

BIO-212. Lecture 6.

Exercises

Question 1.

Which of the following statements are TRUE, and which are FALSE?

- a) Secondary structural elements of a domain generally pack so that a hydrophobic core is formed.
- b) Most protein conformational changes involve breaking and reforming several covalent bonds along the polypeptide chain.
- c) Two proteins that share more than 50% sequence identity over a 100-residue stretch are likely to have the same three-dimensional fold.

During a protein folding event, what happens to the entropy of water molecules? Explain your answer.

- a) It increases
- b) It decreases
- c) It is equal to the protein entropy change
- d) It does not change

A protein has two conformational states with different energy. Which of the following is not true? Explain your answer.

- a) If the energy difference between the two states is equal to kBT , they will be equally populated
- b) With higher temperature it is more probable to visit the state with higher energy
- c) The occupancy of the two states depends on the temperature
- d) The occupancy of the two states depends on the energy difference between the two states

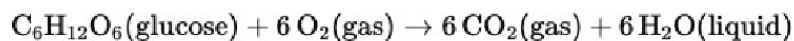
Question 2.

Assume that entropy and enthalpy changes are independent of temperature. A system in state A has an enthalpy of -22 kJ and an entropy of $7 \text{ J}\cdot\text{K}^{-1}$. In state B, it has an enthalpy of -12 kJ and an entropy of $15 \text{ J}\cdot\text{K}^{-1}$. At what temperatures will state B be favored?

	State A	State B
H	-22 kJ	-12 kJ
S	7 J•K ⁻¹	15 J•K ⁻¹

Question 3.

During cellular respiration, a glucose molecule is gradually broken down into carbondioxide and water. Below you have a reaction:



Using a table from the lecture:

Compound	ΔG° (kJ•mol ⁻¹)
acetate ⁻	-369.2
CO ₂ (gas)	-394.4
CO ₂ (aqueous solution)	-386.2
carbonate ion	-587.1
ethanol	-181.5
fructose	-915.4
fructose-6-phosphate ²⁻	-1758.3
α-D-glucose	-917.2
glucose-6-phosphate ²⁻	-1760.2
H ⁺ (aqueous solution)	0.0
H ₂ (gas)	0.0
H ₂ O (liquid)	-237.2
isocitrate ³⁻	-1160.0
lactate ⁻	-516.6
OH ⁻	-157.3
pyruvate ⁻	-474.5
succinate ²⁻	-690.2

a) Calculate the standard Gibbs free energy change (ΔG) for the reaction

b) Interpret the result: Is the reaction thermodynamically favorable under standard conditions?

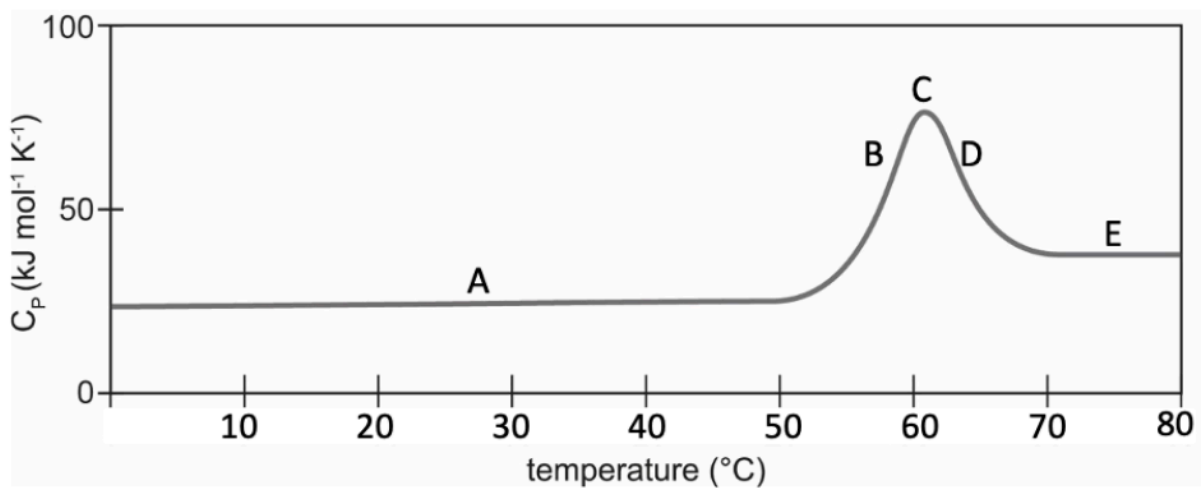
Question 4.

A system at 275 K in state A has an enthalpy of -25 kJ and an entropy of $2 \text{ J}\cdot\text{K}^{-1}$. In state B, it has an enthalpy of -20 kJ and an entropy of $10 \text{ J}\cdot\text{K}^{-1}$. Will state A convert spontaneously to state B?

	State A	State B
H	-25 kJ	-20 kJ
S	$2 \text{ J}\cdot\text{K}^{-1}$	$10 \text{ J}\cdot\text{K}^{-1}$

Question 5.

You are studying a recombinant protein you've designed, expressed, and purified in the lab. You are unsure of its thermal stability so you perform a calorimetry experiment and obtain the melting curve below.



- What is the T_m ?
- At point 'D' on the graph, approximately what percent of proteins are still folded and what percent are unfolded?
- Estimate roughly how much energy it takes to melt the protein.

Question 6.

Using your knowledge about calculating protonation states and the energy of charge-charge interactions, answer the following questions:

- Consider a protein with a surface-exposed histidine residue in a pH 5.5 solution. What is the fraction of protein molecules in which this histidine residue is charged? (Assume that the pK_a is 6.0.)
- For a protein with a surface-exposed aspartic acid, at what pH will this residue be charged in 60% of the protein molecules? (Assume that the pK_a is 3.65)
- Consider an electrostatic interaction between the histidine and the aspartic acid at a distance of 5.0 \AA . What is the energy of interaction if the residues are on the protein surface

($\epsilon=70$) at the pH is 5.0? Define the charge of these amino acids by checking the pKa values below.

TABLE 3-1 Properties and Conventions Associated with the Common Amino Acids Found in Proteins

Amino acid	Abbreviation/ symbol	M_r	pK_a values			pI	Hydropathy index*	Occurrence in proteins (%) [†]
			pK_1 (—COOH)	pK_2 (—NH ₃ ⁺)	pK_R (R group)			
Nonpolar, aliphatic R groups								
Glycine	Gly G	75	2.34	9.60		5.97	-0.4	7.2
Alanine	Ala A	89	2.34	9.69		6.01	1.8	7.8
Proline	Pro P	115	1.99	10.96		6.48	1.6	5.2
Valine	Val V	117	2.32	9.62		5.97	4.2	6.6
Leucine	Leu L	131	2.36	9.60		5.98	3.8	9.1
Isoleucine	Ile I	131	2.36	9.68		6.02	4.5	5.3
Methionine	Met M	149	2.28	9.21		5.74	1.9	2.3
Aromatic R groups								
Phenylalanine	Phe F	165	1.83	9.13		5.48	2.8	3.9
Tyrosine	Tyr Y	181	2.20	9.11	10.07	5.66	-1.3	3.2
Tryptophan	Trp W	204	2.38	9.39		5.89	-0.9	1.4
Polar, uncharged R groups								
Serine	Ser S	105	2.21	9.15		5.68	-0.8	6.8
Threonine	Thr T	119	2.11	9.62		5.87	-0.7	5.9
Cysteine	Cys C	121	1.96	10.28	8.18	5.07	2.5	1.9
Asparagine	Asn N	132	2.02	8.80		5.41	-3.5	4.3
Glutamine	Gln Q	146	2.17	9.13		5.65	-3.5	4.2
Positively charged R groups								
Lysine	Lys K	146	2.18	8.95	10.53	9.74	-3.9	5.9
Histidine	His H	155	1.82	9.17	6.00	7.59	-3.2	2.3
Arginine	Arg R	174	2.17	9.04	12.48	10.76	-4.5	5.1
Negatively charged R groups								
Aspartate	Asp D	133	1.88	9.60	3.65	2.77	-3.5	5.3
Glutamate	Glu E	147	2.19	9.67	4.25	3.22	-3.5	6.3

Question 7*.

The Boltzmann distribution describes the most probable distribution of particles in different energy states for a given system. Thinking about each particle as being a protein and remembering that each different possible conformation of a protein has a different energy, use the Boltzmann distribution to explain why at extremely high temperatures proteins are unfolded.

Question 8*.

The two accessible conformations of a protein differ by 2 kJ/mol. What percentage of protein molecules will be in the higher energy state at 270K?

*** Feel free to work on these exercises now or save them for the next session**