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5.111 Principles of Chemical Science
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5.111 Principles of Chemical Science
Solutions to selected biology-related questions from problem sets for lectures 21-26

Acid-base problems

A.

A pharmaceutical molecule with antifungal properties is only active when deprotonated and negatively charged (A^-). The protonated state (HA) is inactive. If the pK_a of this drug is 10.0, (a) calculate the ratio of protonated to deprotonated compound at physiological pH (7.4). (b) Is this drug likely to be a useful pharmaceutical agent?

(a) calculate the ratio of protonated to deprotonated compound at physiological pH (7.4). Since we are given both the pH and pK_a of the compound, we can use the Henderson-Hasselbalch equation to solve for the ratio of $[HA]$ to $[A^-]$.

$$\begin{aligned} \text{pH} &= \text{p}K_a - \log([HA] / [A^-]) \\ \log([HA] / [A^-]) &= \text{p}K_a - \text{pH} \\ \log([HA] / [A^-]) &= 10.0 - 7.4 \\ \log([HA] / [A^-]) &= 2.6 \\ ([HA] / [A^-]) &= 398.11 \\ ([HA] / [A^-]) &= \mathbf{400} \text{ (correct sig figs)} \end{aligned}$$

The ratio of protonated (inactive) compound to deprotonated (active) compound is 400 to 1 at physiological pH.

(b) *Is this drug likely to be a useful pharmaceutical agent?*

Since the vast majority of the compound is in the inactive form at physiological pH, it is unlikely to be a useful pharmaceutical agent.* Ideally, most of the compound would be active in the body.

*However, if the active compound is highly potent, it is possible that a small fraction of active compound is sufficient for useful antifungal activity.

B.

Absorption of aspirin (acetylsalicylic acid, $C_9H_8O_4$) into the bloodstream occurs only when the molecule is in its conjugate base form.

(a) *If a patient takes two tablets of aspirin (325 mg each), how many grams of aspirin are available for immediate absorption in the stomach? The pH of the stomach is 1.6, and the pK_a of aspirin is 3.5.*

Since we are given both the pH of the stomach and the pK_a of aspirin, we can use the Henderson-Hasselbalch equation to solve for the ratio of $[HA]$ to $[A^-]$.

$$\begin{aligned} \text{pH} &= \text{p}K_a - \log([HA] / [A^-]) \\ \log([HA] / [A^-]) &= \text{p}K_a - \text{pH} \\ \log([HA] / [A^-]) &= 3.5 - 1.6 \\ \log([HA] / [A^-]) &= 1.9 \\ ([HA] / [A^-]) &= \underline{79} \end{aligned}$$

The ratio of protonated aspirin to its conjugate base is 79 to 1.

So one-eightieth (1/80) of the total aspirin taken will be in the conjugate base form and available for immediate absorption in the stomach:

$$2 \times 325 \text{ mg} \times (1/80) = \underline{8.75} \text{ mg}$$

9 mg

(b) Would you expect more or less aspirin to be absorbed in the small intestine (pH ≈ 7.5) compared to the stomach? Briefly explain your answer (no calculation is required).

More aspirin will be absorbed in the small intestine. The higher pH in the intestine means that more aspirin will be in the conjugate base form and therefore available for absorption.

C. (Modified from problem 11.18 in Atkins 3rd ed)

Phosphate buffers are very useful in biochemical experiments. Your research supervisor asks you to make up a phosphate buffer to carry out kinetic assays on an enzyme:

(a) Determine the ratio of molarities of PO_4^{3-} and HPO_4^{2-} ions required to prepare a phosphate buffer with a pH of 12.0?

(b) What mass of K_3PO_4 must be added to 1.00 L of 0.100 M $\text{K}_2\text{HPO}_4(\text{aq})$ to prepare a buffer solution with a pH of 12.0?

(a) We need to think about what happens when you have a solution of PO_4^{3-} and HPO_4^{2-} in water: $\text{HPO}_4^{2-}(\text{aq}) + \text{H}_2\text{O}(\ell) \rightleftharpoons \text{PO}_4^{3-}(\text{aq}) + \text{H}_3\text{O}^+(\text{aq})$. We can look up the K_a for that reaction in table 10.9 (page 391 in the text), recognizing that we are looking at the ionization of the third proton. The K_a is 2.1×10^{-13} . Now to determine the ratios of ions we can substitute into the Henderson-Hasselbach equation:

$$\text{pH} = \text{p}K_a - \log \frac{[\text{HPO}_4^{2-}]}{[\text{PO}_4^{3-}]}$$

$$12.0 = (-\log(2.1 \times 10^{-13})) - \log \frac{[\text{HPO}_4^{2-}]}{[\text{PO}_4^{3-}]}$$

$$12.0 = 12.68 - \log \frac{[\text{HPO}_4^{2-}]}{[\text{PO}_4^{3-}]}$$

$$0.68 = \log \frac{[\text{HPO}_4^{2-}]}{[\text{PO}_4^{3-}]}$$

$$\frac{[\text{HPO}_4^{2-}]}{[\text{PO}_4^{3-}]} = 10^{0.68}$$

$$\frac{[\text{HPO}_4^{2-}]}{[\text{PO}_4^{3-}]} = 4.79 = 5 \text{ (correct sig figs)}$$

$$\frac{[\text{PO}_4^{3-}]}{[\text{HPO}_4^{2-}]} = 0.2$$

The ratio of HPO_4^{2-} to PO_4^{3-} is 5, and the ratio of PO_4^{3-} to HPO_4^{2-} is 0.2 (don't take off points for significant figures)

(b) We need to realize that we are adding the potassium salt of HPO_4^{2-} , so the concentration of HPO_4^{2-} is 0.100 M, so we can substitute that into the expression we calculated in part (a):

$$\frac{[\text{HPO}_4^{2-}]}{[\text{PO}_4^{3-}]} = 4.8$$

$$\frac{0.100}{[\text{PO}_4^{3-}]} = 4.8$$

$$[\text{PO}_4^{3-}] = 2.09 \times 10^{-2} \text{ M}$$

$$\begin{aligned} \text{Molar mass of } \text{K}_3\text{PO}_4 &= [3(39.098) + 30.974 + 4(15.999)] \text{ g mol}^{-1} \\ &= 212.264 \text{ g mol}^{-1} \end{aligned}$$

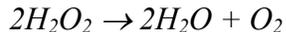
$$\begin{aligned} \text{Mass of } \text{K}_3\text{PO}_4 &= \left(2.09 \times 10^{-2} \frac{\text{mol}}{\text{L}}\right) (212.264 \text{ g mol}^{-1}) (1 \text{ L}) \\ &= 4.4363 \text{ g} \\ &= 4 \text{ g} \end{aligned}$$

We need to add 4 g of K_3PO_4 to 1.0 L. (**don't take off points for significant figures**)

Oxidation-reduction problems

D.

Hydrogen peroxide (H_2O_2) is a harmful and reactive byproduct of metabolism. To prevent H_2O_2 from causing extensive oxidative damage to cells, the enzyme catalase catalyzes the conversion of H_2O_2 to much less reactive molecules, oxygen and water.



Use oxidation numbers to identify which molecules are reduced and/or oxidized in this reaction.

H_2O_2 is both reduced to H_2O (oxidation number of oxygen changes from -1 to -2) **and oxidized** to O_2 (oxidation number changes from -1 to 0).

E.

Oxidative damage of DNA leads to mutation, which can in turn lead to cancer or genetic defects. The redox potentials of the four nucleotides of DNA are listed below. Which nucleotide (A, G, T, C) is the most likely to undergo oxidation? Explain your answer for full credit.

<i>Nucleotide</i>	\mathcal{E} (V)
<i>G</i>	1.33
<i>A</i>	1.42
<i>C</i>	1.60
<i>T</i>	1.70

G is most likely to undergo oxidation. G has the lowest redox potential of the four bases, which indicates that it is the easiest to oxidize

F.

The enzyme known as laccase is a multicopper oxidase that is widely distributed in higher plants and fungi. The $\text{Fe}(\text{CN})_6^{4-}$ complex was used to study the structure of the active site of this enzyme.

(a) Indicate the oxidation number of the central atom in this complex.

Fe is the central atom. Since each of the six cyano (CN^-) groups carries a -1 charge and the total charge of the complex is 4^- , Fe has an oxidation number of 2^+ .

(b) Calculate the d-electron count

The d-electron count of a metal is equal to the group number (from the periodic table) minus the oxidation number of the metal.

The oxidation number of Fe is +2 (see part a)

The group number of Fe is 8

d-electron count = $8 - 2 = 6$

The d-electron count is d^6

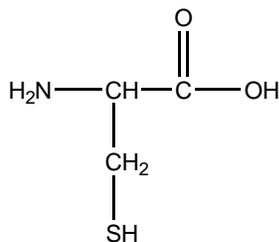
(c) What is the coordination geometry?

The coordination number (CN) is 6, so the geometry is octahedral.

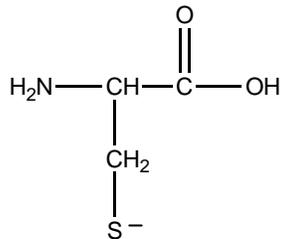
G.

Zinc can act as a Lewis acid, and coordinate amino acids like cysteine by their sulfhydryl (SH) groups. Normally, the sulfhydryl group of cysteine has a pK_a of ~ 8 . However, the interaction with zinc can lower the pK_a of the sulfhydryl group by as much as 4 pH units. Using your knowledge of acid/base chemistry, estimate the approximate ratio of protonated to deprotonated cysteine at neutral pH for (a) free cysteine (pK_a of ~ 8) and

(b) cysteine coordinated to zinc (pK_a of ~ 4). (Since this is an estimate, don't worry about sig figs).



protonated cysteine



deprotonated cysteine

We can treat this like a buffer problem and thus take advantage of the Henderson-Hasselbach equation: $\text{pH} = \text{p}K_a - \log [\text{HA}/\text{A}^-]$

(a) Free cysteine (no zinc present): $\text{p}K_a \sim 8$

$$\text{pH} = \text{p}K_a - \log \frac{[\text{HA}]}{[\text{A}^-]}$$

$$7 = 8 - \log \frac{[\text{HA}]}{[\text{A}^-]}$$

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

When there is no zinc around there is 10 times as much protonated cysteine as there is deprotonated cysteine (activated for nucleophilic attack and therefore the form of cysteine which can partake in chemical reactions).

(b) Cysteine Coordinated to Zinc: $\text{p}K_a \sim 4$

$$\text{pH} = \text{p}K_a - \log \frac{[\text{HA}]}{[\text{A}^-]}$$

$$7 = 4 - \log \frac{[\text{HA}]}{[\text{A}^-]}$$

$$\frac{[\text{HA}]}{[\text{A}^-]} = \frac{1}{1000}$$

When zinc is coordinated to the cysteine there is 1000 times as much deprotonated cysteine as there is protonated cysteine. In this case a much greater portion of the cysteines are deprotonated and ready to partake in a chemical reaction.