Zwitterion behavior of an amino acid -- work with concentration of H^+ rather than pH, and work with K rather than pK.

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An amino acid acts as a zwitterion, i.e., it can be either:

1) a positively charged cation (A^+) in an acid solution,
2) a negatively charged anion (A^-) in an alkaline solution, or
3) a neutral molecule (A) at the isoelectric point.

Zwitterion Reaction:

NH_3^+-CHR-COOH $\longrightarrow$ NH_3^+-CHR-COO^- + H^+

NH_3^+-CHR-COO^- $\longrightarrow$ NH_2-CHR-COO^- + H^+

which can be abbreviated as:

$A^+ \longrightarrow A + H^+ \qquad K_1$

$A \longrightarrow A^- + H^+ \qquad K_2$

The dissociation constants for these steps are K_1 and K_2, which are defined as:

Given

$$K_1 = \frac{A_{neutral} \cdot H}{A_{cation}} \qquad K_2 = \frac{A_{anion} \cdot H}{A_{neutral}}$$

Remember that "p" means "-log", e.g., $pH = -\log(H)$ $\quad pK_1 = -\log(K_1)$ $\quad pK_2 = -\log(K_2)$

Conservation of mass (i.e., all fractions add up to unity): $A_{cation} + A_{neutral} + A_{anion} = 1$

We have six equations and we can solve for any six variables. Below, we shall let Mathcad find how amino acid exists in a solution as a function of pH, pK_1 and pK_2 (via |Math|SmartMath|).

$$\mathrm{Find}(A_{cation}, A_{neutral}, A_{anion}, H, K_1, K_2) \rightarrow \begin{bmatrix} \dfrac{\exp(-pH \cdot \ln(10))^2}{\left(\exp(-pK_1 \cdot \ln(10)) \cdot \exp(-pK_2 \cdot \ln(10)) + \exp(-pK_1 \cdot \ln(10)) \cdot \exp(- \cdots\right.} \\ \exp(-pK_1 \cdot \ln(10)) \cdot \dfrac{\exp(-pH \cdot \ln(10) \cdots}{\left(\exp(-pK_1 \cdot \ln(10)) \cdot \exp(-pK_2 \cdot \ln(10)) + \exp(-pK_1 \cdot \ln(1 \cdots\right.} \\ \exp(-pK_1 \cdot \ln(10)) \cdot \dfrac{\exp(-pK_2 \cdot \ln(10 \cdots}{\left(\exp(-pK_1 \cdot \ln(10)) \cdot \exp(-pK_2 \cdot \ln(10)) + \exp(-pK_1 \cdot \ln(1 \cdots\right.} \\ \exp(-pH \cdot \ln(10)) \\ \exp(-pK_1 \cdot \ln(10)) \\ \exp(-pK_2 \cdot \ln(10)) \end{bmatrix}$$

The expressions are correct, but too messy because Mathcad likes to work in natural log rather than common log.

Let's re-solve the problem. This time, we let Mathcad find how amino acid exists in a solution as a function of H, K_1 and K_2. Now, we have three equations to solve for three variables.

Given

$$K_1 = \frac{A_{neutral} \cdot H}{A_{cation}} \qquad K_2 = \frac{A_{anion} \cdot H}{A_{neutral}} \qquad A_{cation} + A_{neutral} + A_{anion} = 1$$

$$\mathrm{Find}\left(A_{cation}, A_{neutral}, A_{anion}\right) \rightarrow \begin{bmatrix} \dfrac{H^2}{\left(K_1 \cdot K_2 + K_1 \cdot H + H^2\right)} \\ K_1 \cdot \dfrac{H}{\left(K_1 \cdot K_2 + K_1 \cdot H + H^2\right)} \\ K_1 \cdot \dfrac{K_2}{\left(K_1 \cdot K_2 + K_1 \cdot H + H^2\right)} \end{bmatrix}$$

Copy the above analytical formula to the functions below.

$$A_{cation}\left(H, K_1, K_2\right) := \frac{H^2}{K_1 \cdot K_2 + K_1 \cdot H + H^2}$$

$$A_{neutral}\left(H, K_1, K_2\right) := \frac{K_1 \cdot H}{K_1 \cdot K_2 + K_1 \cdot H + H^2}$$

$$A_{anion}\left(H, K_1, K_2\right) := \frac{K_1 \cdot K_2}{K_1 \cdot K_2 + K_1 \cdot H + H^2}$$

Remember that "p" means "-log", e.g., $pH = -\log(H)$ $pK = -\log(K)$

Given the "p" values, we can calculate H and K from the pH and pK values. $H = 10^{-pH}$ $K = 10^{-pK}$

Example: Alanine has the following dissociation constants: $pK_1 := 2.34$ $pK_2 := 9.69$

$K_1 := 10^{-pK_1}$ $K_2 := 10^{-pK_2}$

in a neutral solution: $pH := 7$ $H := 10^{-pH}$

$A_{cation}(H, K_1, K_2) = 2.183 \cdot 10^{-5}$

$A_{neutral}(H, K_1, K_2) = 0.998$ ← Amino acid exists mostly as a neutral molecule.

$A_{anion}(H, K_1, K_2) = 0.002$

in an acid solution: $pH := 1$ $H := 10^{-pH}$

$A_{cation}(H, K_1, K_2) = 0.956$ ← Amino acid exists mostly as a cation A^+.

$A_{neutral}(H, K_1, K_2) = 0.044$

$A_{anion}(H, K_1, K_2) = 8.925 \cdot 10^{-11}$

in an alkaline solution: $pH := 11$ $H := 10^{-pH}$

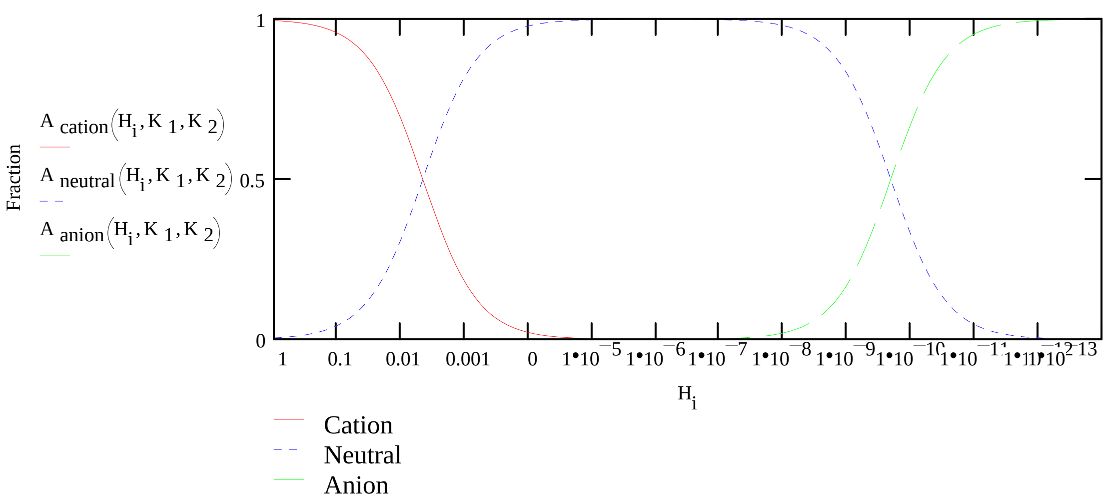
$A_{cation}(H, K_1, K_2) = 1.021 \cdot 10^{-10}$

$A_{neutral}(H, K_1, K_2) = 0.047$

$A_{anion}(H, K_1, K_2) = 0.953$ ← Amino acid exists mostly as an anion A^-.

Plot H dependence for a range of H values, starting from $H_{start} := 1$ over a range of $decade := 13$

Number of H points: $N := 10 \cdot decade$ $i := 0 .. N$ $H_i := H_{start} \cdot 10^{-decade \cdot \frac{i}{N}}$



At $pH=(pK_1+pK_2)/2$ (i.e., midway between two pK's), the zwitterion is mostly neutral. At $pH=pK_1$ or $pH=pK_2$ the fraction of the respective species involved is about half.

$$\text{pH}\cdot\ln(10)) + \exp(-\,\text{pH}\cdot\ln(10))^2\Big)$$

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