}^0(T)$  in terms of  $\Delta H_{unfold}^0(T)$  and  $\Delta S_{unfold}^0(T)$

(c) Express  $\Delta H_{unfold}^0(T)$  in terms of  $C_P^{unfold}$ ; express  $\Delta H_{fold}^0(T)$  in terms of  $C_P^{fold}$

(d) Express  $\Delta S_{unfold}^0(T)$  in terms of  $C_P^{unfold}$ ; express  $\Delta S_{fold}^0(T)$  in terms of  $C_P^{fold}$

You are given the following thermodynamic cycles, where F corresponds to folded and U to unfolded



**(e) Which leg of the following thermodynamic cycle allows us to determine  $\Delta H_{unfold}^0(T)$  and  $\Delta S_{unfold}^0(T)$  and how would I determine it from the other three legs of the cycle?**

**(f) Which leg of the thermodynamic cycle measures  $\Delta H_{unfold}^0(T_M)$  and  $\Delta S_{unfold}^0(T_M)$ ? How would you get these quantities from experiment and what equations would you use?**

**(g) What are the expressions for  $\Delta H_n^0$  and  $\Delta S_n^0$  for the other two legs of the cycle?**

**(h) Write the expressions for  $\Delta G_{unfold}^0(T)$  and show your work**

- 35. For the folding of a 100 residue protein, containing 6 glycines and 4 prolines, at 300K:**
- (i) When unfolded, each residue except glycines and prolines can take 3 conformations of equal energy; glycine can take 4 conformations; proline can take 2 conformations.**
  - (ii) The conformation of the folded state has every residue in 1 possible conformation except glycine which has 2 conformations.**
  - (iii) A His-Asp ion pair, whose interaction energy is  $-350\text{kJ/mol}$  in vacuum, is found in the interior of a folded protein with dielectric constant  $\epsilon_p=4$ . The ion pair remains intact when unfolded in water whose dielectric constant is  $\epsilon_w=80$ .**
  - (iv) Assume water molecules have 6 possible configurations when surrounded by other waters, protein backbone or polar sidechains, otherwise they have only 2 possible configurations.**
  - (v) Every hydrophobic sidechain in unfolded state interacts with 2 water molecules, and all hydrophobic sidechains are buried in folded state.**
  - (v) Assume water-protein interaction energy is zero.**

**(a) Calculate the Helmholtz free energy for the protein-protein interactions only ( $\Delta A_{\text{protein}}$ ). Show your work. Does  $\Delta A_{\text{protein}}$  favor folding?**

**(b) Calculate the free energy for water,non-hydrophobic interactions ( $\Delta A_{\text{non-hphobe,H}_2\text{O}}$ ). Show your work. Does  $\Delta A_{\text{non-hphobe,H}_2\text{O}}$  favor folding over nonfolding?**

**(c) Calculate the free energy for water,hydrophobic interactions ( $\Delta A$  will be per hydrophobic residue). Show your work. What is minimum number of hydrophobic sidechains required to ensure that folding in water is spontaneous at room temperature (300 K)?**

