

CY100

Week 1

(Bio)macromolecules

TYPES OF "Non Living" MATERIALS

Most materials can be classified into one of three basic categories:

1. Metals
2. Ceramics
3. Polymers

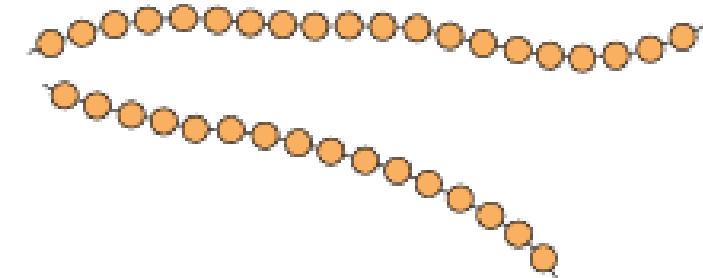
Their chemistries are different, and their mechanical and physical properties are different

In addition, there is a fourth category:

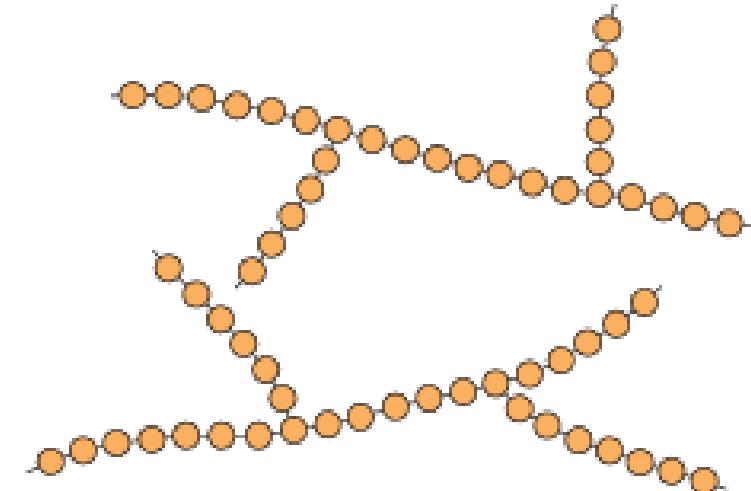
4. Composites

-is a nonhomogeneous mixture of the other three types, rather than a unique category

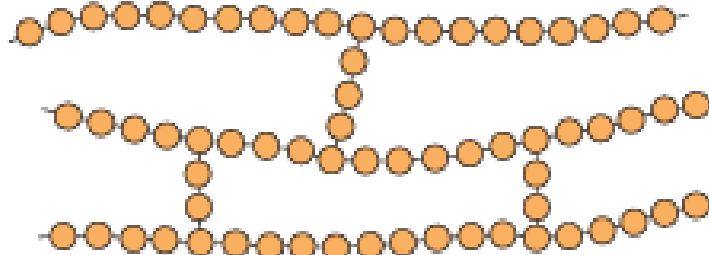
Polymeric Materials



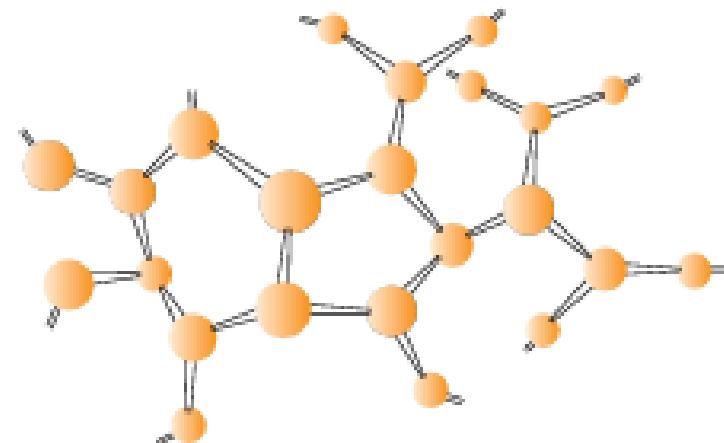
(a)



(b)



(c)

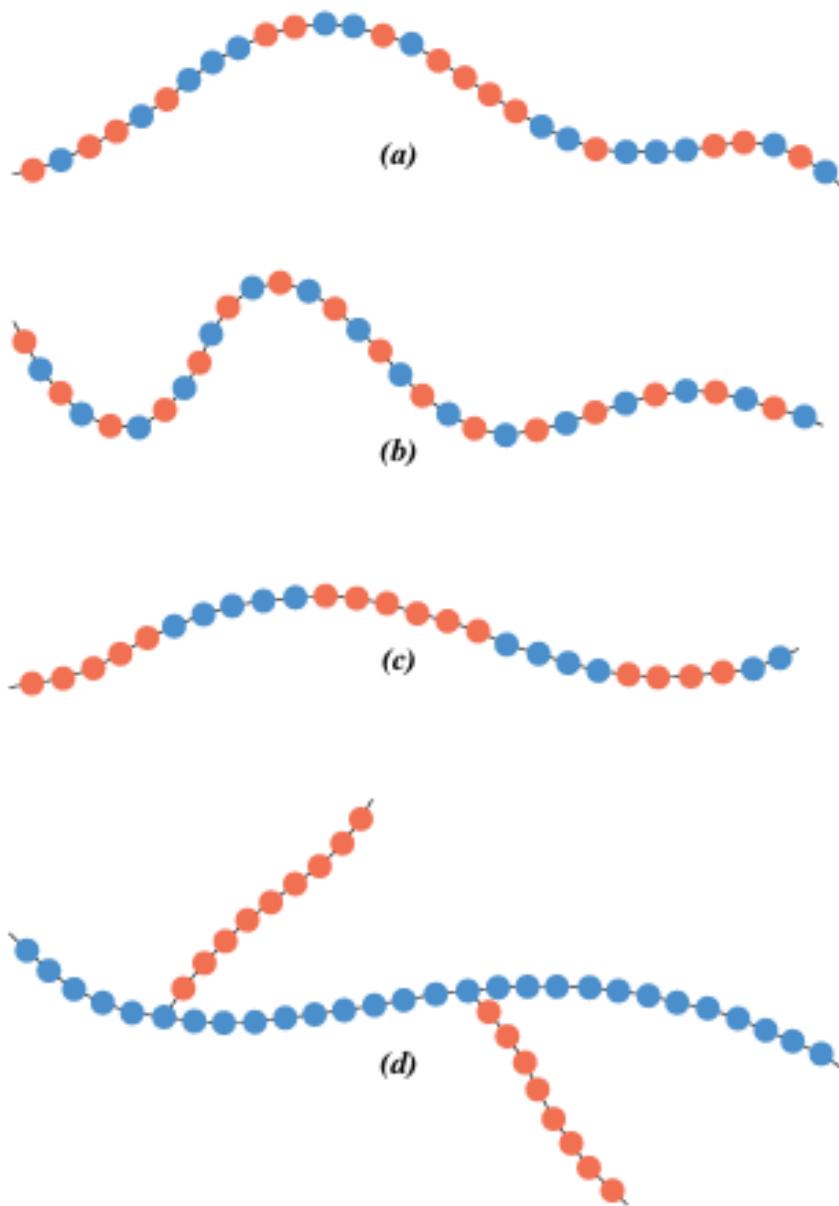


(d)

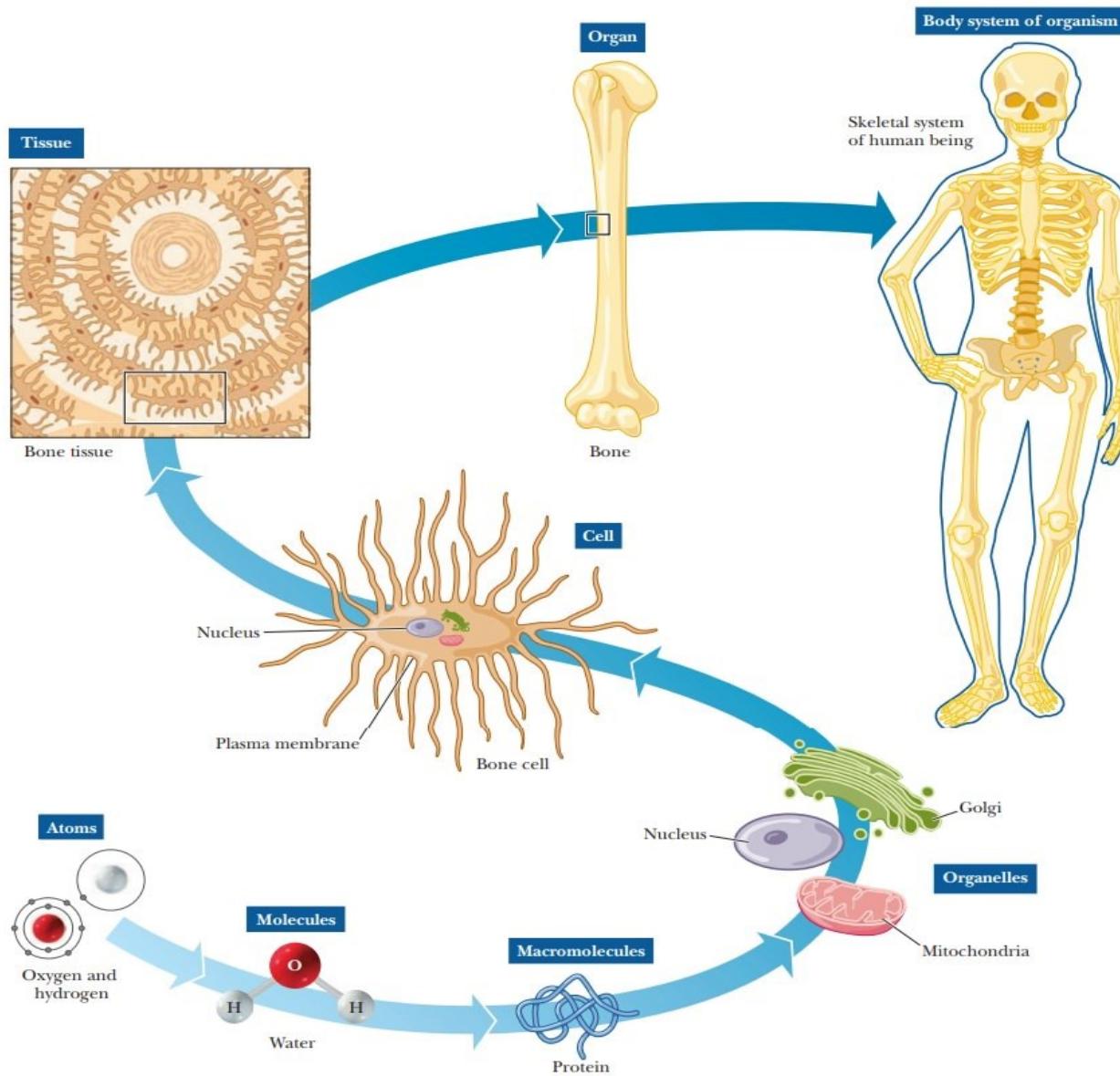
Schematic representations of (a) linear, (b) branched, (c) crosslinked, and (d) network (three-dimensional) molecular structures. Circles designate individual repeat units.

Polymeric Materials

Schematic representations of (a) random, (b) alternating, (c) block, and (d) graft copolymers. The two different repeat unit types are designated by blue and red circles.



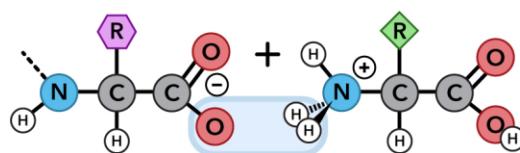
Living organisms



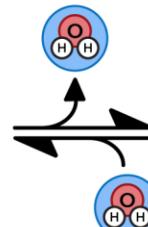
■ FIGURE 1.1 Levels of structural organization in the human body. Note the hierarchy from simple to complex.

Biopolymers

a) synthesis & degradation of protein

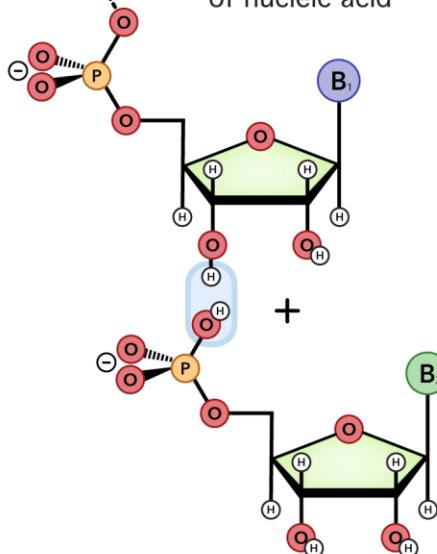


condensation

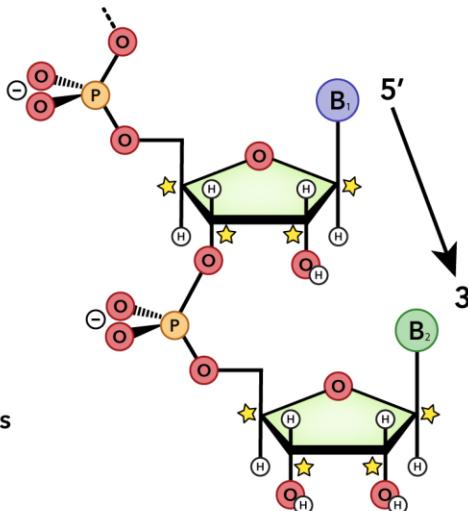
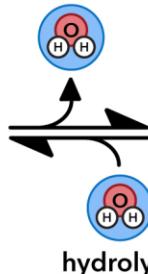


N → C

b) synthesis & degradation of nucleic acid

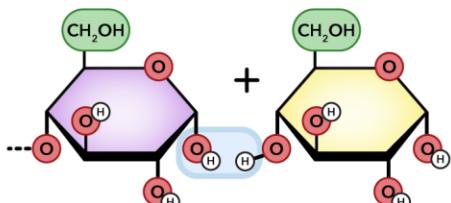


condensation

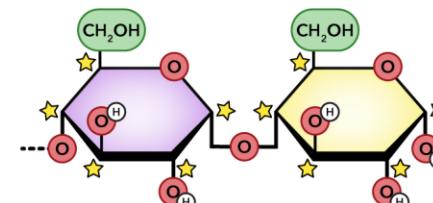
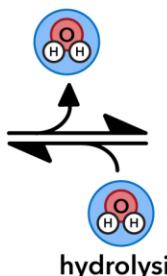


1 → 4

c) synthesis & degradation of polysaccharide

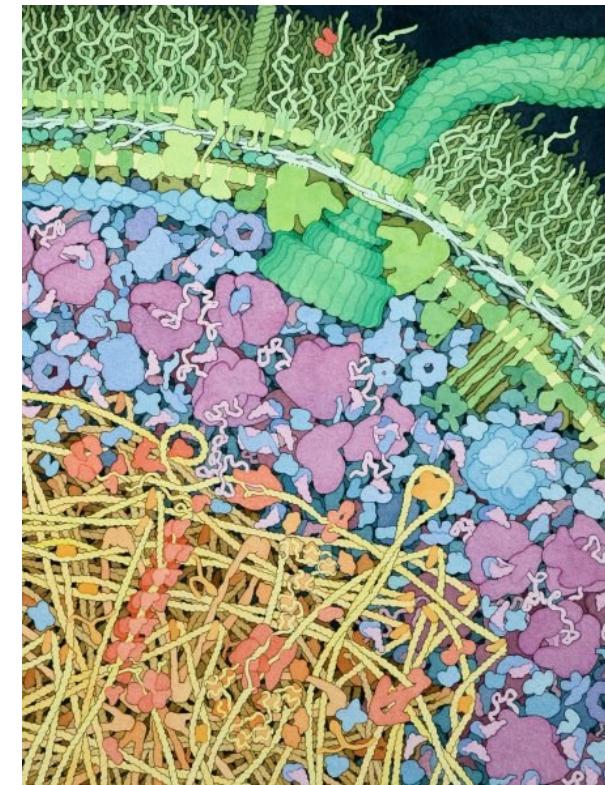


condensation



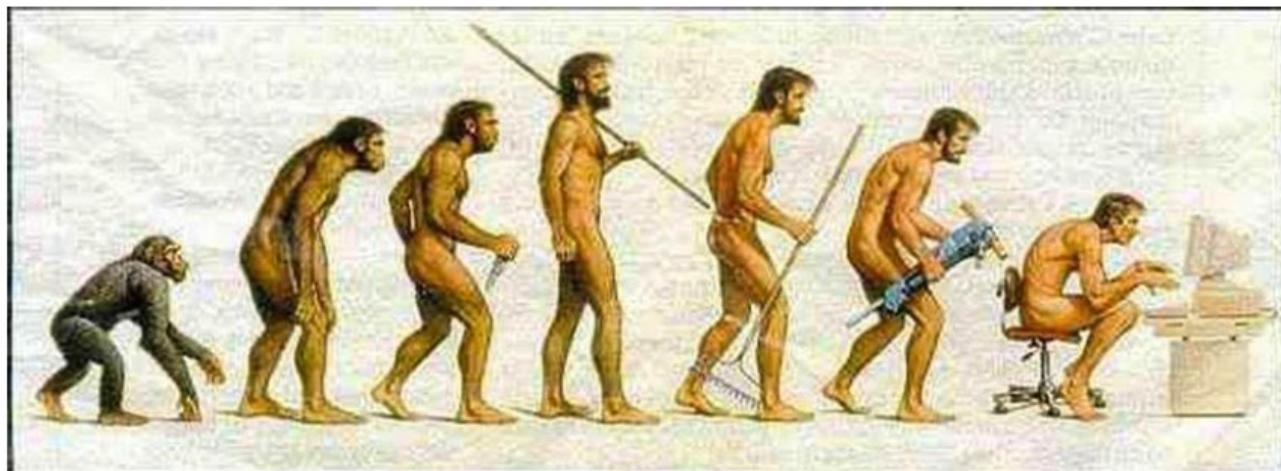
Distinguishing features of living organisms

- A high degree of **chemical complexity** and microscopic organization.
- Systems for **extracting, transforming, and using energy** from the environment.
- **Defined functions** for each of an organism's components and **regulated interactions** among them.



Distinguishing features of living organisms

- Mechanisms for **sensing and responding** to alterations in their surroundings.
- A capacity for **precise self-replication and self-assembly**.
- A capacity to change over time by gradual evolution.



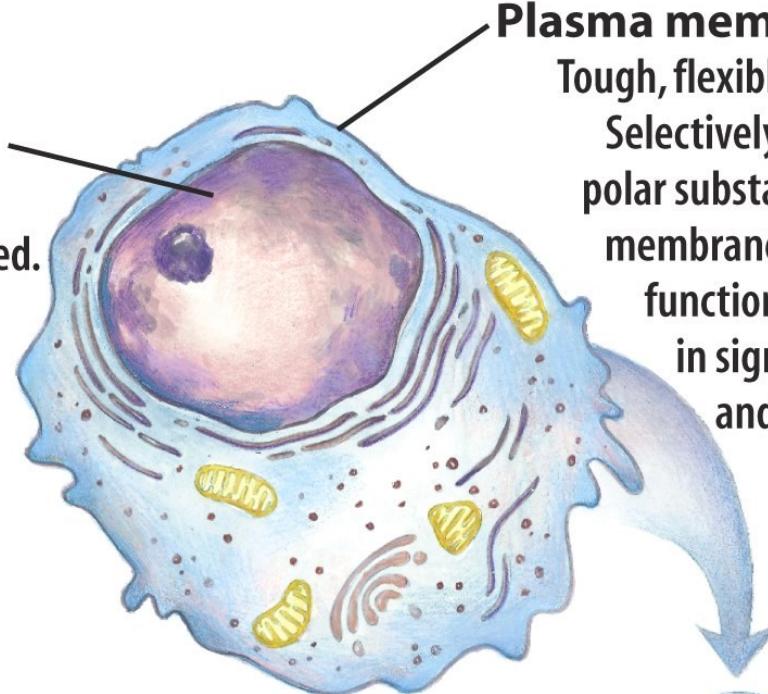
Taken from: <http://hydrodictyon.eeb.uconn.edu/courses/EEB210/evolution.jpg>

The Goals of Biochemistry

- Biochemistry asks how the remarkable properties of living organisms arise from the thousands of different biomolecules.
- Biochemistry describes in molecular terms the structure, mechanisms, and chemical processes shared by all organisms.
- Provides organizing principles that underlie life in all its diverse forms, principles we refer to collectively as the molecular logic of life.

Cells are structural and functional units of all living organisms

Nucleus (eukaryotes) or nucleoid (bacteria)
Contains genetic material—DNA and associated proteins.
Nucleus is membrane-bounded.



Plasma membrane
Tough, flexible lipid bilayer.
Selectively permeable to polar substances. Includes membrane proteins that function in transport, in signal reception, and as enzymes.

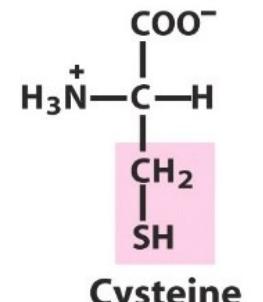
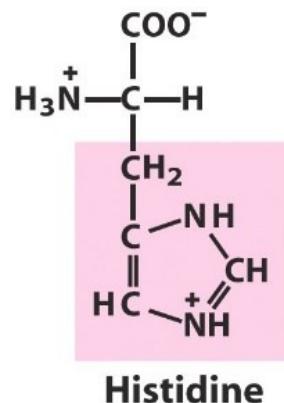
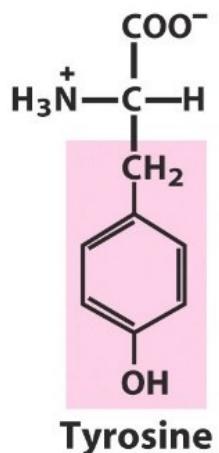
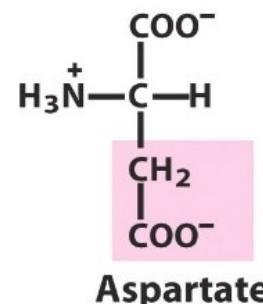
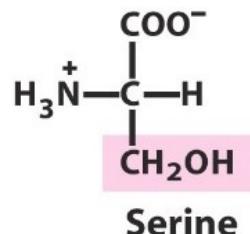
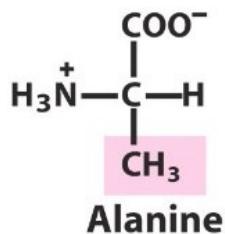
Cytoplasm
Aqueous cell contents and suspended particles and organelles.



Cells build macromolecular structures from simple organic compounds

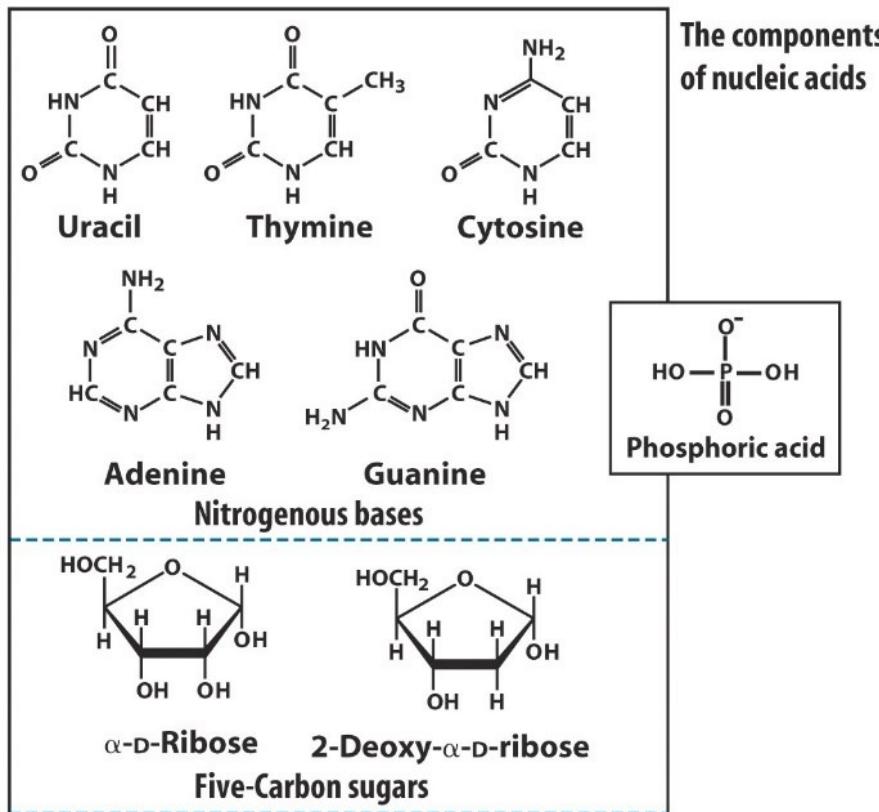
- Amino acids ---> Proteins

(a) Some of the amino acids of proteins

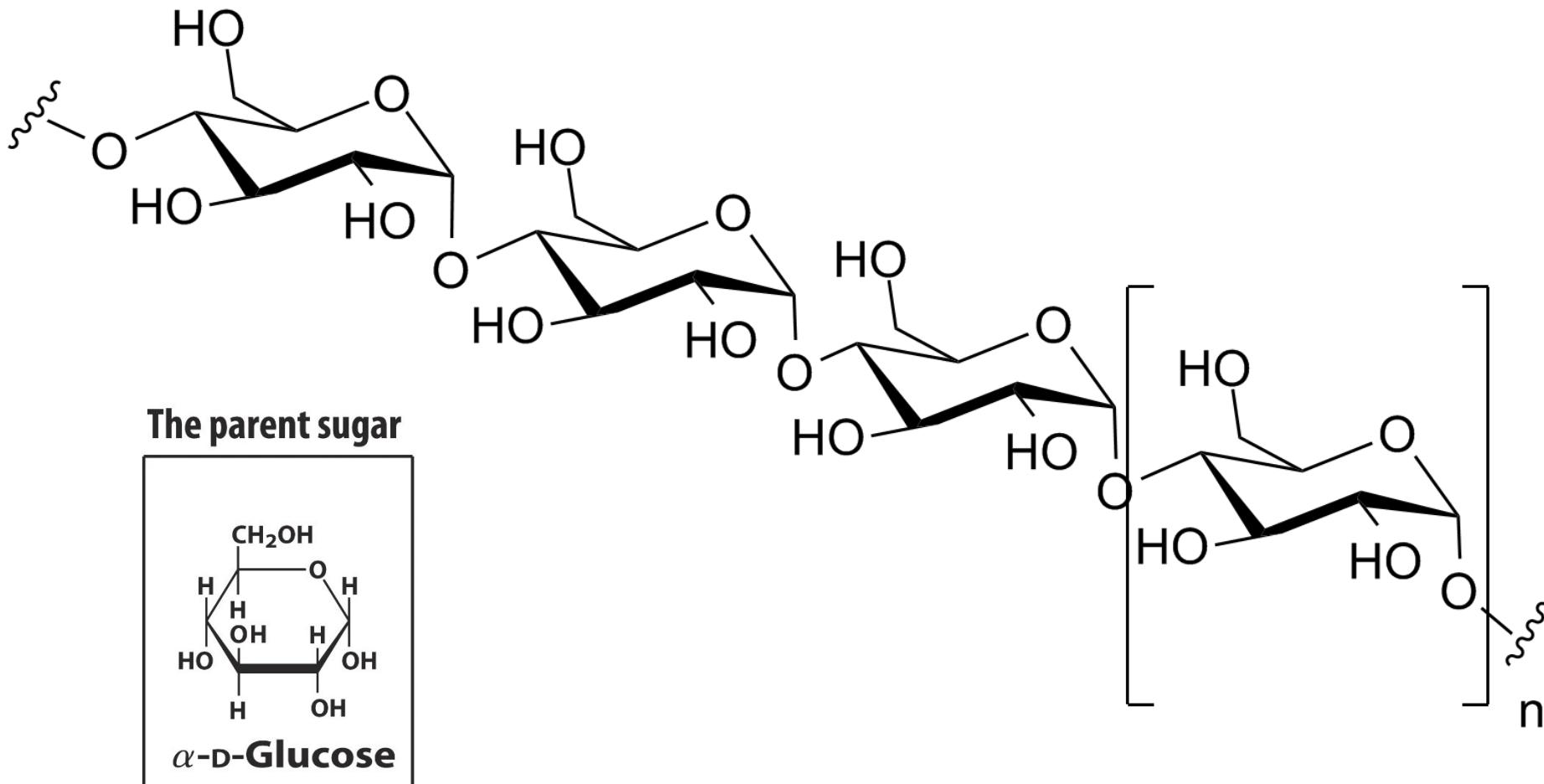


Cells build macromolecular structures from simple organic compounds

- Nucleotides---> DNA & RNA

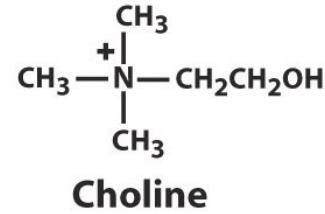
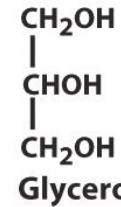
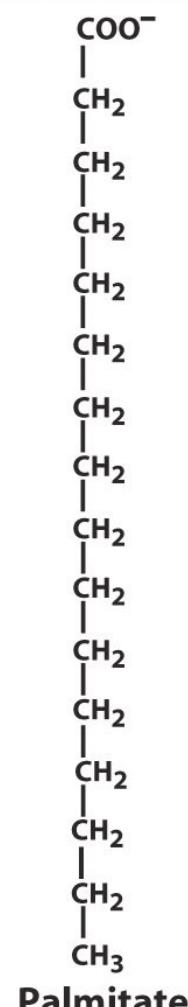
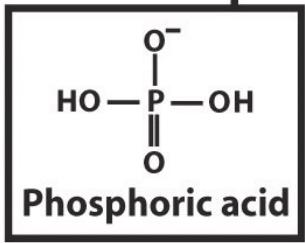


- Sugars ---> polysaccharides

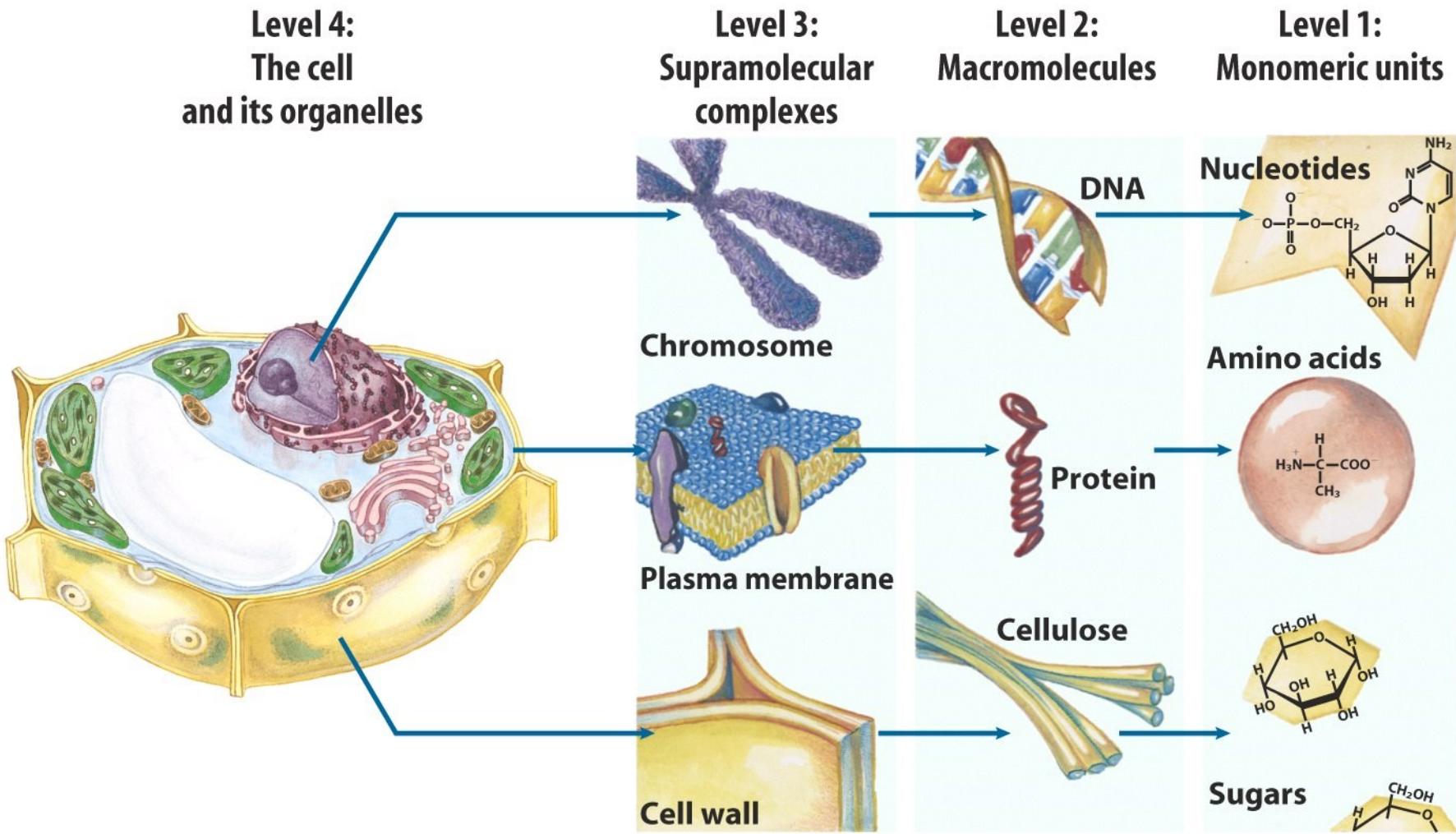


• Fatty acid derivatives ---> Lipids

Some components
of lipids



Structural hierarchy in the molecular organization of cells



1.2 Chemical Foundations

Biochemist's periodic table

1 H																	2 He
3 Li	4 Be																
11 Na	12 Mg																
19 K	20 Ca	21 Sc	22 Ti	23 V	24 Cr	25 Mn	26 Fe	27 Co	28 Ni	29 Cu	30 Zn	31 Ga	32 Ge	33 As	34 Se	35 Br	36 Kr
37 Rb	38 Sr	39 Y	40 Zr	41 Nb	42 Mo	43 Tc	44 Ru	45 Rh	46 Pd	47 Ag	48 Cd	49 In	50 Sn	51 Sb	52 Te	53 I	54 Xe
55 Cs	56 Ba		72 Hf	73 Ta	74 W	75 Re	76 Os	77 Ir	78 Pt	79 Au	80 Hg	81 Tl	82 Pb	83 Bi	84 Po	85 At	86 Rn
87 Fr	88 Ra																

Bulk elements

Trace elements

Lanthanides
Actinides

- Four most abundant elements in living organisms:
H, O, N, C, 99% of the mass of most cells.
- The trace elements are essential to the function of specific proteins.

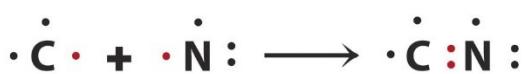
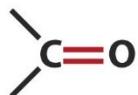
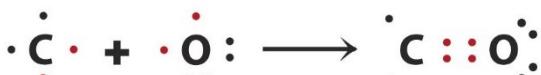
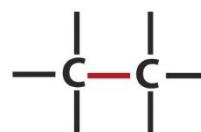
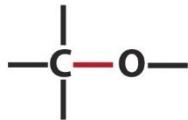
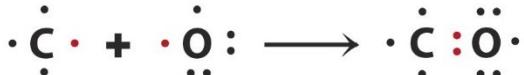
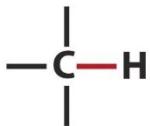
Element	Dry Weight (%)	Element	Dry Weight (%)
C	61.7	Ca	5.0
N	11.0	K	3.3
O	9.3	S	1.0
H	5.7	Cl	0.7
		Na	0.7
		Mg	0.3

- What property unites H, O, C and N and renders these atoms so appropriate to the chemistry of life?
- Answer: Their **ability to form covalent bonds** by electron-pair sharing. They are the lightest elements capable of efficiently forming stable one, two, three and four covalent bonds.

Why carbon based life?

- Covalently linked carbon atoms in biomolecules can form **linear chains, branched chains, and cyclic structures**. It seems likely that the bonding **versatility** of carbon, with itself and with other elements, was a major factor in the selection of carbon compounds for the molecular machinery of cells during the origin and evolution of living organisms. No other chemical element can form **molecules** of such widely different sizes, shapes, and composition.

Versatility of carbon bonding



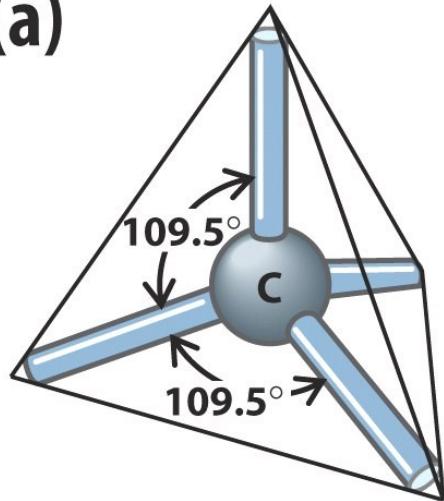
What are the bond energies
of covalent bonds?

<u>Bond</u>	<u>Energy (kJ/mol)</u>
H-H	436
C-H	414
C-C	343
C-O	351

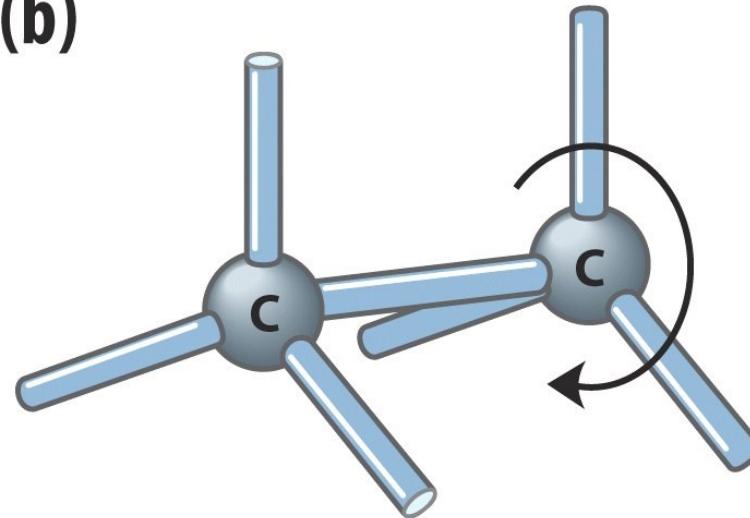
H, C, N and O form the strongest covalent bonds.
P and S are also covalent-bond forming

Geometry of carbon bonding

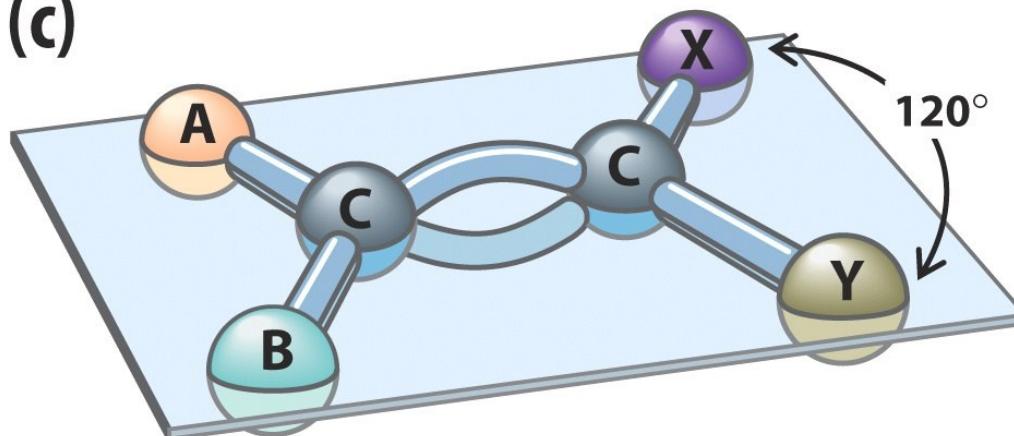
(a)



(b)



(c)



Why not Si based life

Bulk elements

Trace elements

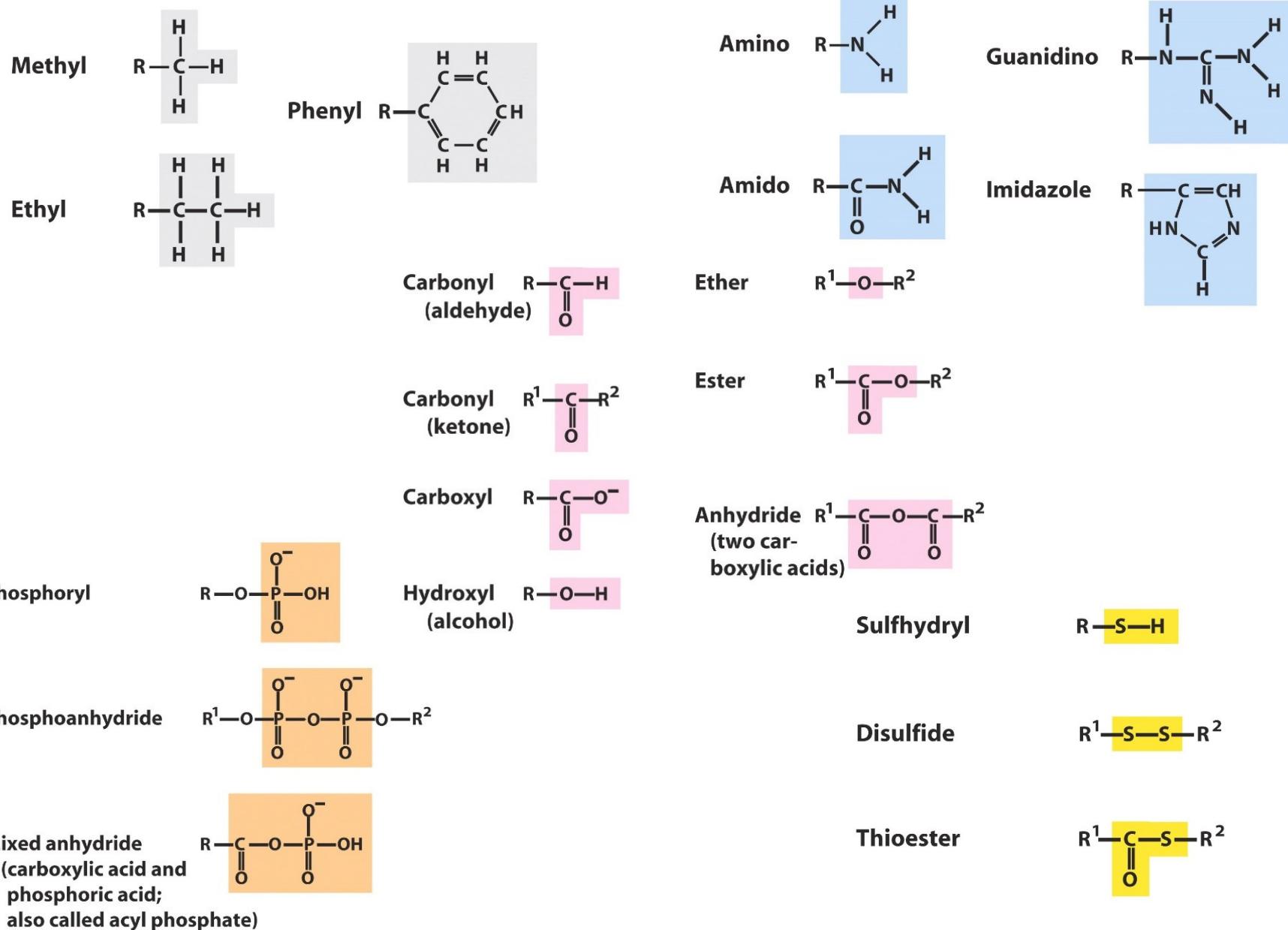
1 H															2 He		
3 Li	4 Be																
11 Na	12 Mg																
19 K	20 Ca	21 Sc	22 Ti	23 V	24 Cr	25 Mn	26 Fe	27 Co	28 Ni	29 Cu	30 Zn	31 Ga	32 Ge	33 As	34 Se	35 Br	36 Kr
37 Rb	38 Sr	39 Y	40 Zr	41 Nb	42 Mo	43 Tc	44 Ru	45 Rh	46 Pd	47 Ag	48 Cd	49 In	50 Sn	51 Sb	52 Te	53 I	54 Xe
55 Cs	56 Ba		72 Hf	73 Ta	74 W	75 Re	76 Os	77 Ir	78 Pt	79 Au	80 Hg	81 Tl	82 Pb	83 Bi	84 Po	85 At	86 Rn
87 Fr	88 Ra																

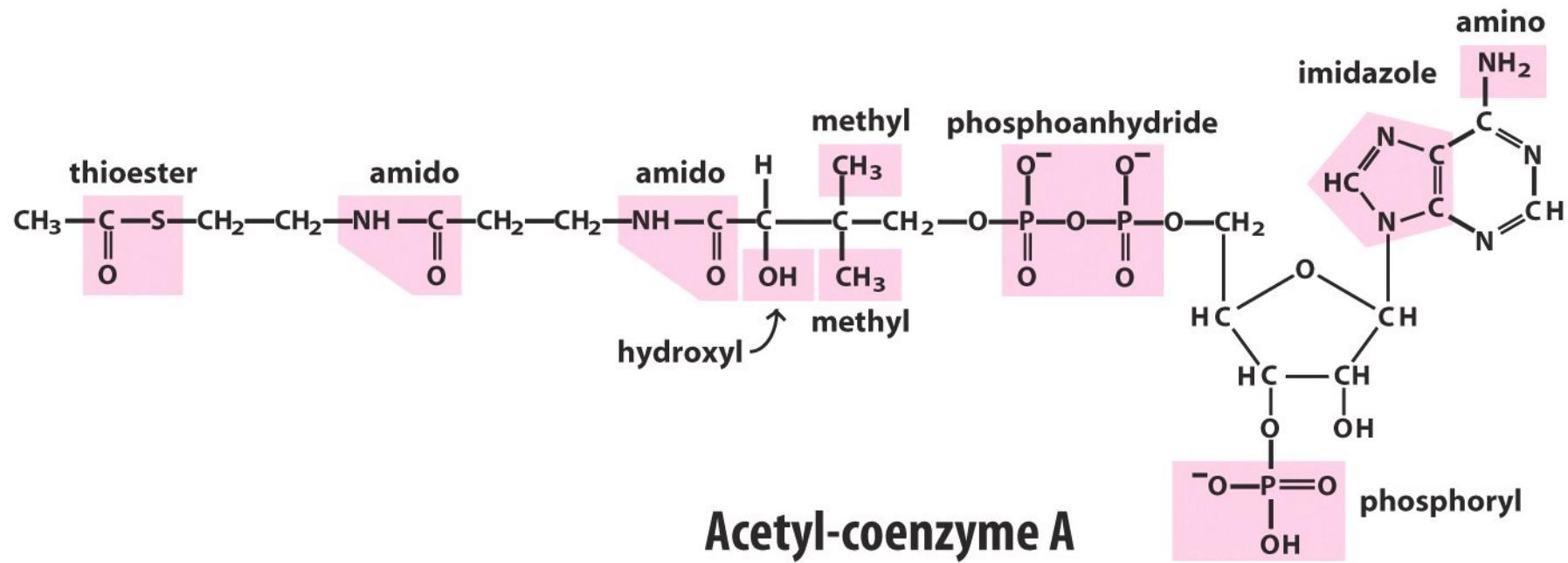
Lanthanides
Actinides

Why not silicon based life?

- Long chains of silicon atoms are not readily synthesized, thus the polymeric macromolecules necessary for more complex functions would not readily form.
- Oxygen disrupt bonds between two silicon atoms, so silicon based life-forms would be unstable in an oxygen-containing atmosphere. Once formed, the bonds between silicon and oxygen are extremely stable and difficult to break, which would prevent the degradation and synthesis of biomolecules.

Common functional groups of biomolecules





An example of several common functional groups in a single biomolecule

Cells contain universal set of small molecules

- A collection of perhaps a thousand different small organic molecules (Molecular weight ($Mr \sim 100$ to 500). These molecules are conserved during evolution, serve as central metabolites in the cell life. They include the common amino acids, nucleotides, sugars, etc.
- These small molecules are trapped in the cell because the plasma membrane is impermeable to them.
- Besides the universal small molecules, there are other small biomolecules specific to only certain types of cells or organisms. They are called secondary metabolites.

Macromolecules are the major constituents of cells

	% of Total Weight of Cell	Approximate Number of Different Molecular Species
Water	70	1
Protein	15	3,000
Nucleic Acids		
DNA	1	1
RNA	6	>3,000
Polysaccharides	3	5
Lipids	2	20
Monomeric Subunits and Intermediates	2	500
Inorganic Ions	1	20

Molecular Components of an *E. coli* Cell

The Diversity of Polymers

- Each cell has thousands of different kinds of macromolecules
- Macromolecules vary among cells of an organism, vary more within a species, and vary even more between species
- An immense variety of polymers can be built from a small set of monomers

Proteins do most of the work of the cell

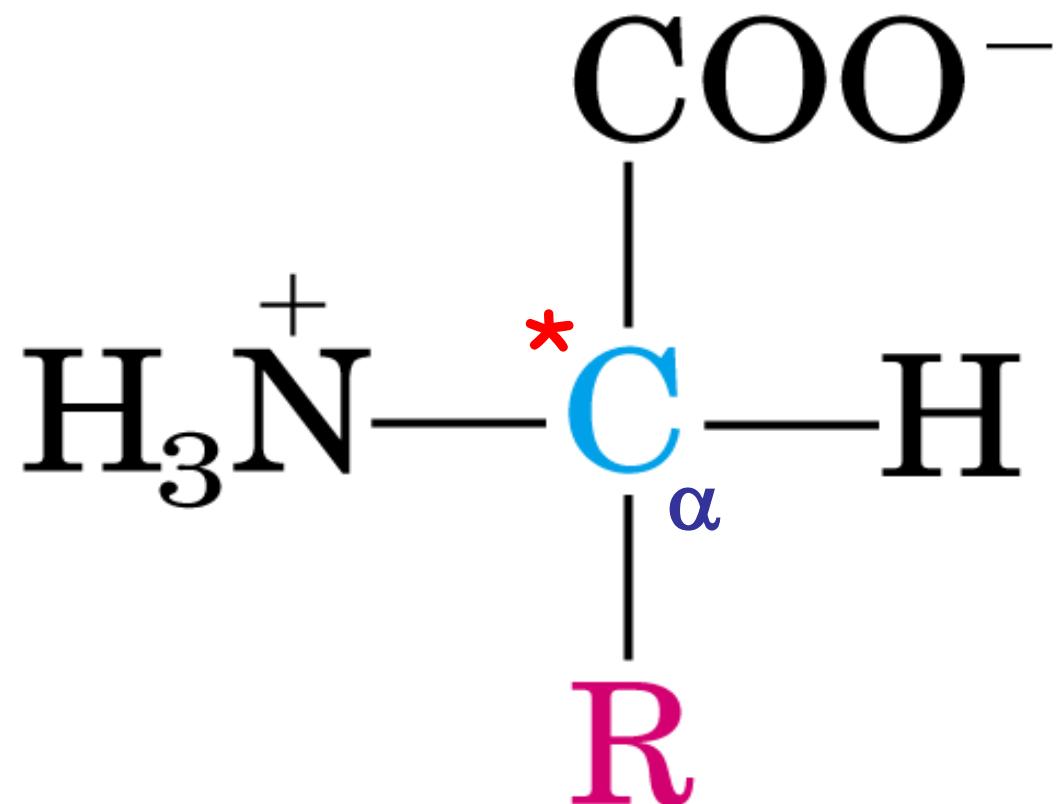
- Each protein is **specialized** to do a certain job.
- Some proteins are **structural**: control shapes of cells and bind cells together. E.g Keratin
- Chemical reactions of the cells are controlled by protein **enzymes**.
- Protein **pumps** move things across the cell membrane.
- Proteins give **mobility**: muscle, flagella, molecular motors

General properties of proteins

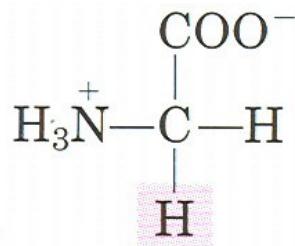
- Most abundant biomolecule; accounts for 50% of dry weight.
- Built by assembling long chains of amino acids (monomers), following by intricate folding.
- Final shape of protein is very specific. Unless correctly folded, is not functional
- Several 1000 different types of proteins in any cell; millions of protein molecules.
- All proteins are composed of 20 "standard" amino acids.

Amino Acids

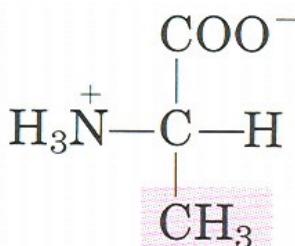
The common amino acids are known as α -amino acids because they have a primary amino group ($-\text{NH}_2$) as a substituent of the α carbon atom, the carbon next to the carboxylic acid group. The 20 standard amino acids differ in the structure of their side chains (R groups).



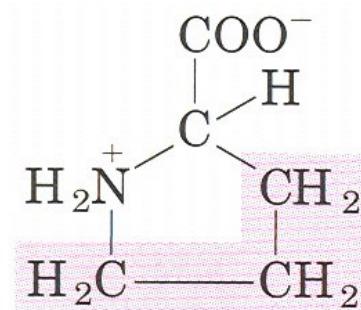
Nonpolar Aliphatic Amino Acids



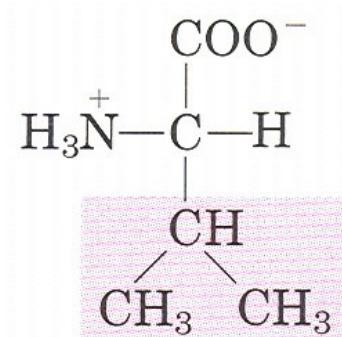
Glycine
Gly, G



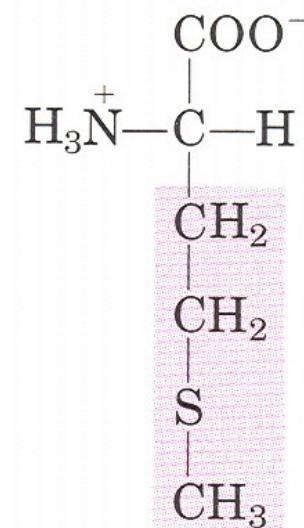
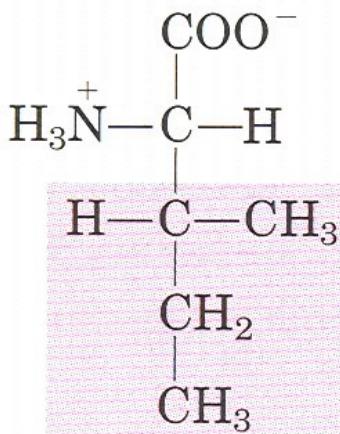
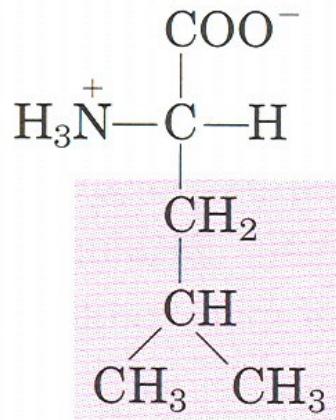
Alanine
Ala, A



Proline
Pro, P



Valine
Val, V

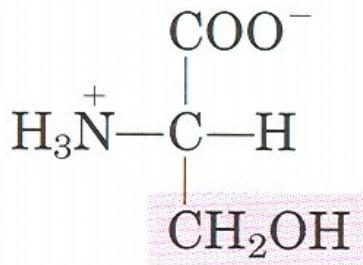


Leucine
Leu, L

Isoleucine
Ile, I

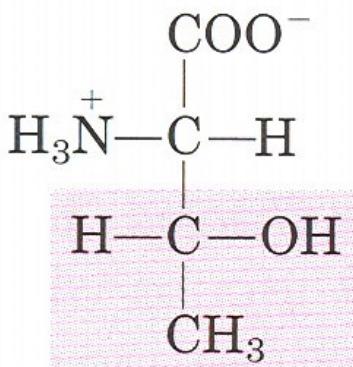
Methionine
Met, M

Polar Uncharged Amino Acids

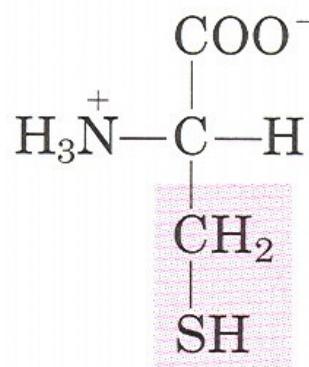


Serine

Ser, S

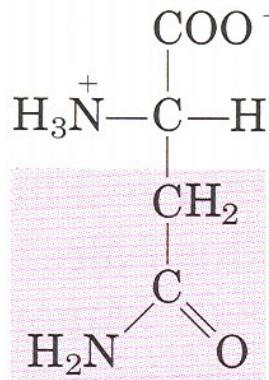


Threonine

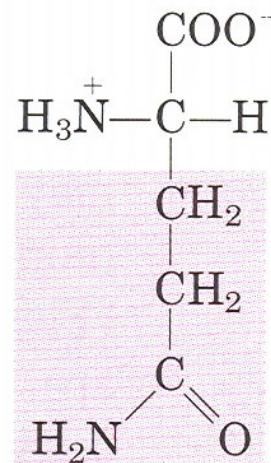


Cysteine

Cys, C

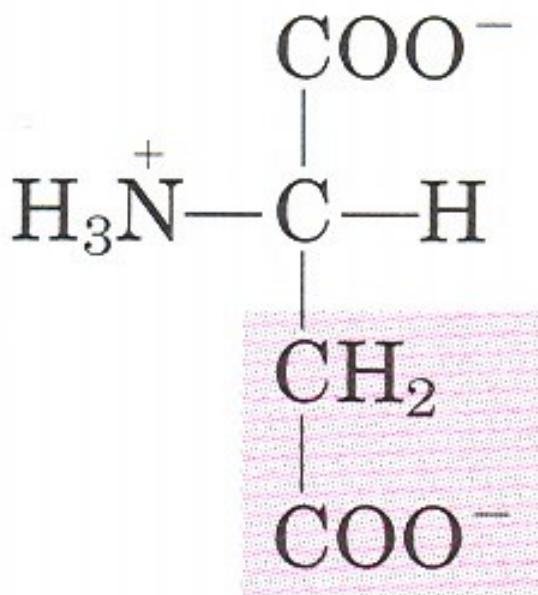


Asn, N Asparagine



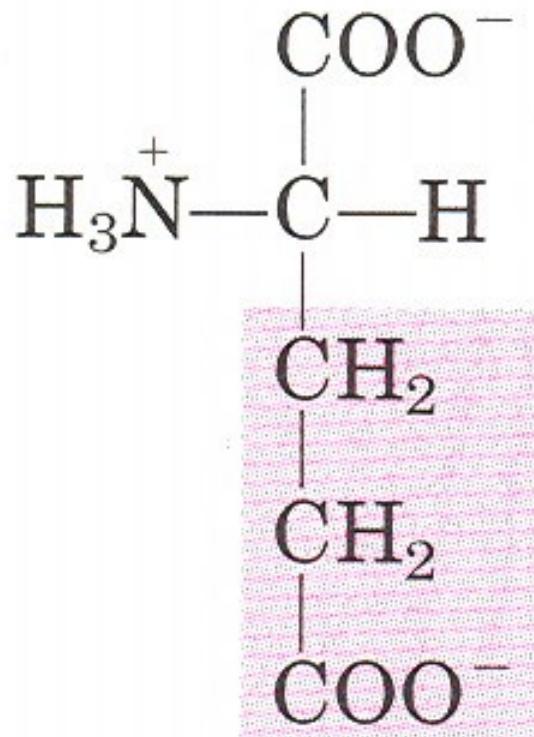
Glutamine Gln, Q

Negatively charged Amino Acids



Aspartate

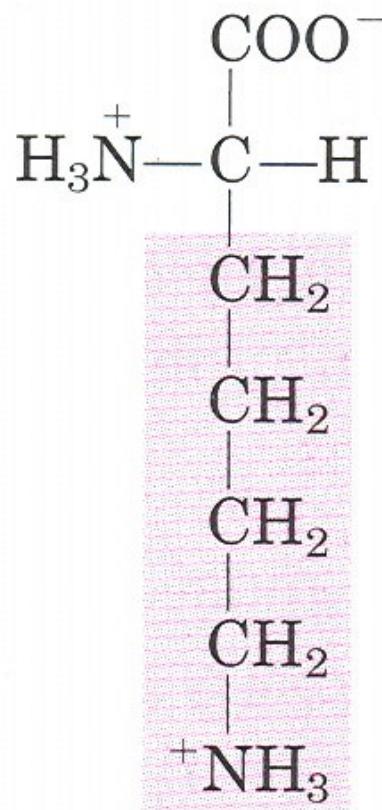
Asp, D



Glutamate

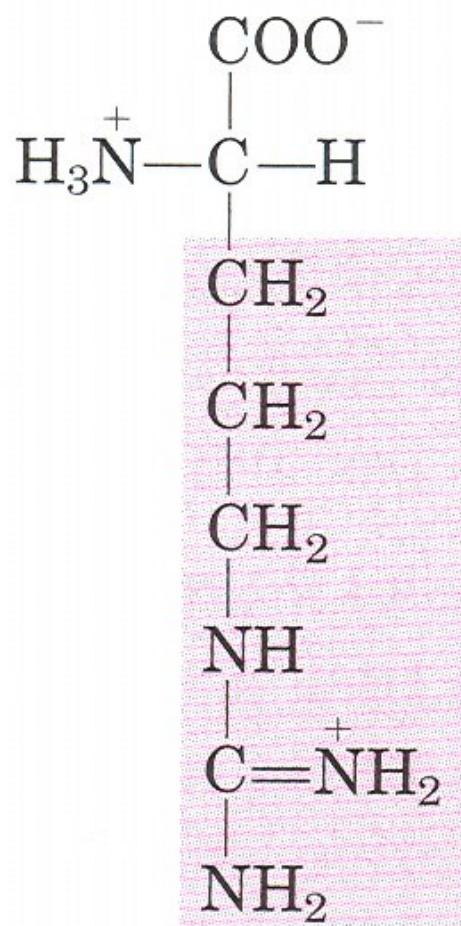
Glu, E

Positively charged Amino Acids



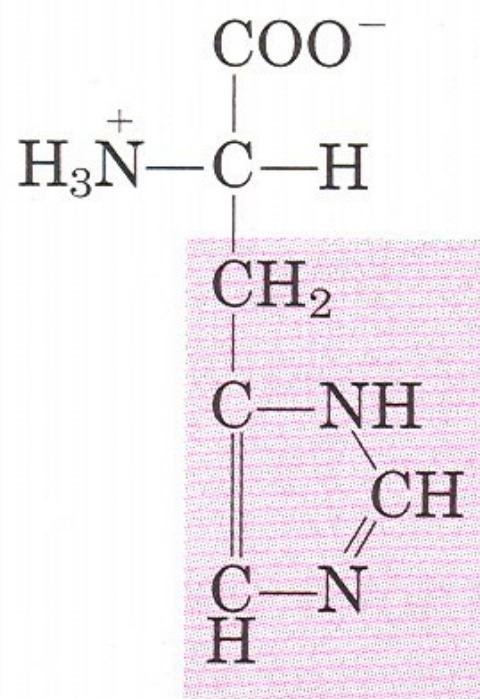
Lysine

Lys, K



Arginine

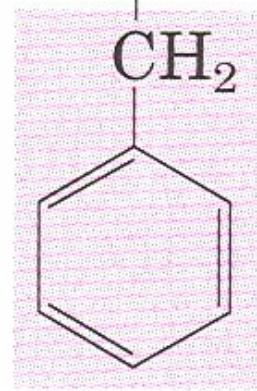
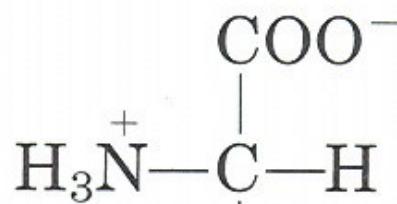
Arg, R



Histidine

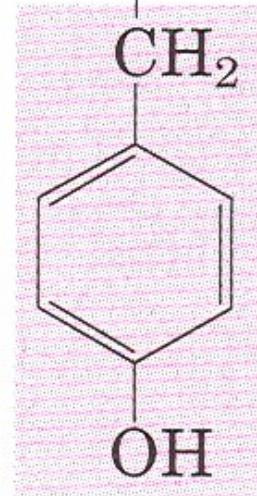
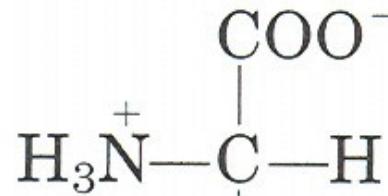
His, H

Aromatic Amino Acids



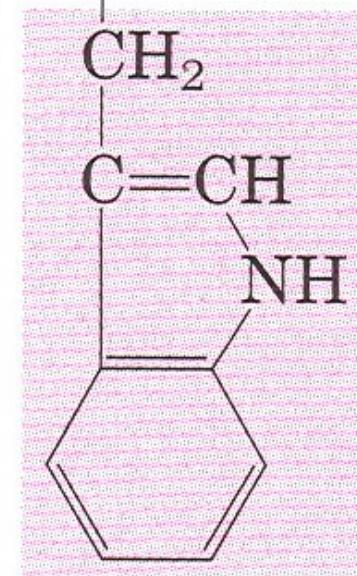
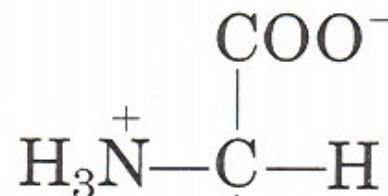
Phenylalanine

Phe, F



Tyrosine

Tyr, Y

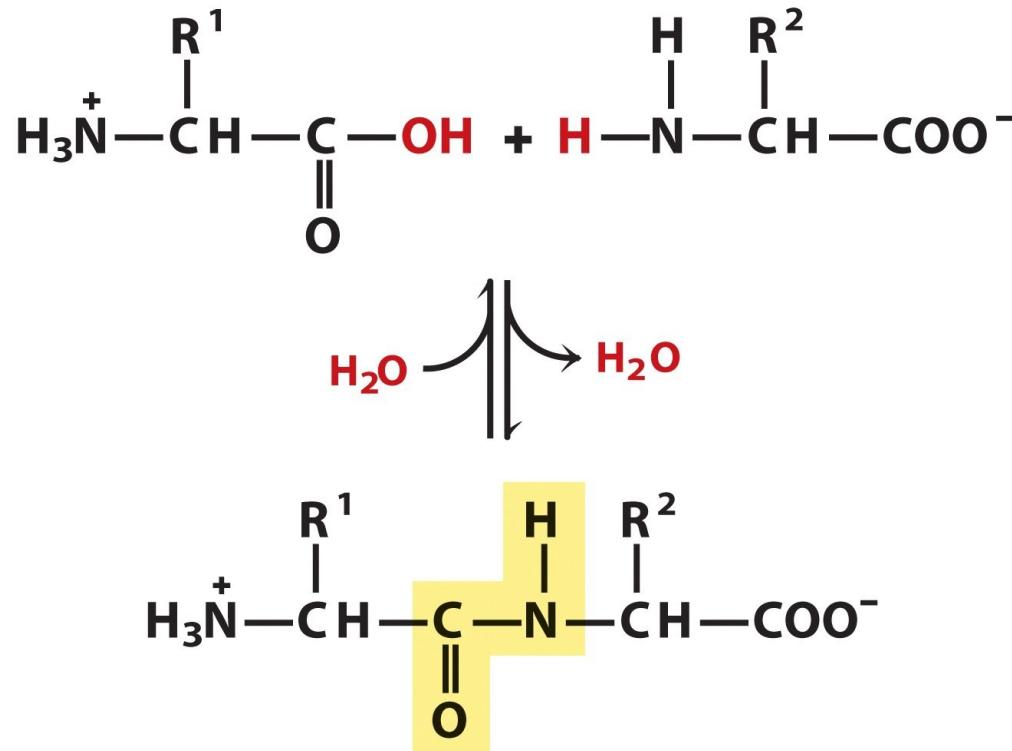


Tryptophan

Trp, W

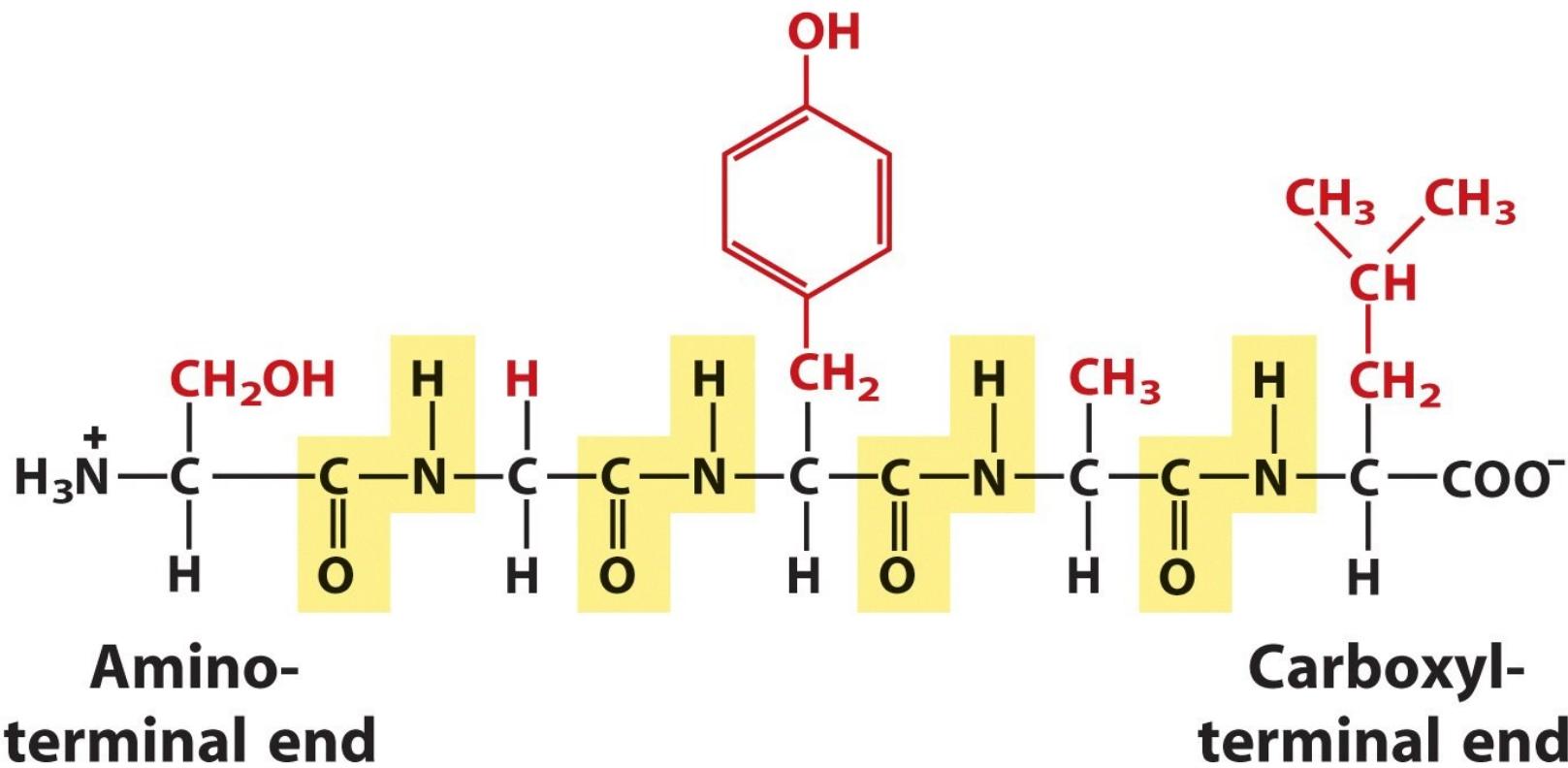
Peptides and proteins

Peptides are chains of amino acids



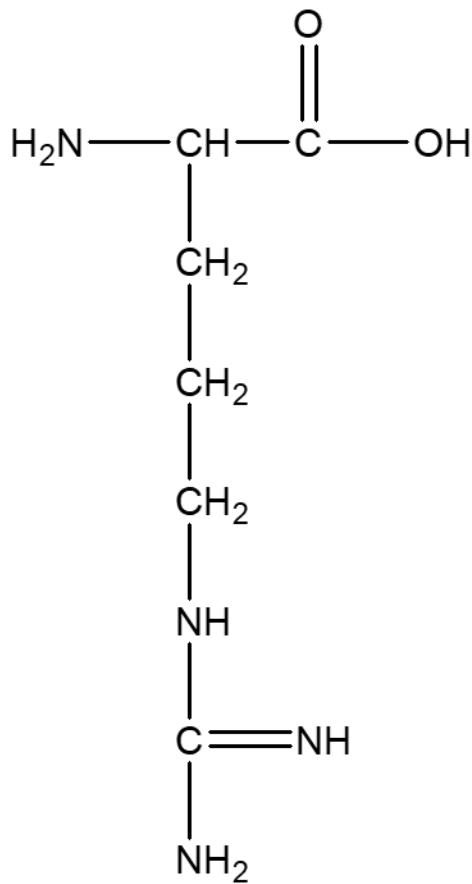
Peptide Bond Formation

Ser-Gly-Tyr-Ala-Lue or SGYAL

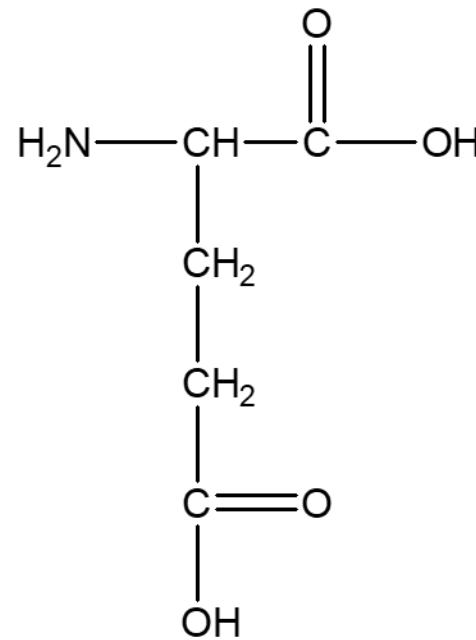


Key convention: display the amino terminal on the left and the carboxyl terminal on the right. The sequence is read left to right.

How many dipeptides can form two of the following AA?



Arg



Glu

Favorable Interactions in Proteins

Electrostatic interactions

Dipolar interactions

 Dipole-dipole interactions

 Dipole-induced dipole interactions

 Charge-dipole interactions

 Fluctuating dipoles (London

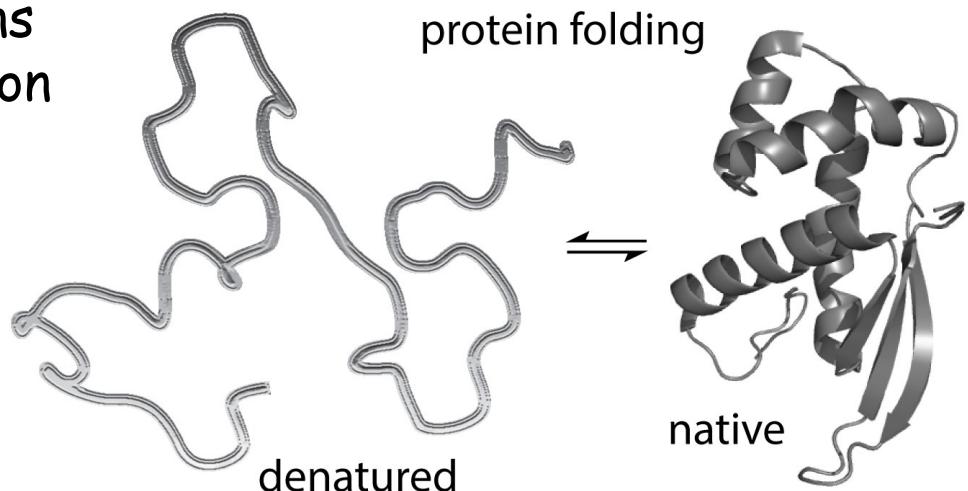
Dispersion)

Cation- π interactions

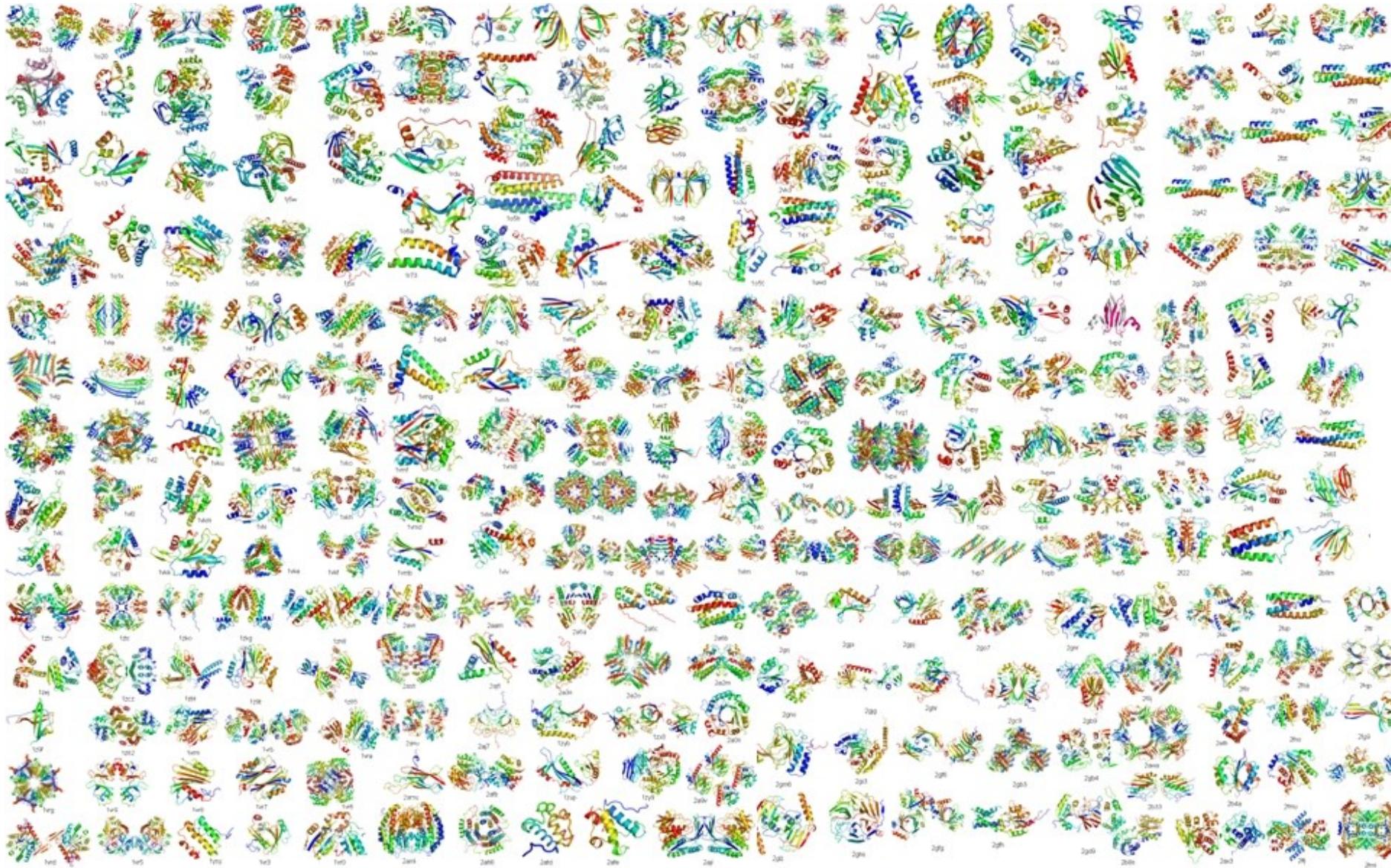
Hydrogen bonding

The hydrophobic effect

Short range repulsion



Proteins are diverse in nature



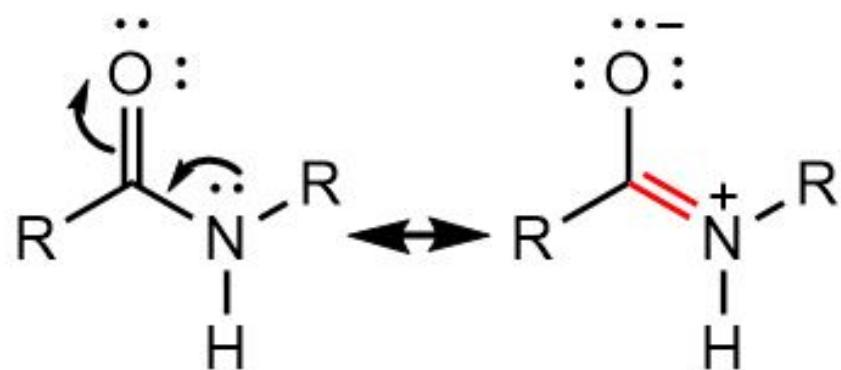
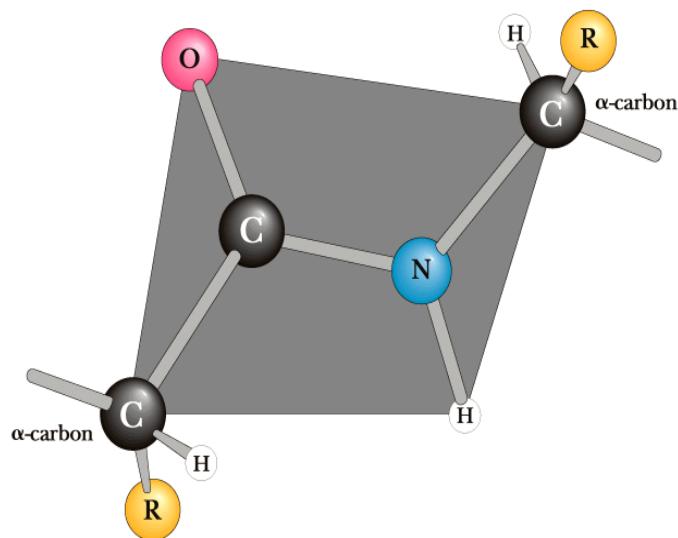
Biologically active peptides and Polypeptides occur in a vast range of sizes and compositions

TABLE 3-2 Molecular Data on Some Proteins

	Molecular weight	Number of residues	Number of polypeptide chains
Cytochrome c (human)	13,000	104	1
Ribonuclease A (bovine pancreas)	13,700	124	1
Lysozyme (chicken egg white)	13,930	129	1
Myoglobin (equine heart)	16,890	153	1
Chymotrypsin (bovine pancreas)	21,600	241	3
Chymotrypsinogen (bovine)	22,000	245	1
Hemoglobin (human)	64,500	574	4
Serum albumin (human)	68,500	609	1
Hexokinase (yeast)	102,000	972	2
RNA polymerase (<i>E. coli</i>)	450,000	4,158	5
Apolipoprotein B (human)	513,000	4,536	1
Glutamine synthetase (<i>E. coli</i>)	619,000	5,628	12
Titin (human)	2,993,000	26,926	1

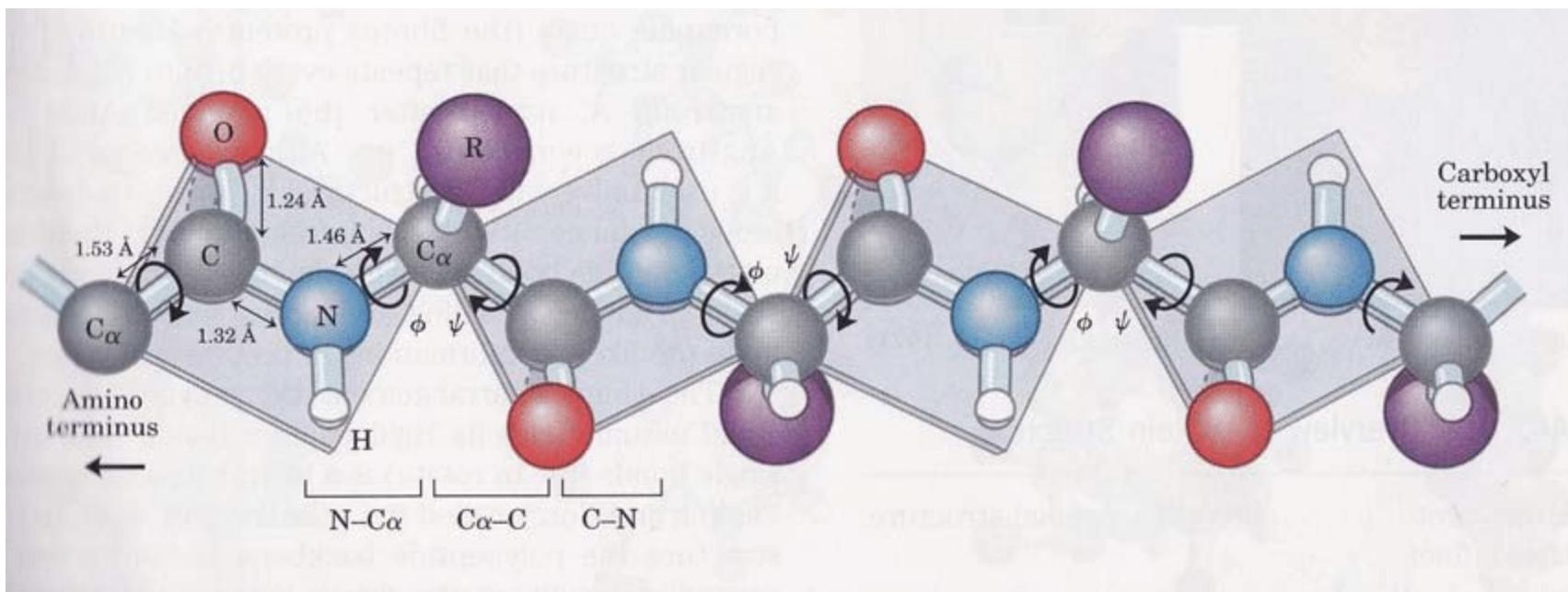
The Coplanar Nature of the Peptide Bond

Six atoms of the peptide group lie in a plane!



The Coplanar Nature of the Peptide Bond

Six atoms of the peptide group lie in a plane!



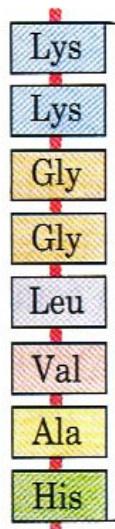
Dihedral angles around C_α-C and N-C_α bonds are named as ψ and ϕ by a common convention. Their values change between -180° and 180° .

Summary of the Peptide Bond

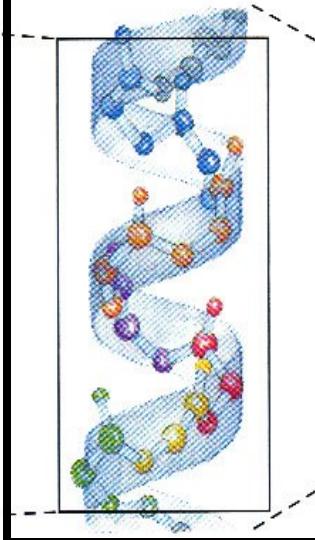
- is usually found in the *trans* conformation
- has partial (40%) double bond character
- due to the double bond character, the six atoms of the peptide bond group are always planar!
- peptide bond is polar: N partially positive; O partially negative

The Four Levels of Protein Structure

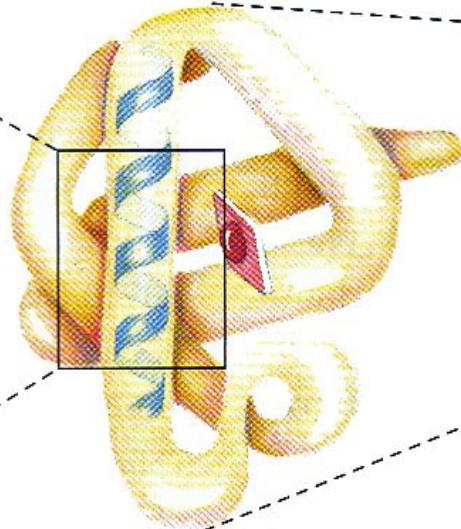
Primary structure



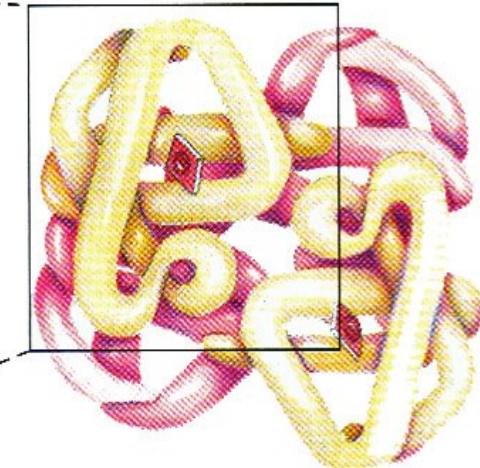
Secondary structure



Tertiary structure



Quaternary structure



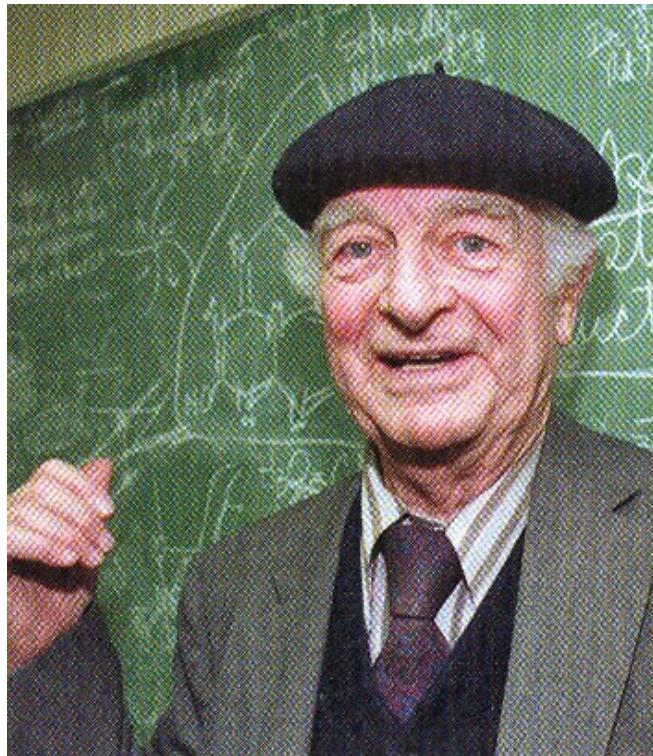
Secondary structure is the local spatial arrangement of a polypeptide's backbone atoms without regard to the conformation of its side chains.

Classes of Secondary Structure

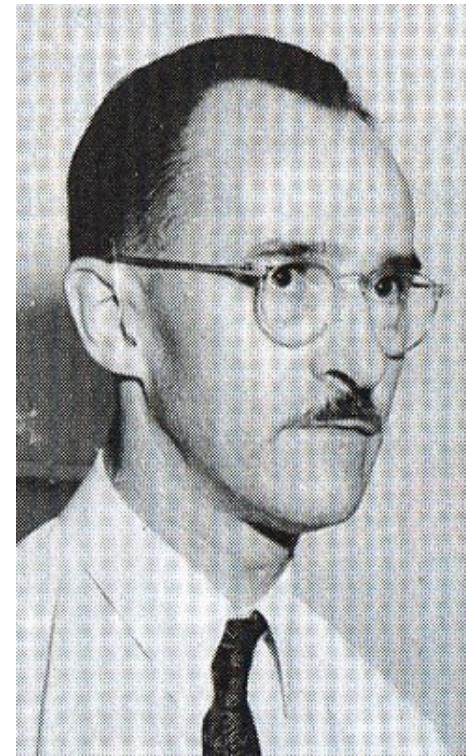
All these are local structures that are
stabilized by hydrogen bonds

- Alpha helix
- Beta sheet
- Beta turns

Papers by Linus Pauling and Robert Corey in 1951 proposed the α -helix and the β -sheet, now known to form the backbones of tens of thousands of proteins.



Linus Pauling (1901-1994), winner of the Nobel Prize in Chemistry in 1954 and the Nobel Peace Prize in 1962.



Robert Corey (1897-1971)

The Alpha Helix

- First proposed by Linus Pauling and Robert Corey in 1951
- Identified in keratin by Max Perutz
- A ubiquitous component of proteins
- Stabilized by H-bonds

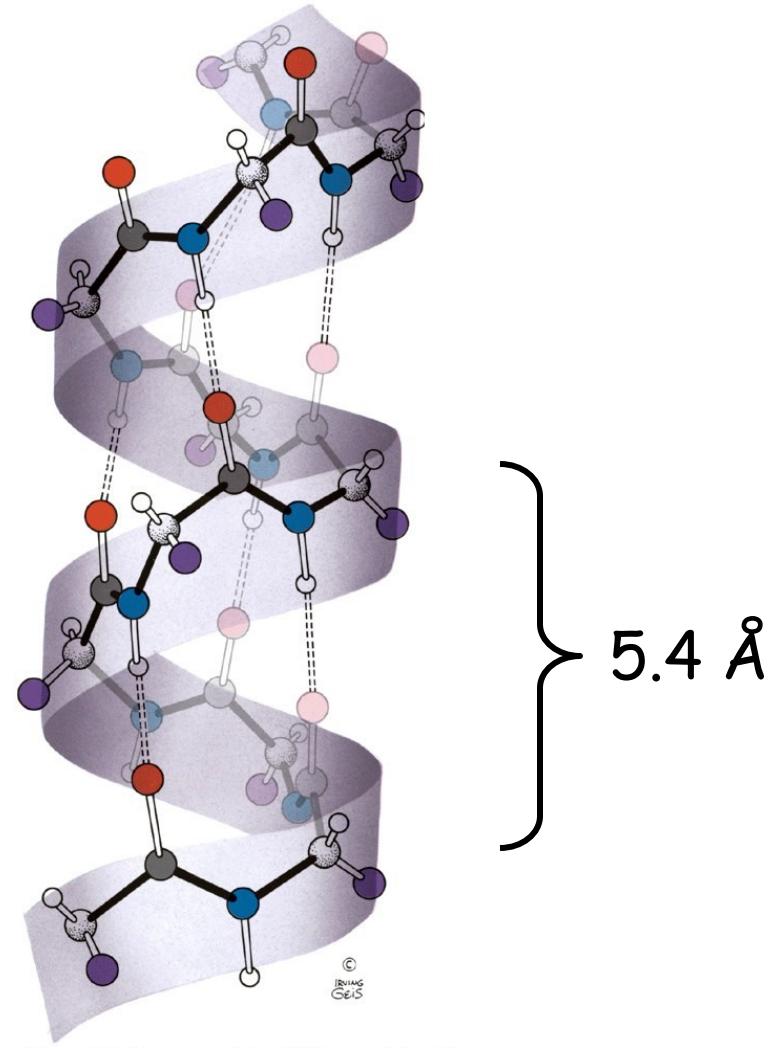
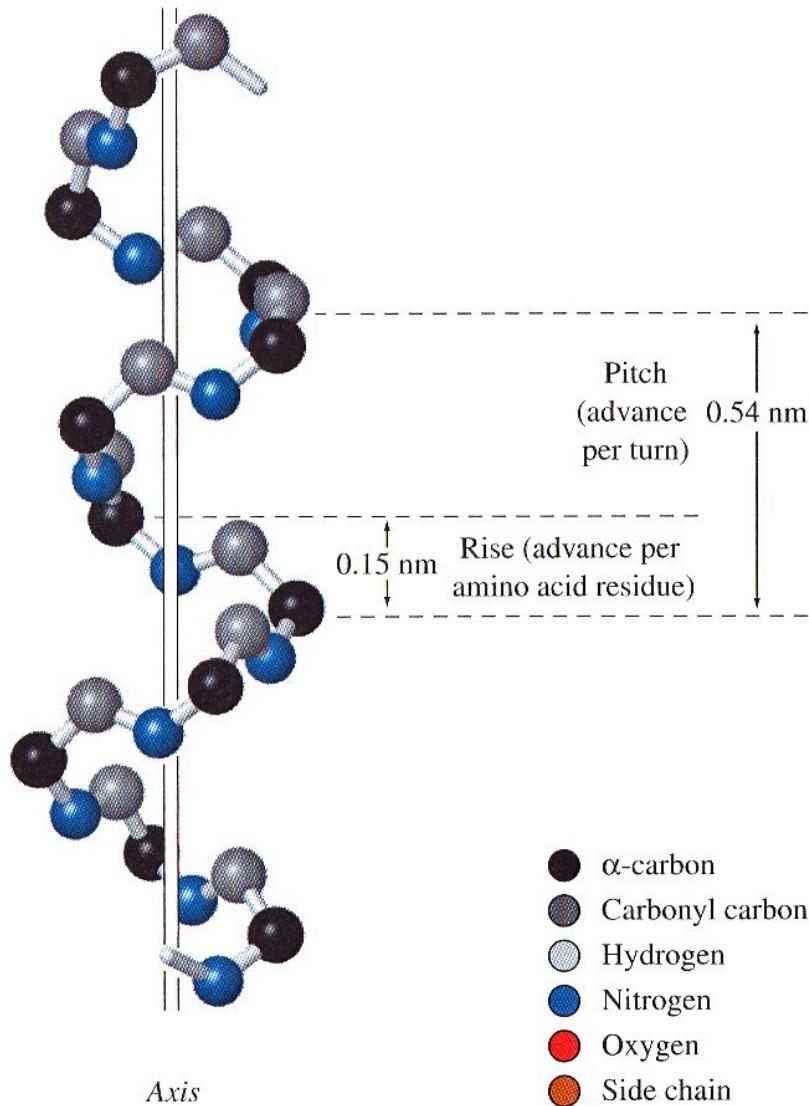
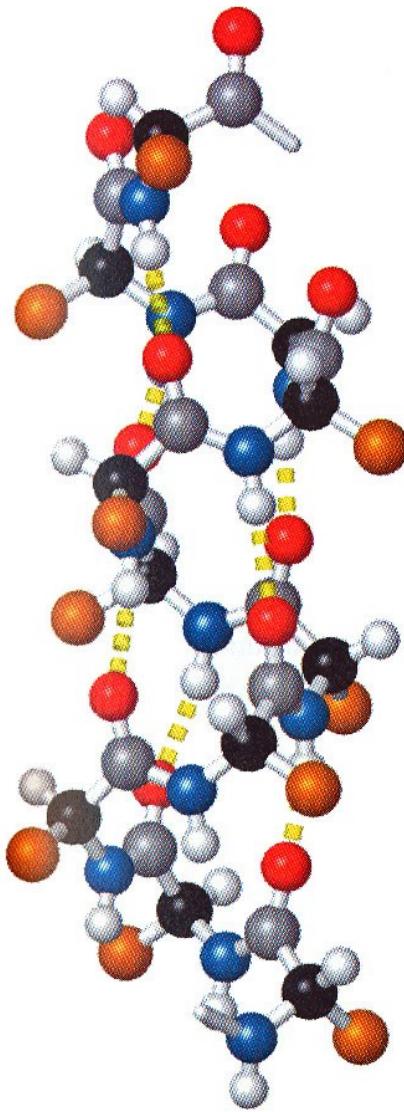


Figure 6-7 Fundamentals of Biochemistry, 2/e

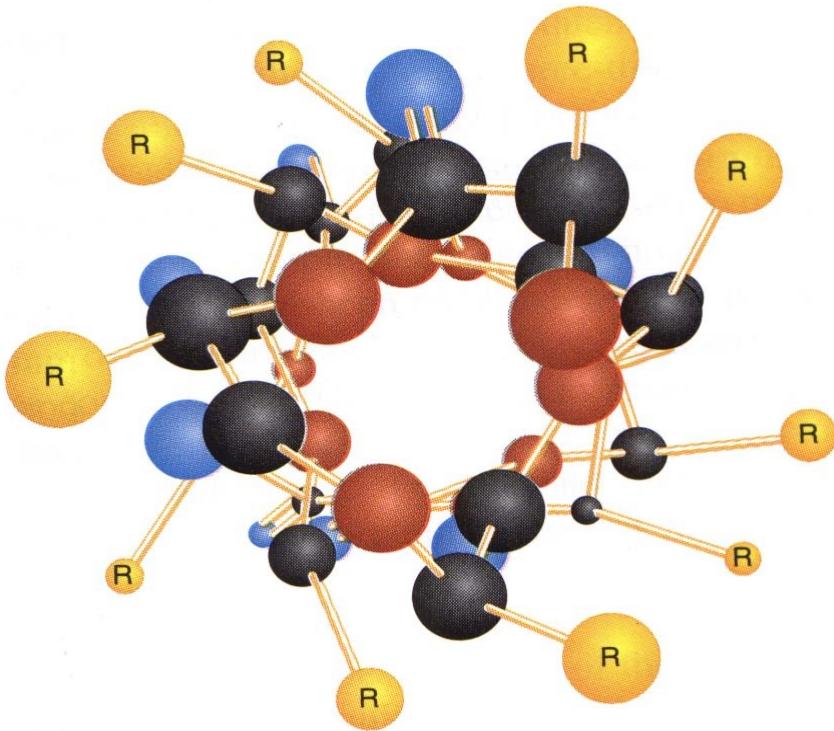
The Alpha-Helix

- Residues per turn: **3.6**
- The non-integral number of residues per turn was a surprise to crystallographers
- Rise per residue: 1.5 \AA
- Rise per turn (pitch): $3.6 \times 1.5 \text{ \AA} = 5.4 \text{ \AA}$

Right-handed Alpha Helix

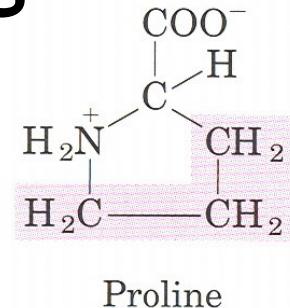


Top View of the Alpha-Helix



The R groups point away from the long axis of the helix

Amino acid sequence affects Alpha-Helix stability

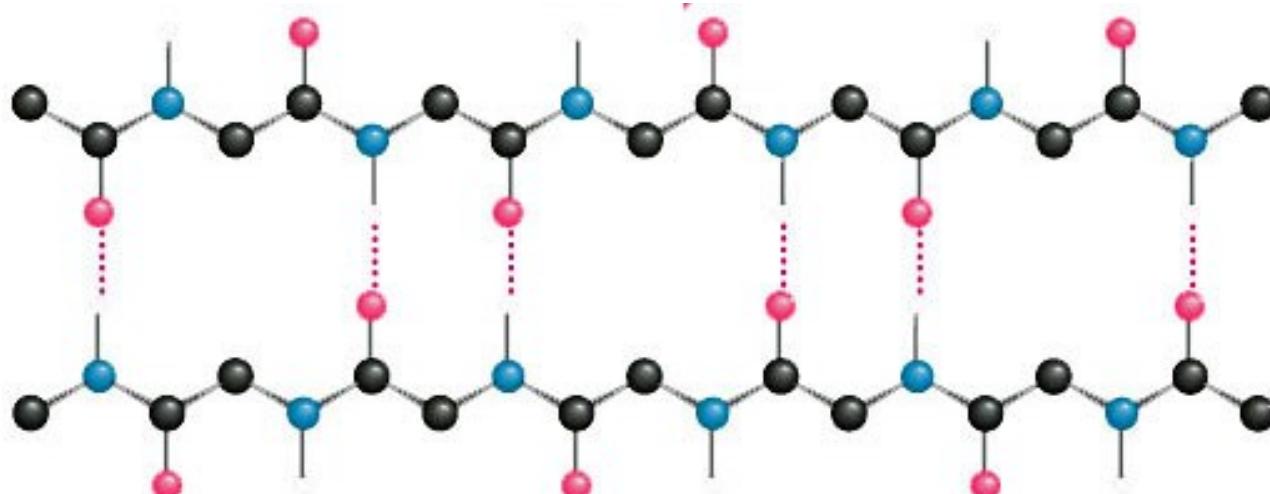


- **proline** creates a bend because
 1. the restricted rotation due to its cyclic structure
 2. its α -amino group has no N-H for hydrogen bonding
- strong electrostatic repulsion caused by the proximity of **several side chains of like charge**, e.g., Lys and Arg or Glu and Asp
- **steric crowding** caused by the proximity of bulky side chains, e.g., Val, Ile, Thr

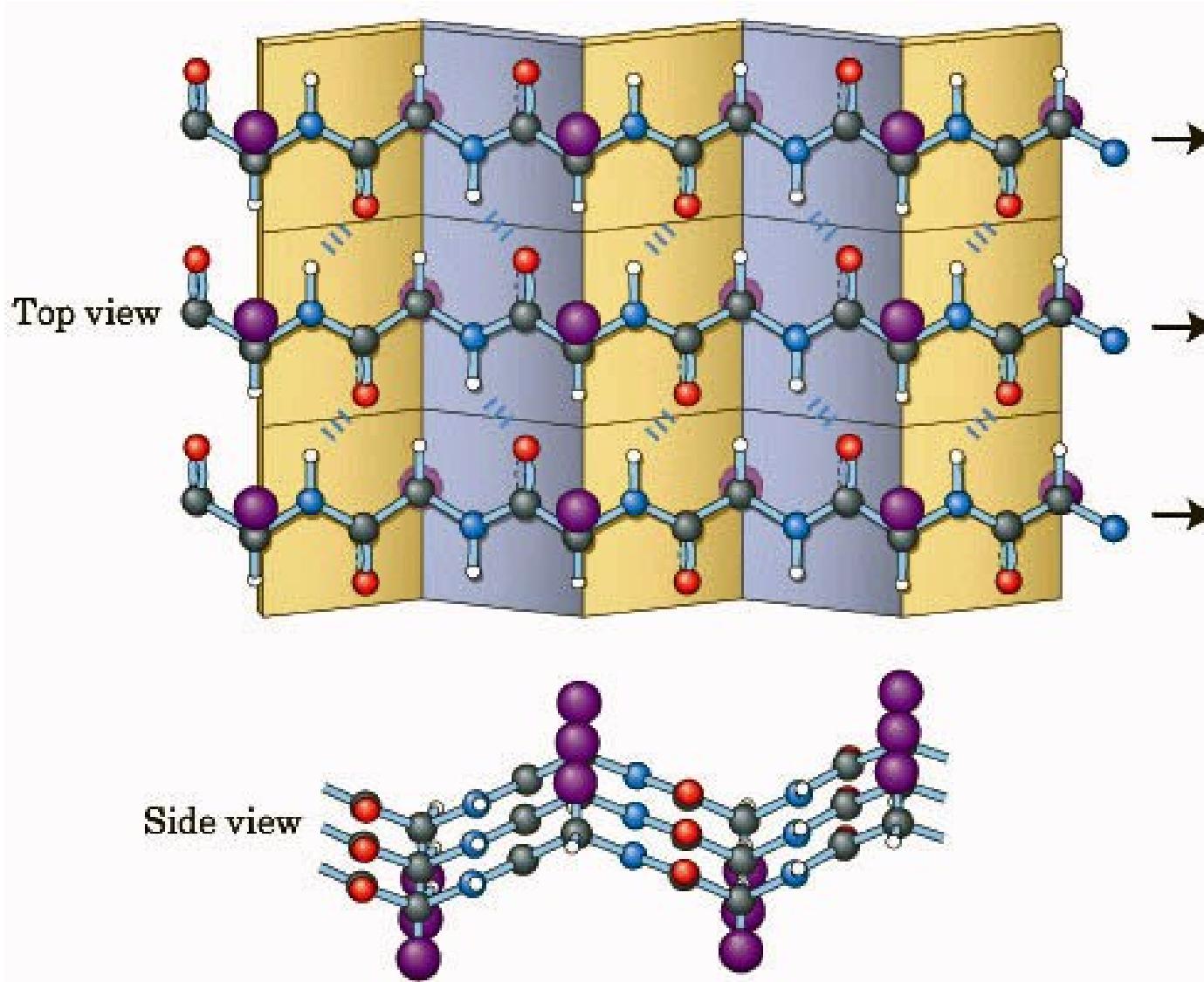
The Beta Sheet

Composed of beta strands

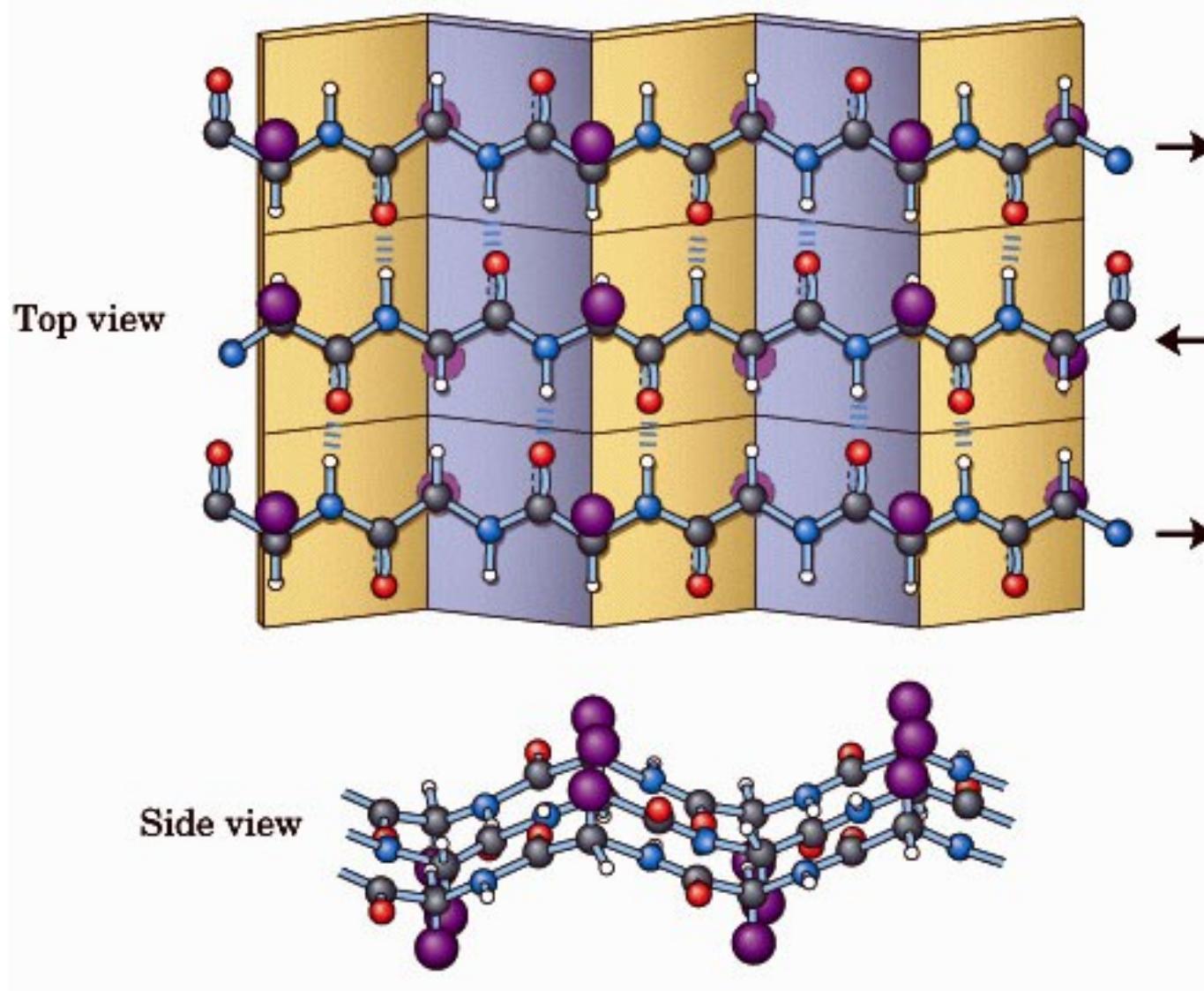
- Also first postulated by Pauling and Corey in 1951
- Strands may be parallel or antiparallel



Parallel Beta-Pleated Sheet

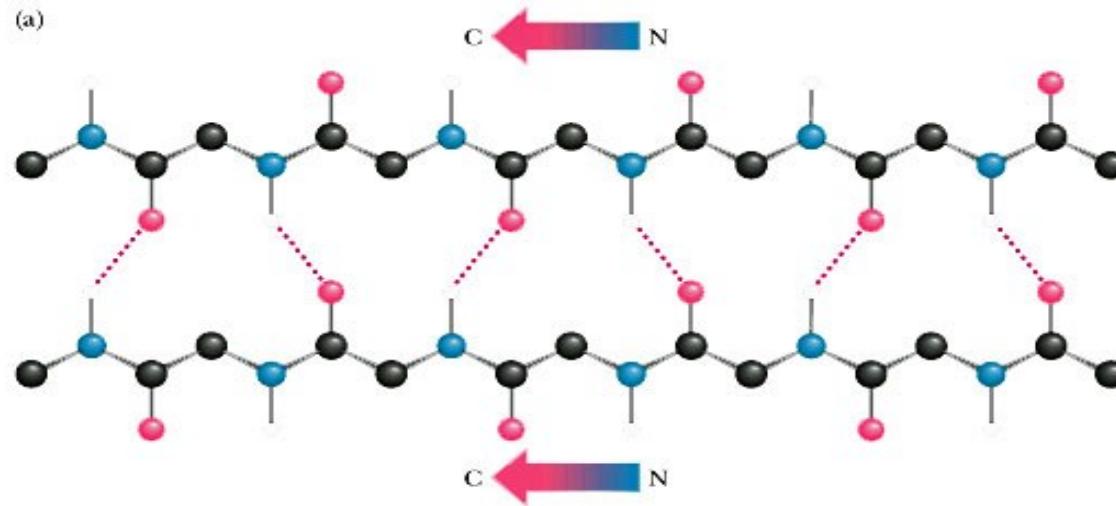


Antiparallel Beta-Pleated Sheet

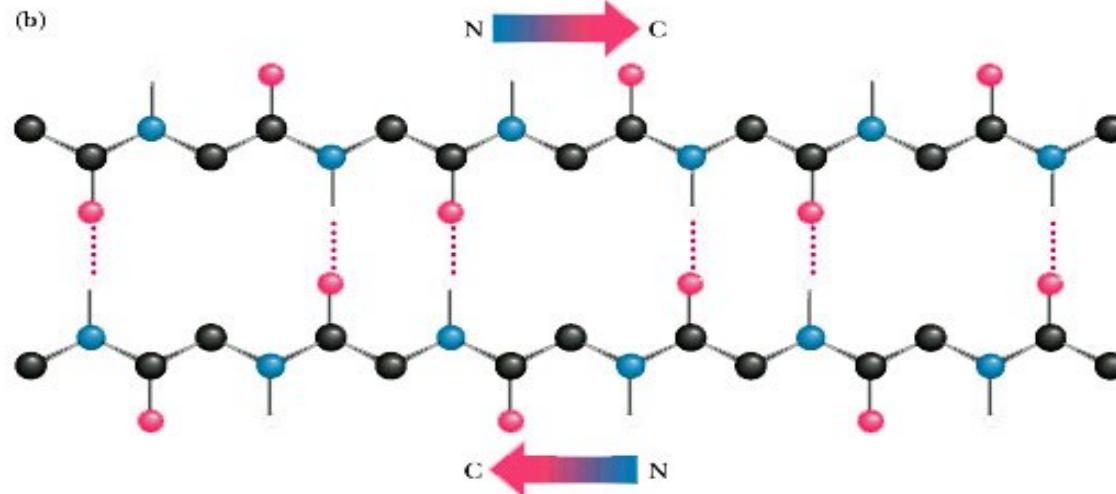


Hydrogen Bond Arrangement in Parallel and Antiparallel Beta-Pleated Sheets

(a)



(b)



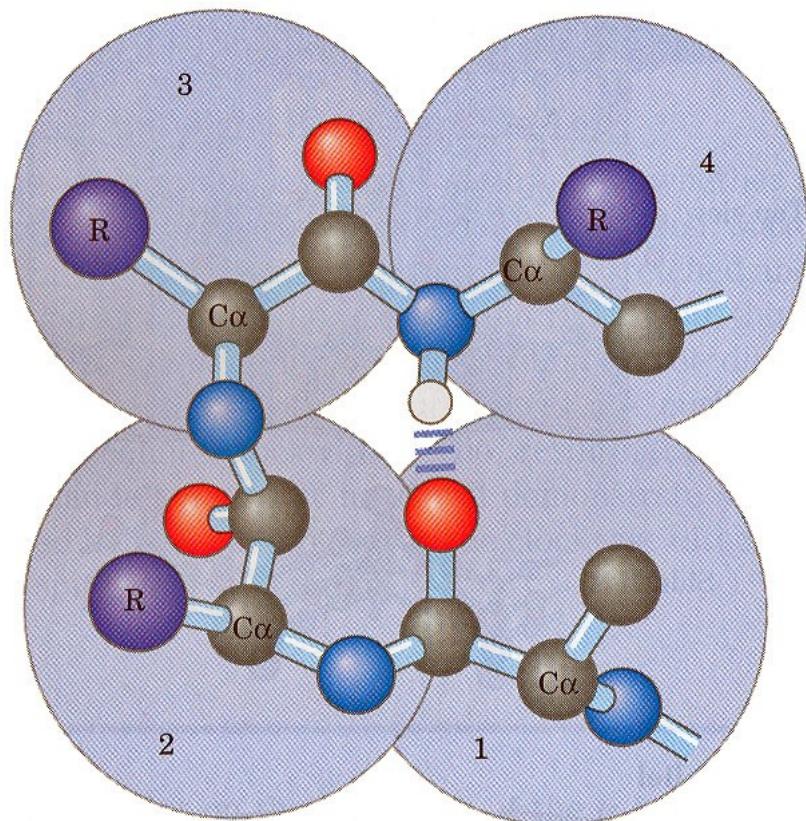
The Beta-Pleated Sheet

- Rise per residue:
 - 3.47 \AA for antiparallel strands
 - 3.25 \AA for parallel strands
 - Compared to 1.5 \AA for α -helix

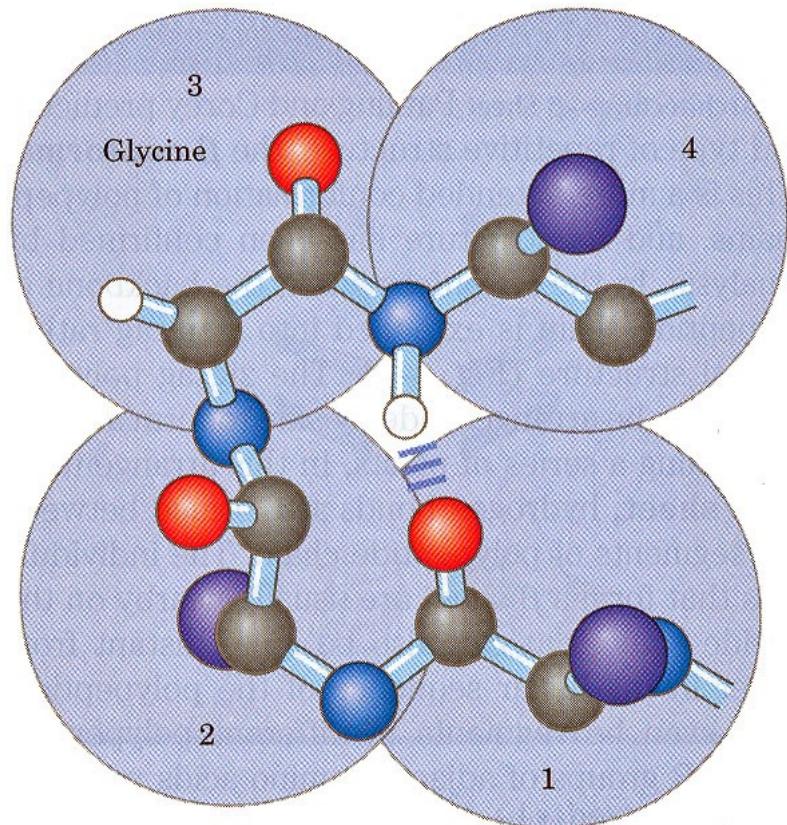
The Beta Turn

- allows the peptide chain to reverse direction
- carbonyl C of one residue is H-bonded to the amide proton of a residue three residues away
- proline and glycine are prevalent in beta turns

Structures of beta-Turns



Type I



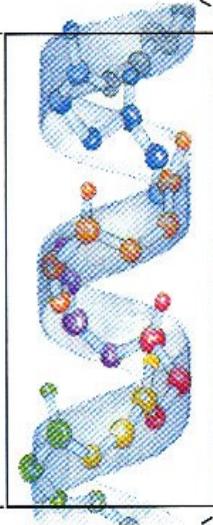
Type II
($\alpha\alpha_3 = \text{gly}$)

The Four Levels of Protein Structure

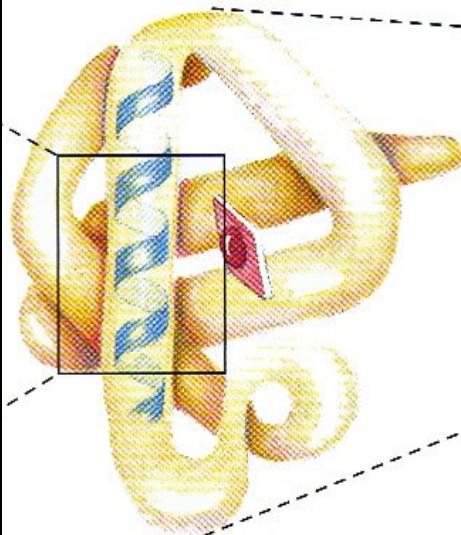
Primary
structure

Lys
Lys
Gly
Gly
Leu
Val
Ala
His

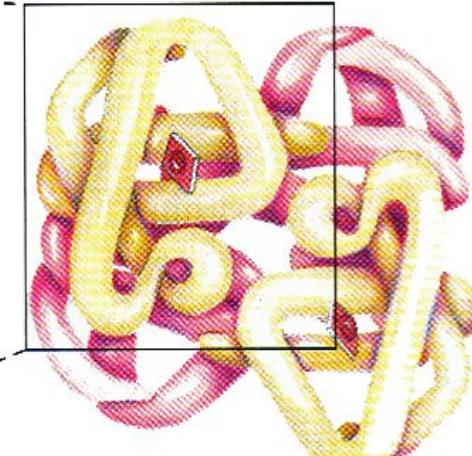
Secondary
structure



Tertiary
structure

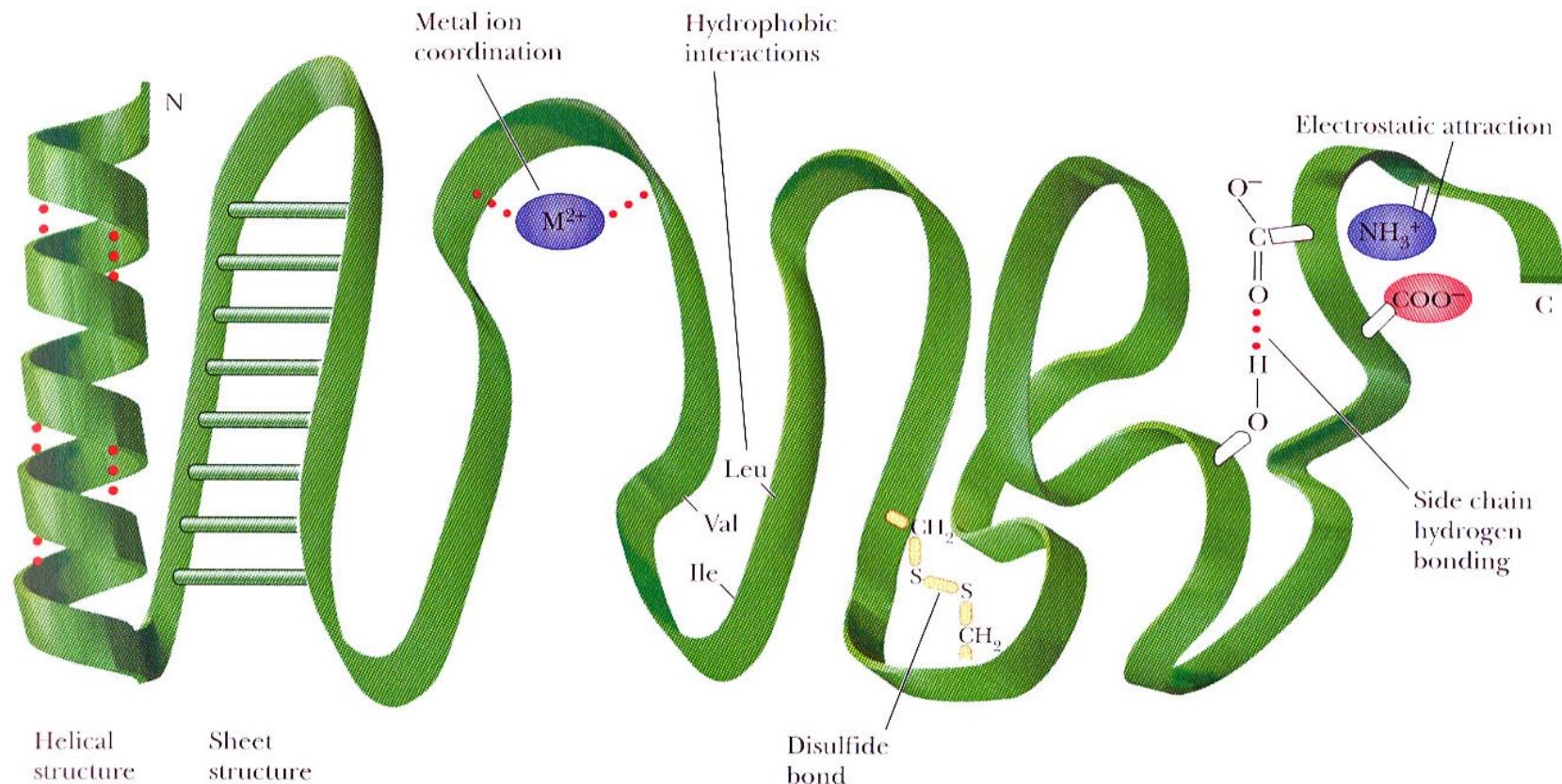


Quaternary
structure



Tertiary structure is the overall three-dimensional arrangement of all atoms in a protein; some proteins contain two or more separate polypeptide chains, or subunits, which maybe identical or different. The arrangement of these protein subunits in three-dimensional complexes constitutes quaternary structure.

Forces that Stabilize the Tertiary Structure of Proteins



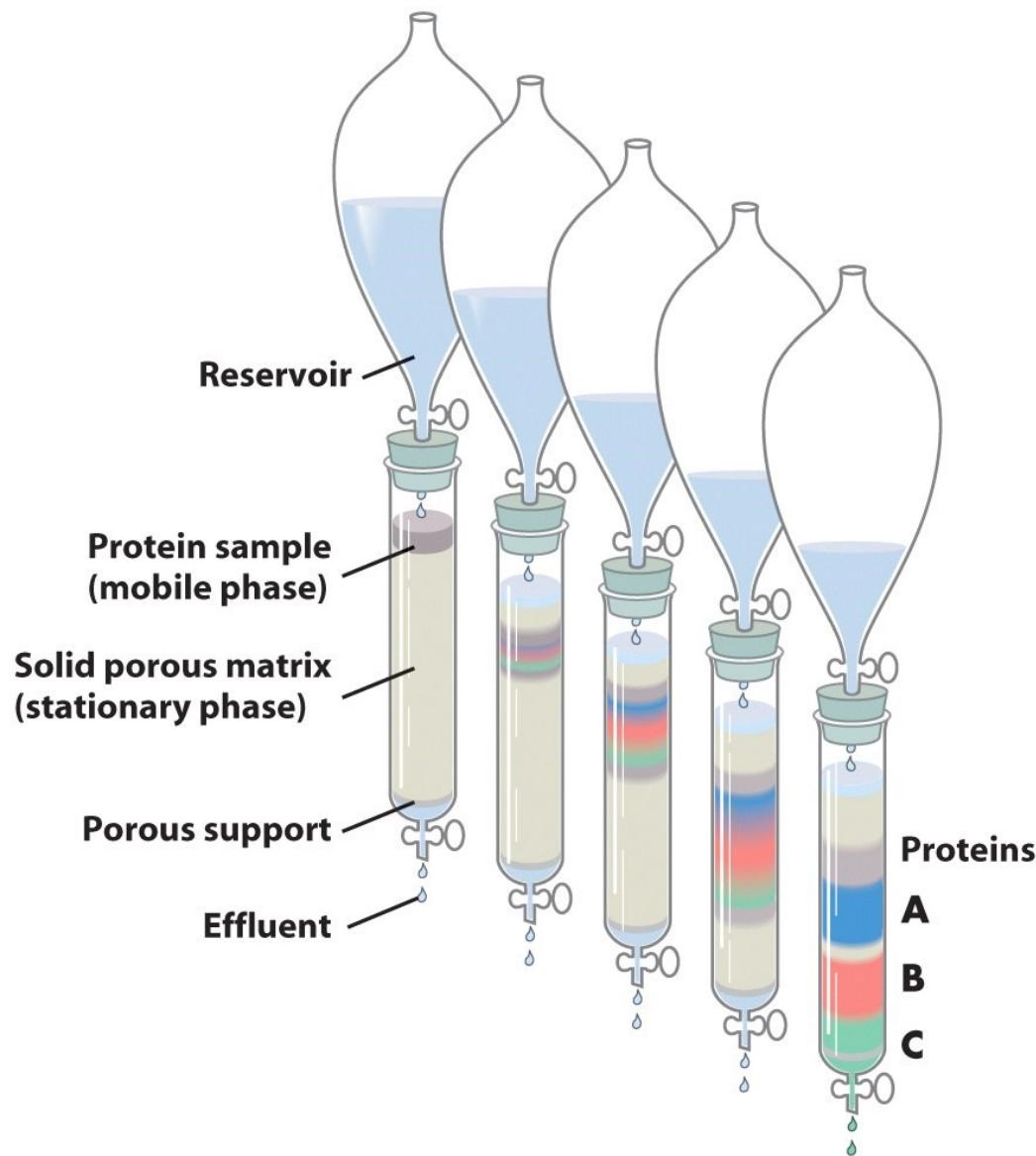
Note that the helical and sheet structures are two kinds of backbone hydrogen bonding. Although backbone hydrogen bonding is part of secondary structure, the conformation of the backbone puts constraints on the possible arrangement of the side chains.

Working with proteins

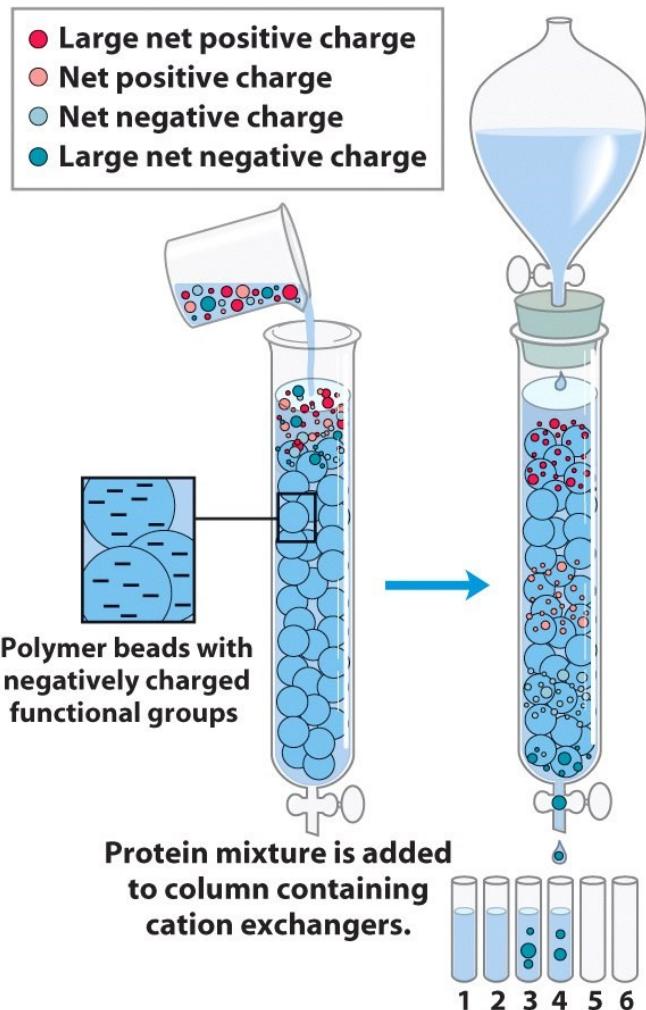
Protein separation and purification

- Protein can be separated according to their size, charge and binding properties etc.
- Initial steps: extraction of protein mixtures from cells/tissues (centrifugation, precipitation, dialysis etc.)
- Separation from a mixture of proteins: Column Chromatography and electrophoresis
- Column Chromatography: ion-exchange chromatography, size exclusion chromatography, affinity chromatography
- Electrophoresis: isoelectric focusing and two-dimensional electrophoresis

Concept of column chromatography



Ion-exchange chromatography



Proteins move through the column at rates determined by their net charge at the pH being used. With cation exchangers, proteins with a more negative net charge move faster and elute earlier.

Cation and Anion Exchange Chromatography Media

A. Anion Exchange Media

Name	Functional Group
DEAE (Diethylaminoethyl)	-OCH ₂ CH ₂ N ⁺ H(CH ₂ CH ₃) ₂
QEA (Quaternary aminoethyl)	-OCH ₂ CH ₂ N ⁺ (C ₂ H ₅) ₂ CH ₂ CH(OH)CH ₃
Q (Quaternary ammonium)	-CH ₂ N ⁺ (CH ₃) ₃

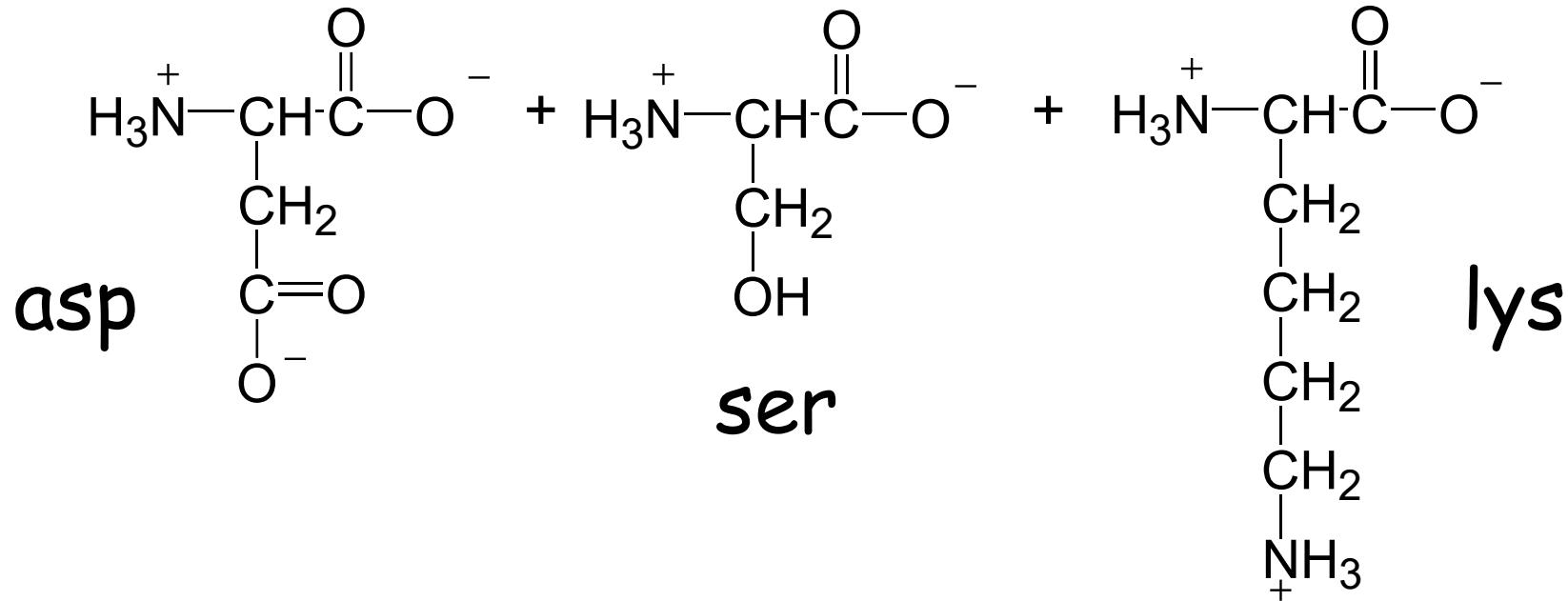
B. Cation Exchange Media

Name	Functional Group
CM (Carboxymethyl)	-OCH ₂ COO ⁻
SP (Sulfopropyl)	-CH ₂ CH ₂ CH ₂ SO ₃ ⁻
S (Methyl sulfonate)	-CH ₂ SO ₃ ⁻

Common Functional Groups

Anion exchangers: Tertiary and quaternary amines
Cation exchangers: Carboxylic and Sulfonic Acids

Separation of Amino Acids by Ion-Exchange Chromatography

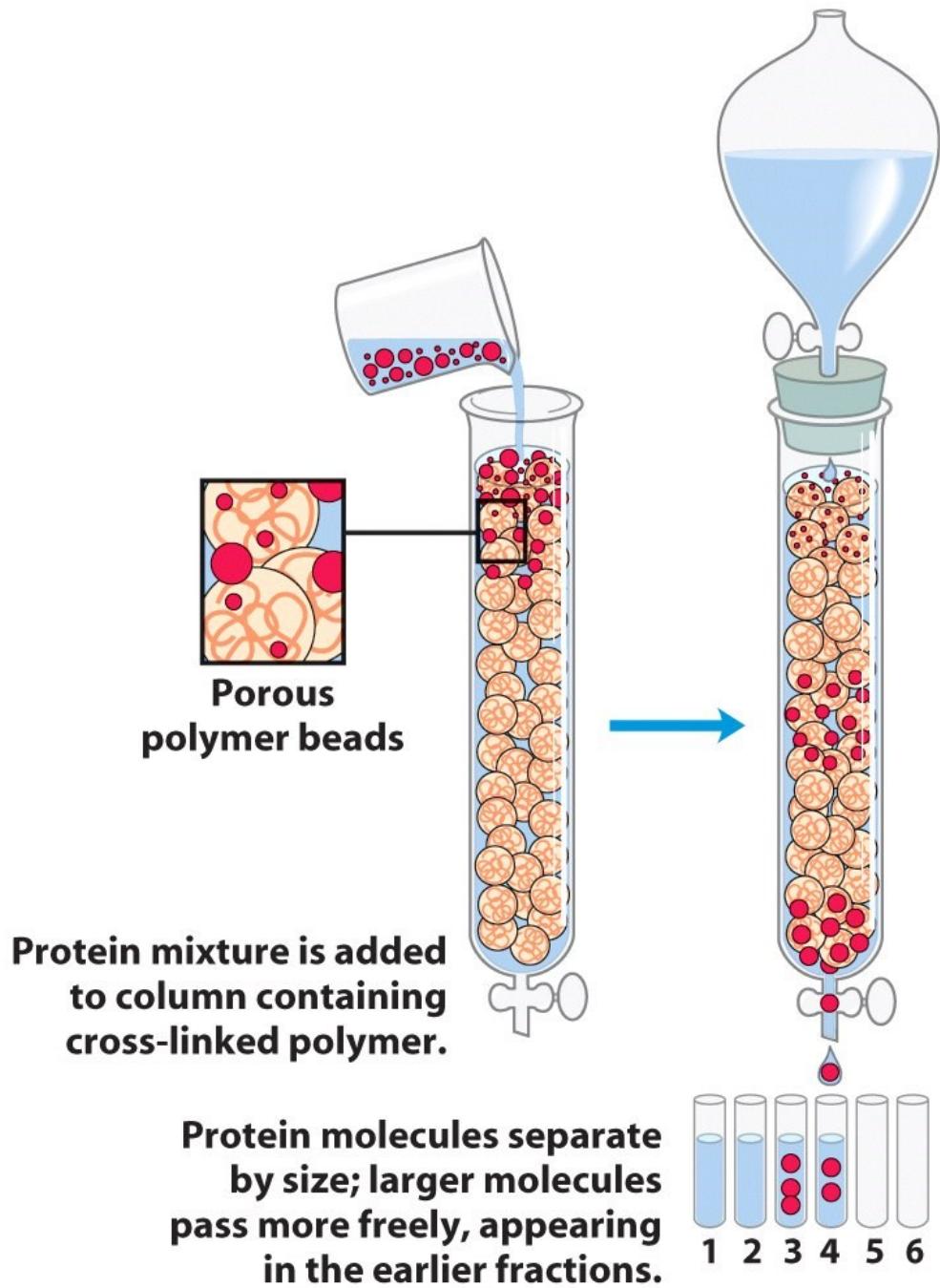


At pH 7, the order of elution is:

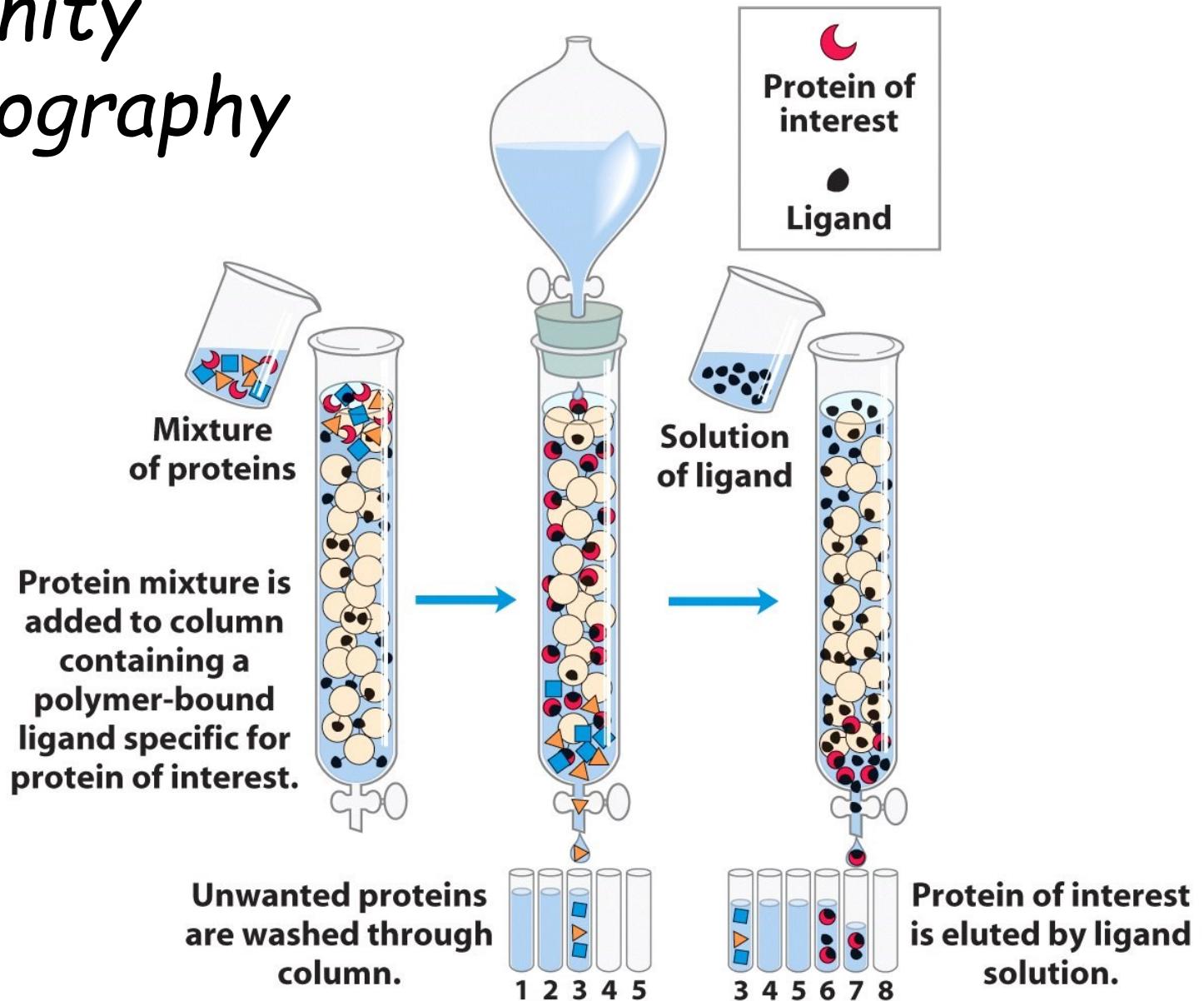
Anion exchange: (1) lys, (2) ser, (3) asp

Cation exchange: (1) asp, (2) ser, (3) lys

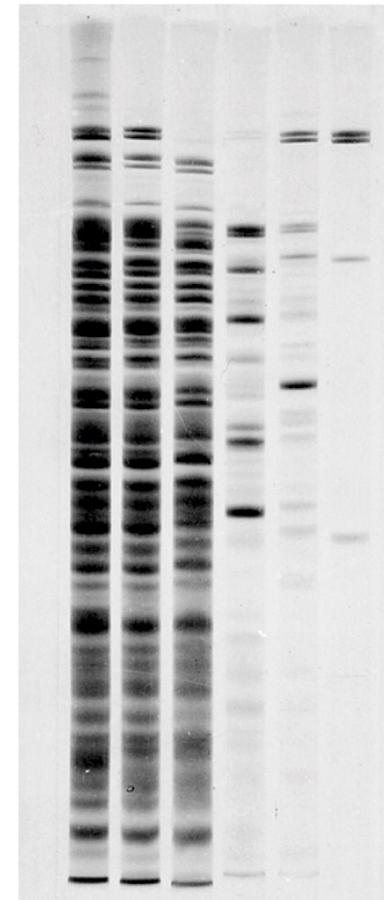
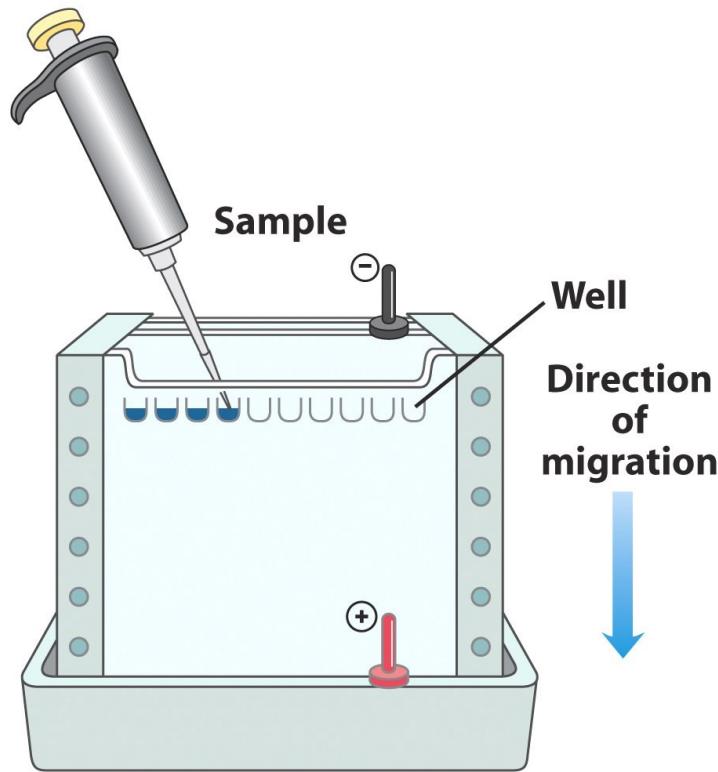
Size exclusion chromatography



Affinity chromatography



Gel Electrophoresis

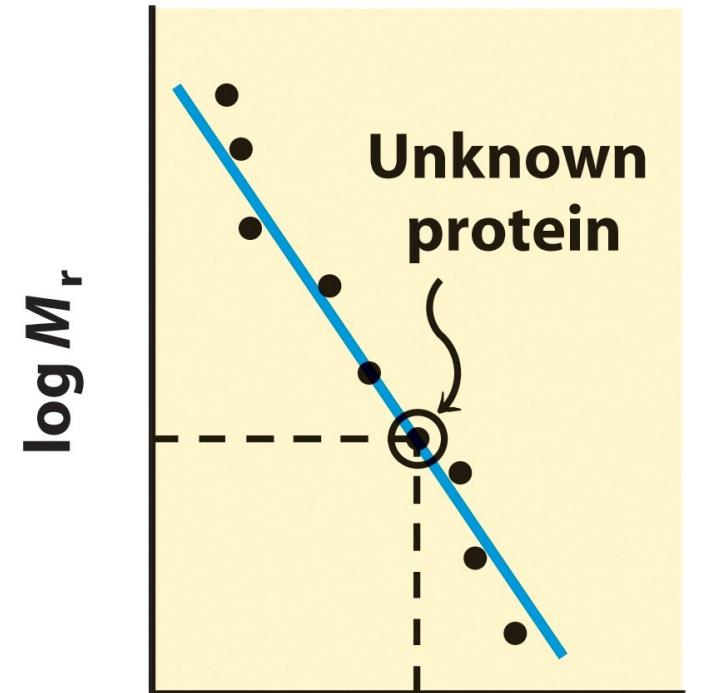
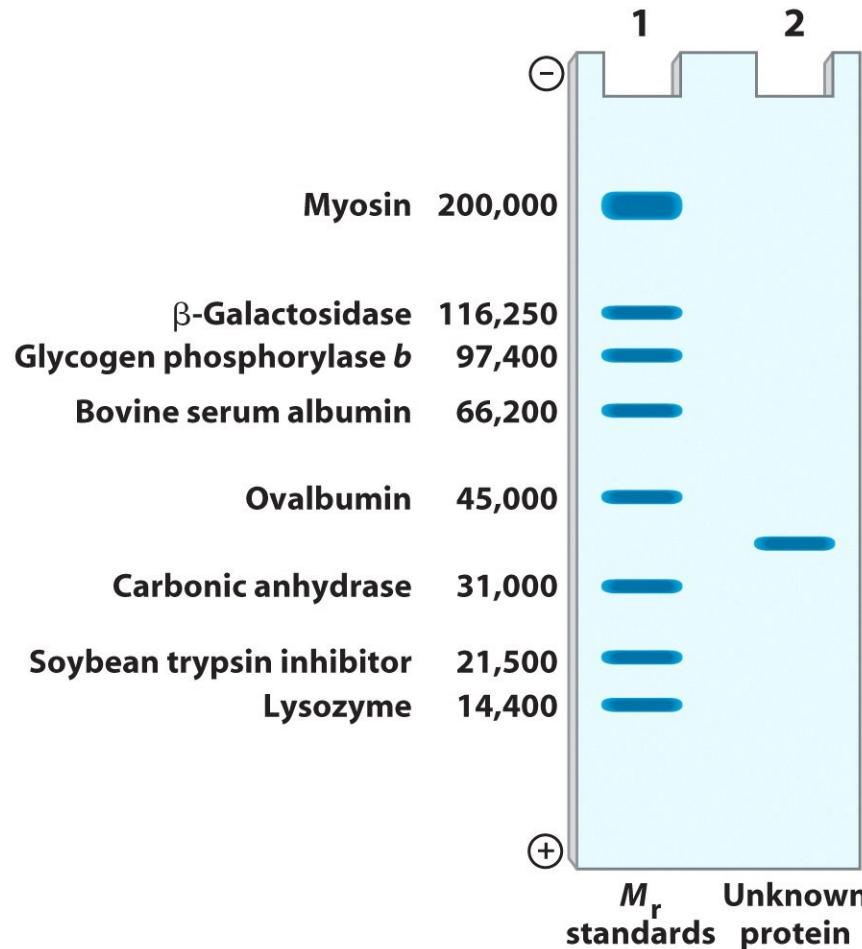


$$U=Z/f$$

Z: net charge, f: frictional coefficient

Migration of proteins in the gel is approximately
Proportional to their charge-to-mass ratio

Estimating the molecular weight of an unknown protein



Relative migration