MDCM601 2020 Exam 4

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1 Problems

Problem 1. In carboxypeptidases two essential catalytic residues are Arg145 and Glu270. How can these two amino acids, 125 residues apart, both be involved in catalysis?

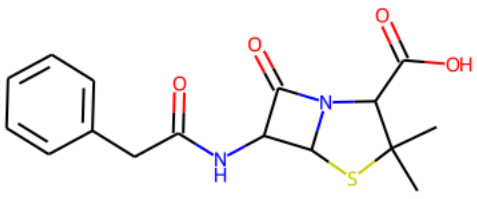
1. Enzyme changes its conformation from one state to another.
2. Substrate first binds one, and then the other active site.
3. These two residues are close in three-dimensional structure.
4. Proton transfer from Arg to Glu is a very fast process.

Problem 2. Rate constant for a reaction is given by the Arrhenius equation (1)

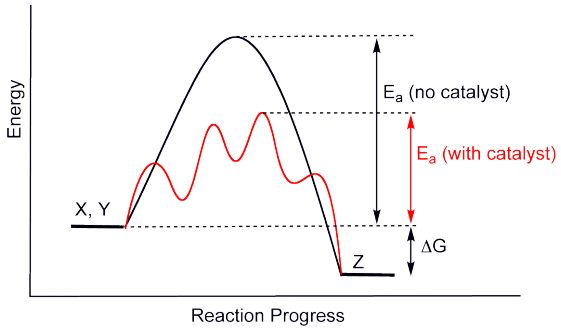
$$k = Ae^{-\frac{E_a}{RT}} \tag{1}$$

If the activation energy is 50 kJ/mol, R = 8.314 J/molK, and A = 1, by what factor does the rate increase when the temperature increases by 10 degrees (e.g. going from 300 K to 310 K)?
The rate at higher temperature is _____(use three significant figures) times greater than the rate at lower temperature.

Problem 3. The molecule shown below reacts covalently with a serine residue in the active site of bacterial carboxypeptidases. Click on the carbon atom that forms this covalent bond.



Problem 4. Catalyzed process (shown in red) consists of 4 distinct steps. Locate on the graph the energy of the transition state corresponding to the slowest step in the catalyzed reaction $X + Y \longrightarrow Z$.

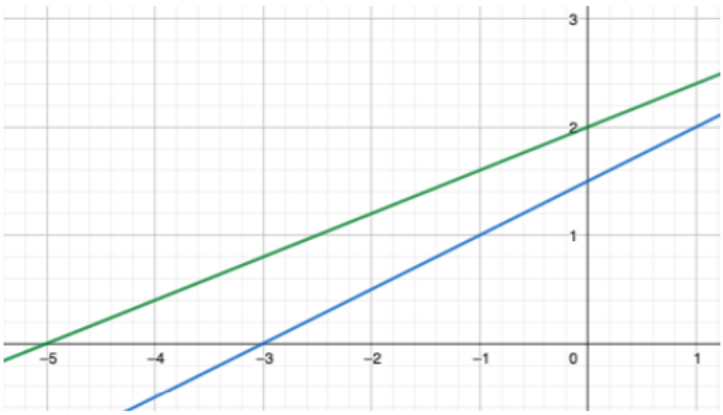


Problem 5. Use Michaelis-Menten equation (2) to determine the concentration of substrate, $[S]$, in terms of K_M, at which the rate of the reaction, v, would be equal to one third of V_{max}.
Michaelis-Menten equation:

$$v = \frac{V_{max} \times [S]}{K_M + [S]} \tag{2}$$

Problem 6. We plotted Lineweaver-Burke plot for two enzymes (green and blue lines in figure below). Determine the K_M and V_{max} for these two enzymes.

1. K_M(green)= 0.2; K_M(blue)= 0.33; V_{max}(green)=0.5; V_{max}(blue)= 0.66
2. K_M(green)= 0.5; K_M(blue)= 0.66; V_{max}(green)=1.5; V_{max}(blue)= 0.5
3. K_M(green)= -5; K_M(blue)= -3; V_{max}(green)=2; V_{max}(blue)= 1.5
4. K_M(green)= 5; K_M(blue)= 3; V_{max}(green)=0.5; V_{max}(blue)= 1.5



Problem 7. True or false?
Enzyme accelerates forward and reverse reaction equally.

Problem 8. True or false?
Enzyme accelerates reactions by stabilizing products of the reaction.

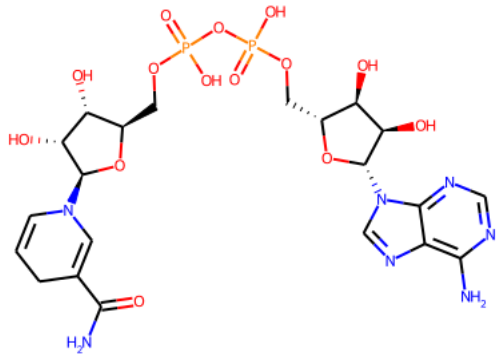
Problem 9. Which of the following statements best describes an allosteric binding site?

1. It is a binding site containing amino acids with aliphatic side chains.
2. It is a binding site that can accept a wide variety of differently shaped molecules.
3. It is a binding site, which is separate from the active site, and affects the activity of an enzyme when it is occupied by a ligand.
4. It is a description of an active site which has undergone an induced fit.

Problem 10. The Michaelis-Menten equation (2) relates the rate of an enzyme-catalysed reaction to which of the following?

1. Substrate concentration
2. Product concentration
3. Activation energy
4. Inhibitor concentration

Problem 11. Click on the carbon atom that bears the deliverable hydride in the structure of NADH.



Problem 12. Which three residues would you expect to find in the active site that requires presence of a hydrophobic environment?

1. Asp, Glu, Lys
2. Ser, His, Pro
3. Phe, Trp, Tyr

4. Gly, Arg, Thr

Problem 13. For an enzyme that follows Michaelis-Menten kinetics, calculate the value of V_{max} if V_0 is 10 µmol/min at 0.4 K_M.

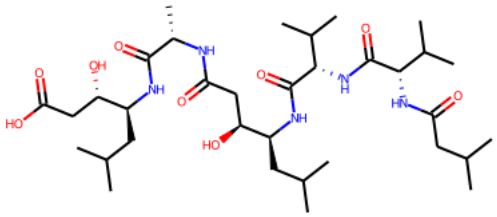
Problem 14. When k_{-1} is much greater than k_2, K_M can be interpreted as which one of the following?

1. Association constant for the process $\mathrm{E} + \mathrm{S} \longrightarrow \mathrm{ES}$
2. Dissociation constant for the process $\mathrm{ES} \longrightarrow \mathrm{E} + \mathrm{S}$
3. k_{cat} for the process $\mathrm{ES} \longrightarrow \mathrm{E} + \mathrm{P}$
4. $\dfrac{1}{k_{cat}}$ for the process $\mathrm{E} + \mathrm{P} \longrightarrow \mathrm{ES}$

Problem 15. Rate constant for the forward reaction catalyzed by carbonic anhydrase (hydration of CO_2) is $1.0 \times 10^6\,\mathrm{s}^{-1}$, and the rate constant for the reverse reaction (dehydration of bicarbonate) is $6.0 \times 10^5\,\mathrm{s}^{-1}$. What is the equilibrium constant for the process? The equilibrium constant $K_{eq} =$ _____ (please use only 3 significant figures)

Problem 16. Michaelis-Menten constant, K_M, for enzyme-substrate complex formation between carbonic anhydrase and CO_2 is 8.3 mM, and between the same enzyme and bicarbonate HCO_3^- is 32 mM.
Is the following stateme true or false?
CO_2 binds to the enzyme with greater affinity compared to bicarbonate.

Problem 17. Structure of pepstatin, a picomolar inhibitor of pepsin, is shown. Click on a carbon atom in the structure that mimics the tetrahedral intermediate encountered during hydrolysis of a regular polypeptide chain.



Problem 18. Which three residues can form a charge-relay system in the active site of some hydrolytic enzymes?

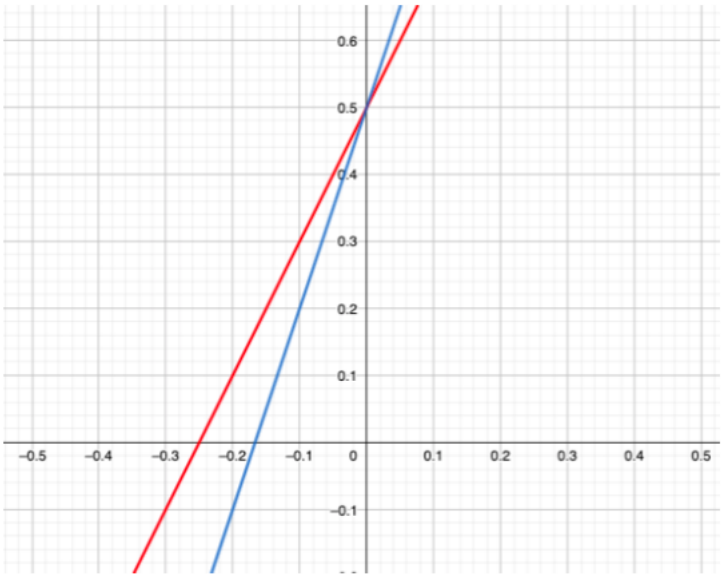
1. Ser, Tyr, Glu
2. Lys, His, Asp
3. Ser, His, Glu
4. Pro, Ser, Gly

Problem 19. Kinetic parameters of an enzymatic reaction were determined in the absence or in the presence of compound A, and the following results were obtained:
1) With A: $-\frac{1}{K_M} = -0.14$; $\frac{1}{V_{max}} = 7.1$
2) Without A: $-\frac{1}{K_M} = -0.08$; $\frac{1}{V_{max}} = 4.0$
What can you say about the activity of A?

1. It is an activator of the enzymatic activity.
2. It is an uncompetitive inhibitor.
3. It is a competitive inhibitor.
4. It is a non-competitive inhibitor.

Problem 20. Careful kinetic experiments of an enzyme with an inhibitor (blue) and without an inhibitor (red) yielded observations that were plotted on a Lineweaver-Burke plot shown here. What type of inhibition is this?

1. Uncompetitive
2. Non-competitive
3. Competitive
4. Mixed



2 Solutions

1. 3
2. 1.91
3.
4.
5. 0.5 K_M
6. 1
7. True
8. False
9. 3
10. 1
11.
12. 3
13. 35 µmol/min
14. 2
15. 1.67
16. True
17.
18. 3
19. 2
20. 3