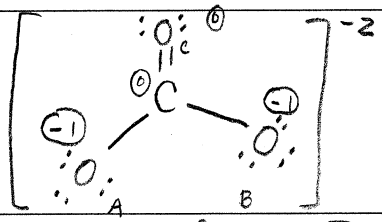
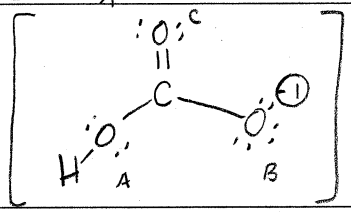
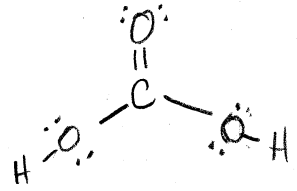
NAME: KEY

Final Exam (Part A 70 points) Always show your work!

1. Bicarbonate ion is the important pH buffer in the blood. (40 points)

a. Fill in the table below for the carbonate anion $[CO_3]^{-2}$, the bicarbonate anion, $[HCO_3]^{-1}$ and carbonic acid, H_2CO_3. If resonance forms exist, just draw one resonance form.

Species	# of Valence Electrons	One reasonable Lewis structure. Indicate the formal charges on each atom in your drawing.	Formal charge FC = valence electrons – [unshared electrons + ½ (shared electrons)]
$[CO_3]^{-2}$	4 + 3(6) +2 = 24e		$O_{A,B} = 6-(6+\frac{1}{2}(2)) = -1$ $O_C = 6-(4+\frac{1}{2}(4)) = 0$ $C = 4-(\frac{1}{2}(8)) = 0$
$[HCO_3]^{-1}$	4 + 3(6) +1 +1 = 24e	 FC on O_B = -1 FC on all other atoms is 0	$O_{AC} = 6-(4+\frac{1}{2}(4)) = 0$ $O_B = 6-(6+\frac{1}{2}(2)) = -1$ $C = 4-(\frac{1}{2}(8)) = 0$ $H = 1-(\frac{1}{2}(2)) = 0$
H_2CO_3	2(1) + 4 + 3(6) = 24e-	 FC	All oxygens $O_x = 6-(4+\frac{1}{2}(2)) = 0$ $C = 4-(\frac{1}{2}(8)) = 0$ All hydrogens $H = 1-(\frac{1}{2}(2)) = 0$

b. Which of the species above can act as acids? Explain by writing down the chemical reaction that demonstrates it is an acid.

carbonic acid : $H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$

bicarbonate $HCO_3^- \rightleftharpoons H^+ + CO_3^{-2}$

c. Which of the species above can act as bases? Explain by writing down the chemical reaction that demonstrates it is a base.

bicarbonate $HCO_3^- + H_2O \rightleftharpoons H_2CO_3 + OH^-$

carbonate $CO_3^{-2} + H_2O \rightleftharpoons HCO_3^- + OH^-$

d. The pK_as for carbonic acid and bicarbonate are $pKa_1 = 6.37$ and $pKa_2 = 10.3$ respectively. Which one of the three species (carbonic acid, bicarbonate, or carbonate) is found in extremely low levels relative to the others in the blood at pH 7.4. Explain your ordering. NO CALCULATION NECESSARY

Carbonate (CO_3^{-2}) lowest level (pKa2 that creates this is furthest away 10.3)
bicarbonate (HCO_3^-) highest level
Carbonic acid (H_2CO_3) high level, but less than HCO_3^-

pH 7.4 of blood sits between pKa_1 carbonic acid that creates HCO_3^- (6.37) and pKa_2 bicarbonate that destroys HCO_3^- (10.3)

e. Use the buffer equation below to predict the ratio of bicarbonate to carbonic acid in the blood at pH 7.4. Show your work
Buffer: pKa = pH – log [A-]/[HA]

relevant reaction is pKa1 $H_2CO_3 \rightleftharpoons HCO_3^- + H^+$ $pKa_2 = 6.37$ $pKa_2 \approx 6.4$

$pKa = pH - \log [A^-]/HA$

$6.4 = 7.4 - \log [A^-]/HA$

$-1 = -\log A^-/HA$

$1 = \log A^-/HA$

$10^1 = \frac{A^-}{HA} = \frac{10}{1}$

Ratio is 10 HCO_3^- to 1 H_2CO_3

f. If you exercise hard, and release lots of H^+ into your blood through lactic acid, how does your body adjust its respiration rate to maintain the pH of your blood close to 7.4? Explain.

A person will exhale more rapidly (breathe more rapidly to get rid of CO_2

$2H^+ + CO_2 \rightleftharpoons H_2CO_3 \xrightarrow{\text{to lungs in blood}} H_2O + CO_2$

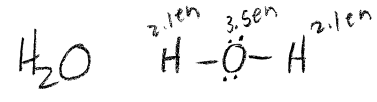
$Hb \cdot CO_2 \xrightarrow{\text{lungs}} Hb + CO_2$

g. Oxygen transported by the blood is eventually turned into water during metabolism. Here is the overall reaction by which this happens, though in the body at least 18 enzymes and five electron transfer complexes participate in the transformation (TAKE MORE BIOCHEM TO INVESTIGATE).

$$6O_2 + \text{glucose} = 6H_2O + 6CO_2$$

Looking only at the conversion of oxygen to water, decide if this is a redox reaction or not by determining the effective oxidation state of the oxygen atoms in the reactant (O_2) and the product (H_2O). If your answer is yes, is the oxygen oxidized or reduced? (Electronegativity of O and H are 3.5 and 2.1 respectively) Effective oxidation state = Valence Electrons – [unshared electrons + shared electrons from bonds made with less electronegative elements]

O_2 oxid state = 0

H_2O 

eff oxid state = −2 (eff oxid state = 6−(4+4) = −2

Yes this is a redox, oxygen must gain electrons to be reduced

h. How would I prepare 10.00 ml of a 50.00 µM stock of sodium carbonate from a stock of 25.62 mM? Show your work.
M = moles/liter; mM = 10^{-3} M ; µM = 10^{-6} M ; 1 mL = 1 x 10^{-3}L

Stock

$$(25.62 \times 10^{-3} M)(V_1) = (50.00 \times 10^{-6} M)(10.00 mL)$$

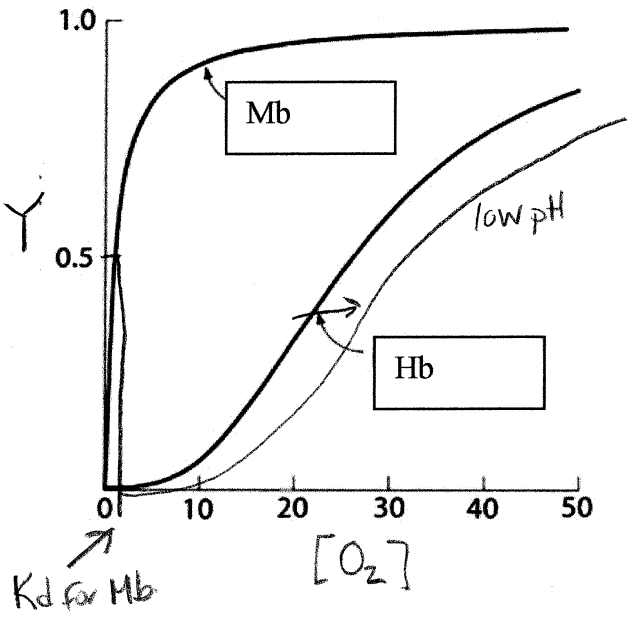
$$V_1 = 0.02000 mL$$

or

$$20.00 \mu L$$

To prepare dilution, take 20.00µL of stock solution and dilute to 10.00 mL with water

2. Oxygen Binding Curve for Myoglobin and Hemoglobin (15 points)



a. The curve associated with Mb binding is precisely described by the formula below. .

$$Y = \frac{[O_2]}{K_D + [O_2]}$$

Give the definition of each of the terms, in this equation: Y = fractional saturation

O_2 = conc. O_2

K_D = dissociation const for O_2 from protein

Label the axes, and show on the graph how you can visually determine Kd for Mb.

b. The Hb binding curve is different in at least two fundamental ways from the curve for Mb. What does the lower value of y for every x mean about Hb's affinity for oxygen? What term would you need to change in the equation above to reflect that change and how would it change (i.e. increase or decrease)?

1. The lower value of Y for every $[O_2]$ for Hb means it binds more weakly, thus allowing transfer from Hb to Mb.

2. Kd term must increase to reflect weaker binding

c. A second way in which the curves differ is in their shape (hyperbolic versus sigmoidal). What does this tell you about the difference between oxygen binding to Mb and Hb?

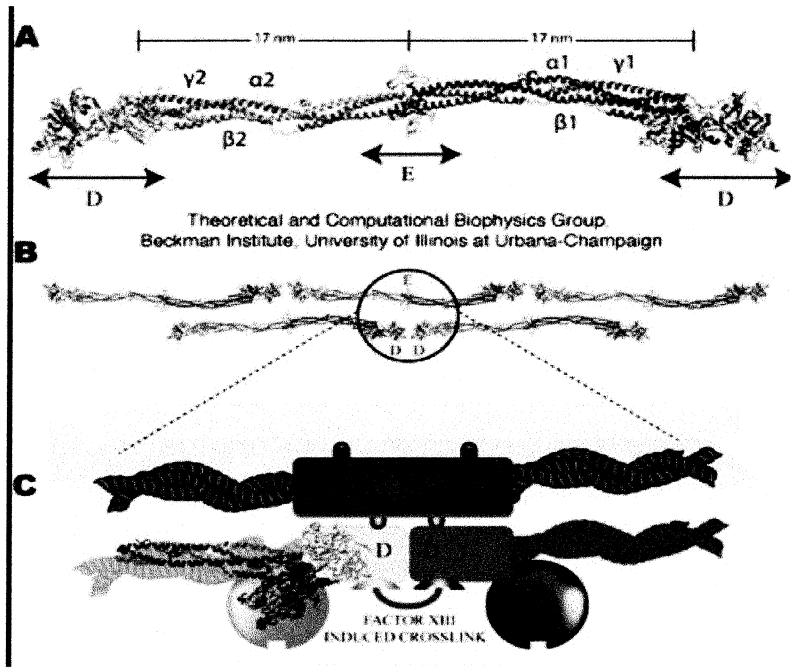
sigmoidal shape for Hb suggests binding affinity of Hb (Kd) is changing as $[O_2]$ increases. This is an example of cooperativity

d. Exercise causes lactic acid to be produced and the pH of the blood to drop. Sketch on the curve above what would happen to the oxygen binding capacity of Hb under these circumstances and explain how that would be beneficial to the exercising person.

At low pH, binding affinity drops and curve shifts to right

3. BioMolecular Structure and Signaling (15 points)

Shown below is the structure of the $\alpha_2\beta_2\gamma_2$ fibrin clotting factor whose cross-linking results in the clots that prevent death from bleeding upon wound formation.



Panel A shows the three different polypeptides α, β, and γ that together make up the protein fibrin. There are two copies of each and together they produce the ~~dimer/trimer/tetramer~~/hexamer (*cross out wrong terms*) shown at top. An unusual aspect of fibrin is the preponderance of a type of secondary structure known as α helix.

The C terminal domains cluster together at each end (labeled D) and the N terminal domains cluster together in the middle (labeled E). Panel B shows how this charge clustering is used to form a clot --- two D domains on different protein interact with one E domain on another protein. The different proteins are held together by crosslinks that are induced by Factor XIII as shown in Panel C

Many clotting factors are activated by cleavage of precursor proteins to form active molecules. Many of the enzymes that cleave the different proteins in the blood clotting cascade contain an active amino acid in their binding site that contains a serine side group.

A second common strategy used by the coagulation factors is activation by binding to Ca^{+2} ions. These ions bind to the protein and cause a conformational change that helps to activate the protein. This is very similar to the Ca^{+2} regulatory protein we studied named calmodulin. An added twist in the blood coagulation cascade is that the proteins don't actually contain a binding site for Ca^{+2} UNTIL they are acted upon by vitamin K, which causes the post-translational modification of the amino acid glu converting it into a super duper Ca^{+2} binder. High levels of Ca^{+2} inside cells is particularly bad because it can cause precipitation with phosphate.

Blood types A, B, AB and O differ by the presence of different types of ~~**fatty acids/nucleic acids**~~/**carbohydrate** (*cross out wrong terms*) molecules on the membrane of the red blood cell.