The Genetic Code

- A codon in messenger RNA is either translated into an amino acid or serves as a translational start/stop signal

First mRNA base (5′ end)	Second mRNA base: U	C	A	G	Third mRNA base (3′ end)
U	UUU Phe	UCU Ser	UAU Tyr	UGU Cys	U
U	UUC Phe	UCC Ser	UAC Tyr	UGC Cys	C
U	UUA Leu	UCA Ser	UAA Stop	UGA Stop	A
U	UUG Leu	UCG Ser	UAG Stop	UGG Trp	G
C	CUU Leu	CCU Pro	CAU His	CGU Arg	U
C	CUC Leu	CCC Pro	CAC His	CGC Arg	C
C	CUA Leu	CCA Pro	CAA Gln	CGA Arg	A
C	CUG Leu	CCG Pro	CAG Gln	CGG Arg	G
A	AUU Ile	ACU Thr	AAU Asn	AGU Ser	U
A	AUC Ile	ACC Thr	AAC Asn	AGC Ser	C
A	AUA Ile	ACA Thr	AAA Lys	AGA Arg	A
A	AUG Met or start	ACG Thr	AAG Lys	AGG Arg	G
G	GUU Val	GCU Ala	GAU Asp	GGU Gly	U
G	GUC Val	GCC Ala	GAC Asp	GGC Gly	C
G	GUA Val	GCA Ala	GAA Glu	GGA Gly	A
G	GUG Val	GCG Ala	GAG Glu	GGG Gly	G

Proteins

Type of Protein	Function	Examples
Enzymatic proteins	Selective acceleration of chemical reactions	Digestive enzymes catalyze the hydrolysis of the polymers in food.
Structural proteins	Support	Insects and spiders use silk fibers to make their cocoons and webs, respectively. Collagen and elastin provide a fibrous framework in animal connective tissues. Keratin is the protein of hair, horns, feathers, and other skin appendages.
Storage proteins	Storage of amino acids	Ovalbumin is the protein of egg white, used as an amino acid source for the developing embryo. Casein, the protein of milk, is the major source of amino acids for baby mammals. Plants have storage proteins in their seeds.
Transport proteins	Transport of other substances	Hemoglobin, the iron-containing protein of vertebrate blood, transports oxygen from the lungs to other parts of the body. Other proteins transport molecules across cell membranes.
Hormonal proteins	Coordination of an organism's activities	Insulin, a homone secreted by the pancreas, helps regulate the concentration of sugar in the blood of vertebrates.
Receptor proteins	Response of cell to chemical stimuli	Receptors built into the membrane of a nerve cell detect chemical signals released by other nerve cells.
Contractile and motor proteins	Movement	Actin and myosin are responsible for the movement of muscles. Other proteins are responsible for the undulations of the organelles called cilia and flagella.
Defensive proteins	Protection against disease	Antibodies combat bacteria and viruses.

Table 5.1

Structures of Proteins

Polypeptides or proteins : Are polymers of amino acid

- **Primary structure:** Peptide bonds

- **Secondary Structure:**

Hydrogen bonds between AAs at different locations, Electrostatic forces, van der Waals forces

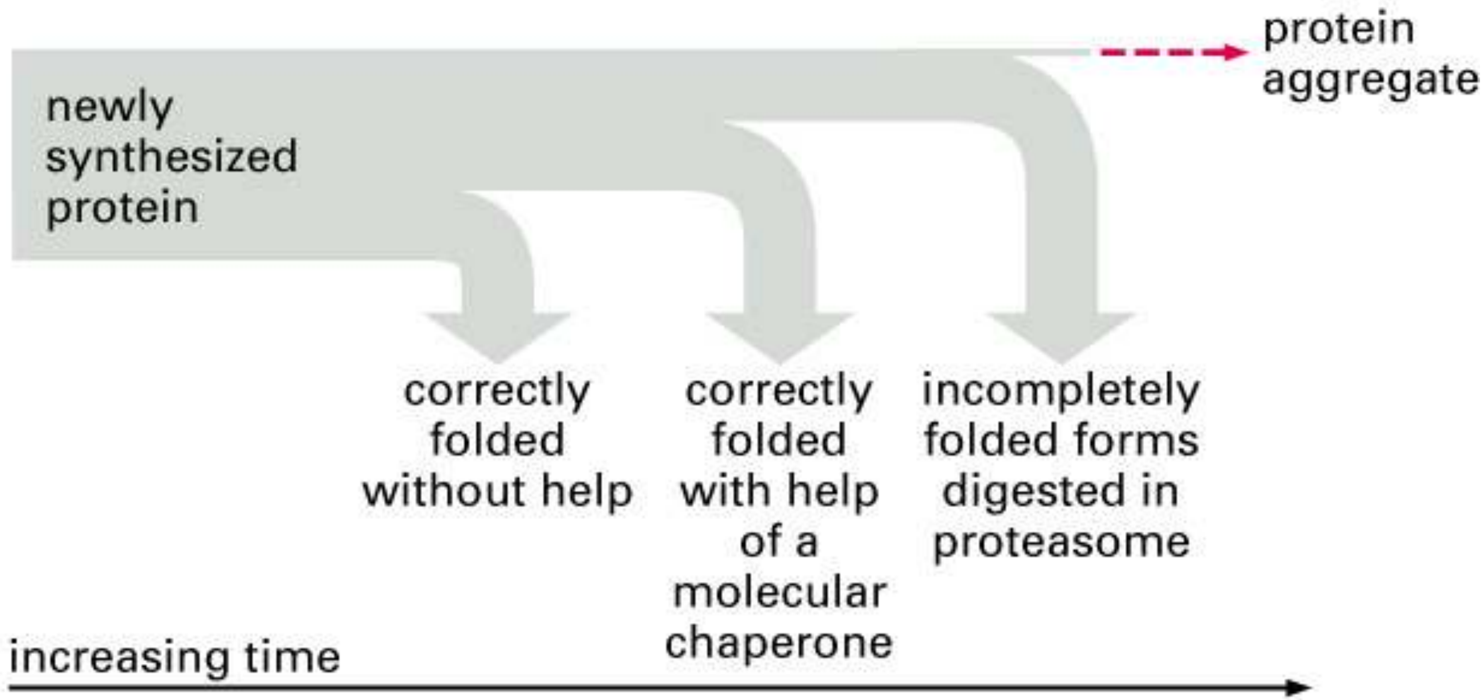
Types: Alpha helices and beta pleated sheets

- **Tertiary structure: +** disulphide bonds,

  formed by folding

- **Quartenary structure:** weak bonds different polypeptides

Protein Folding kinetics



Levels of Protein Structure

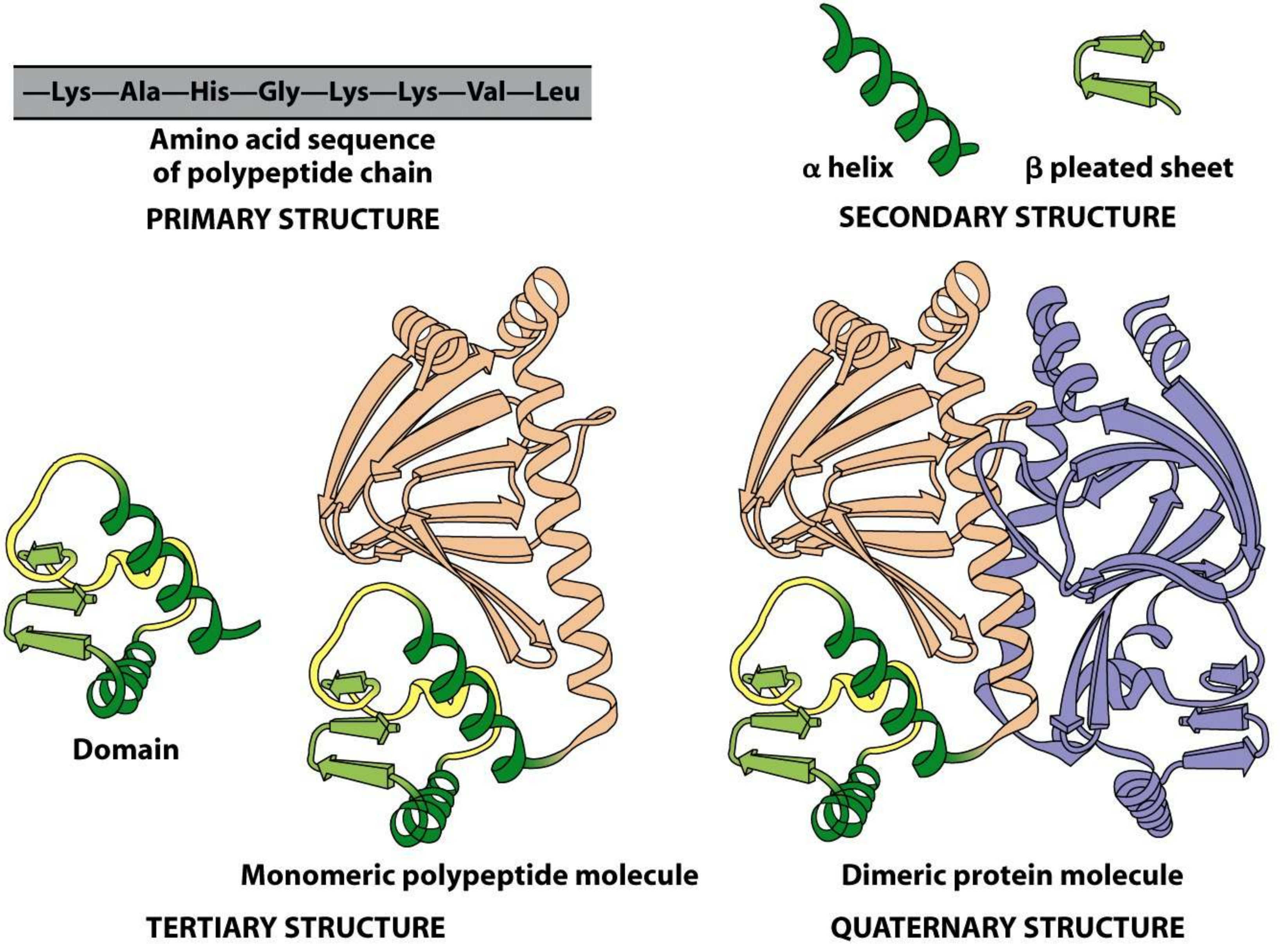
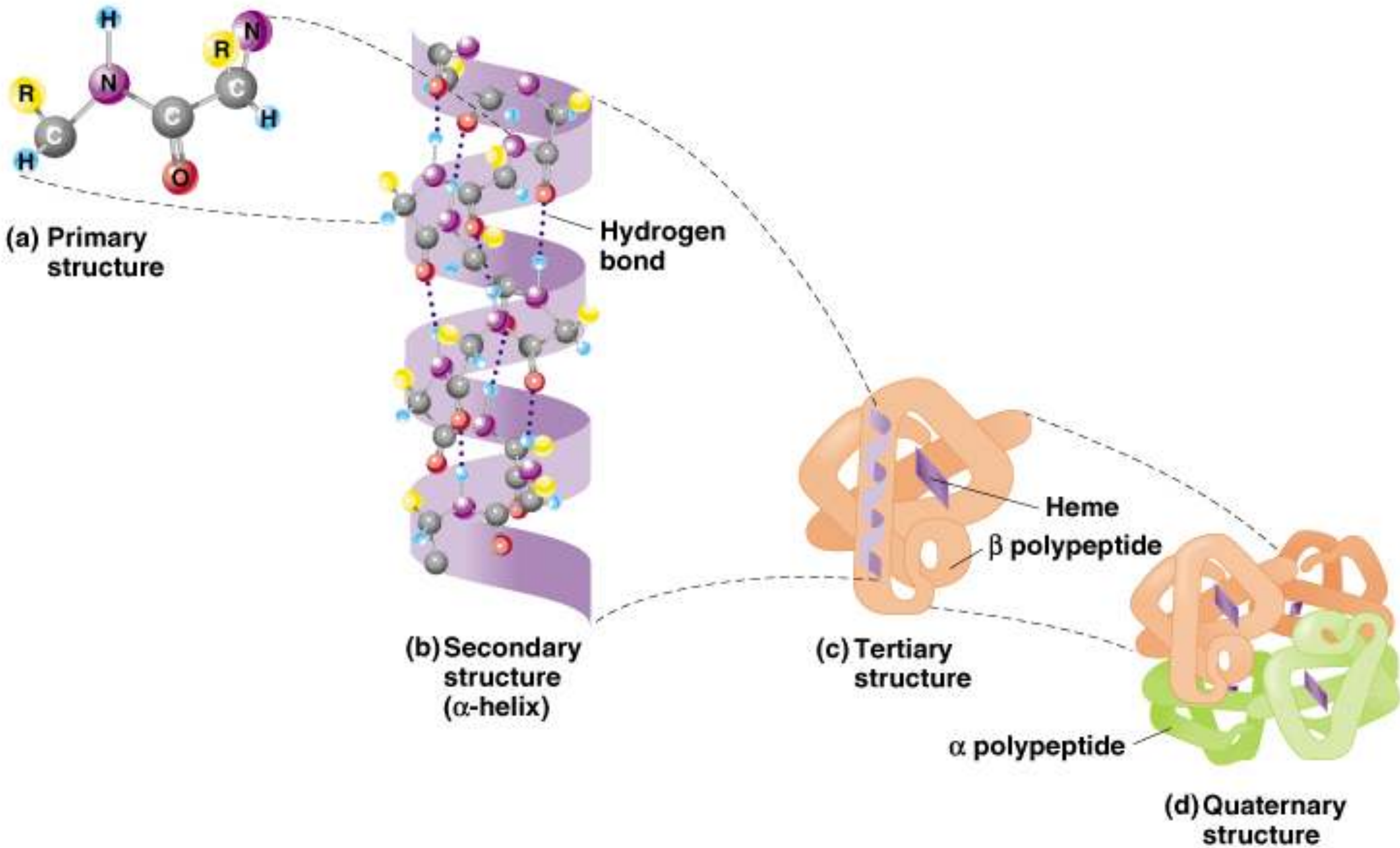
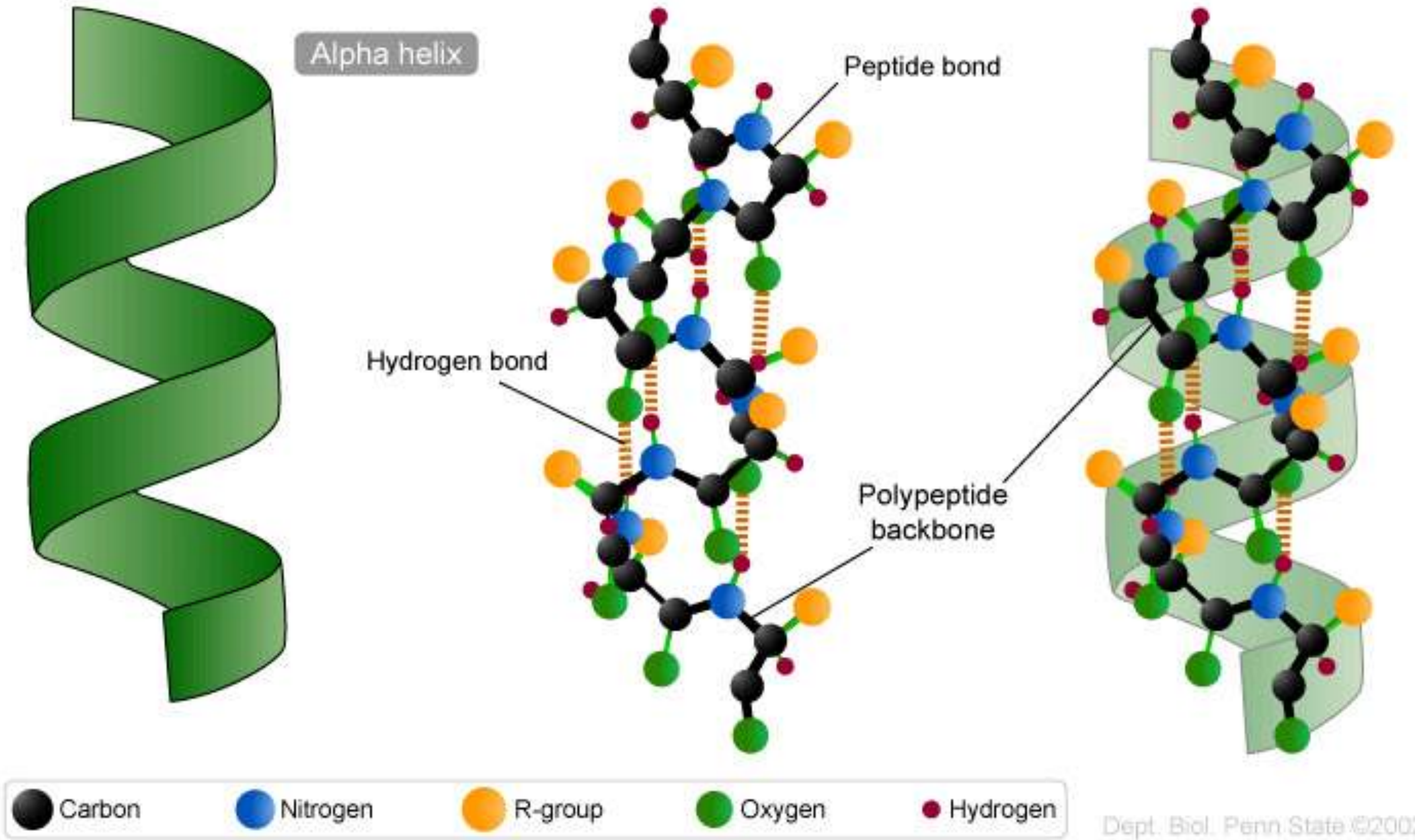


Figure 4-2
Kuby IMMUNOLOGY, Sixth Edition

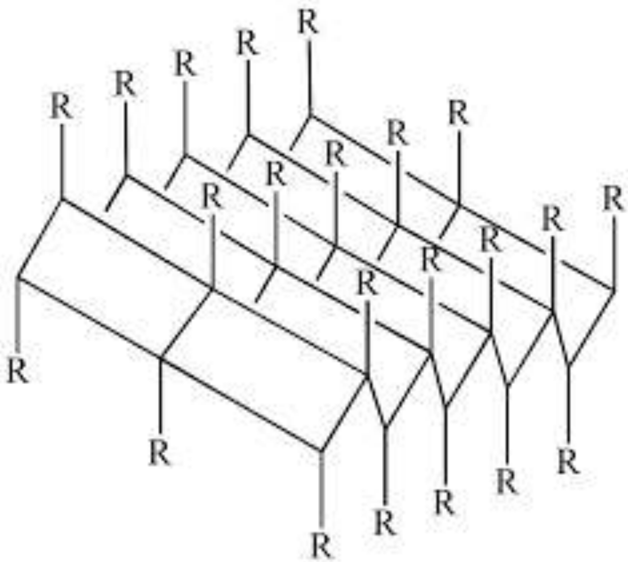
Polypeptides : Are polymers of amino acid

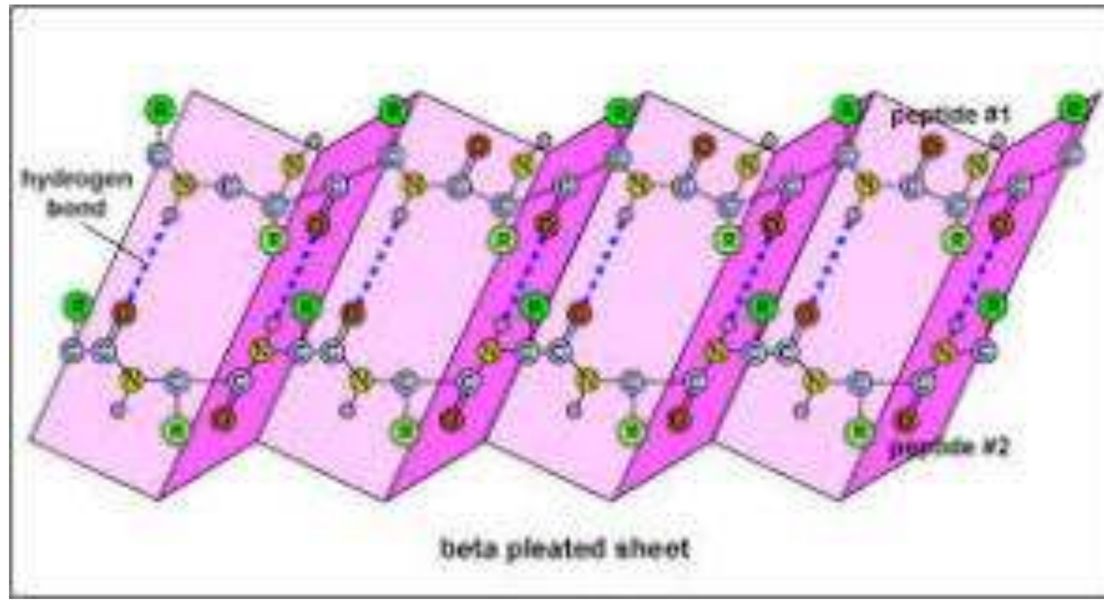


Alpha helical structure

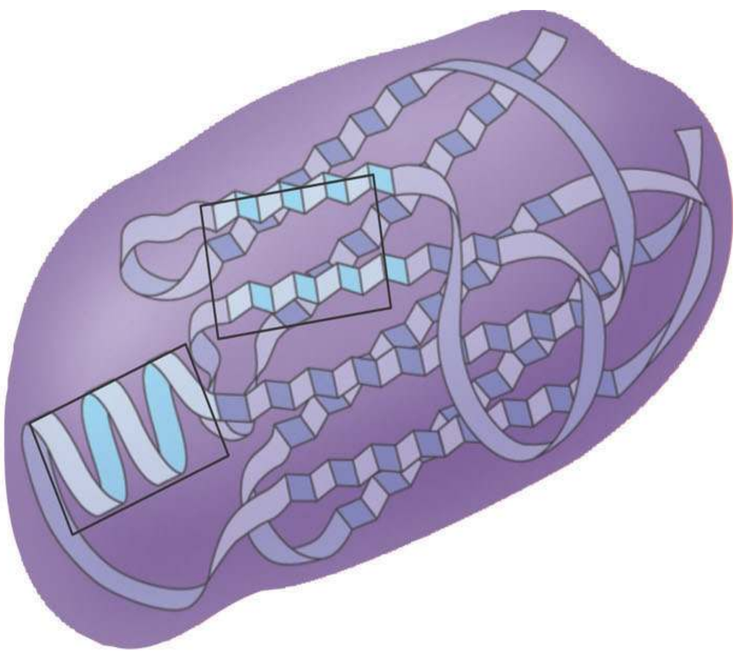


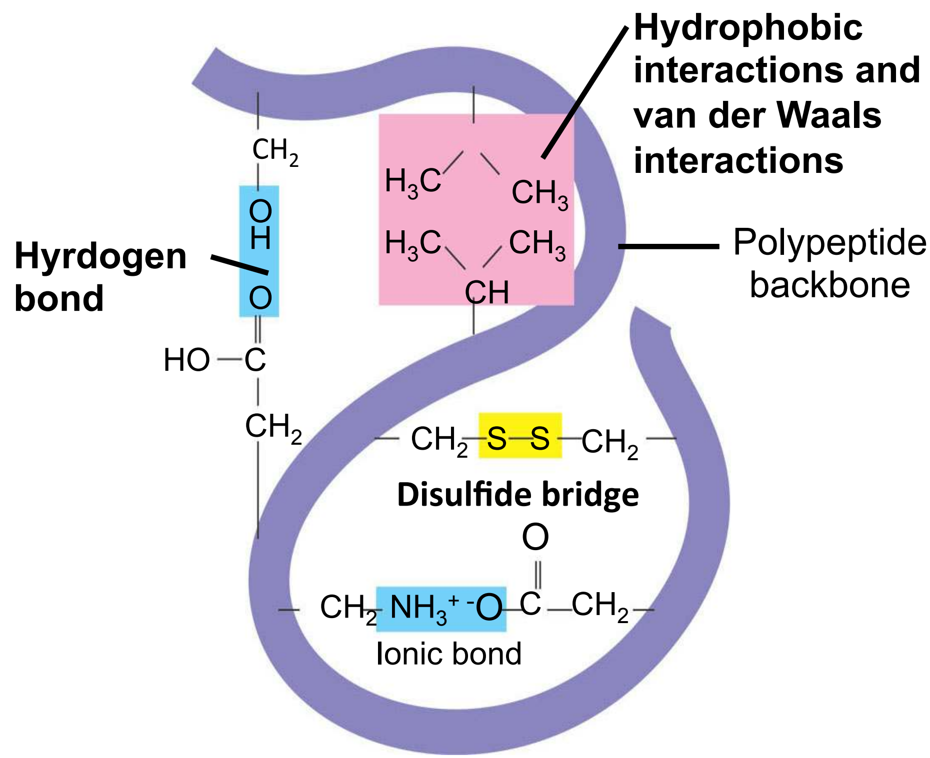
Beta pleated sheet structure





Protein Folding





- Denaturation and Renaturation

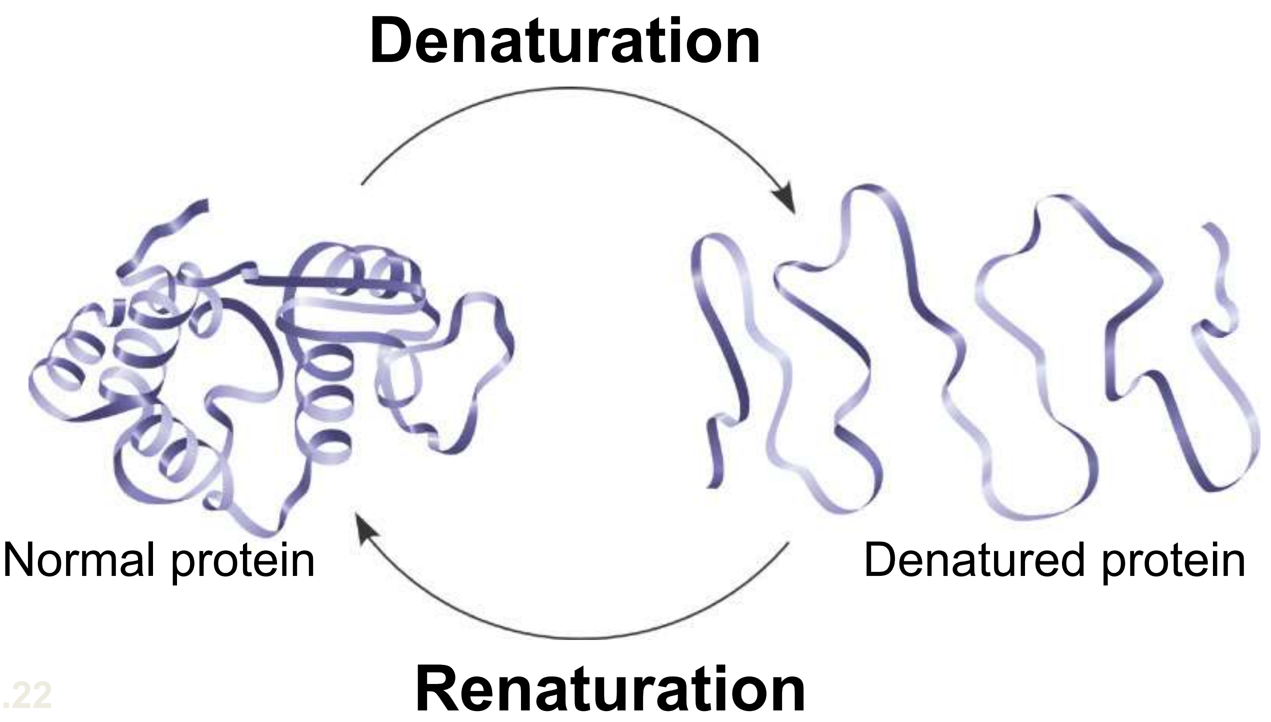
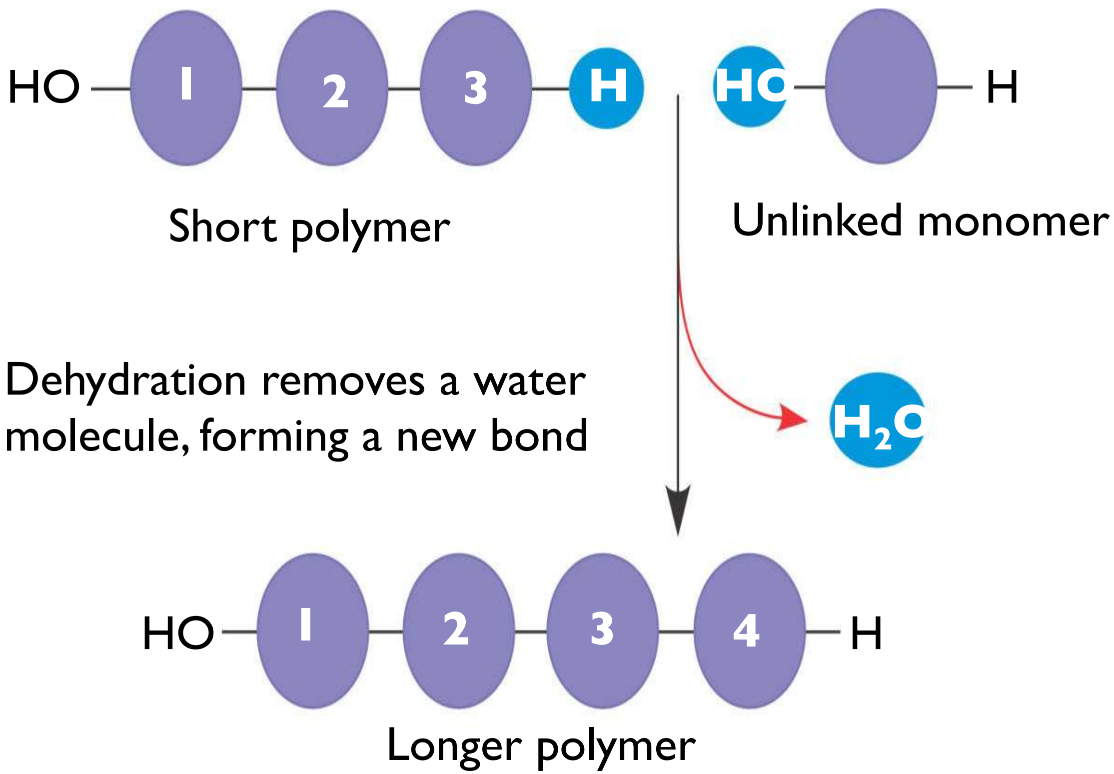
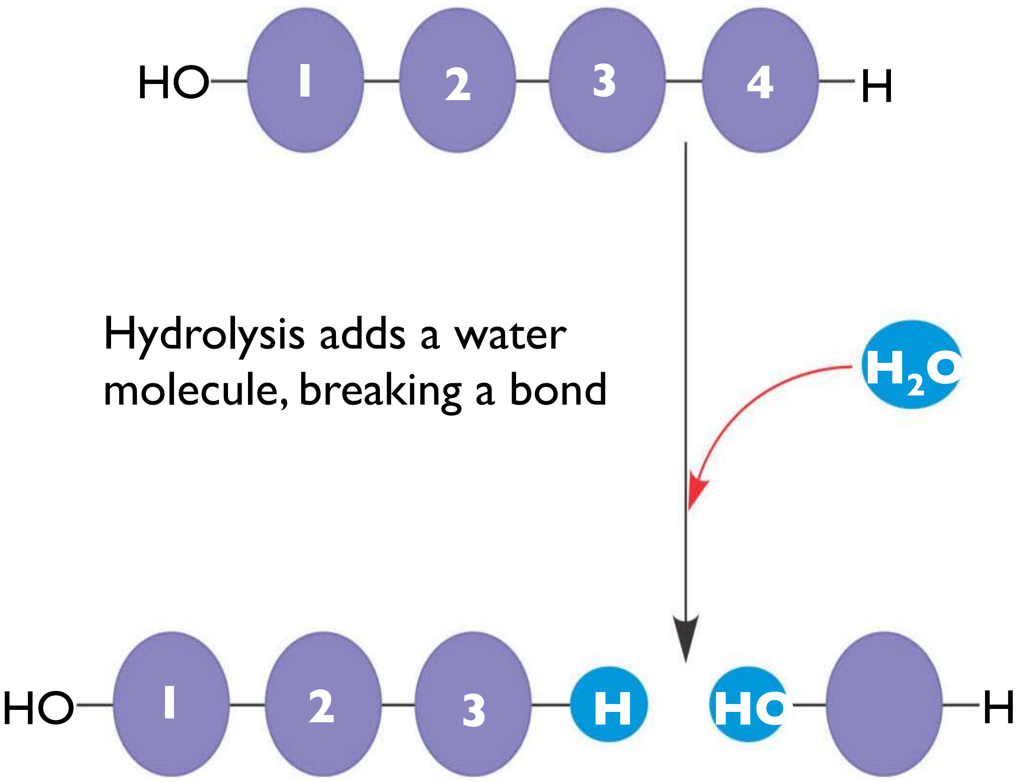


Figure 5.22

The Synthesis and Breakdown of Polymers



(a) Dehydration reaction in the synthesis of a polymer



(b) Hydrolysis of a polymer

Figure 5.2B

Amino Acid Polymers

- Amino acids
  - Are linked by peptide bonds

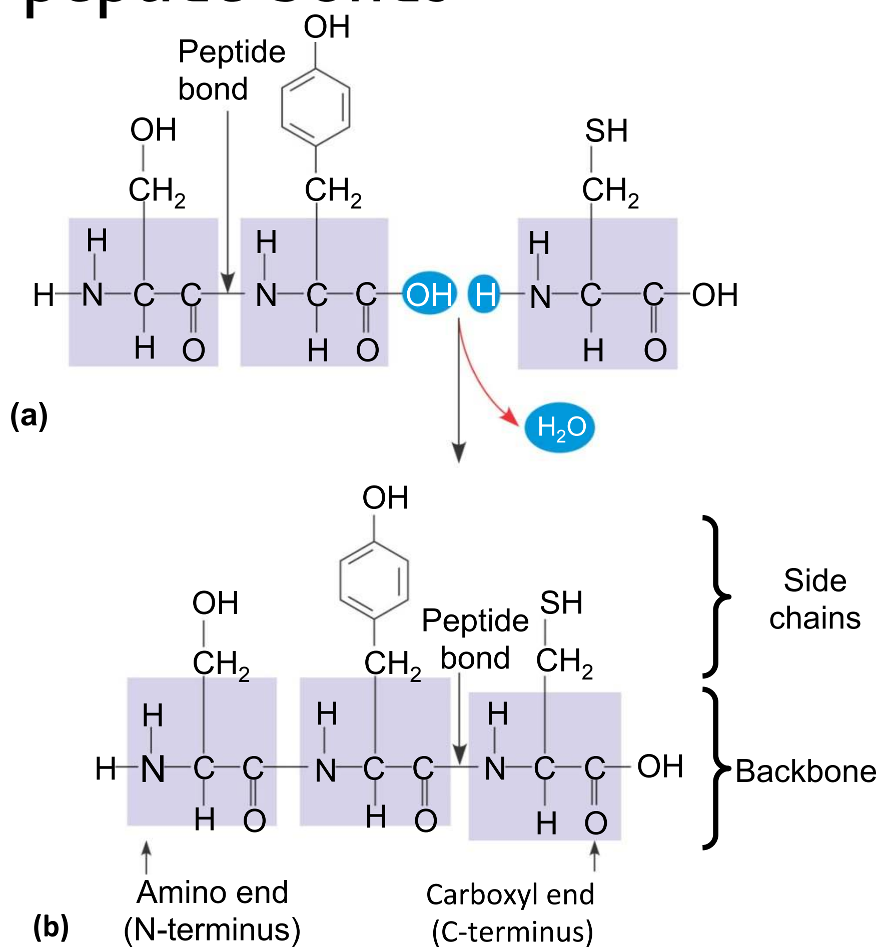


Figure 5.18

Despite this immense diversity, molecular structure and function can still be grouped roughly by class.

Each of the four major classes of large biological molecules:

Sugars, Lipids, Proteins, Nucleic Acids

For each class, the large molecules have emergent properties not found in their individual building blocks.

Salt precipitation of proteins

Proteins is separated in different fractions based on a property such as size or charge :**Fractionation**:

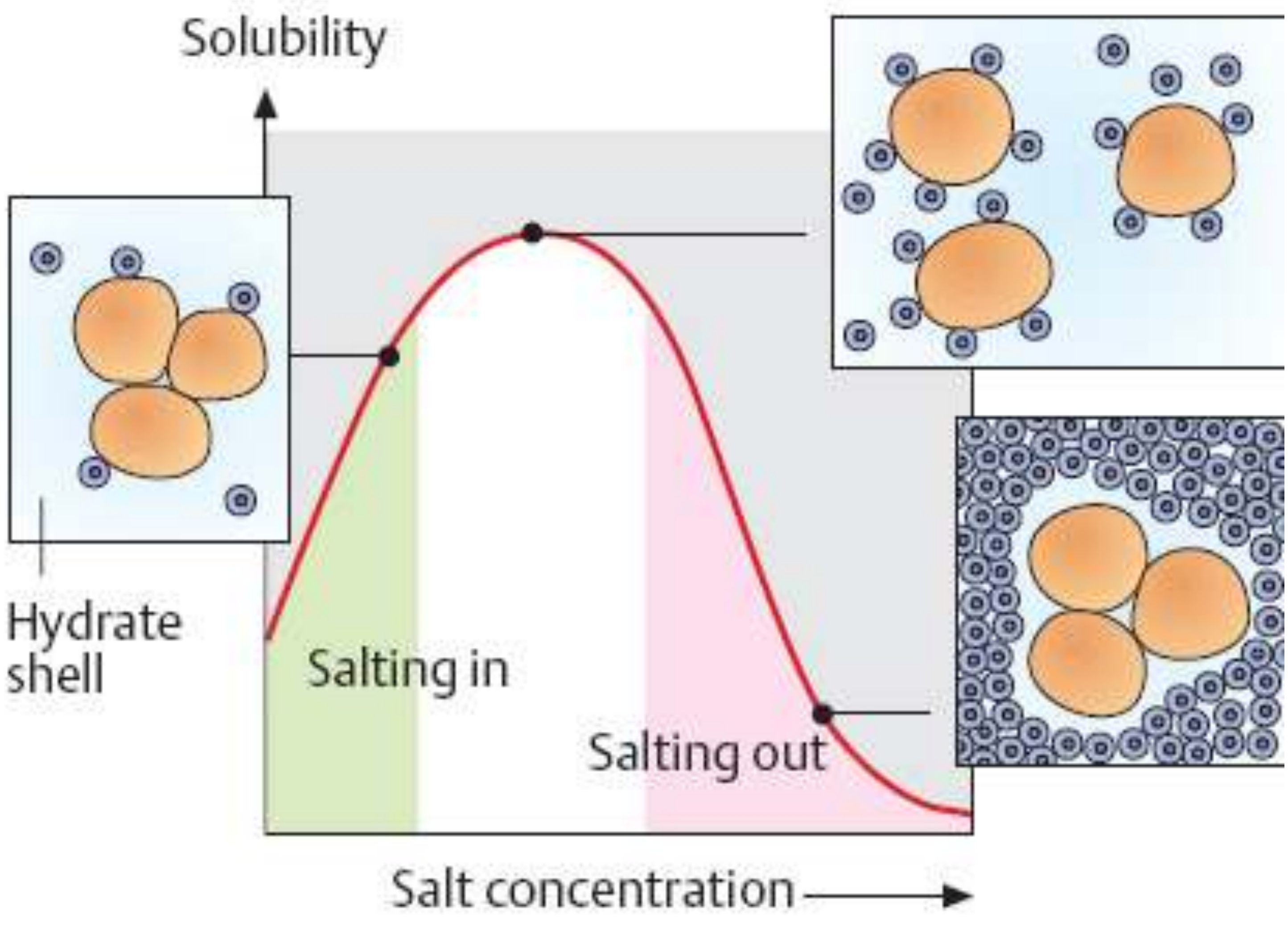
Solubility of proteins depends on multiple charged groups (*concentration of dissolved salts, polarity of solvents, pH, temperature*)

Salting in: The solubility of a protein at low ion concentrations increases as salt is added

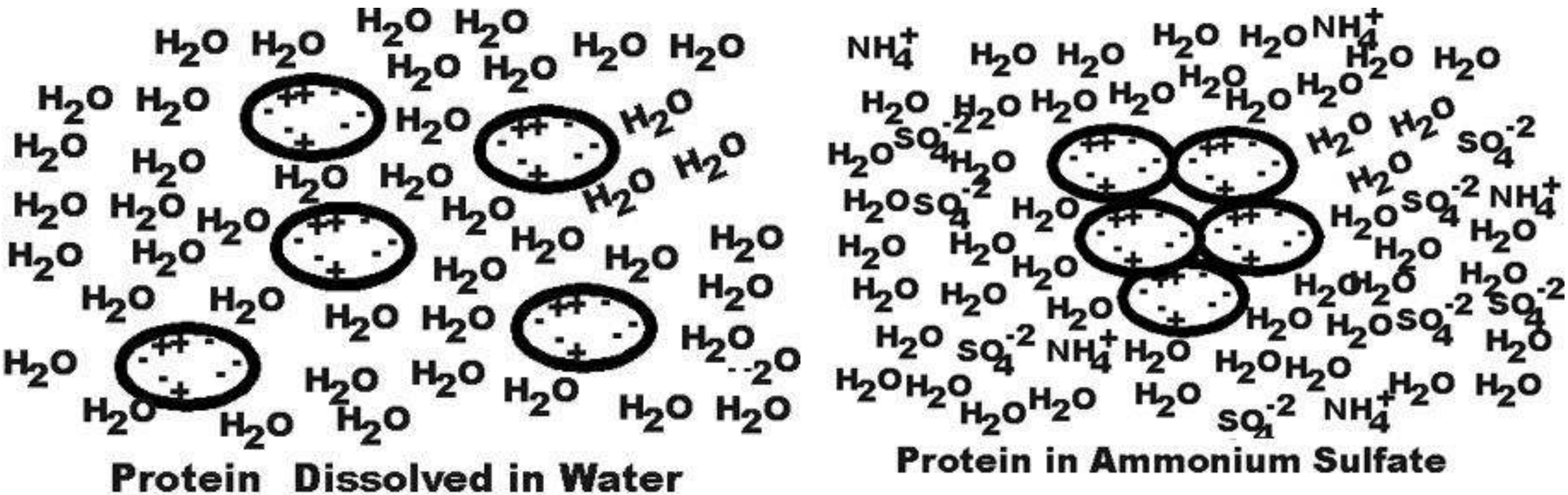
Salting out: As more salt is added, the solubility of protein again decreases due to competition between the added salt ions and the other dissolved solutes (protein molecules) for molecules of solvent (water)

$(NH4)_2SO_4$, is the most commonly used salt for salting out proteins because its large solubility in water, its relative freedom from temperature effects, and it has no harmful effects on most of the proteins. (<3% variations vs Sod sulphate (5x more at 25^0C)

Influence of salts on protein solubility

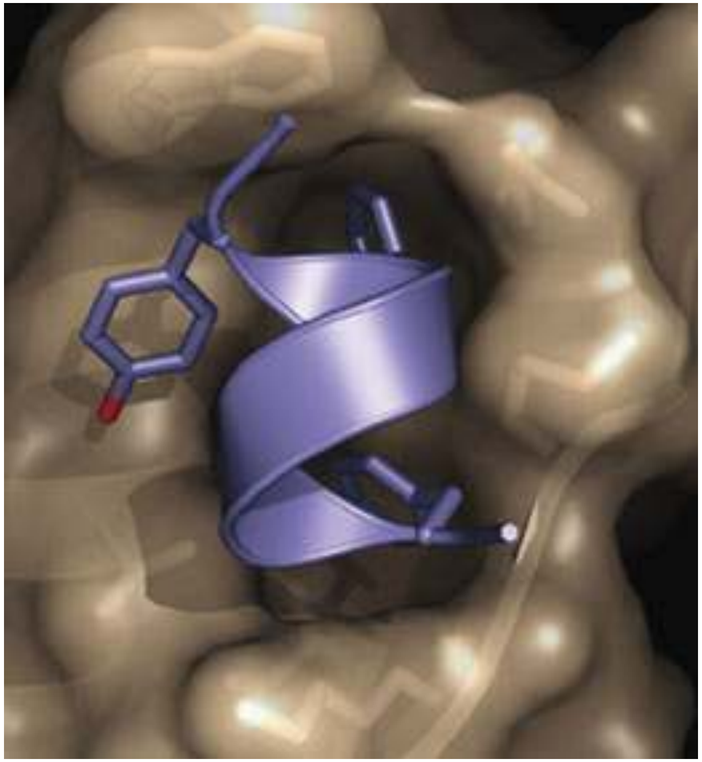


Salt Precipitation



Chromatographic separation of proteins to obtain pure protein preparation

- -Gel filtration
- -ion exchange
- -affinity



Hydrophobic interactions are very weak,

However,

In molecular assemblies involving large numbers of nonpolar contacts, hydrophobic interactions are a potent force.

Non-covalent forces are weak bonds

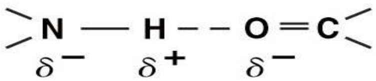
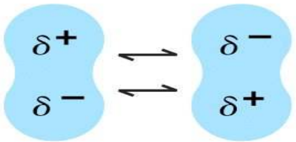
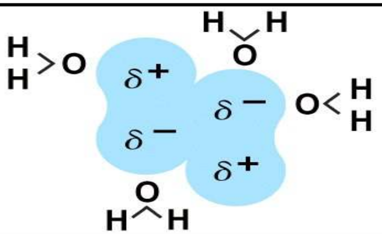
Noncovalent forces	Origin	
Electrostatic forces	Attraction between opposite charges	
Hydrogen bonds	Hydrogen shared between electronegative atoms (N,O)	
Van der Waals forces	Fluctuations in electron clouds around molecules oppositely polarize neighboring atoms	
Hydrophobic forces	Hydrophobic groups interact unfavorably with water and tend to pack together to exclude water molecules. The attraction also involves van der Waals forces	

Figure 3-9 Immunobiology, 6/e. (© Garland Science 2005)

	Bond Length	Energy
Covalent	0.15 nm	90 kcal/mol
Ionic	0.25 nm	3 kcal/mol
Hydrogen	0.30 nm	1 kcal/mol
Van der Waals	0.35 nm	0.1 kcal/mol
Hydrophobic	0.35 nm	0.1 kcal/mol

Bond strength

Amount of energy that must be supplied to break that bond.

Expressed in kilocalories per mole (kcal/mole), Kilocalorie = amount of energy needed to raise the temperature of one liter of water by one degree centigrade.

Bond strength of 1 kcal/mole = 1 kilocalorie must be supplied to break 6×10^{23} bonds of a specific type (that is, 1 mole of these bonds)

Amino Acid Polymers

- Amino acids
  - Are linked by peptide bonds

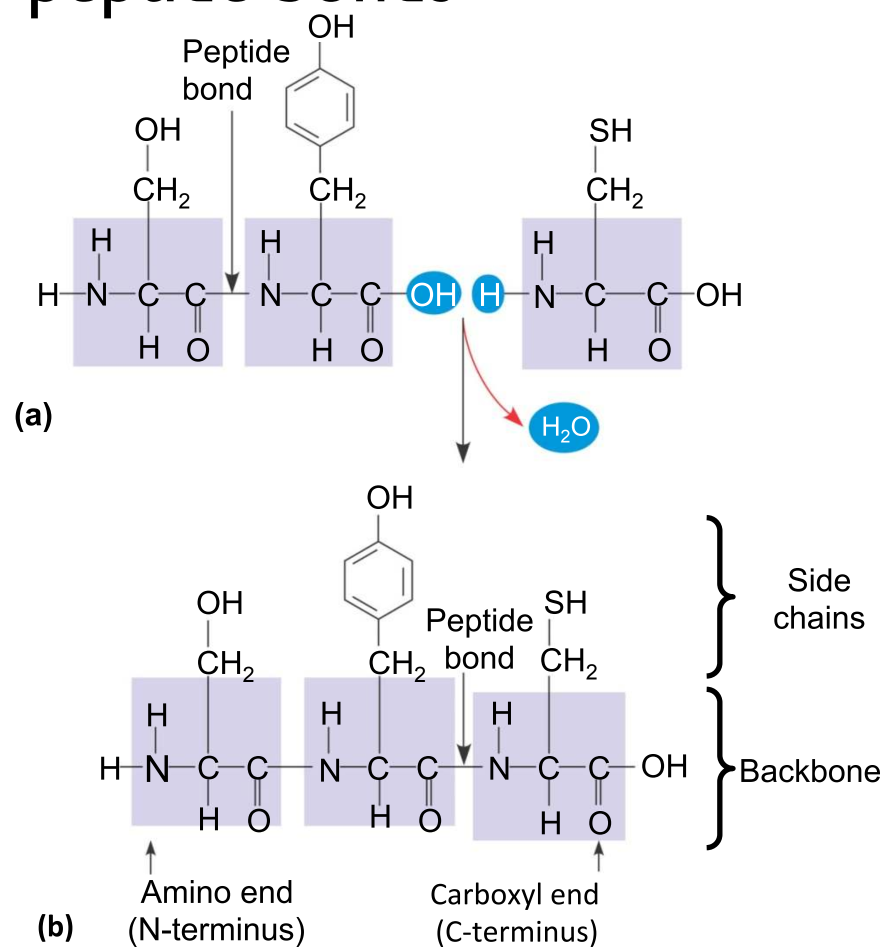
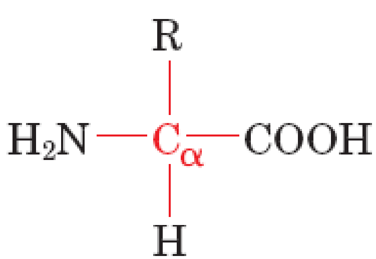


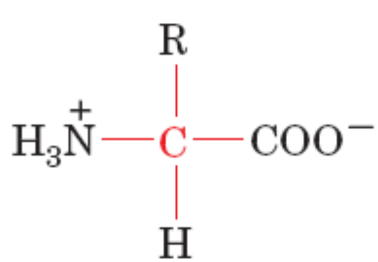
Figure 5.18

Amino Acids

The analyses of a vast number of proteins from almost every conceivable source have shown that *all proteins are composed of the 20 "standard" amino acids.*



General structural formula for α-amino acids.



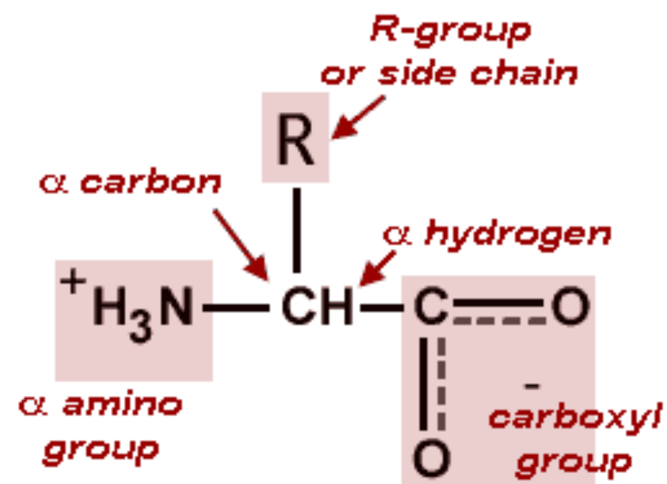
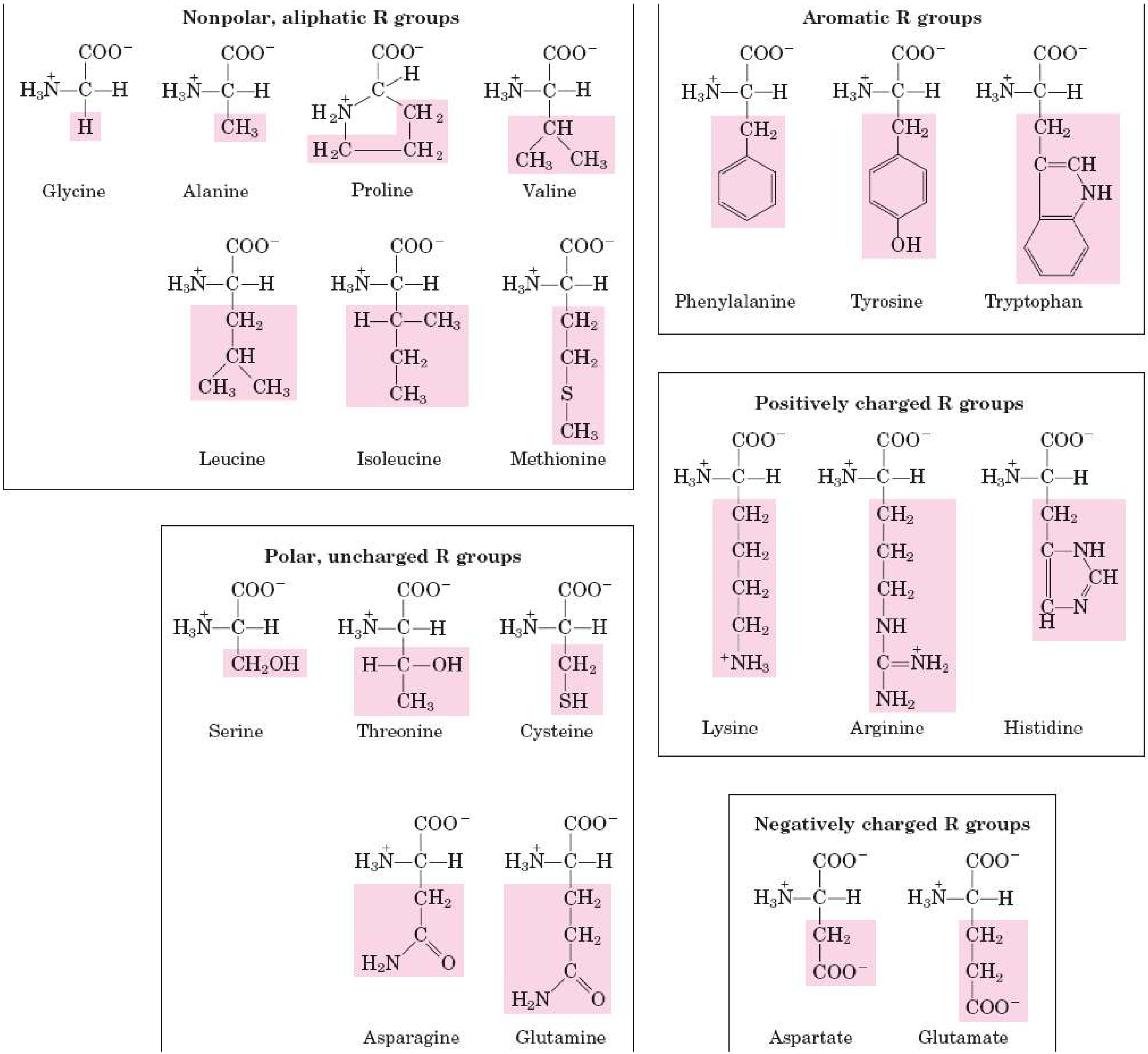


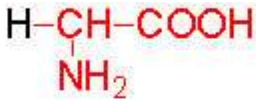
Figure 4-2 Zwitterionic form of the α-amino acids that occurs at physiological pH values.

20 Different Amino Acid Residues: classification and characteristics

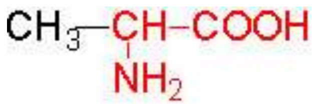


Nonpolar (Hydrophobic) R Groups

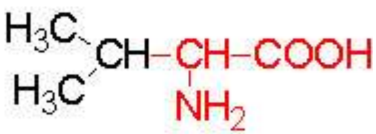
Glycine (Gly)



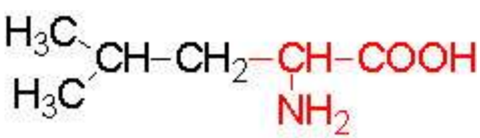
Alanine (Ala)



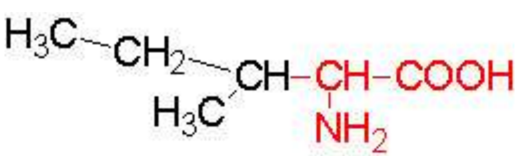
Valine (Val)



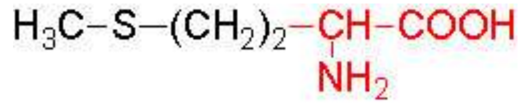
Leucine (Leu)



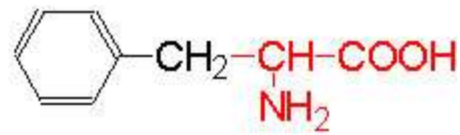
Isoleucine (Ile)



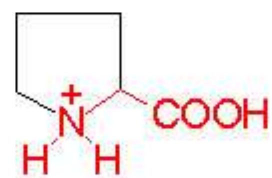
Methionine (Met)



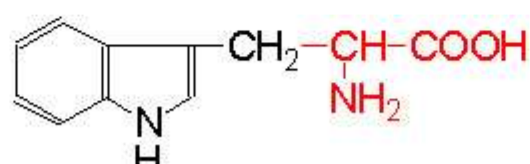
Phenylalanine (Phe)



Proline (Pro)



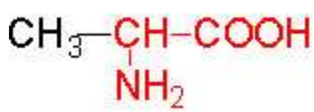
Tryptophan (Trp)



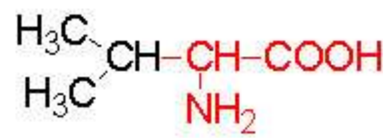
http://www.indstate.edu/thcme/mwking/amino-acids.html

The simplest amino acid is Glycine, which has a single hydrogen atom as its side chain.

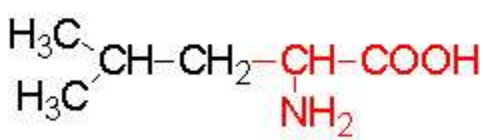
Alanine, Valine, Leucine and Isoleucine have saturated hydrocarbon R groups (i.e. they only have hydrogen and carbon linked by single covalent bonds). Leucine and Isoleucine are isomers of each other.



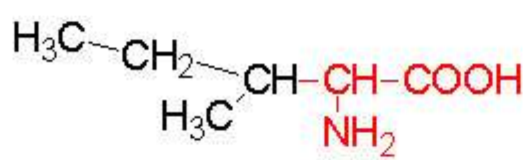
Alanine



Valine

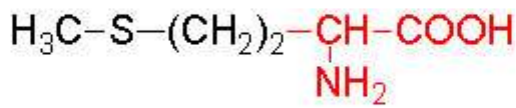


Leucine



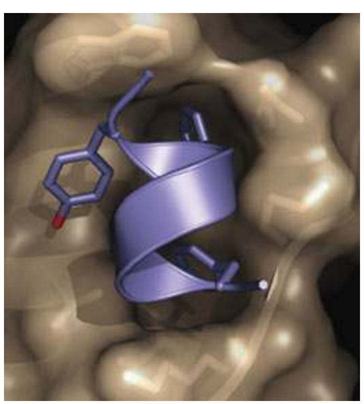
Isoleucine

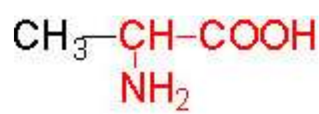
- The side chain of Methionine includes a sulphur atom but remains hydrophobic in nature.

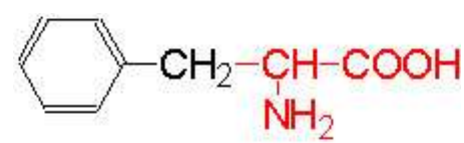


Methionine

- Phenylalanine is Alanine with an extra benzene (sometimes called a Phenyl) group on the end. Phenylalanine is highly hydrophobic and is found buried within globular proteins.





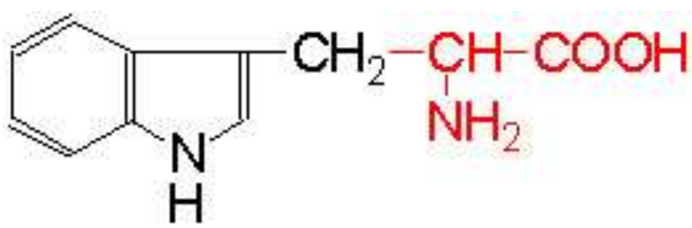


Phenylalanine

- Tryptophan is highly hydrophobic and tends to be found immersed inside globular proteins.

- Structurally related to Alanine, but with a two ring (bicyclic) indole group added in place of the single aromatic ring found in Phenylalanine.

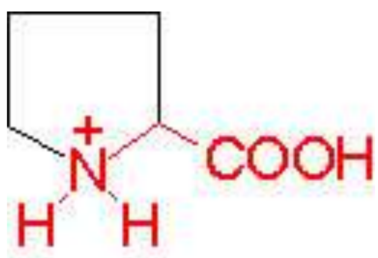
- The presence of the nitrogen group makes Tryptophan a little less hydrophobic than Phenylalanine.

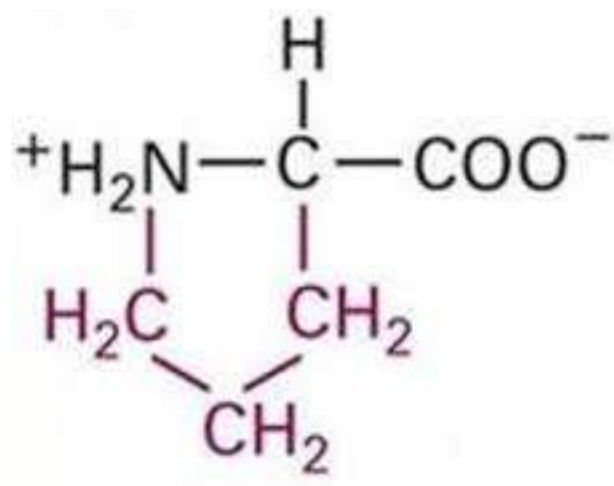


- Proline is unique amongst the amino acids – its side chain is bonded to the backbone nitrogen as well as to the a-carbon.

- Because of this proline is technically an *imino* rather than an amino acid.

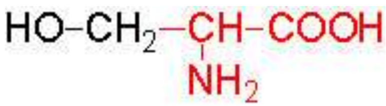
- The ring is not reactive, but it does restrict the geometry of the backbone chain in any protein where it is present.



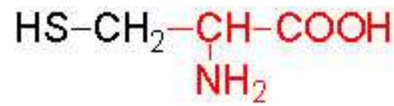


Polar (Hydrophilic) R Groups

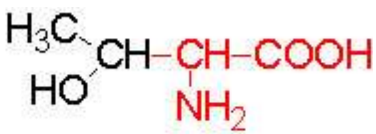
Serine (Ser)



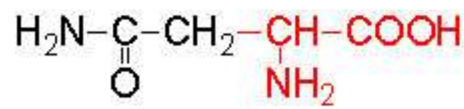
Cysteine (cys)



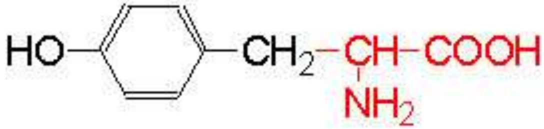
Threonine (Thr)



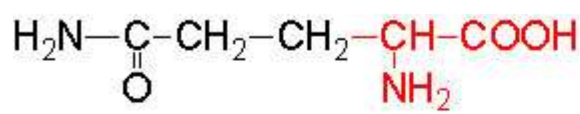
Asparagine (Asn)



Tyrosine (Tyr)



Glutamine (Gln)



http://www.indstate.edu/thcme/mwking/amino-acids.html

Essential Amino Acids in Humans

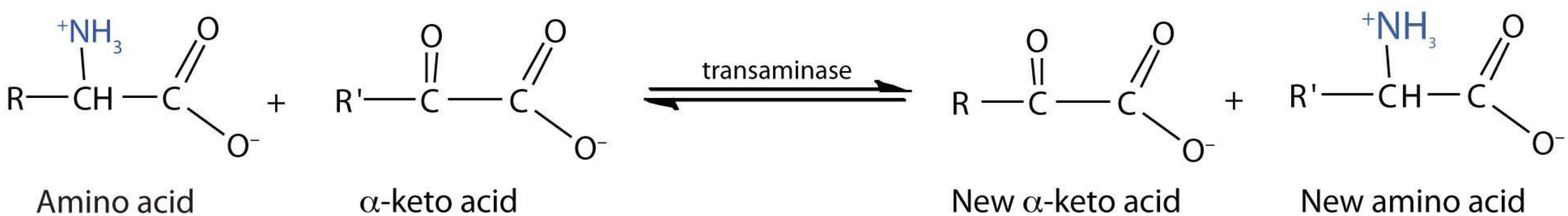
- Required in diet
- Humans incapable of forming requisite carbon skeleton

Arginine*	Lysine
Histidine*	Methionine
Isoleucine	Threonine
Leucine	Phenylalanine
Valine	Tryptophan

* Essential in children, not in adults

Non-Essential Amino Acids in Humans

- Not required in diet
- Can be formed from α-keto acids by transamination and subsequent reactions

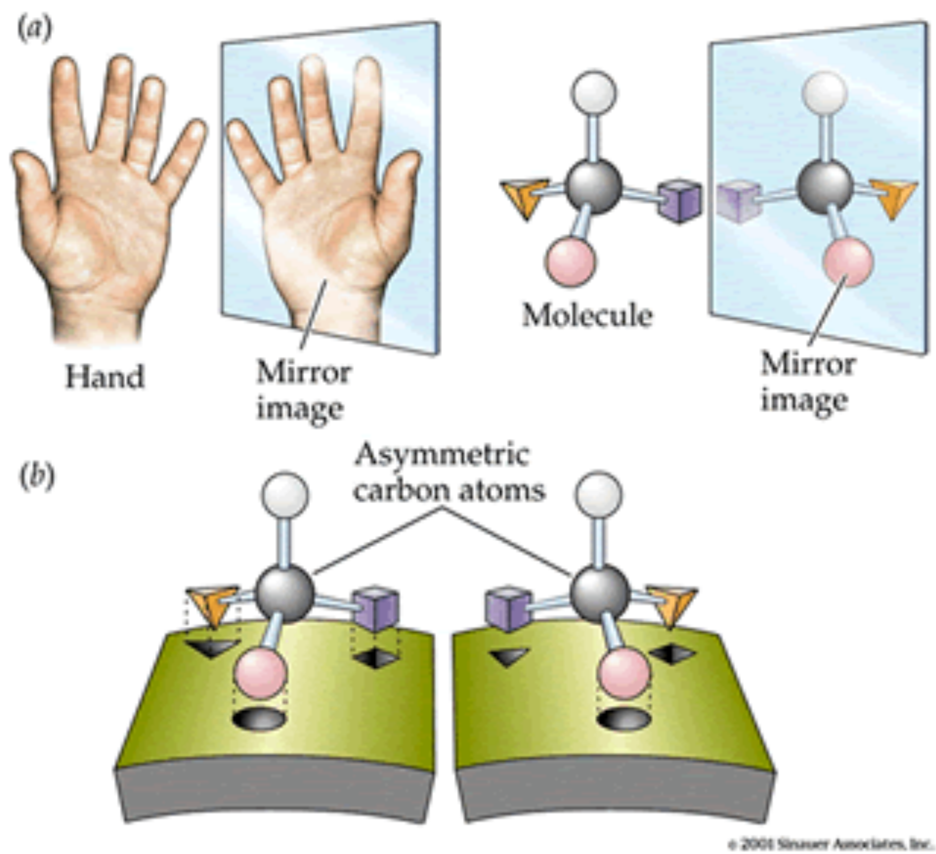


Alanine	Glycine
Asparagine	Proline
Aspartate	Serine
Glutamate	Cysteine (from Met*)
Glutamine	Tyrosine (from Phe*)

* Essential amino acids

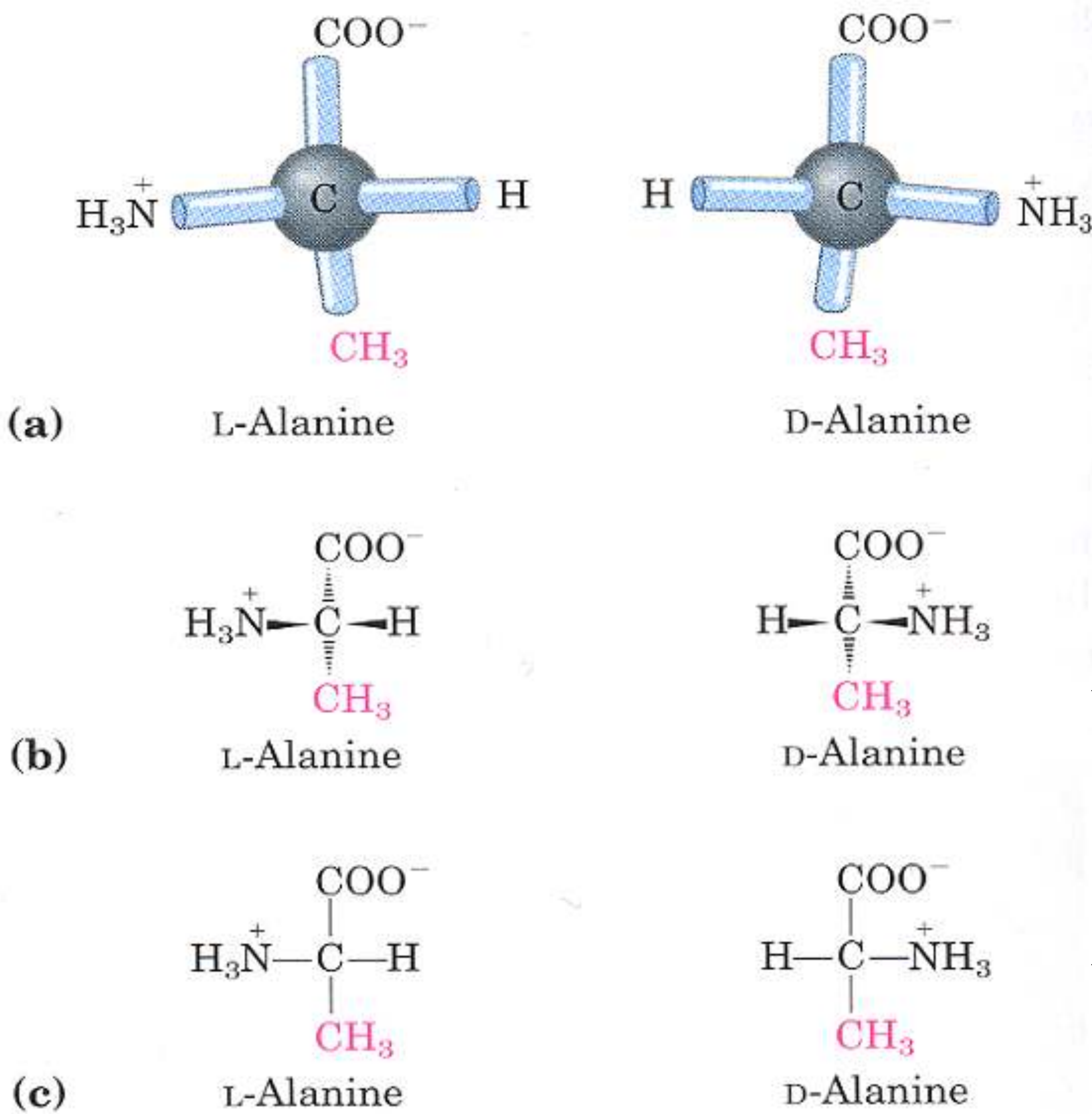
The Stereochemistry of Amino Acids

Chiral molecules existing in two forms



http://www.imb-jena.de/~rake/Bioinformatics_WEB/gifs/amino_acids_chiral.gif

The two stereoisomers of alanine

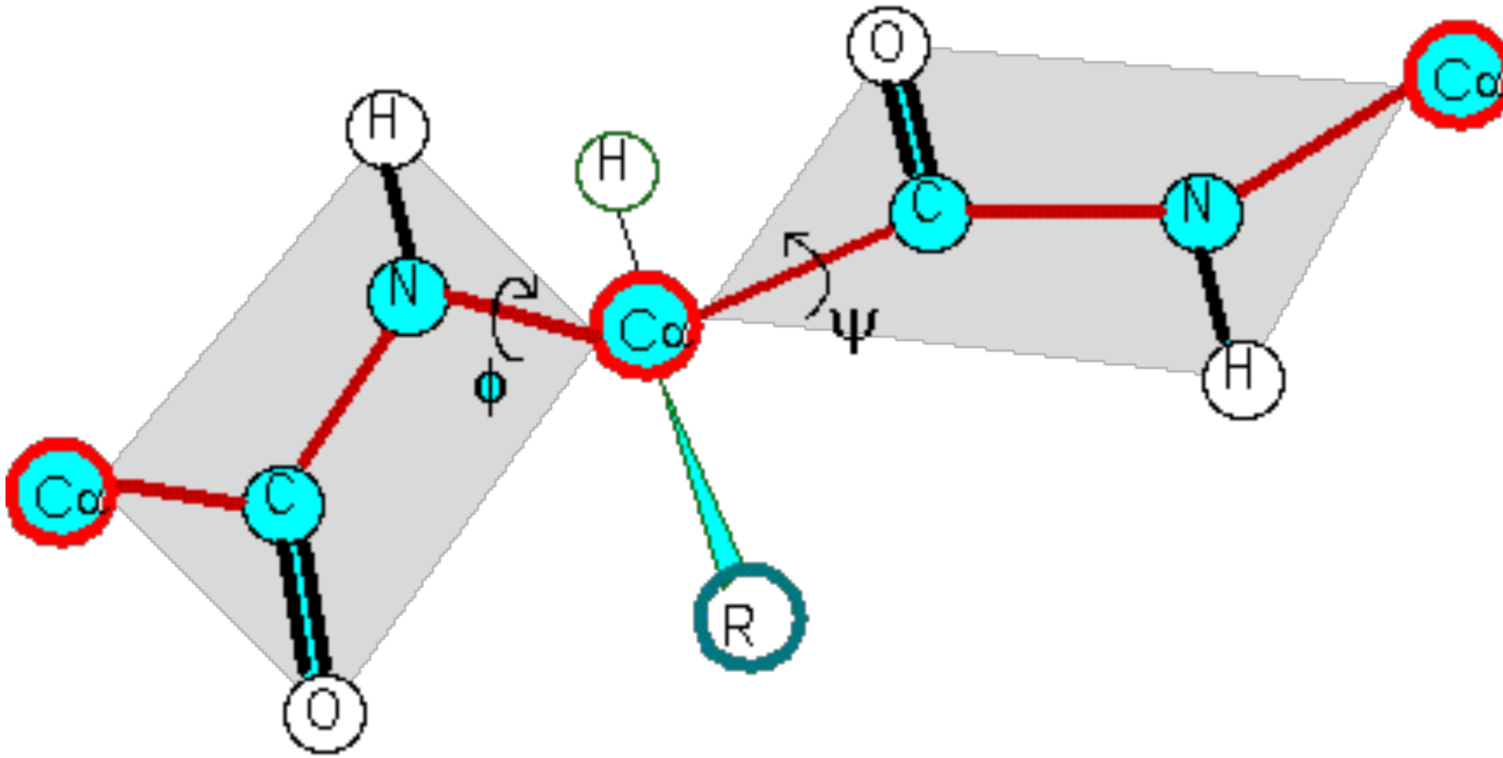


alpha-carbon is a **chiral center**

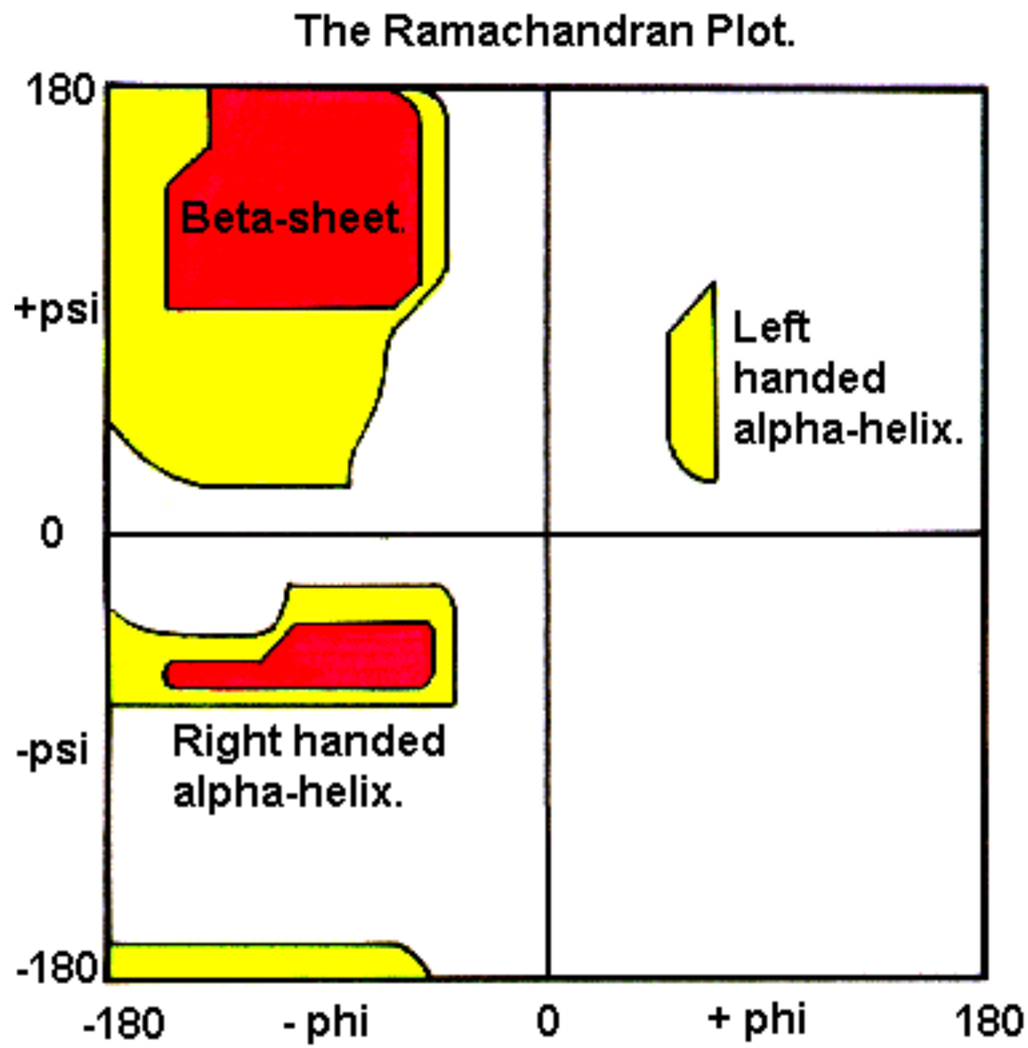
Two stereoisomers are called **enantiomers.**

The solid wedge-shaped bonds project out of the plane of paper, the dashed bonds behind it.

The horizontal bonds project out of the plane of paper, the vertical bonds behind.

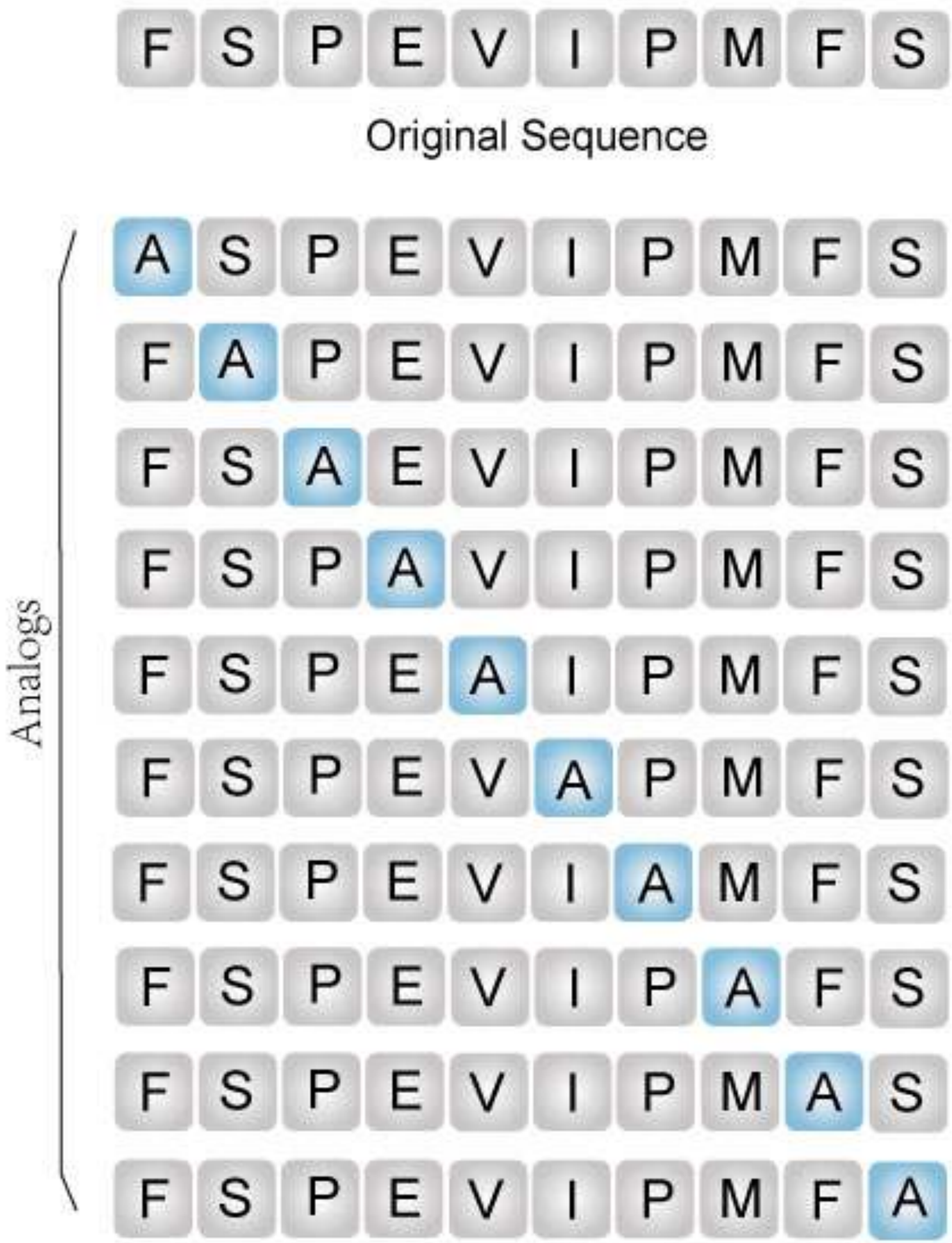


Due to the specific electronic structure of the peptide bond, the atoms on its two ends cannot rotate around the bond. Hence, the atoms of the group, O=C-N-H, are fixed on the same plane, known as the **peptide plane**. The whole plane may rotate around the N-Cα bond (ϕ angle) or C-Cα bond (ψ angle). Cα is the carbon atom connected to the R group. → **Ramachandran plot**



The Ramachandran Plot.
180
+psi
0
-psi
-180
-180
- phi
0
+ phi
180
Beta-sheet.
Left
handed
alpha-helix.
Right handed
alpha-helix.

Alanine Scan or mutational scanning



Glycine	G
Alanine	A
Valine	V
Cysteine	C
Proline	P
Leucine	L
Isoleucine	I
Methione	M
Tryptophan	W
Phenylalanine	F
Lysine	K
Arginine	R
Histidine	H
Serine	S
Threonine	T
Tyrosine	Y
Asparagine	N
Glutamine	Q
Aspartic acid	D
Glutamic acid	E