10.6: BIOLOGICAL AMINES AND THE HENDERSON-HASSELBALCH EQUATION

OBJECTIVES

1. identify the form that amine bases take within living cells.
2. use the Henderson-Hasselbalch equation to calculate the percentage of a base that is protonated in a solution, given the pK_a value of the associated ion and the pH of the solution.
3. explain why organic chemists write cellular amines in their protonated form and amino acids in their ammonium carboxylate form.

The Henderson-Hasselbalch equation is very useful relating the pKa of a buffered solution to the relative amounts of an acid and its conjugate base. In **Section 20-3**, we used the Henderson-Hasselbalch equation to show that under physiological pH, carboxylic acids are almost completely dissociated into their carboxylate ions.

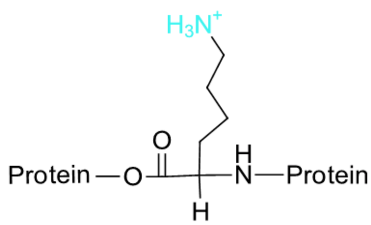
$$\mathrm{pH} = \mathrm{pK_a} + \log\left(\frac{\text{concentration of conjugate base}}{\text{concentration of weak acid}}\right) \quad \text{(Henderson-Hasselbalch equation)}$$

So, what does the side chain of a lysine amino acid residue look like if it is on the surface of a protein in an aqueous solution buffered pH 7.0? Is it protonated or deprotonated? The values in the Henderson-Hasselbalch can be used for an amine with the ammonium salt written as, HA = RNH_3^+, and the amine as being, A^- = RNH_2. With an approximate pK_a of 10.8 for the protonated amine HA, it should be >99% protonated, in the positively-charged, ammonium form:

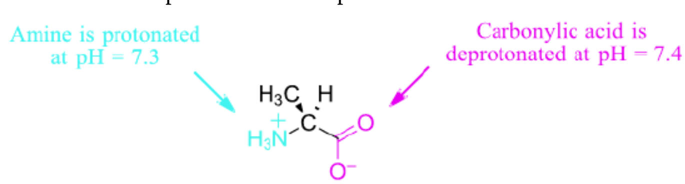
$$7.0 = 10.8 + \log\left(\frac{[\mathrm{RNH_2}]}{[\mathrm{RNH_3^+}]}\right)$$

$$\frac{[\mathrm{RNH_2}]}{[\mathrm{RNH_3^+}]} = 1.6 \times 10^{-4}$$

So, $[\mathrm{RNH_3^+}] \gg [\mathrm{RNH_2}]$ at this pH. Consequently, in an aqueous solution buffered at pH 7, carboxylic acid groups can be expected to be essentially 100% deprotonated and negatively charged (ie. in the carboxylate form), and amine groups essentially 100% protonated and positively charged (i.e., in the ammonium form).



Alcohols are fully protonated and neutral at pH 7, as are thiols. The imidazole group on the histidine side chain has a pK_a near 7, and thus exists in physiological solutions as mixture of both protonated and deprotonated forms.



Alanine
(Amino Acid)

? EXERCISE 10.6.1

Would you expect an aromatic hetererocycle, pyrrole, to be protonated at pH = 7.3? Use the Henderson-Hasselbalch equation to determine your answer. pKa of protonated pyrrole is 0.4.

Answer

$$7.3 = 0.4 + \log\left(\frac{[\mathrm{RNH_2}]}{[\mathrm{RNH_3^+}]}\right)$$

$$\frac{[\mathrm{RNH_2}]}{[\mathrm{RNH_3^+}]} = 7.9 \times 10^6$$

So, $[\mathrm{RNH_2}] \gg [\mathrm{RNH_3^+}]$. Thus pyrrole would be almost completely unprotonated at pH = 7.