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			Exa	ım 1		
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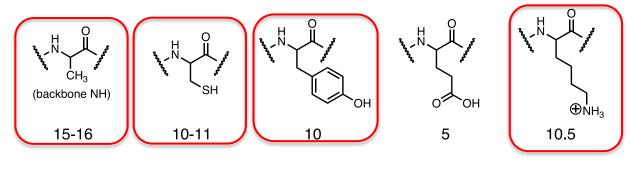
The exam starts on the next page. It has 10 questions, worth a total of 100 points. Please write legibly and don't assume that long answers are required if there is a lot of space left for your response.

A test-taking tip: go through the whole exam and do the easy questions first. Then tackle the ones you find to be more difficult. Good luck.

- 1. (5 points) A new drug to treat stomach ulcers has a critical amino group (pKa<sub>NH2</sub> = 9.4) and a carboxylic acid group (pKa<sub>COOH</sub> = 4.1). In order for the drug to be effective both functional groups need to be protonated. Would this drug be effective if taken orally? (Hint, stomach pH=2)
  - a. No, both groups will be deprotonated
  - **b.** No, only the amino group would be protonated
  - c. No, only the carboxylic acid group would be protonated
  - d. Yes, both groups will be protonated
  - e. Yes, both groups will be deprotonated
- **2.** (**5 points**) You add an enzyme to the reaction shown below. How does the enzyme help drive the reaction forward?

 $\Delta G$ = + 0.6 kcal/mol;  $\Delta G^{\ddagger}_{uncat}$  = 10 kcal/mol;  $K_{eq}$  = 0.1

- **a.** The enzyme increases the Keq of the reaction.
- **b.** The enzyme makes the free energy ( $\Delta G$ ) of the reaction negative
- c. The enzyme lowers the activation free energy ( $\Delta G^{\ddagger}_{uncat}$ ) of the reaction
- **d.** The enzyme makes the enthalpy of the reaction negative ( $\Delta H < 0$ )
- **e.** The enzyme makes the entropy of the reaction positive ( $\Delta S>0$ )
- (10 points) Shown here are protein building blocks (amino acid units) that have the indicated pK<sub>a</sub> values. Under each, draw the dominant form of that unit at pH 7. If the dominant form is unchanged from the drawing, just circle the drawing.
   2 points per correct answer.



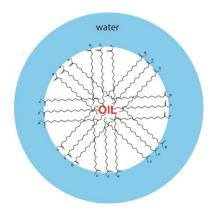
**4.** (**10 points**) Dishwashing detergent is used to clean animals affected by oil spills. This approach has worked well along the cost of the Gulf of Mexico, due to the presence of "soft water". However, this approach does not work well along the Atlantic coast, due to the presence of "hard water". "Hard water" contains a high calcium ion concentration.



$$Na \oplus O$$

Most common component of detergent

a. Using a diagram, explain how detergent can remove the oil from the animals' surface. Be sure to explain what type of structure the detergent forms. (5 points)



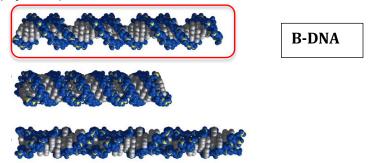
- The detergent forms a micelle around the oil. (2.5 points)
- The carboxylic acid groups will point towards the water engaging in hydrogen bonds with the water. (2.5 points)
- b. Using a diagram, explain why this approach does not work well in the presence of "hard water". Be sure to explain what type of structure the detergent forms. (5 points)



- A calcium ion has a +2 charge and can chelate with the negatively charged fatty acid. (2points)
- Each calcium in will bind two fatty acids (2 points)
- Calcium bound fatty acids will precipitate out of the water. Given that there is less detergent to bind oil, the detergent does not work well in hard water (1 point)

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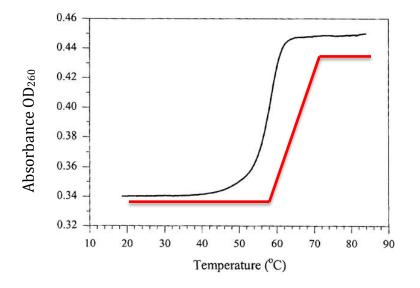
5. (8 points) Shown below are the three forms that DNA can adopt.



- a) Circle and label the DNA form most likely to be found in nature (2 points)
- b) List 3 major differences between A-form and B-form DNA (6 points)

## Any three differences found in table 24-1. For example

- The base pairs are tilted about 20° on A-form DNA but they are almost not tilted (only 6°) in B-form DNA
- There is a hole in the middle of A-form DNA but not in B-form DNA
- A-form DNA is broader (about 26Å) than B-DNA (about 20 Å)
- A-form DNa has a C3'-endo shugar puckering while B-DNa has a C2'-endo sugar puckering
- In B-form of DNA the major and minor groove are clearly different. The major groove is wide, while the minor groove is narrow. However, in A-form DNa the major and minor groups looks very similar. The major groove is narrow while the minor groove is wide.
- **6.** (**5 points**) The human genome has a 40% GC content, while the genome of microbes that live at high temperatures (thermophiles) have a higher GC content, sometimes as high as 70%. Below is the melting curve for human DNA. Draw in the graph below the melting curve you expect to see for the DNA of a thermophilic microbe.



Expect the Tm of the DNA from a thermophile to be higher than the Tm of a mesophile.

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- 7. (15 points) An RNA hairpin undergoes a structural transition from an extended conformation to a hairpin structure with enthalpy  $\Delta H = -38$  kcal/mol and entropy  $\Delta S = -110$  cal/(molK)
  - a) What is the Gibbs Free energy ( $\Delta$ G) for this transition at 37°C and 100°C (0°C = 273°K) (**5 points**)
- 1.5 pts to set up the calculation correctly. 1 point for the right answer.

## At 37°C

 $\Delta G = \Delta H - T \Delta S$ 

- = -38000 cal/mol (310K \* -110 cal/(mol K)) = -38000 cal/mol + 34100 cal/mol
- = -3900 cal/mol
- 1.5 pts to set up the calculation correctly. 1 point for the right answer.

At 100°C

- = -38000 cal/mol (373K \* -110 cal/(mol K)) = -38000 cal/mol + 41030 cal/mol
- = 3030 cal/mol
  - b) At what temperature is this transition "spontaneous"? (2 points)

At 37°C

c) What is the melting temperature, or " $T_m$ ", for this transition? The  $T_m$  is defined as the temperature at which the populations of extended and hairpin structures are equal (8 points)

The populations of extended and hairpin RNA structures will be equal at equilibrium, that is  $\Delta G = 0$  (4 points)

$$\wedge G = \wedge H - T \wedge S = 0$$

 $T \triangle S = \triangle H \rightarrow Tm = \triangle H/\triangle S$  (2points)

Tm= 38000 cal/mol/ -110 cal/(mol K) = -345.45 °K (1point)

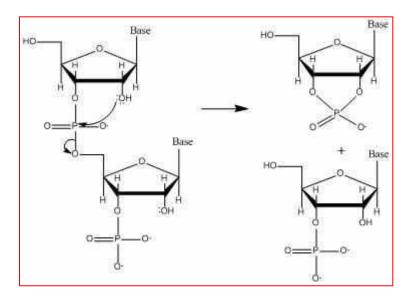
- **8.** (**10 points**) It is your first day of summer research and your advisor asks you to choose between working with DNA or working with RNA. You have taken "Survey of Biochemistry" and know that RNA is less stable than DNA, thus you choose to work with DNA. Your advisor asks you to prove this. You proceed to:
  - a. Draw the structure of the adenine ribonucleotide (5 points)

2pt for correct base

2pt for correct sugar

1pt for correct location and structure of the phosphate

b. Draw the chemical mechanism that proves that RNA is less stable than DNA (5 points)



Showing that 2' OH attachs the 3' phosphate 2.5 points
Showing the pentacoordinated phosphate intermediate 2.5 points.

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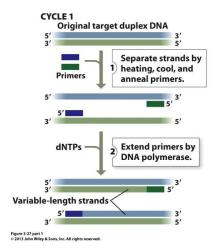
9. (12 points) At the beginning of DNA-RNA hybrids, we often find DNA triplets called "Hoogsteen base pairs". Fill in the structure of the GGC triplet in the Hoogsteen base pair shown below. Be sure to highlight the hydrogen bonds with dashed lines. Two of these figures are shown in case you mess up, so that you don't have to re-draw the positions of the bases. Only one answer is needed.

Hydrogen bonds

3 points per correct base

- $1.5\ points$  for correct hydrogen bonding between G and C
- $1.5\ points\ correct\ hydrogen\ bonding\ between\ G\ and\ G$

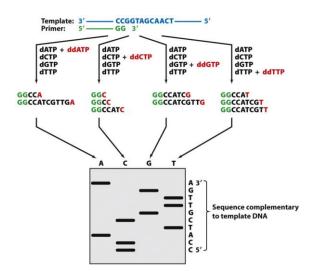
- **10.** (**20 points**) DNA technologies allow us to read, write and amplify DNA. Using diagrams, explain how the two technologies below work and what are they used for.
  - a. Polymerase chain reaction (10 points)



## **Important:**

- Heating to separate the double stranded DNA
- Annealing of primers
- Extension of the DNa using dNTPs and DNa polymerase
- Results in semi conservative replication of DNA.
- DNA amplification grows exponentially.

b. DNA sequencing (10 points)



## **Important:**

- The use of ddNTP to stop the reaction.
- The labeling of the ddNTP to identify the base pair were the raction stops.
- The detection method, either gel electrophoresis (radioactivity) or capillary electrophoresis with fluorescent probes.