Exercises – Lecture 10
BIO-212

Question 1

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

Answer: 29.2%

Solution

To calculate the percentage of proteins in the higher energy state, we use the Boltzmann distribution formula:

$$\frac{N_2}{N_1} = e^{-\Delta G/RT}$$

Where:

- N2: Population of the higher energy state.
- N1: Population of the lower energy state.
- ΔG=5 kJ/mol=2000 J/mol: Energy difference between the states.
- R=8.314 J/mol*K = 8.314 : Gas constant.
- T: Temperature in Kelvin.

Step 1: Compute the ratio of populations: N1/N2

$$\frac{N_2}{N_1} = e^{-2000/(8.314 \cdot 270)}$$

$$\frac{N_2}{N_1} = e^{-0.887} \approx 0.412$$

Step 2: Compute the fraction in the higher energy state

The fraction of proteins in the higher energy state is:

$$\text{Fraction in higher energy state} = \frac{N_2}{N_1 + N_2} = \frac{\frac{N_2}{N_1}}{1 + \frac{N_2}{N_1}}$$

Substitute $\frac{N_2}{N_1} = 0.412$:

$$\text{Fraction in higher energy state} = \frac{0.412}{1 + 0.412} \approx \frac{0.412}{1.412} \approx 0.292$$

Step 3: Convert to a percentage: 0.292*100 = 29.2%

Question 2

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.

Answer:

The Boltzmann distribution is given by:

$$P_i = \frac{e^{-\frac{U_i}{K_B T}}}{\sum_i^N e^{-\frac{U_i}{K_B T}}}$$

Let's assume that at extremely high temperatures we are working in a regime where T -> ∞.This means that the exponent of our terms will go to zero for any energy value U_i:

$$P_{i(T\rightarrow\infty)} = \frac{e^0}{\sum_i^N e^0}$$

$$P_{i(T\rightarrow\infty)} = \frac{1}{\sum_i^N 1}$$

$$P_{i(T\rightarrow\infty)} = \frac{1}{N}$$

What this means is that, at extremely high temperatures, any possible energy state is equallyaccessible to the protein. In this situation, the protein is as likely to be in any of the very few **n** states where it is properly folded state as it is to be in any of the (much more numerous) **N-n** unfolded conformations.

Question 3

A protein can transition between two conformations which differ by 5 kJ/mol. Which of the following statements is false?

a. 15 % of the protein is in the higher energy state at 350 K
b. 10 % of the protein is in the higher energy state at 270 K
c. The protein can change conformation at room temperature
d. 90 % of the protein is in the lower energy state at 300 K

Answer: d

Solution

To solve this, we'll calculate the relative populations of the two conformations at the given temperatures using the **Boltzmann distribution**:

$$\frac{N_2}{N_1} = e^{-\Delta G/RT}$$

Where:

- N2: Population of the higher energy state.
- N1: Population of the lower energy state.
- ΔG=5 kJ/mol=5000 J/mol: Energy difference between the states.
- R=8.314 J/mol*K = 8.314 : Gas constant.
- T: Temperature in Kelvin.

The **fraction in the higher energy state** is given by:
Fraction in higher energy state = N2 / (N1+N2)=1/(1+$e^{\Delta G/RT}$)

a) At T=350 K:

$$\frac{N_2}{N_1} = e^{-5000/(8.314\cdot 350)} = e^{-1.729} \approx 0.177$$

$$\text{Fraction in higher energy state} = \frac{1}{1+\frac{1}{0.177}} \approx 0.15\,(15\%)$$

b) At T=270 K:

$$\frac{N_2}{N_1} = e^{-5000/(8.314\cdot 270)} = e^{-2.228} \approx 0.108$$

$$\text{Fraction in higher energy state} = \frac{1}{1+\frac{1}{0.108}} \approx 0.10\,(10\%)$$

c) The statement **"The protein can change conformation at room temperature"** is qualitative and generally true, given the significant energy difference and the thermal energy available at room temperature (300 K).

d) At T = 300K:

$$\frac{N_2}{N_1} = e^{-5000/(8.314\cdot 300)} = e^{-2.006} \approx 0.135$$

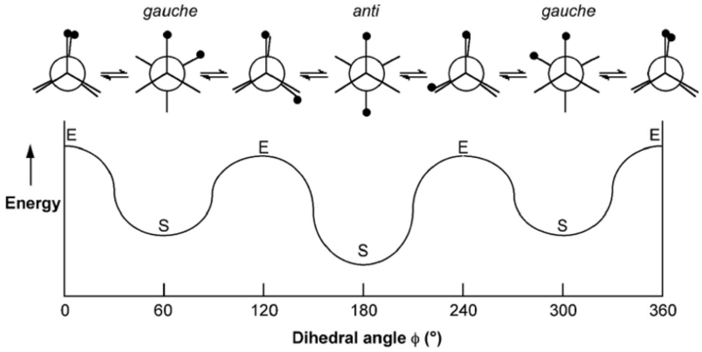
$$\text{Fraction in lower energy state} = \frac{1}{1+0.135} \approx 0.88\,(88\%)$$

Question 4

A particular sidechain has a dihedral angle for which the energy is governed by the following equation:

$U_{\text{dihedral}} = 2 \times \cos(3\times angle)$ kJ/mol

A. What is the torsional energy of the sidechain when the angle is 60 °?



$$U_{dihedral} = 2 \times \cos(3\times60)\left[\frac{kJ}{mol}\right] = -2\left[\frac{kJ}{mol}\right]$$

B. And when the angle is 120°?

$$U_{dihedral} = 2\ x \cos(3x120)\left[\frac{kJ}{mol}\right] = 2\left[\frac{kJ}{mol}\right]$$

C. What is the relative population of sidechains with an angle of 60 ° vs 120 ° at 300 K?

$$\frac{N_2}{N_1} = e^{-\Delta U/k_B T}$$

$$\frac{P60}{P120} = e^{\frac{-(P60-P120)}{RT}}$$

Again use the ideal gas constant.

$$\frac{P60}{P120} = e^{\frac{-(-2000\left[\frac{J}{mol}\right]-2000\left[\frac{J}{mol}\right])}{8.31\left[\frac{J}{Kmol}\right]x300K}}$$

$$\frac{P60}{P120} = e^{1.60} = 4.95$$

4.95 times more 60° conformation compared to the 120° conformation. Which is expected because 120° conformation has a higher energy than the conformation with the dihedral angle equal to 60°.

D. Would it be possible to visit a state with a dihedral angle of 180° at 300 K, given that the initial dihedral angle is 60°? Explain your answer considering possible energy barriers.

Yes, it would be possible. Conformations of 60° and 180° have the same energy -2 kJ/mol, so they are equally likely to be populated. But given that a specific transition (60° -> 180°) has been proposed, one needs to consider the height of the energy barrier between these states, which as calculated in the previous exercise is 4 kJ/mol (plotting the equation will reveal that a maximum of energy exists at 120°). At 300 K, the thermal fluctuation energy of the system (R*T) is 2.5 kJ/mol, which has the same order of magnitude of the energy barrier, thus it is reasonable to propose that this barrier can be surpassed by random kinetic energy transfer from collision with other atoms in the system (you can even calculate that 17% of the population will be at a state with an angle of 120°, which is not a negligible amount).

Question 5

The energy associated a specific torsional angle of a given molecule can be described by the following potential: $U(\vartheta) = U_0 (1 + \cos 4\vartheta)$ with $U_0 = 6$ kJ/mol. Which of the following statements is false?

a. The maximum energy value associated with the interaction is 12 kJ/mol
b. The torsional angle has 4 possible minima
c. At the minima the energy is zero
d. The minimal amount of energy required to jump between two minima is 6 kJ/mol

Answer:

d) The actual minimal amount of energy required is 12 kJ/mol

Solution

a) Maximum Energy Value

The potential energy U(θ) depends on cos(4θ) which oscillates between −1 and +1. Substituting these extreme values:

- Maximum energy cos(4θ)= +1:

$$U_{\max} = 6 \cdot (1 + 1) = 12\,\mathrm{kJ/mol}.$$

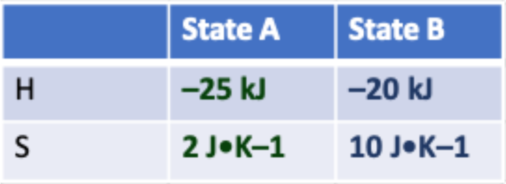
- Minimum energy cos(4θ)= -1:

$$U_{\min} = 6 \cdot (1 - 1) = 0\,\mathrm{kJ/mol}.$$

Statement **a** is **true**; the maximum energy is 12 kJ/mol.

Question 6

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



	State A	State B
H	–25 kJ	–20 kJ
S	2 J•K–1	10 J•K–1

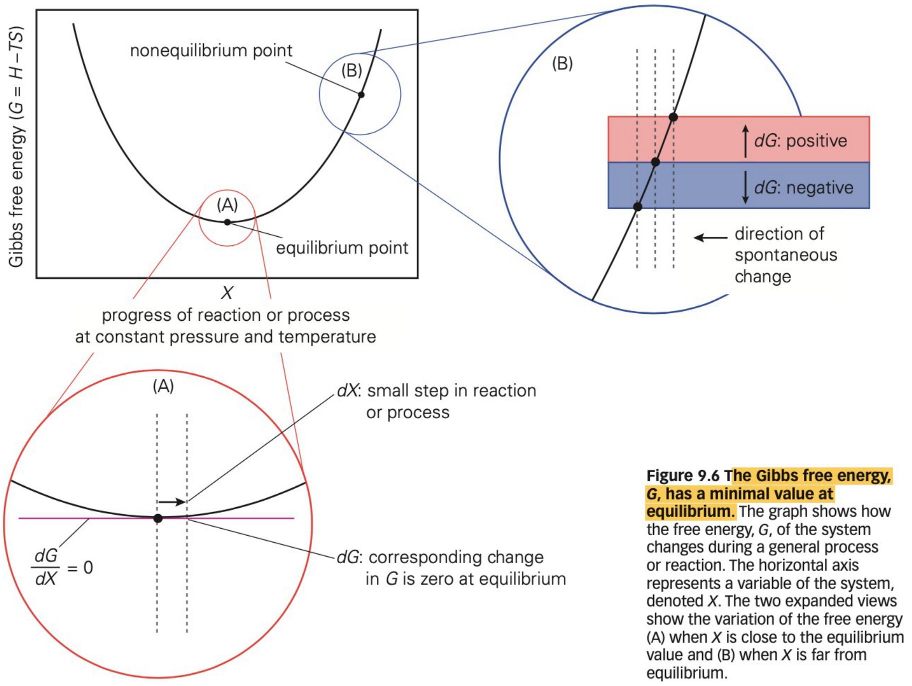


Figure 9.6 The Gibbs free energy, *G*, has a minimal value at equilibrium. The graph shows how the free energy, *G*, of the system changes during a general process or reaction. The horizontal axis represents a variable of the system, denoted *X*. The two expanded views show the variation of the free energy (A) when *X* is close to the equilibrium value and (B) when *X* is far from equilibrium.

A spontaneous process at constant temperature and pressure always involves a **decrease** in the Gibbs free energy of the system (dG < 0)

$$G = H - TS$$

$$G_A = -25kJ - 275K \times 2JK^{-1} = -25.55\ kJ$$

$$G_B = -20kJ - 275K \times 10J\ .K^{-1} = -22.75\ kJ$$

** don’t forget to convert units

$G_A < G_B$ Therefore state A will not spontaneously convert to state B

Question 7

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 J•K^{-1}. In state B, it has an enthalpy of –12 kJ and an entropy of 15 J•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

$$G_B < G_A$$

$$H_B - TS_B < H_A - TS_A$$

$$\frac{H_B - H_A}{S_B - S_A} < T \quad \text{->} \quad \frac{-12000\ J + 22000\ J}{15\ J*K - 7\ J*k} < T;\ -1250\ K < T$$

T must be higher than 1250K for B to be favored

Question 8

The potential energy between two atoms is described by a **Lennard-Jones potential**:

$$U_{VdW} = \sum_{i>j}^{N} \epsilon \left[\left(\frac{r_0}{r_{ij}} \right)^{12} - 2 \left(\frac{r_0}{r_{ij}} \right)^{6} \right]$$

Given:

- ϵ=2 kJ/mol,
- r0=0.4 nm

a) Calculate the potential energy U(r) at r=0.45 nm.

b) At what distance r is the potential energy at its minimum?
c) Choose the correct interpretation of the potential:

- The term $(\frac{r0}{r})^{12}$ describes the attractive force.
- The term $(\frac{r0}{r})^{6}$ describes the repulsive force.
- The potential U(r) accounts for both attractive and repulsive interactions.
- The distance r = r0 corresponds to the strongest attractive force.

Answer

Solution

a) Calculate the potential energy at r=0.45 :
Here you could do calculations just with formula, since you had just 2 atoms.

$$U(r) = \epsilon \left[\left(\frac{r_0}{r} \right)^{12} - 2 \left(\frac{r_0}{r} \right)^{6} \right],$$

Substitute the given values into the formula

Calculate the ratio $\frac{r_0}{r}$:

$$\frac{r_0}{r} = \frac{0.4}{0.45} \approx 0.8889.$$

Raise the ratio to the powers of 6 and 12:

$$\left(\frac{r_0}{r}\right)^6 = (0.8889)^6 \approx 0.5133,$$

$$\left(\frac{r_0}{r}\right)^{12} = (0.8889)^{12} \approx 0.2635.$$

Substitute these into the Lennard-Jones formula:

$$U(r) = 2\left[(0.2635) - 2\,(0.5133)\right].$$

Simplify the expression:

$$U(r) = 2\left[0.2635 - 1.0266\right],$$

$$U(r) = 2\left[-0.7631\right].$$

Final calculation:

$$U(r) = -1.5262\,\mathrm{kJ/mol}.$$

You could also see that there is another form of L-J potential, which looks like:
And so calculations will be (with sigma = 0.4)

$$U(r) = 4\epsilon\left[\left(\frac{\sigma}{r}\right)^{12} - \left(\frac{\sigma}{r}\right)^{6}\right].$$

$$U(0.45) = 4(2)\left[\left(\frac{0.4}{0.45}\right)^{12} - \left(\frac{0.4}{0.45}\right)^{6}\right].$$

1. Calculate $\frac{\sigma}{r} = \frac{0.4}{0.45} \approx 0.889$.
2. Compute $(0.889)^{12} \approx 0.275$ and $(0.889)^6 \approx 0.524$.
3. Substitute:
$$U(0.45) = 4(2)\left[0.275 - 0.524\right] = 8 \cdot (-0.249) = -1.992\,\mathrm{kJ/mol}.$$

The second formula is **standard Lennard-Jones potential** used in many textbooks and simulations. In standart L-J potential usually used sigma!

σ represents the distance where U(r)=0 and it is related to r0 (the equilibrium distance) by r0=2^(1/6)*σ

b) At what distance rrr is the potential energy at its minimum?

The minimum of the Lennard-Jones potential occurs at the equilibrium distance r_{min} , where the attractive and repulsive forces balance. This happens when:

$$\frac{dU}{dr_{ij}} = \epsilon \cdot \left[-12 \cdot \left(\frac{r_0}{r_{ij}} \right)^{13} + 12 \cdot \left(\frac{r_0}{r_{ij}} \right)^{7} \right]$$

Set $\frac{dU}{dr_{ij}} = 0$:

$$-12 \left(\frac{r_0}{r_{ij}} \right)^{13} + 12 \left(\frac{r_0}{r_{ij}} \right)^{7} = 0$$

Factor out $\left(\frac{r_0}{r_{ij}} \right)^{7}$:

$$\left(\frac{r_0}{r_{ij}} \right)^{7} \left[- \left(\frac{r_0}{r_{ij}} \right)^{6} + 1 \right] = 0$$

$$\left(\frac{r_0}{r_{ij}} \right)^{6} = 1$$

$$\frac{r_0}{r_{ij}} = 1 \qquad r_{ij} = r_0$$

r_{min}=r0=0.4 nm

c) Multiple Choice Interpretation:

- a. **False**: $(\frac{\sigma}{r})^{12}$ describes the **repulsive** force due to Pauli exclusion.
- b. **False**: $(\frac{\sigma}{r})^{6}$ describes the **attractive** van der Waals interaction.
- c. **True**: The Lennard-Jones potential combines **attractive** and **repulsive** forces.
- d. **False**: At r=σ, the potential energy is zero, not the strongest attraction.