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Chapter 4—Amino Acids

The building blocks of proteins

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Amino Acid Structure

- **Alpha** amino acids-typical structure
  - See Figure 4.1
- Amide bond called **peptide** bond
  - See Figure 4.2
- Amino acids differ in **R-group**
  - Structures of the 20 common amino acids
  - See Figure 4.3

(**LEARN structures, names, and abbreviations!!**)

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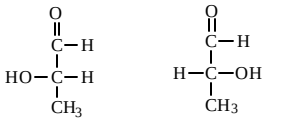
Amino Acid Stereochemistry

- Natural amino acids are L
  - Configuration based on glyceraldehyde
  - Fischer projection convention:



L glyceraldehyde (l-glyceraldehyde)

D glyceraldehyde (d-glyceraldehyde)

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Amino Acid Stereochemistry, con't

- Cahn, Ingold, Prelog System
  - R, S configuration (Web site explanation)
  - L glyceraldehyde is S
  - D glyceraldehyde is R
  - L alanine is S
    - See Figure Page 99
- All amino acids are S except:
  - Glycine (no chiral carbon)
  - Cysteine (why?)

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Amino Acids are Polyprotic

- Neutral Side Chain (See Fig. 4.7)
- Acidic Side Chain (See Fig. 4.8a)
- Basic Side Chain (See Fig. 4.8b)

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pK's of Amino Acid Groups

- See Table 1 for actual values
- Approximate values:
  - Alpha carboxyl ~2
  - Alpha amino ~9.5
  - Side chain carboxyl ~4
  - His side chain ~6
  - Cys side chain ~8.5
  - Lys and Tyr side chain ~10
  - Arg side chain ~12

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Structure Effect on pK's

- Carboxyl group
  - Alkyl carboxyl ~4.5
  - Side chain carboxy ~4
  - Alpha carboxyl ~2
  - Peptide terminal carboxy ~3
- Amino group
  - Alkyl amino ~10.5
  - Side chain amino ~10.5
  - Alpha amino ~9.5
  - Peptide terminal amino~8.

Demonstrate with structures how electron withdrawing properties of neighboring functional groups affects the pK's.

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Isoionic Point

- When Σ neg.charges = Σ pos. charges
- pH = $(pK_a + pK_b)/2$ where
  - pK_a is for protonation of neutral species
  - pK_b is for deprotonation of neutral species
- Illustration for neutral, acidic and basic amino acids
- Illustration for peptides

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Determining Charge on a Peptide

- Note pK's of all functional groups
- Calculate charge when totally protonated
- Determine number of dissociable protons, and charge on each intermediate
- Determine pK's involving neutral species
- pI is average of these pK's
  - pH>pI, peptide is negatively charged
  - pH<pI, peptide is positively charged

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Determining Charge on a Peptide, con't.

- Consider the peptide **ACKRDM**
- Estimate its pI
- Estimate its charge at
  - pH = 4.0, pH = 7.0, and pH = 10.0
- How to proceed?
- First, determine the protonatable groups and their pK's

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Functional Groups of ACKRDM

- Peptide amino terminal, pK ~ 8
- Cysteine side chain, pK ~ 8.5
- Lysine side chain, pK ~ 10
- Arginine side chain, pK ~ 12
- Aspartate side chain, pK ~ 4
- Peptide carboxy terminal, pK ~ 3

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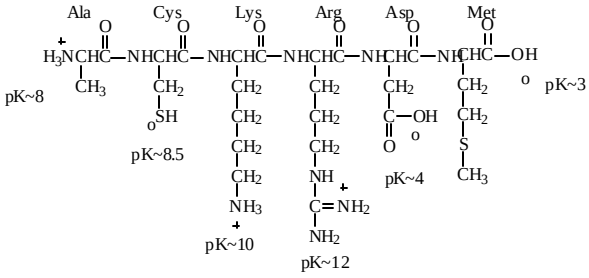
Charge of Fully Protonated ACKRDM



Total charge of fully protonated form = +3

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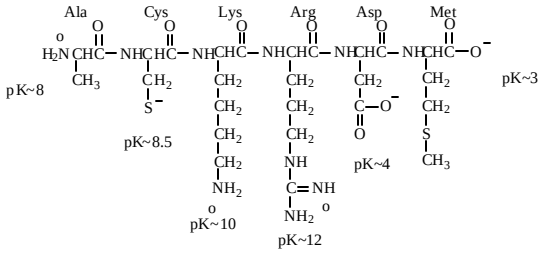
Charge of Fully Unprotonated ACKRDM



Total charge of fully unprotonated form = -3

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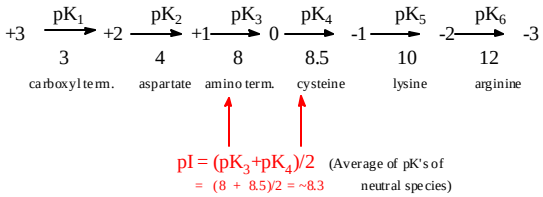
Dissociation Steps for ACKRDM



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ACKRDM Charge at various pH's)

Group	pH = 4.0	pH = 7.0	pH = 10.0
Amino Term.	+1	~+0.9	~+0.03
Cysteine	~0	~-0.03	~-0.97
Lysine	+1	+1	~+0.5
Arginine	+1	+1	~+.99
Aspartate	~-0.5	-1	-1
Carbox. Term.	~-0.9	-1	-1
Total	~+1.6	~+0.9	~-1.5

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Other Properties of Amino Acids

- Ultraviolet Spectra (See Figure 4.15)
- Reactions of Carboxyl Group (See Figure 4.9a)
- Reactions of Amino Group (See Figure 4.9b)
- Ninhydrin Reaction (See Figure 4.10)
- Reactions of Cysteine SH (See Figure 4.11a and 4.11b)
- ^{13}C Chemical Shifts with pH (See Figure 4.17)

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Chromatographic Separation of Amino Acids

- Ion Exchange Chromatography
  - Cation Exchange Resin
    - Structure (See Figure 4.18a)
    - Operation (See Figure 4.19)
  - Anion Exchange Resin (See Figure 4.18b)
- Analysis on Ion Exchange
  - See Figure 4.21a
  - See Figure 4.21b
- HPLC Reversed Phase Chromatography of Chemical Derivative
  - See Figure 4.22