Exam2

Wednesday, March 22, 2017 11:33 AM

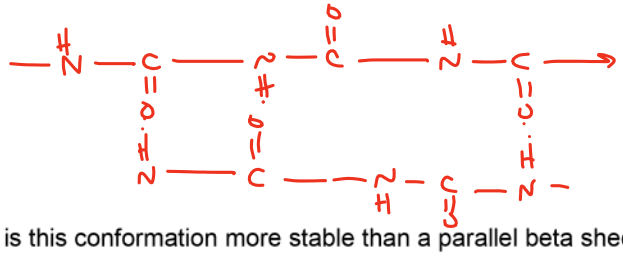
Chem 106 Exam 2 Name_____

This exam is schedule for 75 minutes and I anticipate it to take the full time allotted. You are free to leave if you finish. In multiple part problems, points awarded will not be penalized for incorrect answer on previous parts, so simply **move on if you get stuck on one part**. If you need to, make up an answer for the previous part. Always neatly show work for partial credit.

1. For each of the following, indicate whether backbone or side chain interactions are more important in stabilizing the structure.
   a. Secondary protein structure backbone
   b. Tertiary protein structure side chains

2. What is the major stabilizing force that keeps a protein folded in the correct conformation? Explain why this is so effective.
   Hydrophobic effect → hydrophobic side chain are packed together at the protein core. This results in a huge restructuring of H_2O that $\Delta S > 0$.

3. Clearly describe the H-bonding pattern than stabilizes an anti-parallel beta sheet. You are encouraged to use a sketch to support your answer.



H bonds between backbone C=O + NH — line up perfectly

   Why is this conformation more stable than a parallel beta sheet?
   same pattern, but longer H-bonds so weaker

4. Consider a reaction that has an activation energy of 8.6 kJ mol^{-1}. What percent of molecules will have enough energy to react at 300 °C?

$e^{-E_a/RT}$ $T = 573.15\ K$ $E_a = 860.\ \frac{J}{mol}$

$e^{-860/8.314 \cdot 573.15} = 0.1645$

16.45%

5. Compare the two peptides below. Circle the peptide that has the largest log P value?

$P = \frac{[\,]_{oct}}{[\,]_{H_2O}}$ ↑ log P = soluble in octanol

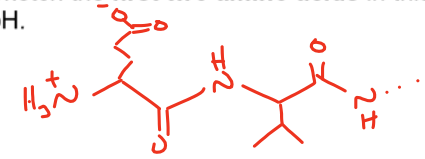
Tryptophan – Alanine – Serine – Leucine

Isoleucine – Alanine – Phenylalanine - Methionine All nonpolar

6. Consider a peptide:

glutamic acid – valine – serine – lysine – alanine – leucine - cysteine.

a. Sketch the **first two amino acids** in this this peptide as you would expect to see it at neutral pH.



b. Determine the pI of this peptide.

$H_5X^{+2} \rightleftharpoons H_4X^{+1} \rightleftharpoons H_3X \rightleftharpoons H_2X^{-1} \rightleftharpoons HX^{-2} \rightleftharpoons X^{-3}$

2.10 4.07 8.37 10.71

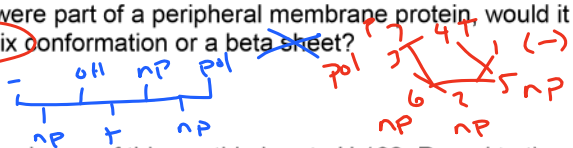
$pI = 6.22$

c. Is this peptide susceptible to disulfide bond formation? Why?

yep - cysteine is present

d. Answer **one** of these:

i. If this peptide were part of a peripheral membrane protein, would it be more likely to be in an alpha helix conformation or a beta sheet?

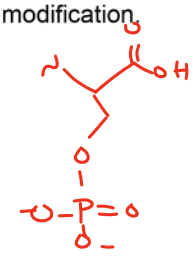


ii. What would the charge of this peptide be at pH 10? Round to the nearest whole number.

mostly H_7X^{-1} −1

iii. Which amino acid side chain in this peptide is most susceptible to phosphorylation? Sketch product of the phosphorylation modification.

serine



7. Clearly explain three ways that the rate of a reaction can be changed. In your answer, make sure to explain why each change would result in a modified reaction rate.

rate = k [A]

① ΔT → changes k

② ΔEa by adding a catalyst → changes k

③ Δ [A] → change rate by influencing # of collisions

8. The reaction A → B has been shown to have a rate constant of 72.60 $M^{-1}s^{-1}$.

a. Write a rate law for this reaction.

units → 2nd order!

$rate = 72.6\ M^{-1}s^{-1}[A]^2$

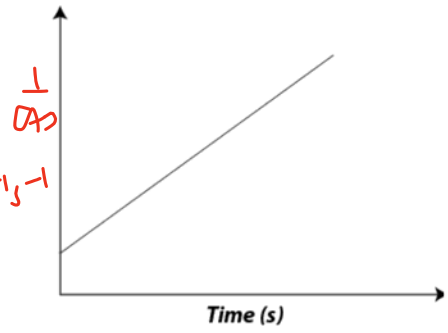
b. What is the rate if [A] = 100 mM?

100 mM → 0.1 M

$rate = 72.6(0.1)^2 = 0.726\ \frac{M}{s}$

c. Label the Y-axis with [A], ln[A] or 1/[A] for the reaction above.

2nd order



d. What is the slope of the graph? Make sure to include units.

$\frac{1}{[A]} = kt + \frac{1}{[A]_0}$ ↑ slope

$k = 72.6\ M^{-1}s^{-1}$

e. The y-intercept of this graph is 0.03. What is the concentration of A at t = 0?

$\frac{1}{[A]_0} = 0.03$ $[A]_0 = 33.33\ M$

f. How much A is remaining after 1 ms?

$\frac{1}{[A]} = 72.6(0.001) + 0.03$

$\frac{1}{[A]} = 0.1026$ $[A] = 9.75\ M$

9. The enzyme CON-2 is responsible for catalyzing the following reaction:

a. What type of reaction is this? How do you know?

condensation

b. The turnover number ($3.5 \times 10^{-6}\ s^{-1}$) and the catalytic efficiency ($1.4 \times 10^{7}\ \mu M^{-1}s^{-1}$) were determined in an experiment using 0.1 μM CON-2 and a very large excess of the 2nd reactant (so only the carboxylic acid containing reactant (S) influences the rate).

i. Determine Km for S

$cat.\ eff. = \frac{k_{cat}}{K_M}$ $\quad 1.4\times10^{7}\ \mu M^{-1}s^{-1} = \frac{3.5\times10^{6}\ s^{-1}}{K_M}$ $\quad K_M \sim 0.25\ \mu M$

ii. Determine Vmax

$k_{cat} = \frac{V_{max}}{E_{TOT}}$ $\quad 3.5\times10^{6} = \frac{V_{max}}{0.1}$ $\quad V_{max} = 3.5\times10^{5}\ \frac{\mu M}{s}$

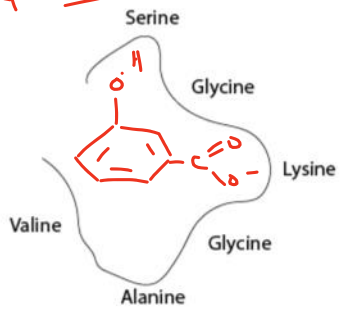
iii. Calculate the rate of the reaction when [S] = 360 nM.

$V = \frac{V_{max}[S]}{K_M + [S]} = \frac{3.5\times10^{5}\ (0.36\ \mu M)}{0.25 + 0.36} = 206557\ \frac{\mu M}{s}$

c. A sketch of the active site of CON-2 is shown below. Orient the carboxylic acid containing substrate into the active site and explain why the active site is ideal for binding to this compound.

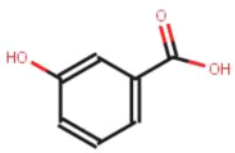
deprotonate!

- Serine → H-bonds with OH
- Lys → ion pair with COO^-
- other non-polar interact with np regions of substrate

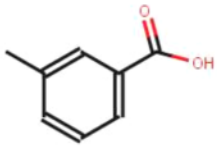


CON-2

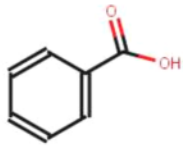
d. As you have seen before, some enzymes can recognize multiple substrates. CON-2 can catalyze identical reactions with these two substrates:



A



B



C

i. Which of these compounds will bind to the active site with the lowest affinity? Why?

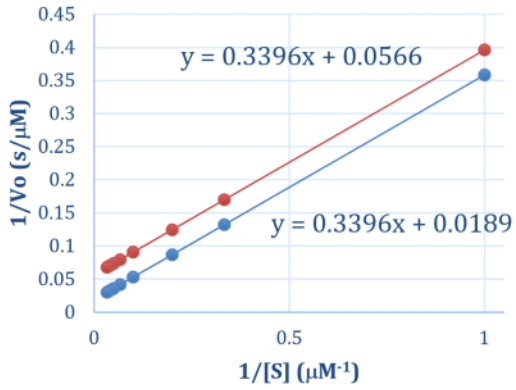
B or C are ok answers B: -CH3 does not interact well with serine C: nothing to interact with serine

ii. Rank these compounds by **increasing** Km.

small = high affinity

A < C < B or A < B < C (depending on your answer to i)

e. The graph below shows the CON-2 reaction in the presence of an inhibitor.



What type of an inhibitor is this?

uncompetitive

On the reaction scheme below, show where the inhibitor will interact.

$$E + S \rightleftharpoons ES \rightarrow E + P$$

+ I ↓ ESI

Circle the true statements (the asterisk means the value was determined in the presence of the inhibitor).

Km* > Km or Km* < Km

Vmax* > Vmax or Vmax* < Vmax

Bonus: Calculate Ki noting that this data was collected with 100 nM inhibitor

$V_{max}' = 17.67$

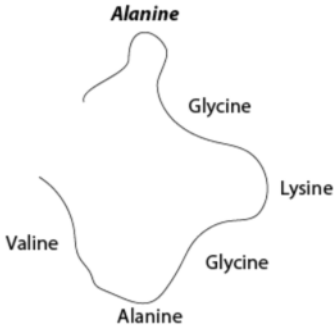
$V_{max} = 52.91$

$V_{max}' = \frac{V_{max}}{\alpha}$ $17.67 = \frac{52.91}{\alpha}$

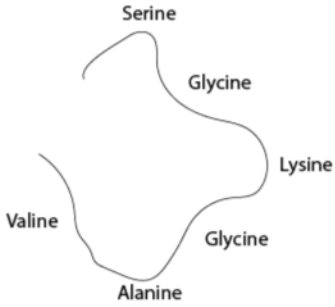
$\alpha = 2.99 = 1 + \frac{[I]}{K_I} = 1 + \frac{100}{K_I}$

$K_I = 50\ nM$

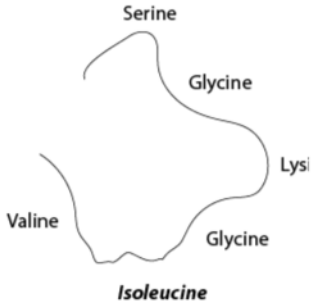
10. Three different isoforms of the enzyme from the previous problem have been discovered. The active site of each of these is shown below with the single difference from CON-2 emphasized by bold labeling.



CON-1

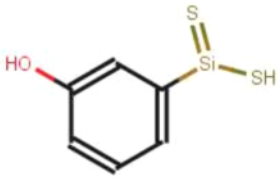


CON-2



CON-3

a. The molecule shown to the right has been shown to be an effective inhibitor of CON-2 but not CON-1.

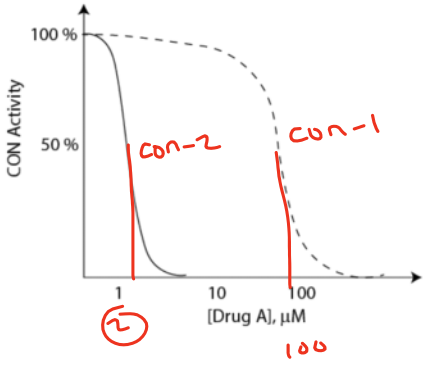


Drug A

i. Why? The OH group will bind to serine but not alanine. This means it will inhibit CON-2, not CON-1.

ii. Consider the graph below, which shows the activity of CON-1 and CON-2 (100% = no inhibition, 0% = fully inhibited) vs. [Drug A].

Label the line that most likely corresponds to CON-1. Do the same for CON-2. → low [Drug] → inhibited @ high [Drug]



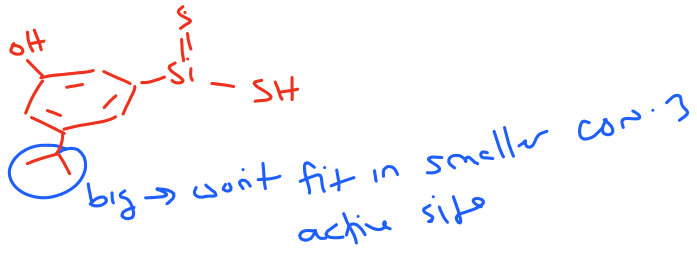
Estimate the IC_{50} value for each enzyme.

CON-1 = 100 CON-2 = 2

What concentration of Drug A would you administer so that only one enzyme is inhibited?

10 µM would work

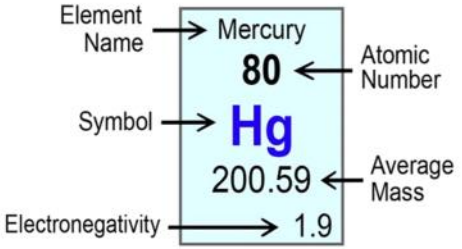
iii. Using Drug A as a template, design a drug that would inhibit CON-2 but not CON-3.



Periodic Table of the Elements

Average relative masses are rounded to two decimal places.

All average masses are to be treated as measured quantities, and subject to significant figure rules.



1																		18
Hydrogen 1 H 1.01 2.1	2											13	14	15	16	17		Helium 2 He 4.00 ---
Lithium 3 Li 6.94 1.0	Beryllium 4 Be 9.01 1.5											Boron 5 B 10.81 2.0	Carbon 6 C 12.01 2.5	Nitrogen 7 N 14.01 3.0	Oxygen 8 O 16.00 3.5	Fluorine 9 F 19.00 4.0		Neon 10 Ne 20.18 ---
Sodium 11 Na 22.99 0.9	Magnesium 12 Mg 24.31 1.2		3	4	5	6	7	8	9	10	11	12	Aluminum 13 Al 26.98 1.5	Silicon 14 Si 28.09 1.8	Phosphorus 15 P 30.97 2.1	Sulfur 16 S 32.07 2.5	Chlorine 17 Cl 35.45 3.0		Argon 18 Ar 39.95 ---
Potassium 19 K 39.10 0.8	Calcium 20 Ca 40.08 1.0		Scandium 21 Sc 44.96 1.3	Titanium 22 Ti 47.88 1.5	Vanadium 23 V 50.94 1.6	Chromium 24 Cr 52.00 1.6	Manganese 25 Mn 54.94 1.5	Iron 26 Fe 55.85 1.8	Cobalt 27 Co 58.93 1.8	Nickel 28 Ni 58.69 1.8	Copper 29 Cu 63.55 1.9	Zinc 30 Zn 65.39 1.6	Gallium 31 Ga 69.72 1.6	Germanium 32 Ge 72.61 1.8	Arsenic 33 As 74.92 2.0	Selenium 34 Se 78.96 2.4	Bromine 35 Br 79.90 2.8		Krypton 36 Kr 83.80 3.0
Rubidium 37 Rb 85.47 0.8	Strontium 38 Sr 87.62 1.0		Yttrium 39 Y 88.91 1.2	Zirconium 40 Zr 91.22 1.4	Niobium 41 Nb 92.91 1.6	Molybdenum 42 Mo 95.94 1.8	Technetium 43 Tc (98) 1.9	Ruthenium 44 Ru 101.07 2.2	Rhodium 45 Rh 102.91 2.2	Palladium 46 Pd 106.42 2.2	Silver 47 Ag 107.87 1.9	Cadmium 48 Cd 112.41 1.7	Indium 49 In 114.82 1.7	Tin 50 Sn 118.71 1.8	Antimony 51 Sb 121.76 1.9	Tellurium 52 Te 127.60 2.1	Iodine 53 I 126.90 2.5		Xenon 54 Xe 131.29 2.6
Cesium 55 Cs 132.91 0.7	Barium 56 Ba 137.33 0.9	57-70 *	Lutetium 71 Lu 174.97 1.1	Hafnium 72 Hf 178.49 1.3	Tantalum 73 Ta 180.95 1.5	Tungsten 74 W 183.84 1.7	Rhenium 75 Re 186.21 1.9	Osmium 76 Os 190.23 2.2	Iridium 77 Ir 192.22 2.2	Platinum 78 Pt 195.08 2.2	Gold 79 Au 196.97 2.4	Mercury 80 Hg 200.59 1.9	Thallium 81 Tl 204.38 1.8	Lead 82 Pb 207.20 1.8	Bismuth 83 Bi 208.98 1.9	Polonium 84 Po (209) 2.0	Astatine 85 At (210) 2.2		Radon 86 Rn (222) 2.4
Francium 87 Fr (223) 0.7	Radium 88 Ra (226) 0.9	89-102 **	Lawrencium 103 Lr (262) ---	Rutherfordium 104 Rf (261) ---	Dubnium 105 Db (262) ---	Seaborgium 106 Sg (266) ---	Bohrium 107 Bh (264) ---	Hassium 108 Hs (269) ---	Meitnerium 109 Mt (268) ---	Darmstadtium 110 Ds (271) ---	Roegentium 111 Rg (272) ---	Copernicium 112 Cn (277) ---	Ununtrium 113 Uut (284) ---	Flerovium 114 Fl (289) ---	Ununpentium 115 Uup (288) ---	Livermorium 116 Lv (293) ---	Ununseptium 117 Uus (294) ---		Ununoctium 118 Uuo (294) ---

*lanthanides	Lanthanum 57 La 138.91 1.1	Cerium 58 Ce 140.12 1.1	Praseodymium 59 Pr 140.91 1.1	Neodymium 60 Nd 144.24 1.1	Promethium 61 Pm (145) 1.1	Samarium 62 Sm 150.36 1.2	Europium 63 Eu 151.97 1.1	Gadolinium 64 Gd 157.25 1.2	Terbium 65 Tb 158.93 1.1	Dysprosium 66 Dy 162.50 1.2	Holmium 67 Ho 164.93 1.2	Erbium 68 Er 167.26 1.2	Thulium 69 Tm 168.93 1.3	Ytterbium 70 Yb 173.04 1.1
**actinides	Actinium 89 Ac (227) 1.1	Thorium 90 Th 232.04 1.3	Protactinium 91 Pa 231.04 1.5	Uranium 92 U 238.03 1.4	Neptunium 93 Np (237) 1.4	Plutonium 94 Pu (244) 1.3	Americium 95 Am (243) 1.3	Curium 96 Cm (247) 1.3	Berkelium 97 Bk (247) 1.3	Californium 98 Cf (251) 1.3	Einsteinium 99 Es (252) 1.3	Fermium 100 Fm (257) 1.3	Mendelevium 101 Md (258) 1.3	Nobelium 102 No (259) 1.3

$k = Ae^{\frac{-E_a}{RT}}$ $R = 8.314\, Jmol^{-1}K^{-1}$ $v_0 = \frac{v_{max}[S]}{Km\ \ [S]}$

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

$\propto = 1 + \frac{[I]}{K_I}$ $v_{max} = k_2[E]_{total}$

Amino Acid	**-NH_3^+**	**-CO_2H**	**Side chain**
Glycine, Gly	9.78	2.35	
Alanine, Ala	9.87	2.35	
Valine, Val	9.74	2.29	
Leucine, Leu	9.74	2.33	
Isoleucine, Ile	9.76	2.32	
Phenylalanine, Phe	9.31	2.20	
Tryptophan, Trp	9.41	2.46	
Tyrosine, Tyr	9.21	2.20	10.46
Histidine, His	9.33	1.80	6.04
Serine, Ser	9.21	2.19	
Threonine, Thr	9.10	2.09	
Methionine, Met	9.28	2.13	
Cysteine, Cys	10.70	1.92	8.37
Aspartic Acid, Asp	9.90	1.99	3.90
Glutamic Acid, Glu	9.47	2.10	4.07
Asparagine, Asn	8.72	2.14	
Glutamine, Gln	9.13	2.17	
Lysine, Lys	9.06	2.16	10.54
Arginine, Arg	8.99	1.82	12.48
Proline, Pro	10.64	1.95	