CHEM 204
Introductory Biochemistry

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Text

- Lehninger Principles of Biochemistry
  - 5th edition
  - D.L. Nelson and M.M. Cox
- Website

Organic Chemistry

- Dates back to 1770's
  - unexplainable differences between molecules isolated from living (organic) sources and those derived from minerals
- Differences attributed to a vital force until 1820's when inorganic converted to organic
- Characteristic of organics is that they all contain carbons
  - Each has unique chemical and physical properties based upon their functional group.

Biochemistry

- Dates to 1897
- Buchner demonstrated while sugar is fermented by yeast, it could also be fermented by the juices of yeast
- Simplest definitions
  - Chemistry of life
  - Collection of organic reactions which occur within a cell

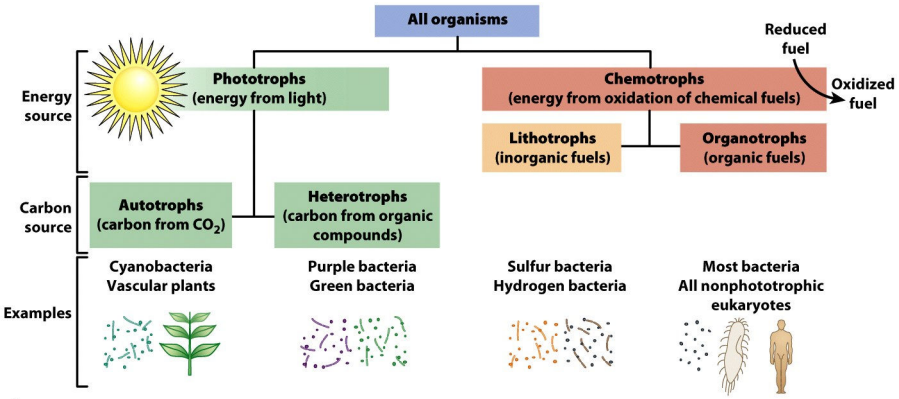

Figure 1-5
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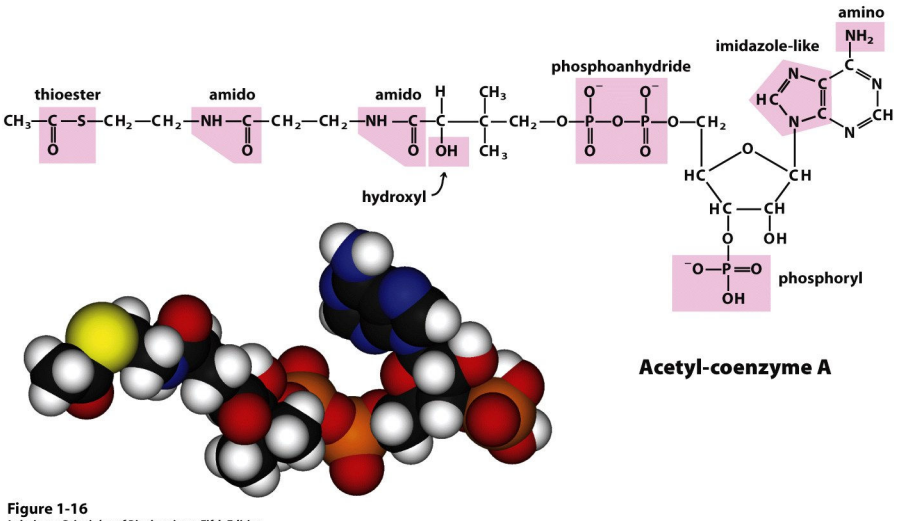

Figure 1-16
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Things/Definitions to remember from prior chemistry

- G – Gibbs free energy
  - ΔG – free energy change
    - must be negative (-) for a process to be spontaneous
- H – enthalpy
  - Making/breaking bonds
  - ΔH – enthalpy change
    - Is positive (+) for melting and evaporation
- S – entropy
  - Randomness
- Remember : $\Delta G = \Delta H - T\Delta S$
- Solvent; solute
- Atomic structure (nucleus, electron)
- Covalent, non-covalent

Biomolecules

- Amino Acids
  - proteins
- Carbohydrates
  - polysaccharides
- Nucleotides
  - Nucleic acids
- Lipids

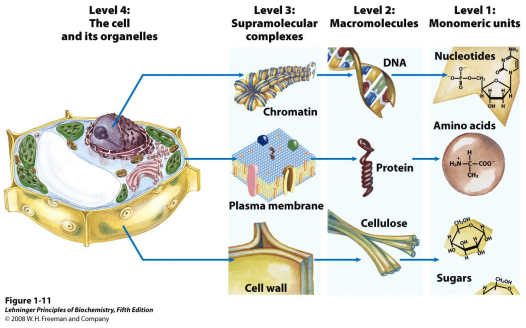

Figure 1-11
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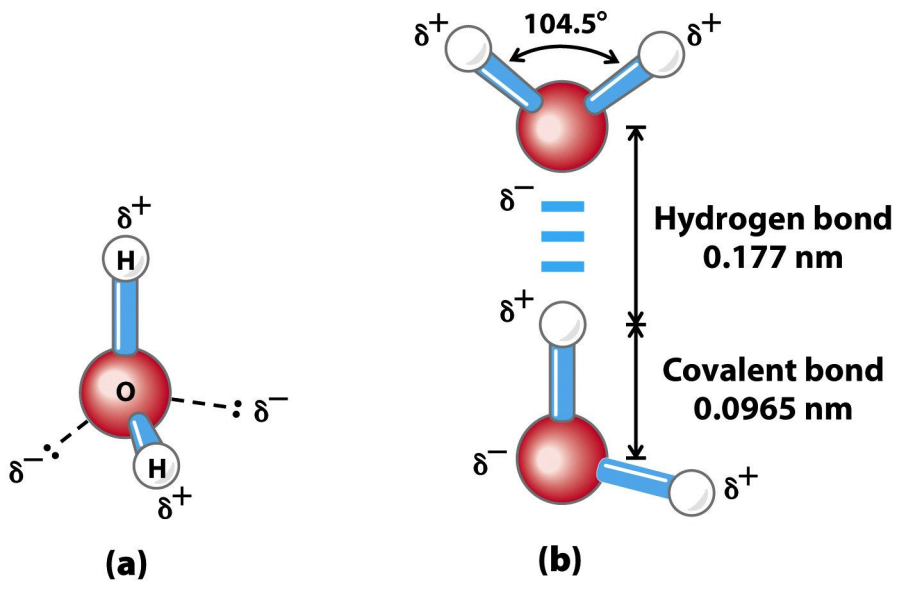
Aqueous Systems

- Everything in biochemistry occurs in aqueous (water-based) systems
- Higher melting point, boiling point, heat of vaporization than other common solvents of similar molecular weight
- Properties due to interactions between adjacent molecules of water and with the solutes dissolved into it



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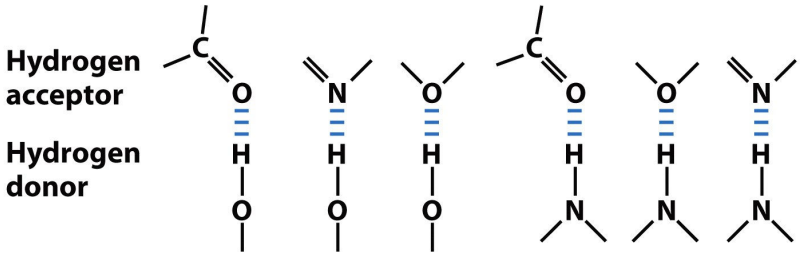

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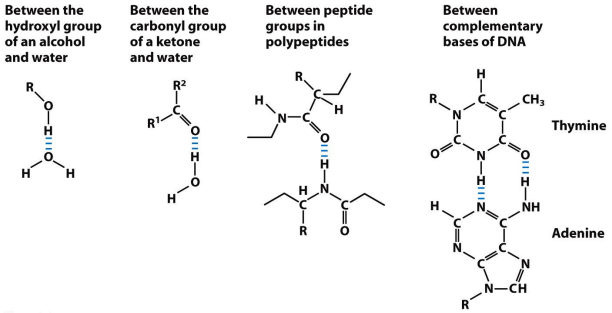

Figure 2-4
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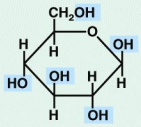
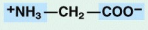
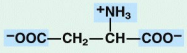
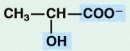
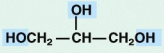
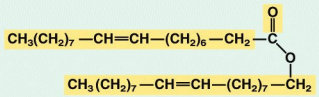
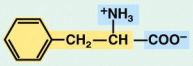
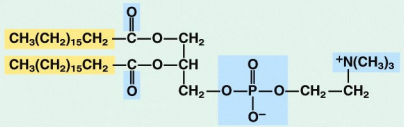
TABLE 2–2 Some Examples of Polar, Nonpolar, and Amphipathic Biomolecules (Shown as Ionic Forms at pH 7)

Polar	
Glucose	
Glycine	
Aspartate	
Lactate	
Glycerol	
Nonpolar	
Typical wax	
Amphipatic	
Phenylalanine	
Phosphatidylcholine	

Polar groups Nonpolar groups

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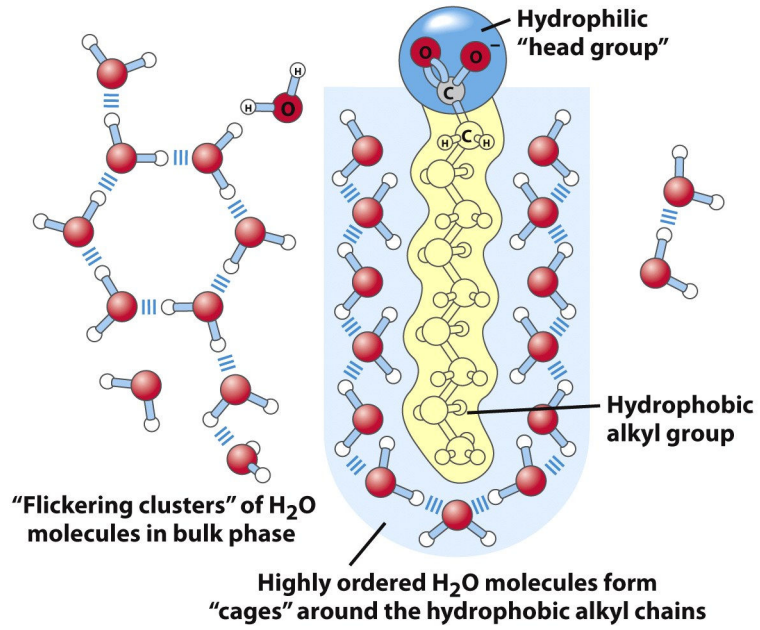

Figure 2-7a
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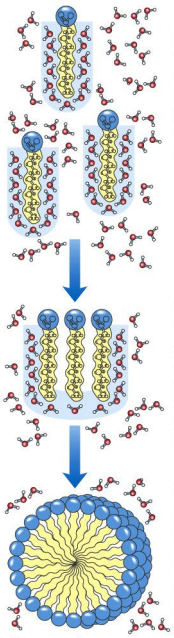

Dispersion of lipids in H_2O

Each lipid molecule forces surrounding H_2O molecules to become highly ordered.

Clusters of lipid molecules

Only lipid portions at the edge of the cluster force the ordering of water. Fewer H_2O molecules are ordered, and entropy is increased.

Micelles

All hydrophobic groups are sequestered from water; ordered shell of H_2O molecules is minimized, and entropy is further increased.

Figure 2-7b
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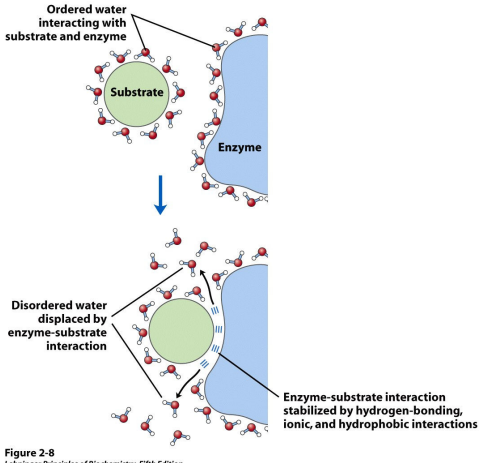

Figure 2-8
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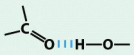
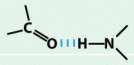
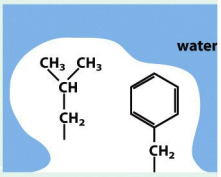
TABLE 2–5 Four Types of Noncovalent ("Weak") Interactions among Biomolecules in Aqueous Solvent

Hydrogen bonds	
Between neutra groups	
Between peptide bonds	
Ionic interactions	
Attraction	
Repulsion	
Hydrophobic interactions	
Van der Waals interactions	Any two atoms in close proximity

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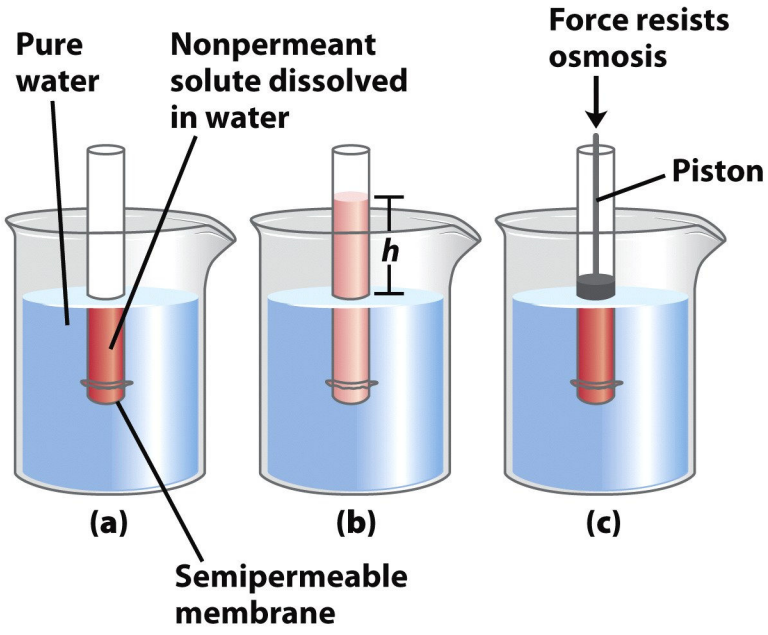

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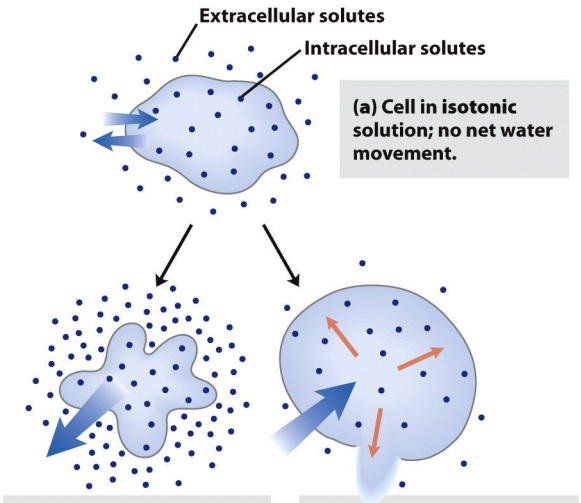

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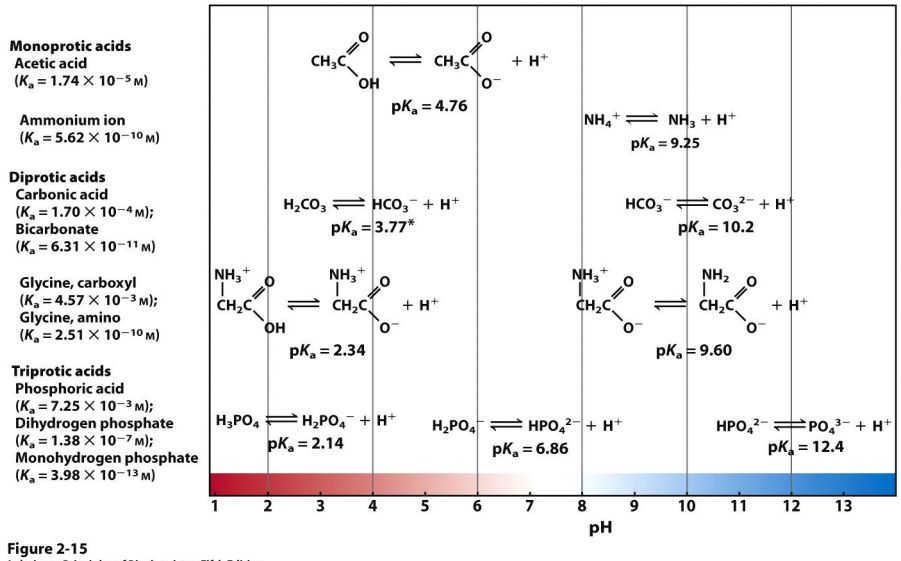

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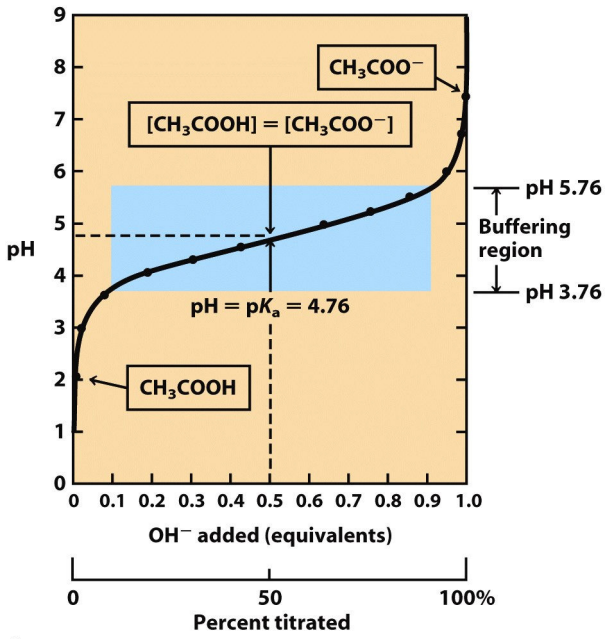

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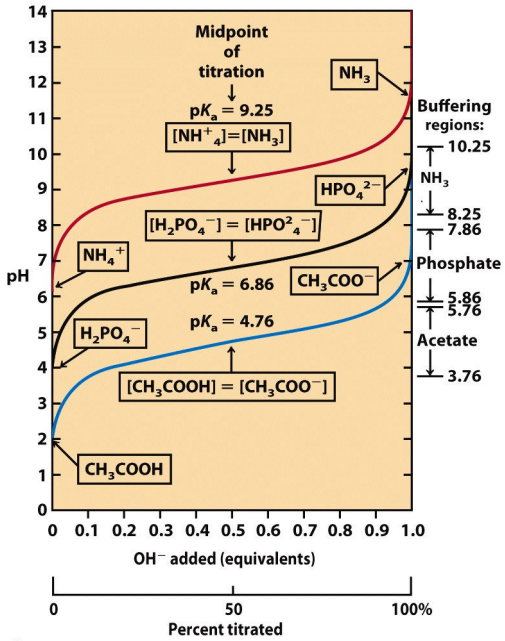

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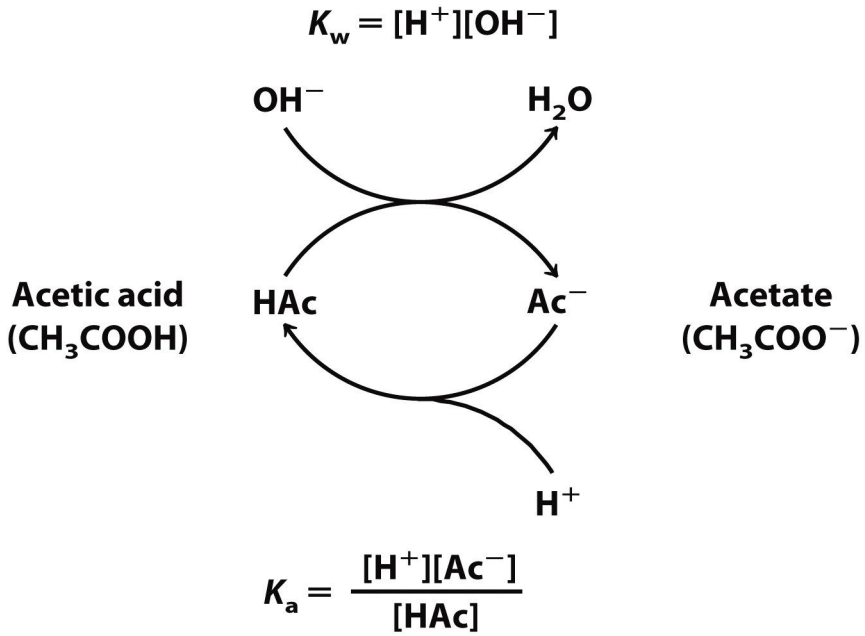

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K_{eq} and Henderson-Hasselbach

- Definition of pH
- Henderson-Hasselbach equation
  - Defined as: $pH=pK_a + \text{Log } [A^-]/[HA]$

Examples

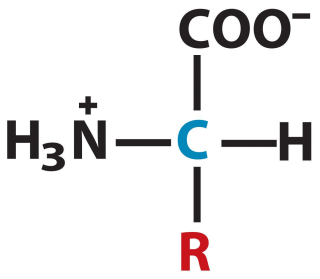
- What is the pH of a solution containing 0.2 M acetic acid (pK_a=4.7) and 0.1 M NaAcetate?
- A weak acid (HA) has a pK_a of 5.0. If 1 mol of this acid and 0.1 mol of NaOH were dissolved in 1L of H2O, what would the final pH be?

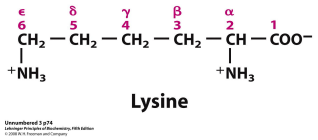
Proteins

- are the most abundant biomolecule
- great variety of functions
  - **Structural**
    - Collagen- skin and connective tissue (tendons)
    - Keratin- hair,fingernails
    - Silk
  - **Catalysts:** These are enzymes.
    - Hexokinase
    - trypsin
  - **Movement:** Muscle Proteins, flagella & cilia
    - skeletal
    - smooth muscle (digestive tract)
    - cardiac tissue
  - **Transport of other biomolecules:**
    - O_2 transport- hemoglobin in blood and myoglobin in muscle tissue
    - HDL/LDL –cholesterol transport

Amino Acids

- Monomeric unit of proteins
- Ubiquitous
  - 20 commonly found
- 4 different groups bound to the C_α
  - an amino group ($-NH_2$)
  - carboxylic acid (-COOH)
  - Proton (H)
  - Side-chain or R-group
- Carbon called the C_α
  - numbering from the carboxyl group
  - is a chiral center
- Named for their functional groups
- Nomenclature based upon historical basis
  - 3-letter and 1-letter abbreviations





Lysine

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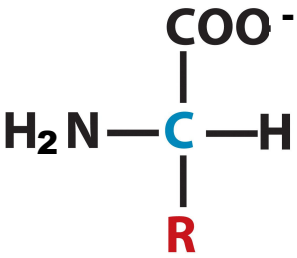
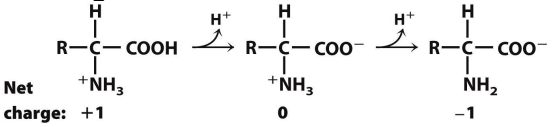
Amino acids are all Zwitterions

- Zwitterion
  - From German “hybrid”
  - Dipolar ion due to intramolecu acid-base reaction
- Net charge is 0
- Amphoteric
  - can act as either acid or base
  - COOH proton donor; NH_2 proton acceptor





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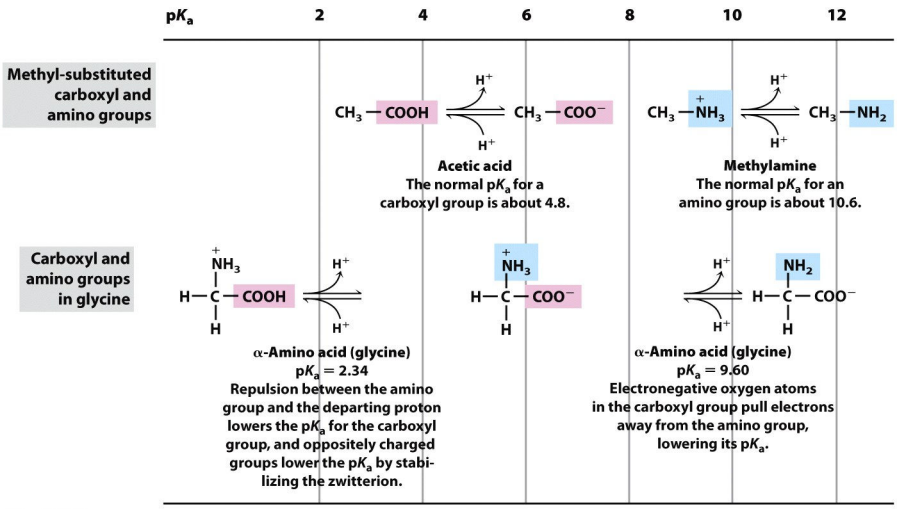

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Titration Curve

- Dipolar measures specific pK_a for ionizable groups
  - pKa defined as the pH at which 50% of each form is present
- **Isoelectric point (pI)** is the pH where the amino acid is neutral (net charge = 0)
  - For amino acids with a single carboxylic acid and a single amino group, the isoelectric point is the average of pK_1 and pK_2
- Specific titration curves for each amino acid

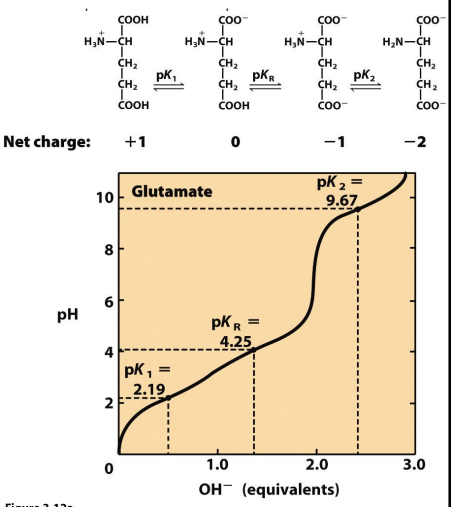

Figure 3-12a
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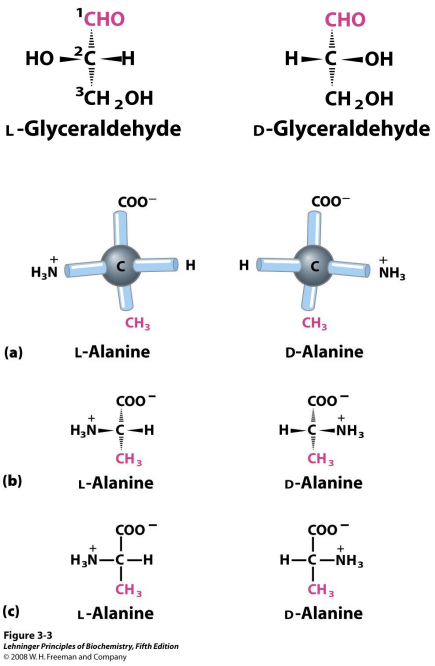
Stereoisomers

- Use fisher Convention of assigning D,L configuration
- D, L distinct from *d,l* and refers only to the absolute configuration about the chiral carbon
- Biologically relevant isomers are the L-stereoisomers



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Amino Acid Side Chains : R group

- Names are historical and non-systematic
- Twenty standard R groups differing in
  - Size
  - shape
  - charge
  - hydrogen-bonding capacity
  - hydrophobic character
  - chemical reactivity

Things you should know

- Be able to draw the structure of one amino acid from each of the 5 groups
- If given the structure of an amino acid, be able to place the amino acid into one of the 5 groups
- If given the structure of an amino acid, be able to give its name
- Know all of the 3-letter abbreviated names
  - Table 3.1 (5.1) gives the 3-letter abbreviated names and single letter codes for the 20 common amino acids

TABLE 3–1 Properties and Conventions Associated with the Common Amino Acids Found in Proteins

Amino acid	Abbreviation/ symbol	M_r*	pK_a values: pK_1 (—COOH)	pK_2 ($—NH_3^+$)	pK_R (R group)	pI	Hydropathy index†	Occurrence in proteins (%)‡
Nonpolar, aliphatic R groups								
Glycine	Gly G	75	2.34	9.60		5.97	−0.4	7.2
Alanine	Ala A	89	2.34	9.69		6.01	1.8	7.8
Proline	Pro P	115	1.99	10.96		6.48	1.6	5.2
Valine	Val V	117	2.32	9.62		5.97	4.2	6.6
Leucine	Leu L	131	2.36	9.60		5.98	3.8	9.1
Isoleucine	Ile I	131	2.36	9.68		6.02	4.5	5.3
Methionine	Met M	149	2.28	9.21		5.74	1.9	2.3
Aromatic R groups								
Phenylalanine	Phe F	165	1.83	9.13		5.48	2.8	3.9
Tyrosine	Tyr Y	181	2.20	9.11	10.07	5.66	−1.3	3.2
Tryptophan	Trp W	204	2.38	9.39		5.89	−0.9	1.4
Polar, uncharged R groups								
Serine	Ser S	105	2.21	9.15		5.68	−0.8	6.8
Threonine	Thr T	119	2.11	9.62		5.87	−0.7	5.9
Cysteine§	Cys C	121	1.96	10.28	8.18	5.07	2.5	1.9
Asparagine	Asn N	132	2.02	8.80		5.41	−3.5	4.3
Glutamine	Gln Q	146	2.17	9.13		5.65	−3.5	4.2
Positively charged R groups								
Lysine	Lys K	146	2.18	8.95	10.53	9.74	−3.9	5.9
Histidine	His H	155	1.82	9.17	6.00	7.59	−3.2	2.3
Arginine	Arg R	174	2.17	9.04	12.48	10.76	−4.5	5.1
Negatively charged R groups								
Aspartate	Asp D	133	1.88	9.60	3.65	2.77	−3.5	5.3
Glutamate	Glu E	147	2.19	9.67	4.25	3.22	−3.5	6.3

*M_r values reflect the structures as shown in Figure 3–5. The elements of water (M_r 18) are deleted when the amino acid is incorporated into a polypeptide.

†A scale combining hydrophobicity and hydrophilicity of R groups. The values reflect the free energy (ΔG) of transfer of the amino acid side chain from a hydrophobic solvent to water. This transfer is favorable ($\Delta G <$ 0; negative value in the index) for charged or polar amino acid side chains, and unfavorable ($\Delta G >$ 0; positive value in the index) for amino acids with nonpolar or more hydrophobic side chains. See Chapter 11. From Kyte, J. & Doolittle, R.F. (1982) A simple method for displaying the hydropathic character of a protein. *J. Mol. Biol.* **157,** 105–132.

‡Average occurrence in more than 1,150 proteins. From Doolittle, R.F. (1989) Redundancies in protein sequences. In *Prediction of Protein Structure and the Principles of Protein Conformation* (Fasman, G.D., ed.), pp. 599–623, Plenum Press, New York.

§Cysteine is generally classified as polar despite having a positive hydropathy index. This reflects the ability of the sulfhydryl group to act as a weak acid and to form a weak hydrogen bond with oxygen or nitrogen.

Table 3-1
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Classifications

- Based upon charge at pH 7.0
- Classifications
  - Non-polar aliphatic R groups
  - Aromatic
  - Polar, Uncharged
  - Positively charged (basic)
  - Negatively charged (acidic)

Non-polar aliphatic R groups

- Carbon chain participates in hydrophobic interactions
  - Gly, Ala, Pro, Val, Leu, Ile, Met
  - G, A, P, V, L, I , M
- Glycine only non-chiral amino acid
- Met has thioether group
- Pro is technically not an amino acid
  - imino acid due to cyclic structure

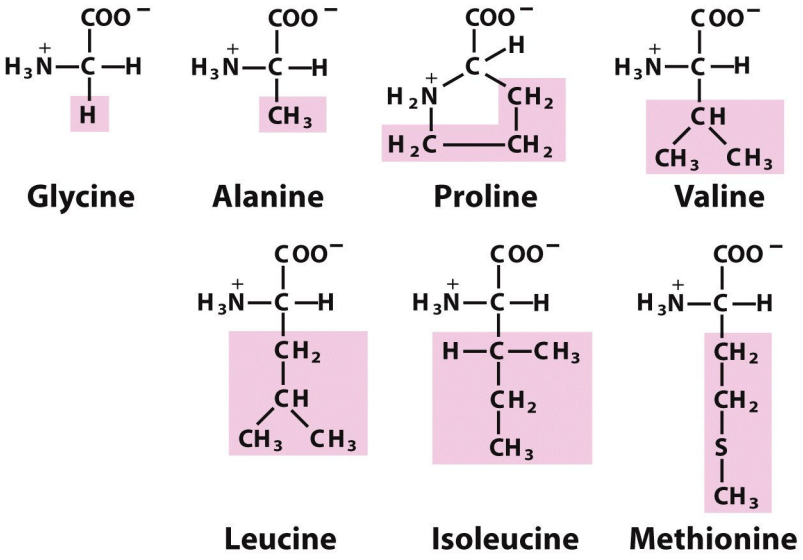

Figure 3-5 part 1
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Aromatic Amino Acids

- Contain an aromatic group
  - Phe, Tyr, Trp
  - F, Y, W
- Relatively hydrophobic (non-polar), though Tyr can participate in hydrogen bonds
- Are UV absorbers (Y&W more than F)

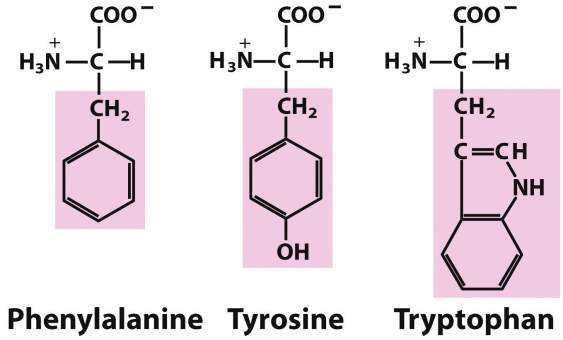

Figure 3-5 part 2
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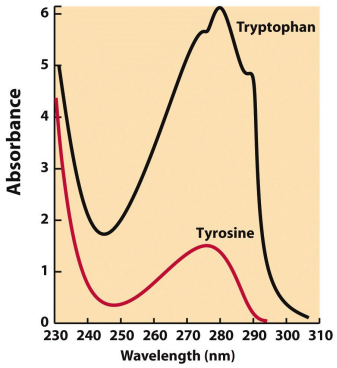

Figure 3-6
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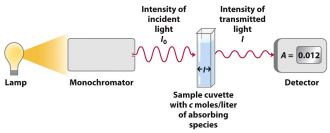

Box 3-1 Figure 1
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Polar, Uncharged

- Are more hydrophilic as they can form H-bonds
  - Thr, Cys, Asn, Gln, Ser
  - T, C, N, Q, S
- Cys special case - ability to form di-sulfides; a covalent bond
  - the disulfide is non-polar

Polar, uncharged R groups

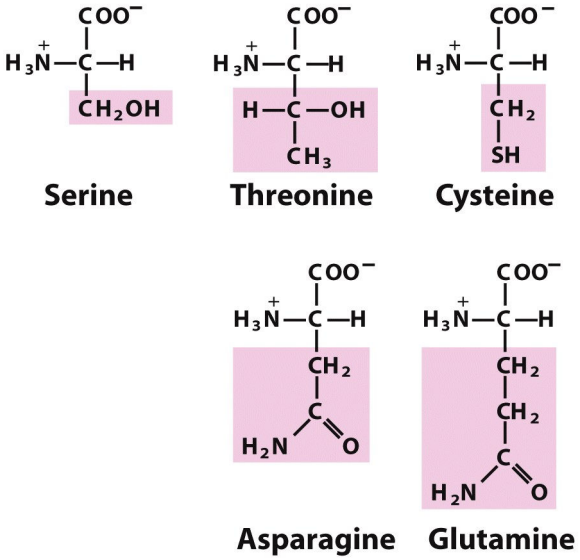

Figure 3-5 part 3
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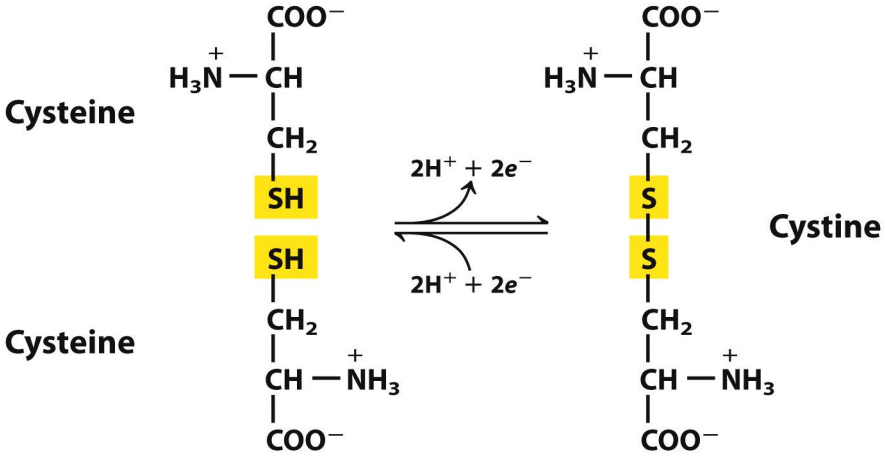

Figure 3-7
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Positively charged (basic)

- Have ability to accept proton
  - Lys, His, Arg
  - K, H, R
- His is only ionizable group at a neutral pH
  - pI of 6.0
- Are positively charged at neutral pH

Positively charged R groups

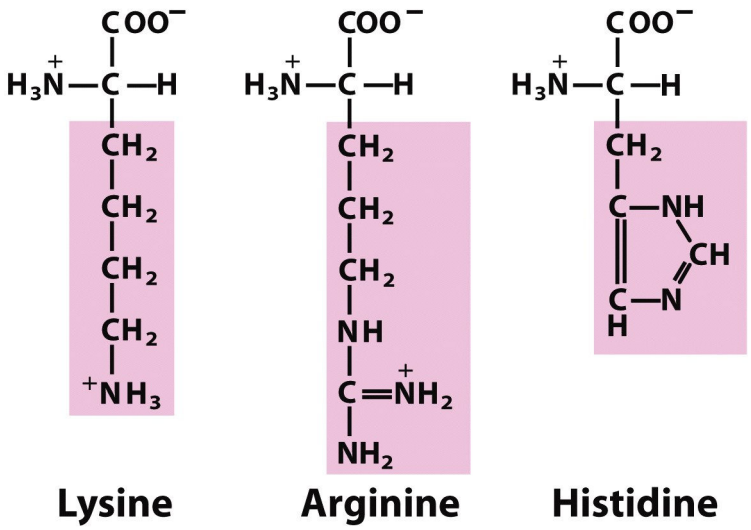

Figure 3-5 part 4
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Negatively charged (acidic)

- Donate protons
  - Asp, Glu
  - D, E
- Second carboxyl group on side chain of amino acid

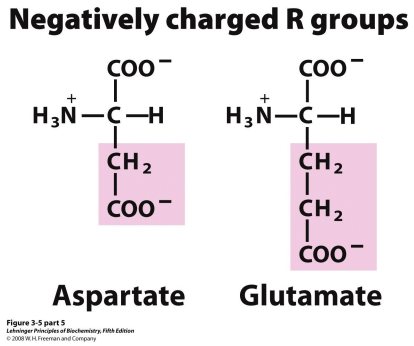

Figure 3-5 part 5
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Non-standard/uncommon amino acids

- can be metabolic intermediates, not found in proteins
  - Ornithine and citrulline
- can be made by modification of common residues incorporated in chain
- can be utilized as neurotransmitters
- selenocystine special as it is coded for in genome

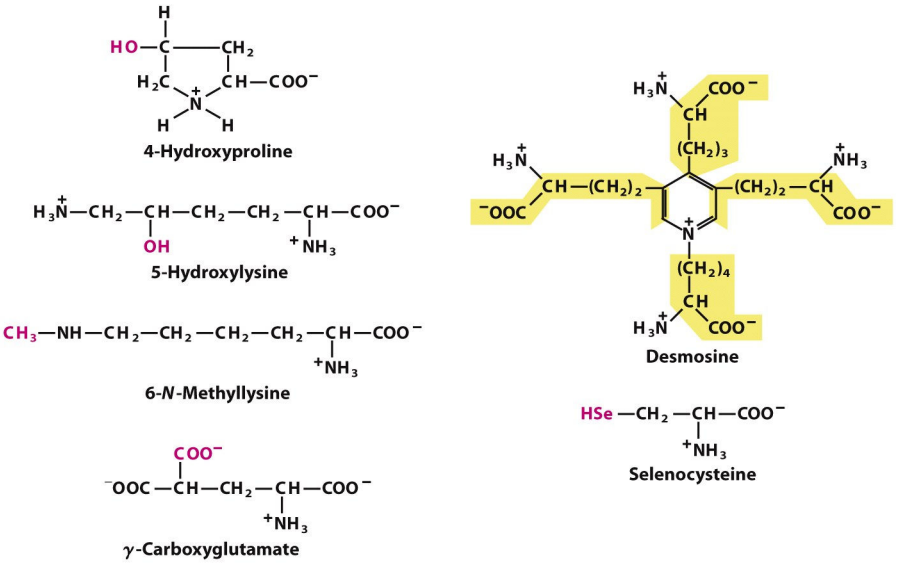

Figure 3-8a
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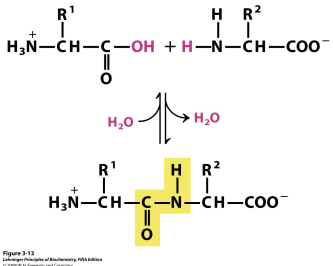
Peptides and Proteins

- two amino acids joined together is a dipeptide
- Bond formed between the carboxyl of one amino acid and amino of another amino acid in a dehydration reaction
  - Amino acid of 2nd to carboxyl of 1st amino acid



- Covalent bond formed
  - called a peptide bond
- reaction is NOT spontaneous under standard conditions
  - $t_{1/2}$ for bond is approx 7 yrs
- Order of amino acids is important
  - Thr-Asp-Ala vs. Ala-Thr-Asp (TEA vs ATE)

Writing Conventions

- NH_2 (NH_3^+)on left, -COOH (COO^-)on right
- Top to bottom of page
- NH_3^+ free is N-terminus
- COO^- free is C-terminus

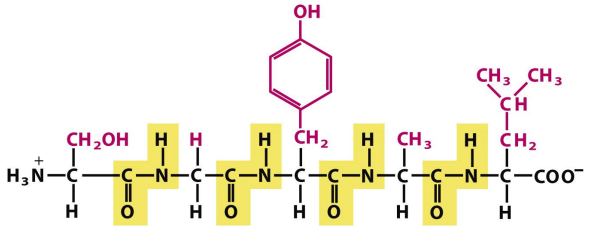


Figure 3-14
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Polymers are peptides

- length gives different names
  - Oligopeptides
    - i.e. di-, tri-, tetra-
    - generally less than 15 or 20
  - Polypeptides
    - <50 residues
    - < 10000MW)
  - Proteins
    - <50 residues,
    - >10000MW

Protein Structure

- four levels found in proteins
  - Primary
  - Secondary
  - Tertiary
  - Quaternary
- describes the conceptual hierarchy

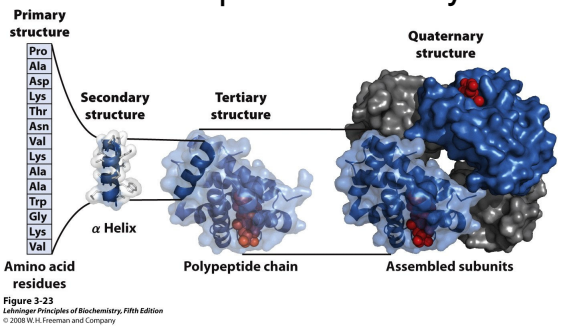

Figure 3-23
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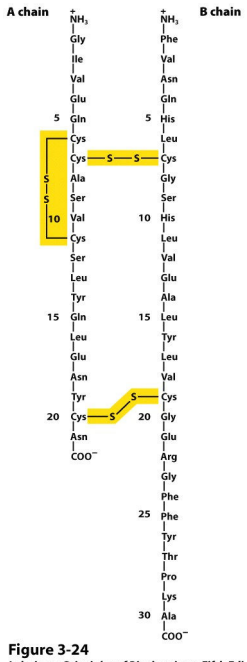
Primary Structure

- Sequence of amino acids
- All covalent bonds in the 1° chain
  - Peptide bond sequence
  - Disulfide bonds



Secondary Structure

- Local structure
  - Adjacent segments of the protein
- Stable arrangements of amino acids in recurring structural patterns
- Two most common
  - Alpha helices
  - Beta sheets

Tertiary Structure

- Overall structure of the entire protein
- All the 3D folding of polypeptide
- Conformation
  - spatial arrangement of atoms in a protein
  - any structural state that can occur without breaking covalent bonds

Quaternary Structure

- Association of more than one protein
  - Can be same or different polypeptide chains
  - Referred to by chain number
    - Dimer, trimer, tetramer
  - Referred to by chain type
    - Homomer or heteromer
    - i.e. homodimer (α_2) or heterodimer ($\alpha\beta$)
- Arrangement in space of the polypeptide chains

Covalent structure of proteins

- Function depends upon 1° sequence
  - Can be polymorphic - aa variants within a protein with the same function
- First protein sequenced was insulin
  - 1953 Sanger took10 yrs
  - 50 a.a. now common in 24-48 hrs

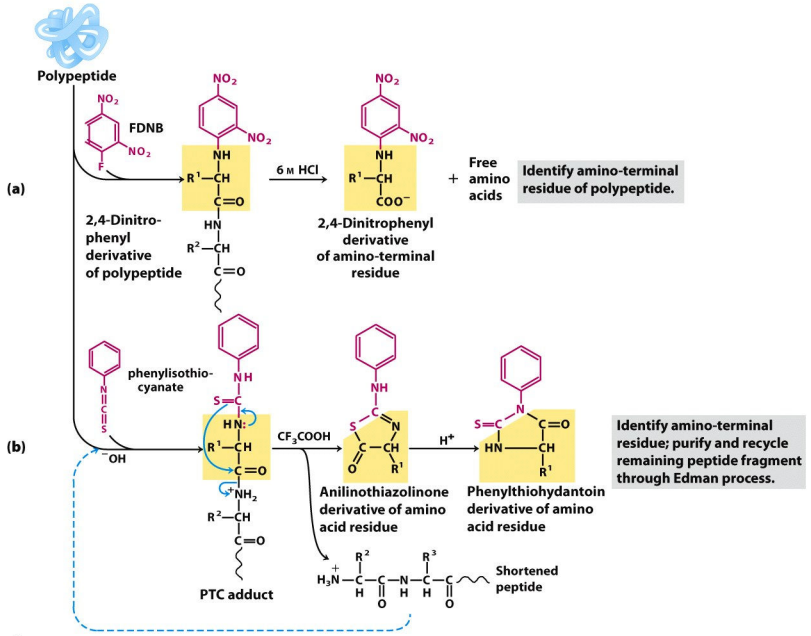


Figure 3-25
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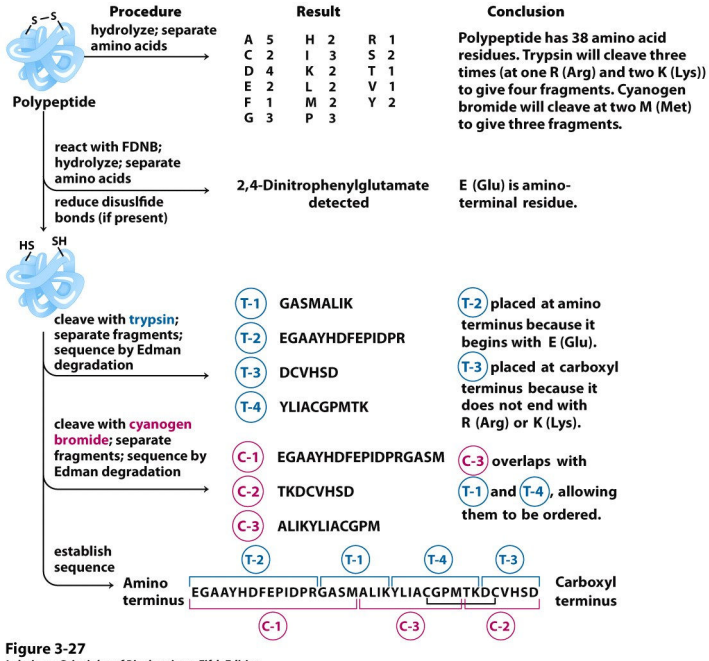

Figure 3-27
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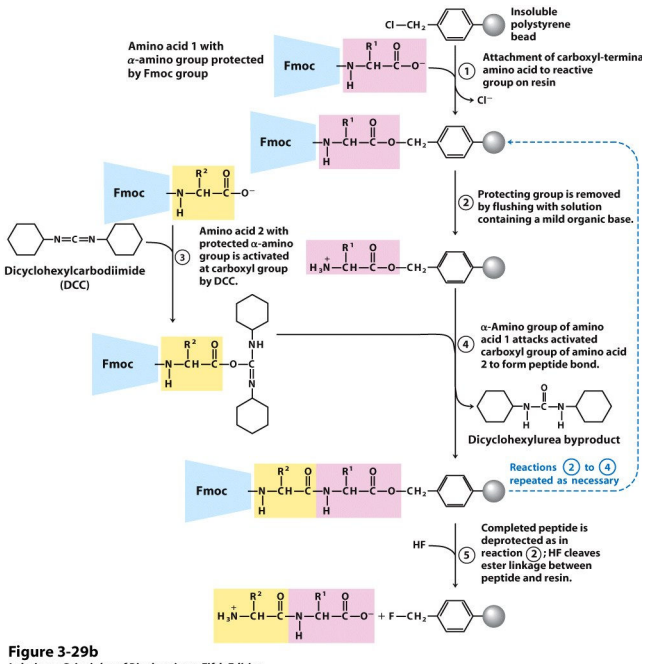

Figure 3-29b
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Peptide Bond

- peptide bond is the carbon of adjacent aa residues are separated by 3 covalent bonds
  - C_α-C-N-C_α
- N-CH-CO-N- repetitive chain is called the backbone
- C-N bond is shorter than in a simple amine
  - therefore resonance between the carbonyl O and amide N
  - e^--pair shared by interaction with the carbonyl group
  - sets up a dipole
  - Planar
  - N-H is 180° to the C=O

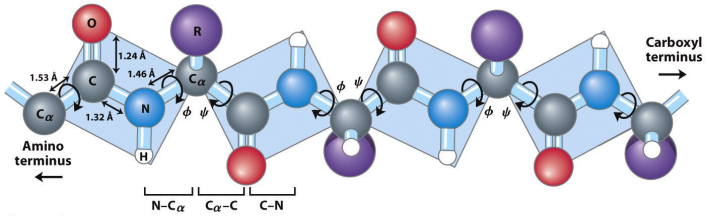

Figure 4-2b
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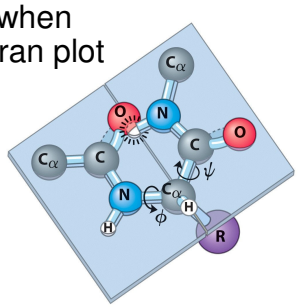
Angle Convention

- Phi (ϕ) is N-Cα
- Psi (ψ) is Cα-C=O
- Convention is that they are 180° when all peptide groups are in same plane
  - but this is sterically prohibited in proteins
  - atoms would overlap
- Allowed values of ϕ and ψ are revealed when plotted as an x/y graph in a Ramachandran plot



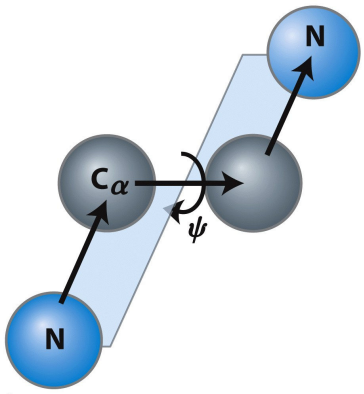


Figure 4-2c
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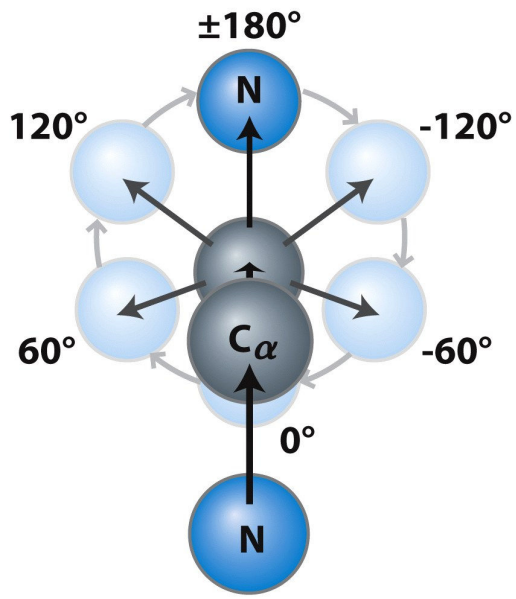

Figure 4-2d
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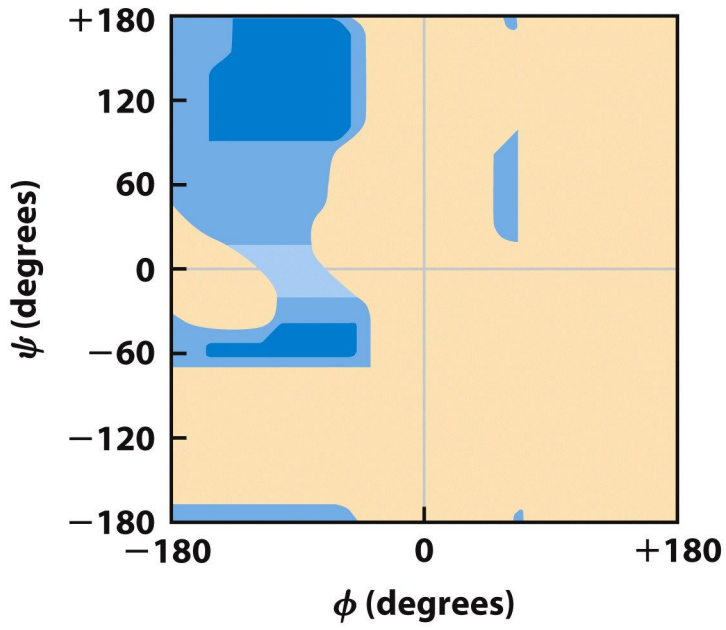

Figure 4-3
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