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**Rec. Exam Biophysics. January 2021**  
***Bioinformatics degree. Part 1***

1) (0.5 point) Consider the following two configurations with the same energy. Configuration A: {150, 150, 320, 180, 50, 25, 15} and configuration B: {160, 140, 340, 160, 40, 35, 15}. Calculate which configuration has the greatest weight. Discuss which configuration is most probable.

2) (1.5 points) Initially, we have two separated systems with CO<sub>2</sub> and O<sub>2</sub> molecules in two containers.

- a) Calculate the kinetic energy of a single molecule of CO<sub>2</sub> in a container of 0.5 litres having  $2 \cdot 10^{18}$  molecules of CO<sub>2</sub> at 35°C; and calculate the kinetic energy of a single molecule of O<sub>2</sub> in a container of 0.6 litres having  $3 \cdot 10^{18}$  molecules of O<sub>2</sub> at 55°C.
- b) Calculate the total energy of the CO<sub>2</sub> container, and also the total energy of the O<sub>2</sub> container.
- c) Consider now that both containers are put together (having a global volume of 1.1 litre), mixing CO<sub>2</sub> and O<sub>2</sub> molecules and reaching the thermodynamic equilibrium. Calculate: i) the total energy of the global system; ii) the kinetic energy of each of a single CO<sub>2</sub> or O<sub>2</sub> molecule; iii) and the final temperature of the system. In all calculations, assume ideal gases having only kinetic energy.

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- 3) (1.0 points) An enzyme with a flexible inner cavity could adopt three different macromolecular conformations: open, semi-open or closed conformations. One experiment carried out at 37°C determined the following populations 55%, 45% and 5%, for open, semi-open and closed conformations, respectively. a) Assuming that the degeneration of open and closed conformations are 1, and the degeneration of the semi-open conformation is 2, calculate the relative energy of these conformations.
- b) Calculate the proportions of these conformations if we make a new experiment at 4°C.

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4) (1.0 points) In the second order reaction  $A \rightarrow \text{Products}$ , the concentration of A is  $[A] = 0.16 \text{ M}$  at the initial time of the reaction, and  $[A] = 0.08 \text{ M}$  after 42 minutes. a) Determine the value of the rate constant.  
b) Which will be the concentration of  $[A]$  at 3.5 h?

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5) (1.0 points) It is studied a reaction  $A+B \rightarrow P$  using different initial concentrations of the both reactants at several temperatures. A summary of the experiments is provided in the table.

a) Determine the partial order of A and B, and the rate constant at 30°C

b) Determine the activation energy of this reaction.

Experiment	$[A]_0 / (\text{mol dm}^{-3})$	$[B]_0 / (\text{mol dm}^{-3})$	$v_0 / (\text{mol dm}^{-3} \text{s}^{-1})$	Temperature/°C
1	0.252	0.142	1.35	30
2	0.504	0.142	5.43	30
3	0.504	0.213	5.44	30
4	0.252	0.142	2.79	70

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6) (2 points) Justify briefly the following sentences (all them are true)

- a) A classical forcefield applied to a single structure cannot be used to evaluate solvation energy in water.
- b) The choice of the simulation temperature in NVE molecular dynamics define the limits of the conformational space.
- c) Flexible residues like Gly decrease protein stability
- d) In both proteins and nucleic acids, hydrogen bonds do not contribute to the stabilization energy.
- e) Properly folded protein structures cannot be identified with classical forcefields only.
- f) Protein folding in vivo is much more efficient than in vitro

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- g) NPT is the most realistic simulation ensemble
  
  
  
  
  
  
  
  
  
  
- h) The binding energy between the two components in a protein complex requires to estimate their solvation energies.
  
  
  
  
  
  
  
  
  
  
- i) A hyperbolic curve when representing the degree of saturation in a binding process indicates that a protein is involved
  
  
  
  
  
  
  
  
  
  
- j) Folding “in vivo” is helped by accelerating the isomerization of Pro residues.

7) (1 point) Indicate which of the following energy terms are Favourable (F), Unfavourable (U) or Indifferent (I) for protein folding

- \_\_\_ Conformational entropy
- \_\_\_ Solvent entropy
- \_\_\_ Hydrogen bonds
- \_\_\_ Electrostatic interactions inside the protein
- \_\_\_ Electrostatic interactions in the surface of the protein
- \_\_\_ Van der Waals interactions



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8) (2 points) We wish to evaluate the influence of several amino acid residues in the stability of a protein-protein complex (R-L), by analysing the interaction energy change after mutations to Ala. The following table summarizes calculated changes in interaction and solvation energies due to the modification:

Mutation	$\Delta\Delta G_{\text{elec.int}}$ (Kcal mol <sup>-1</sup> )	$\Delta\Delta G_{\text{vdw.int}}$ (Kcal mol <sup>-1</sup> )	$\Delta\Delta G_{\text{solv}}$ (Kcal mol <sup>-1</sup> )
Glu 300 Ala	10.0	0.5	-3.0
Trp 260 Ala	-0.1	1.2	3.2
Val 310 Ala	0.0	0.1	0.3
Gln 302 Ala	0.7	0.5	-1.1

- Order these residues from less to more important in the stability of the complex.
- Suggest explanations for the observed energy changes. Consider that Glu is a negative charged residue while Gln is polar but neutral. Trp and Val are both hydrophobic but Trp is much larger than Val.
- Knowing that the experimental dissociation constant for the unmutated complex is 2.4 nM, evaluate
  - the expected dissociation constants for the mutants
  - the degree of complex formation at a concentration of L necessary for getting a 50% of the wild-type complex.

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## **Additional data and equations:**

M(H)=1 g mol<sup>-1</sup>; M(C)=12 g mol<sup>-1</sup>; M(O)=16 g mol<sup>-1</sup>; M(N)=14 g mol<sup>-1</sup>

k<sub>B</sub>=1.3806488·10<sup>-23</sup> J K<sup>-1</sup>

R=1.987 cal K<sup>-1</sup> mol<sup>-1</sup> = 8.314 J K<sup>-1</sup> mol<sup>-1</sup> = 0.082 atm L K<sup>-1</sup> mol<sup>-1</sup>

N<sub>A</sub>=6.022·10<sup>23</sup> mol<sup>-1</sup>

$$v^{mp} = \sqrt{(2 RT/M)}$$

$$\bar{v} = \sqrt{(8 RT/(\pi M))}$$

$$v^{rms} = \sqrt{(3 RT/M)}$$

$$f(v) = 4\pi \left(\frac{m}{2\pi k_B T}\right)^{3/2} v^2 e^{-mv^2/(2k_B T)}$$

$$\frac{1}{[A]_0 - [B]_0} \ln \frac{[B]_0[A]}{[A]_0[B]} = kt$$

## **Electrostatic interaction**

$$E_{pot} = 332.16 \frac{q_i q_j}{\epsilon r_{ij}}$$

q<sub>i</sub>, q<sub>j</sub>: partial charges (e); ε: relative dielectric constant; r<sub>ij</sub>: distance (Å). Resulting energy is Kcal mol<sup>-1</sup>

## **VdW interaction energy between equal atoms**

$$E_{pot} = 4\epsilon \left( \left(\frac{\sigma}{r}\right)^{12} - \left(\frac{\sigma}{r}\right)^6 \right)$$

ε: well depth (Kcal mol<sup>-1</sup>), σ: Distance at E<sub>pot</sub>=0 (Å)

## **Free energy related to dissociation constants**

$$\Delta G = RT \ln K_D$$

ΔG: Process free energy (units: energy mol<sup>-1</sup>, depending on the R value used). R (gas constant), T: Temperature (K); K<sub>D</sub>: Dissociation constant (Concentrations in M)

## **Saturation degree in a simple binding process**

$$Y = \frac{L}{K_D + L}$$

Y: Saturation degree, K<sub>D</sub>: Dissociation constant, L: Concentration of free ligand