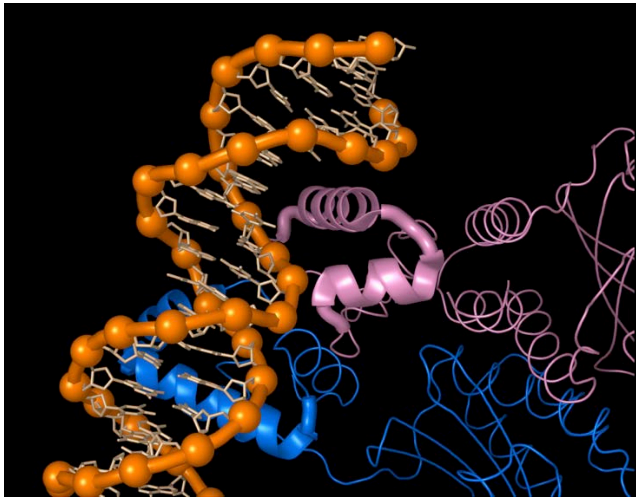
Amines, Amino Acids, Peptides and Proteins

Amines, McMurry Ch 12

•Structures, naming, properties, water solubility, basicity

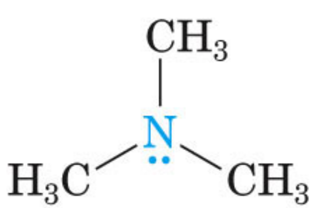
Amino acids, peptides and proteins, McMurry Ch 15

•Their structures, stereochemistry, effect of pH and reactions, biological importance

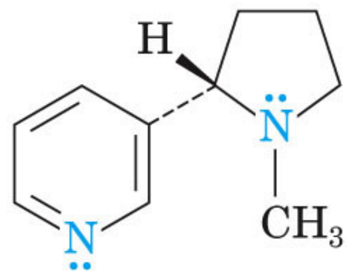


Amines

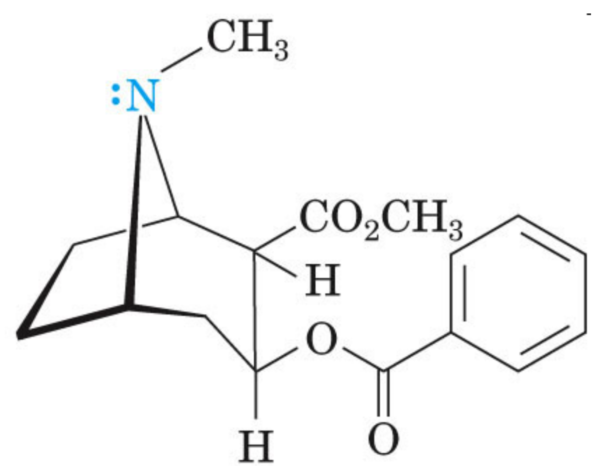
- **Amines** contain at least one carbon chain attached to a nitrogen
- **Nitrogen atom is typically sp^3 hybridised with a lone pair of electrons, making amines both basic and nucleophilic**
- Occur in many biological systems and are often **bioactive**



Trimethylamine



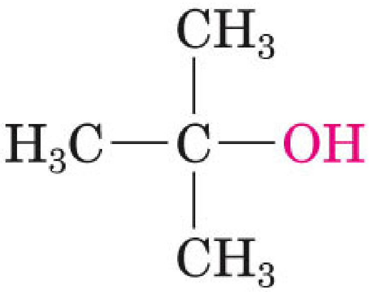
Nicotine



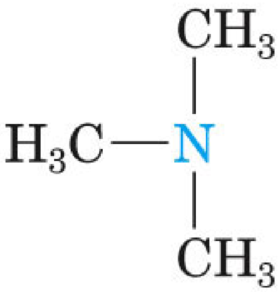
Cocaine

Classification of Amines

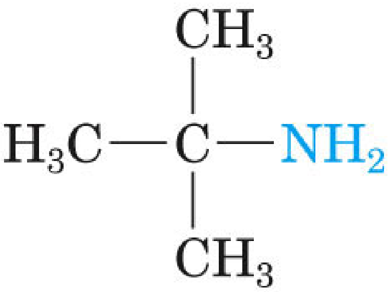
- Classified as methyl (CH_3NH_2), 1° (RNH_2), 2° (R_2NH), 3° (R_3N) amines based on the degree of substitution around the N atom



tert-Butyl alcohol
(a tertiary alcohol)



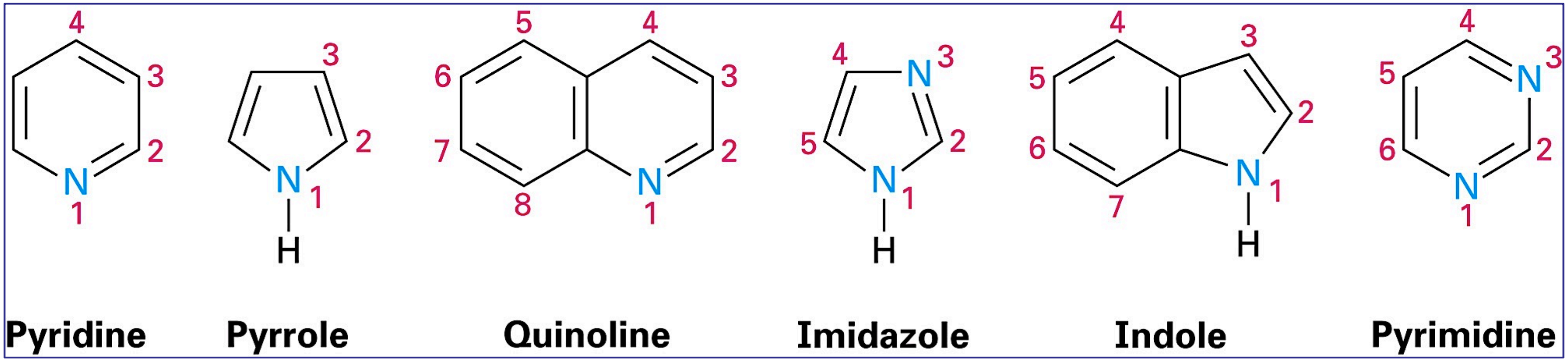
Trimethylamine
(a tertiary amine)



tert-Butylamine
(a primary amine)

Amines

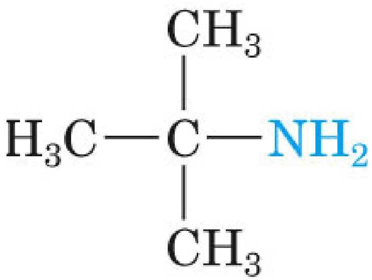
- In a **heterocyclic amine**, the N atom forms part of the ring



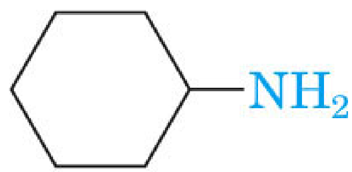
Will not be asked to remember these names – will see some of them
As part of important biomolecules

IUPAC Names – Simple Amines

- For simple amines, the suffix -*amine* is added to the name of the alkyl substituent



tert-Butylamine



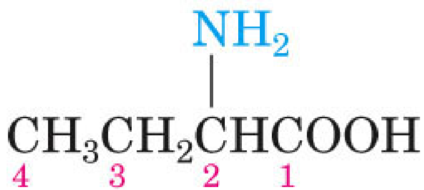
Cyclohexylamine

$H_2NCH_2CH_2CH_2CH_2NH_2$

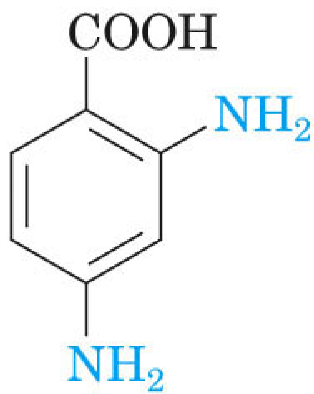
Butane-1,4-diamine

IUPAC Names – Amines With More Than One Functional Group

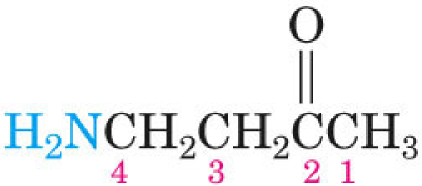
- Consider the —**<u>NH_2 as an *amino*</u>** substituent on the parent molecule



2-Aminobutanoic acid



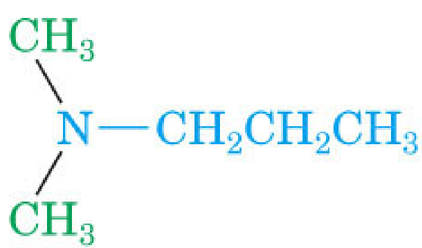
2,4-Diaminobenzoic acid



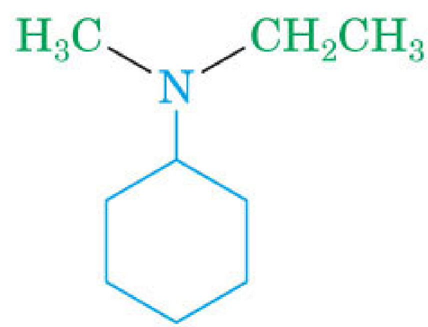
4-Aminobutan-2-one

IUPAC Names – Multiple, Different Alkyl Groups

- Named as *N*-substituted primary amines
- Largest alkyl group is the parent name, and other alkyl groups are considered *N*-substituents



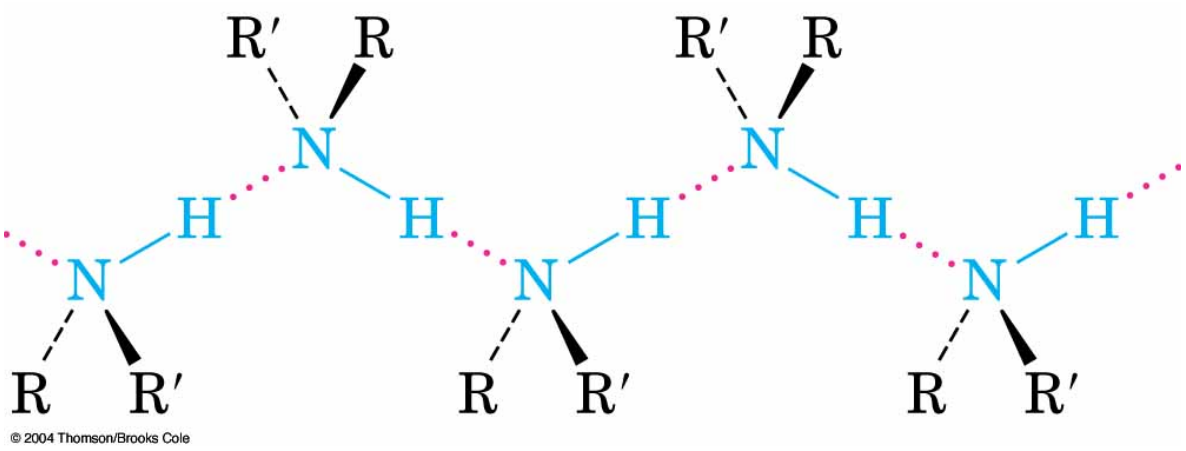
***N,N*-Dimethylpropylamine**
(propylamine is the parent name; the two methyl groups are substituents on nitrogen)



***N*-Ethyl-*N*-methylcyclohexylamine**
(cyclohexylamine is the parent name; methyl and ethyl are *N*-substituents)

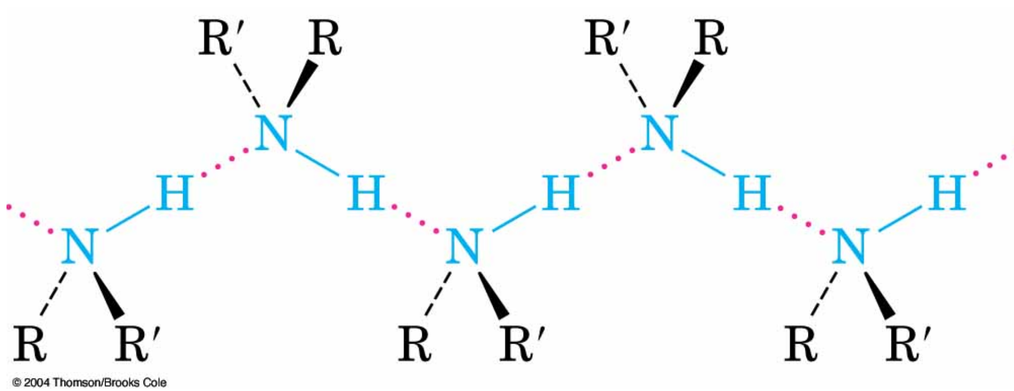
Properties of Amines

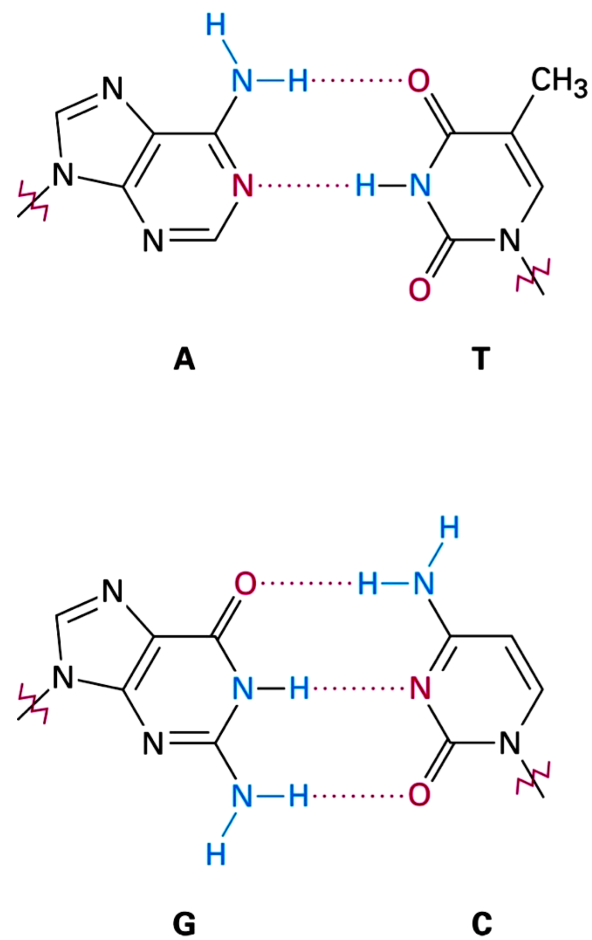
- Amines (like alcohols) are polar
- Primary and secondary amines form hydrogen bonds – enhances water solubility and increases their boiling points
- Amines with fewer than five carbons are water-soluble



- Low molecular weight amines have fishy odour

Properties of Amines – H-bonding



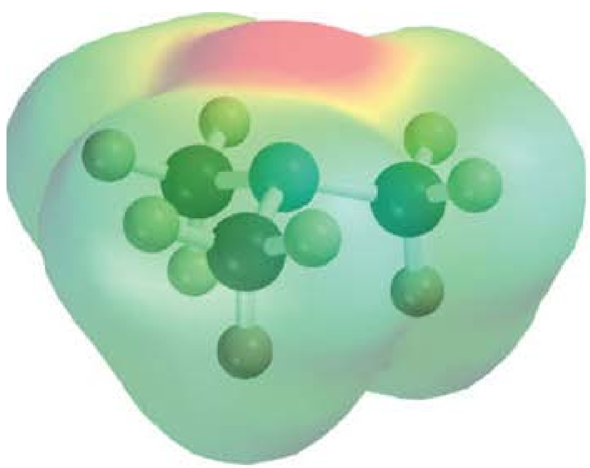


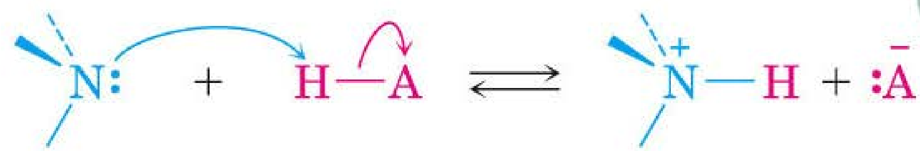
Watson-Crick base pairing

N-H----N is slightly weaker than
O-H----O

Chemistry of Amines

- The lone pair of electrons on nitrogen makes amines basic and nucleophilic
- They react with electrophiles – this includes acids to form salts





An amine (a Lewis base) **An acid** **A salt**

Basicity of Amines

- Amines are much stronger bases than alcohols, ethers or water
- When an amine dissolves in water it forms hydroxide ions and makes pink litmus paper blue
- Measure basicity in water by pK_b

- $RNH_2 \quad + \quad H_2O \rightleftharpoons RNH_3^+ \quad + \quad HO^-$

- $$K_b = \frac{[RNH_3^+]\,[HO^-]}{[RNH_2]}$$

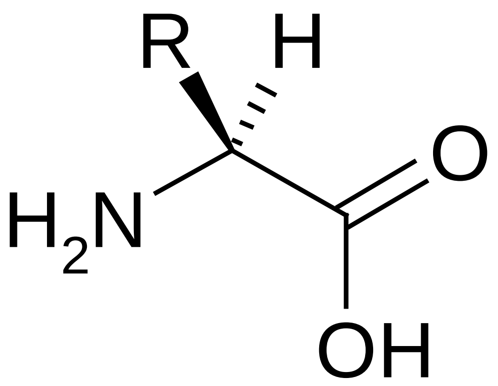
$pK_b = -\log K_b$

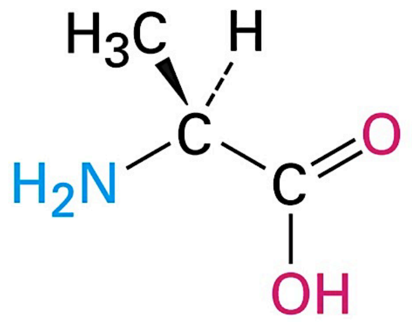
Amino acids, peptides and proteins

- **Proteins** are polymers (poly = many, mer = unit)
- Proteins occur in every living organism and have many different biological functions
- Made up of alpha (α) **amino acids** joined together with amide bonds to form long chains
- Smaller chains of amino acids joined together (with amide bonds) give **peptides**

α-amino acid structure

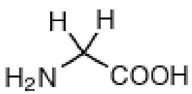
each amino acid contains
a basic amino group
+
an acidic carboxylic acid group



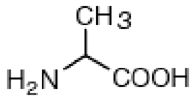


Alanine, an amino acid

Small

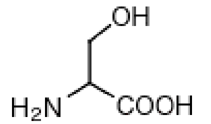


Glycine (Gly, G)
MW: 57.05

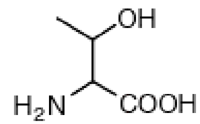


Alanine (Ala, A)
MW: 71.09

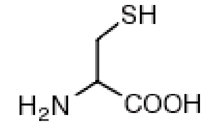
Nucleophilic



Serine (Ser, S)
MW: 87.08, $pK_a \sim 16$

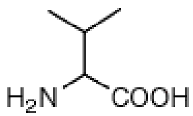


Threonine (Thr, T)
MW: 101.11, $pK_a \sim 16$

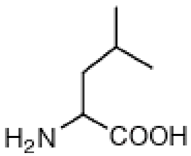


Cysteine (Cys, C)
MW: 103.15, $pK_a = 8.35$

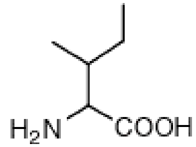
Hydrophobic



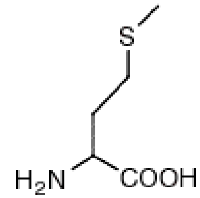
Valine (Val, V)
MW: 99.14



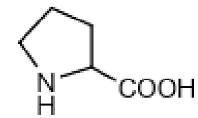
Leucine (Leu, L)
MW: 113.16



Isoleucine (Ile, I)
MW: 113.16

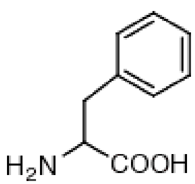


Methionine (Met, M)
MW: 131.19

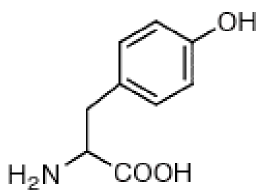


Proline (Pro, P)
MW: 97.12

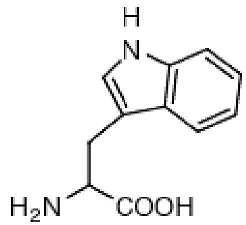
Aromatic



Phenylalanine (Phe, F)
MW: 147.18

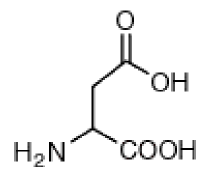


Tyrosine (Tyr, Y)
MW: 163.18

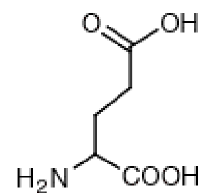


Tryptophan (Trp, W)
MW: 186.21

Acidic

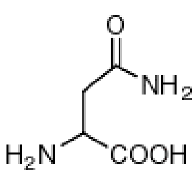


Aspartic Acid (Asp, D)
MW: 115.09, $pK_a = 3.9$

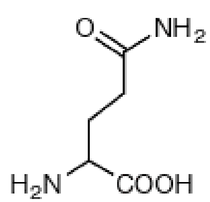


Glutamic Acid (Glu, E)
MW: 129.12, $pK_a = 4.07$

Amide

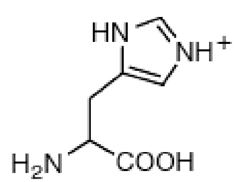


Asparagine (Asn, N)
MW: 114.11

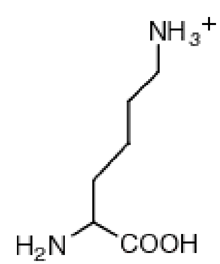


Glutamine (Gln, Q)
MW: 128.14

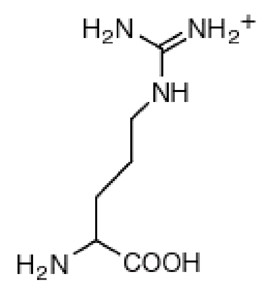
Basic



Histidine (His, H)
MW: 137.14, $pK_a = 6.04$

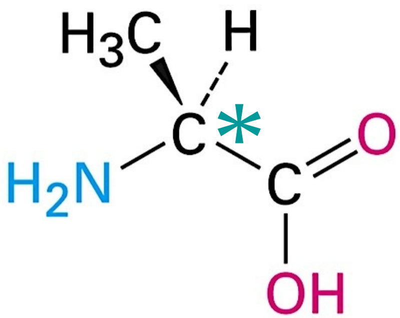


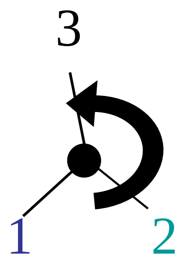
Lysine (Lys, K)
MW: 128.17, $pK_a = 10.79$



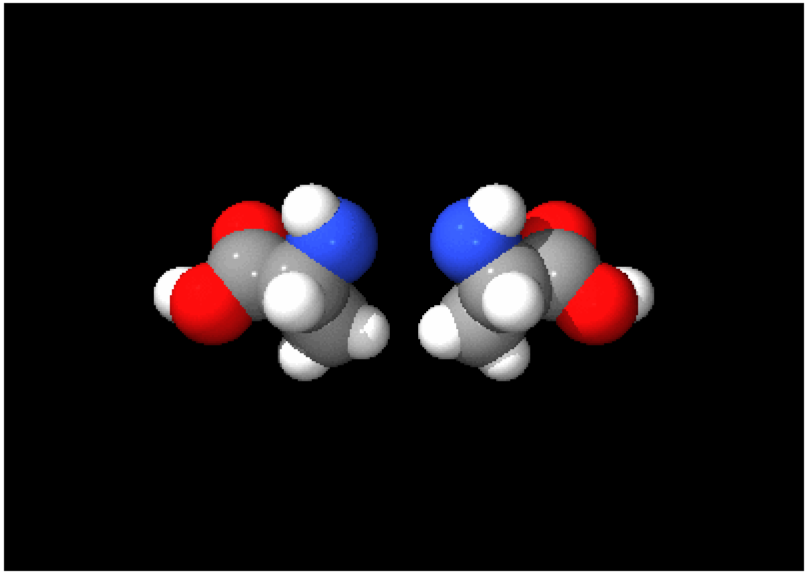
Arginine (Arg, R)
MW: 156.19, $pK_a = 12.48$

α-amino acids are chiral





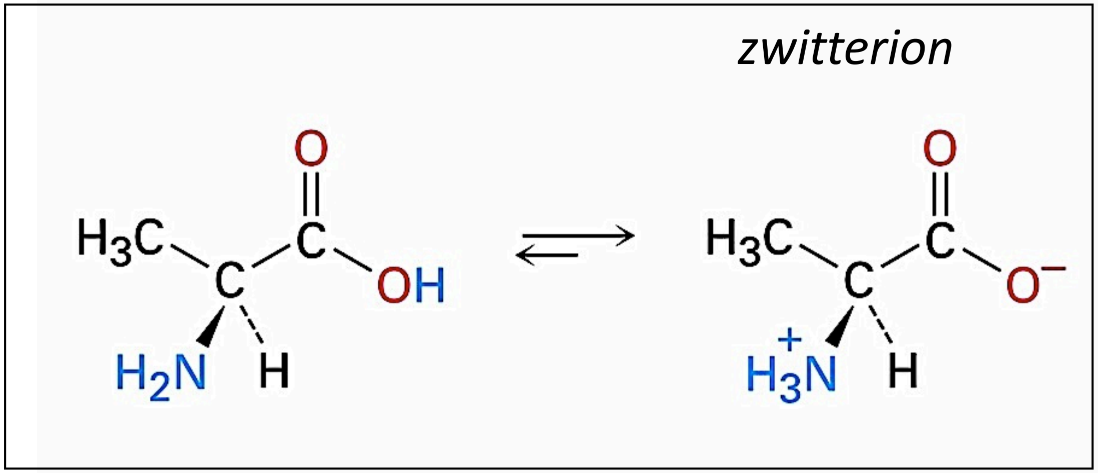
i.e. this is the S enantiomer

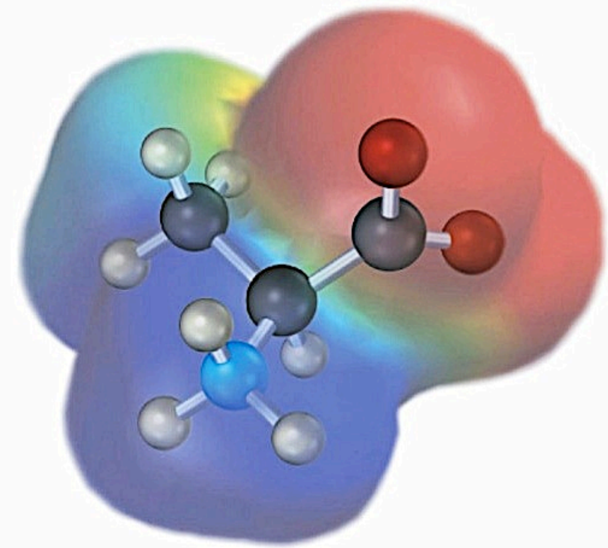


Glycine (R=H) is only achiral amino acid

the two optical isomers of alanine

α-amino acids exist as zwitterions





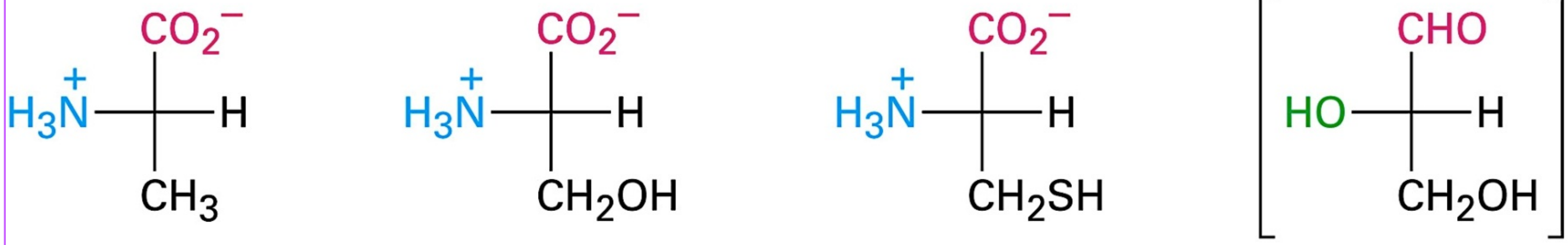
With both acidic and basic groups attached to the same framework, amino acids contain anion (CO_2^-) and cation ($^+NH_3$) groups <u>at the same time</u>.

Creates a water-soluble charged molecule.

zwitterion is favoured
$\Rightarrow$ mixed hybrid form

BUT still neutral overall

Using Fischer projections



L-Alanine
(*S*)-Alanine

L-Serine
(*S*)-Serine

L-Cysteine
(*R*)-Cysteine

L-Glyceraldehyde

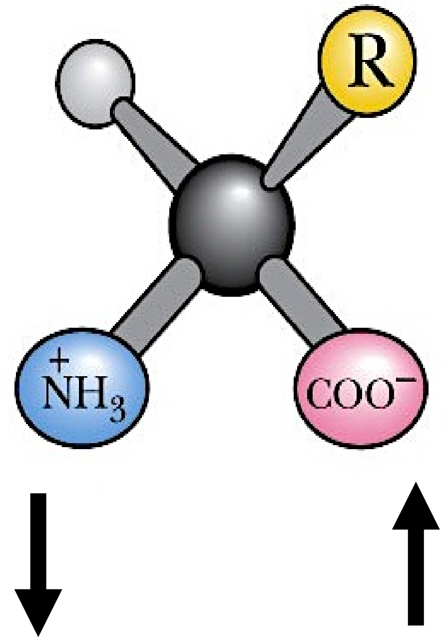
Draw out in a similar way to sugars (CHO at top)

the variable –R group is then at the bottom.

Naturally-occuring enantiomers are the L-amino acids, i.e. related to L-glyceraldehyde, with N group on left.

Effect of pH

Amino acids have both acidic and basic capacity

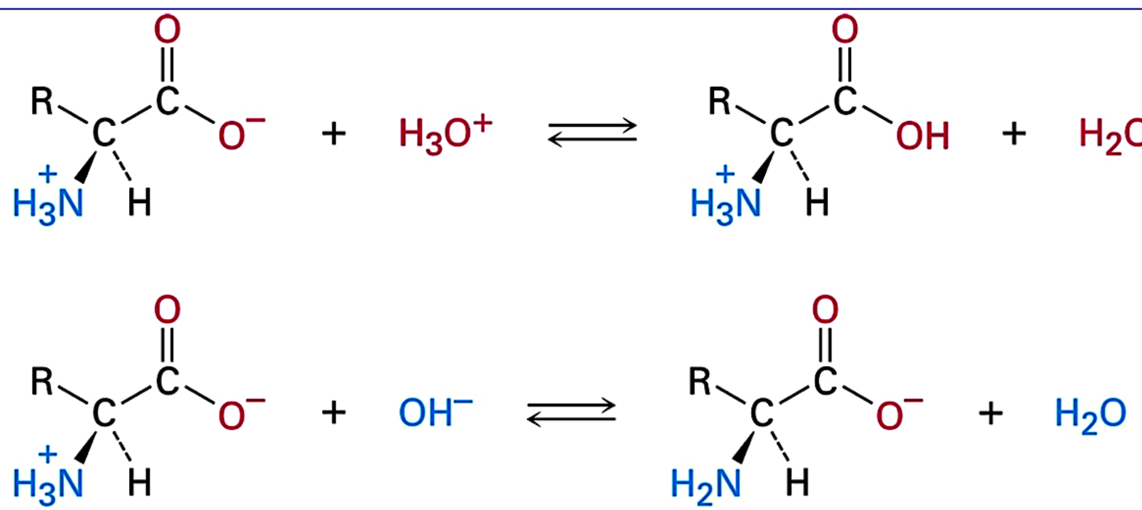


loses protons (to a base)

gains protons (from an acid)

In acid solution

In base solution



creates cation

creates anion

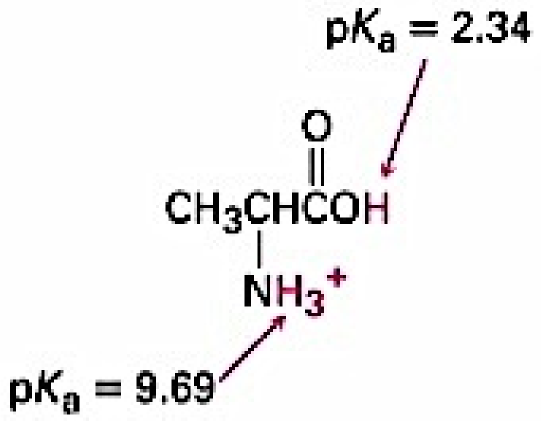
Effect of pH

Can determine the ionisation state of an amino acid given pH and pka's of functional groups

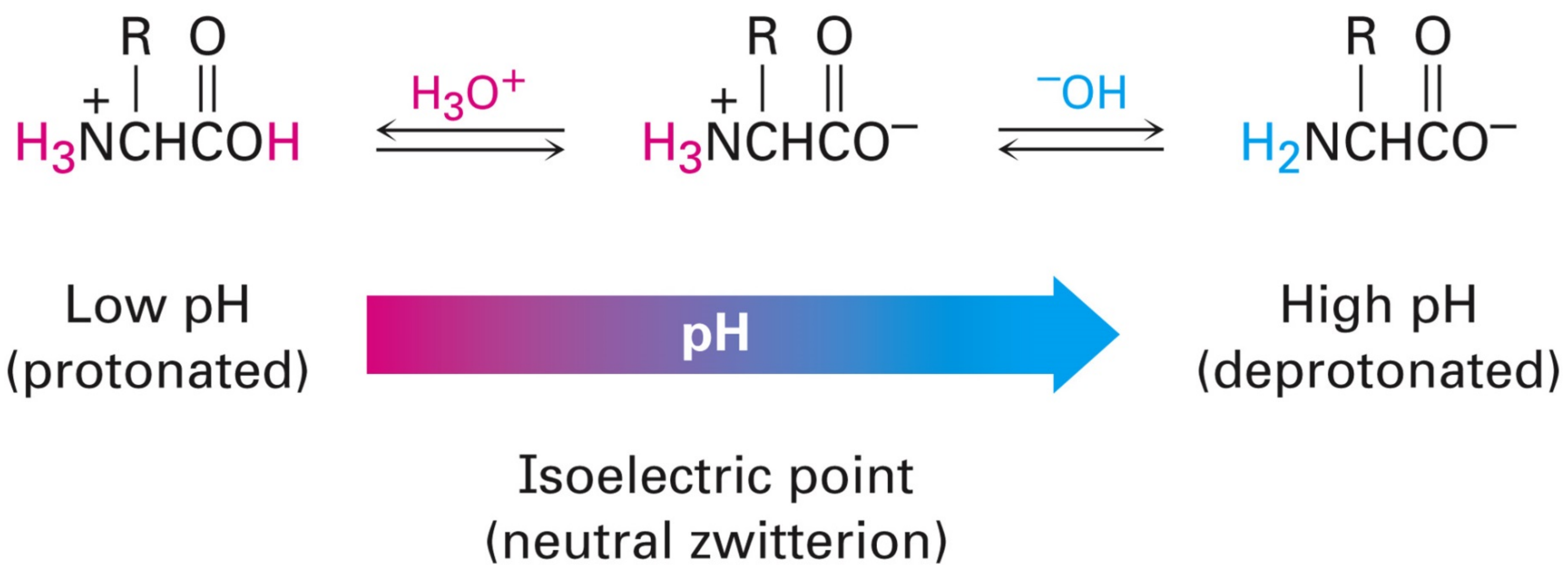
Note handy rule:
If pH = pKa, have 1:1 mix of protonated & deprotonated form

If pH < pKa (more acidic) conditions have more of protonated form

If pH > pKa (more basic) have more of deprotonated form

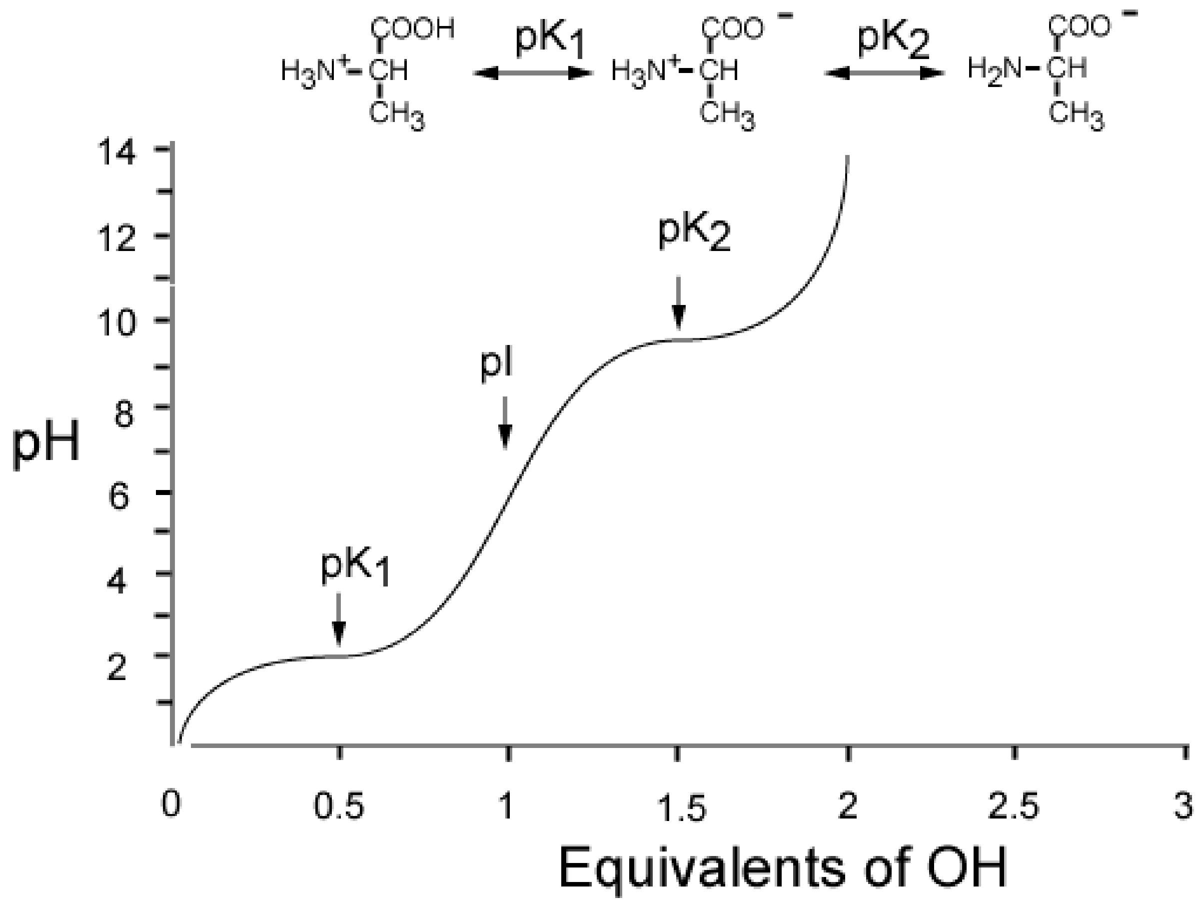


Effect of pH



H_3O^+
^-OH
$H_3\overset{+}{N}CHCOH$ (R, O)
$H_3\overset{+}{N}CHCO^-$ (R, O)
H_2NCHCO^- (R, O)
Low pH
(protonated)
pH
High pH
(deprotonated)
Isoelectric point
(neutral zwitterion)

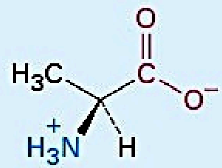
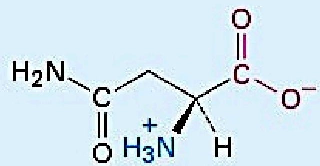
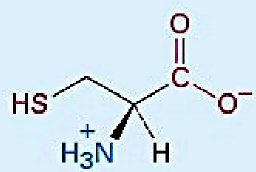
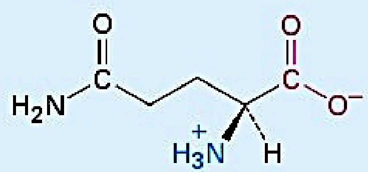
Effect of pH



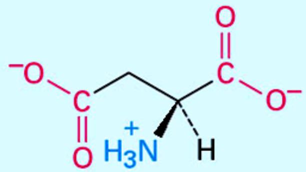
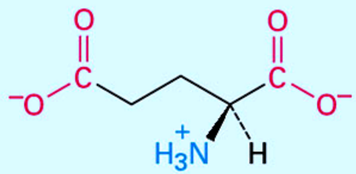
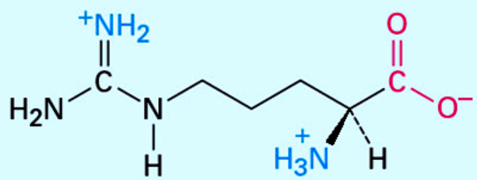
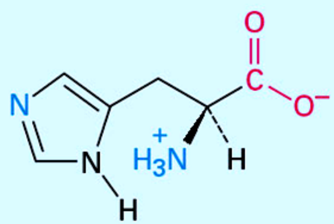
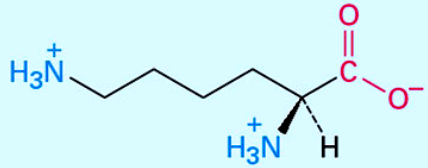
COOH
H_3N^+- CH
CH_3
pK1
COO -
H_3N^+- CH
CH_3
pK2
COO -
H_2N- CH
CH_3
pH
14
12
10
8
6
4
2
pK2
pI
pK1
0
0.5
1
1.5
2
2.5
3
Equivalents of OH

pI – when no overall charge - many amino acids have “neutral” pI

Table 15.1 **Structures of the 20 Common Amino Acids Found in Proteins**

Name	Abbreviations		MW	Stucture	pK_a α-CO_2H	pK_a α-NH_3^+	pK_a side chain	pI
Neutral Amino Acids								
Alanine	Ala	A	89		2.34	9.69	—	6.01
Asparagine	Asn	N	132		2.02	8.80	—	5.41
Cysteine	Cys	C	121		1.96	10.28	8.18	5.07
Glutamine	Gln	Q	146		2.17	9.13	—	5.65

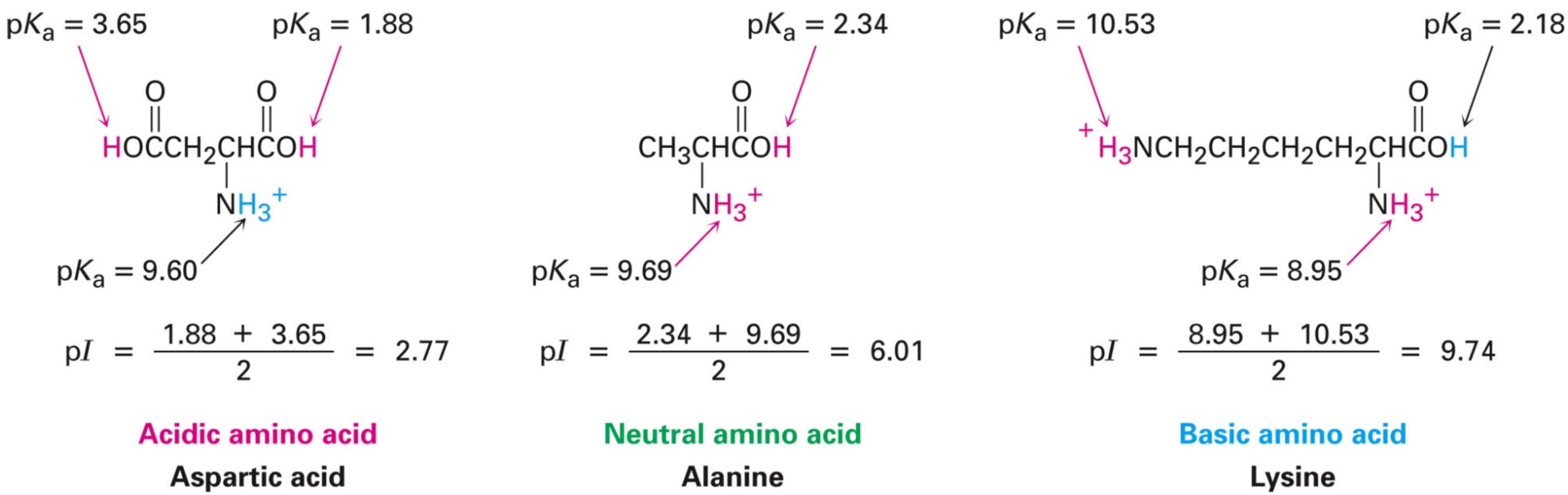
pI (neutral point) depends on the R group

					pK$_1$ (CO_2H)	pK$_2$ (NH_3+)	pK(R)	pI
Acidic Amino Acids								
Aspartic acid	Asp	D	133		1.88	9.60	3.65	2.77
Glutamic acid	Glu	E	147		2.19	9.67	4.25	3.22
Basic Amino Acids								
Arginine	Arg	R	174		2.17	9.04	12.48	10.76
Histidine	His	H	155		1.82	9.17	6.00	7.59
Lysine	Lys	K	146		2.18	8.95	10.53	9.74

These have isoelectric points AWAY from neutral pH

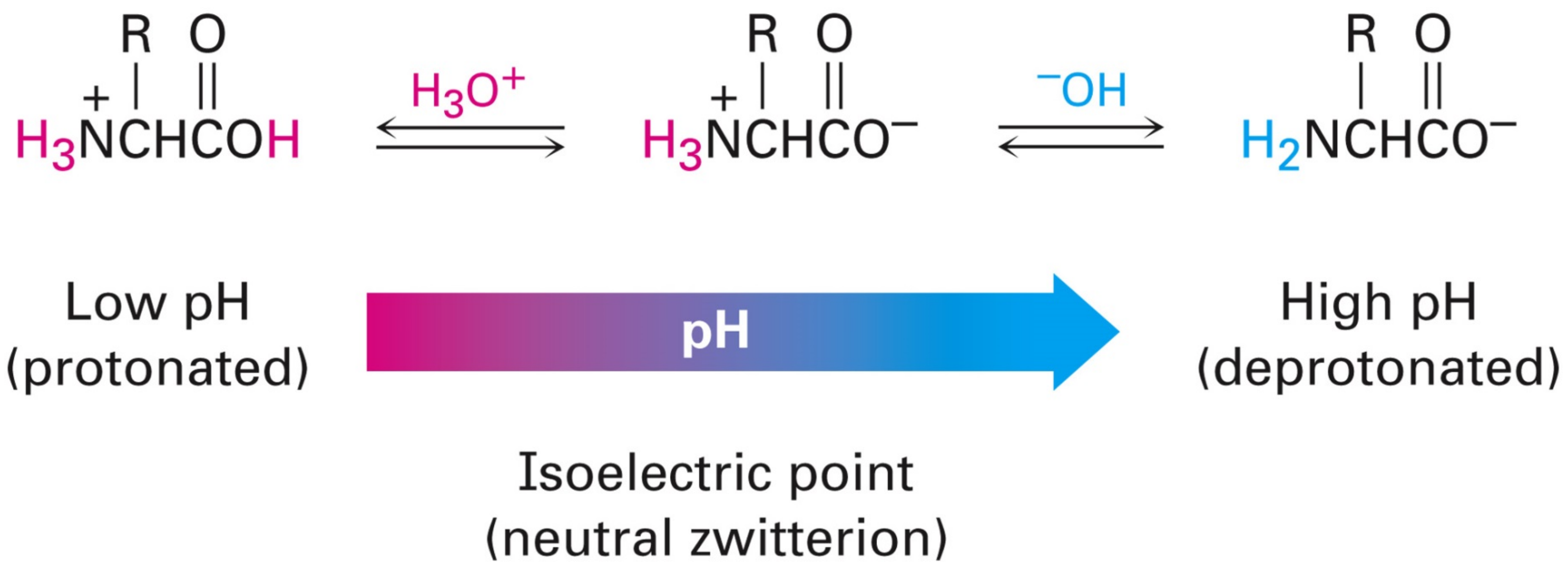
pI (neutral point) depends on the R group

- For amino acids with neutral side chains, pI = average of pKas
- For amino acids with acidic side chains, pI = average of two lowest pKa's
- For amino acids with basic side chains, pI = average of two highest pKa's



pI and solubility

- Solubility or amino acid is lowest at pH = pI where no net charge
- Solubility is higher above or below pI, where there is charged species

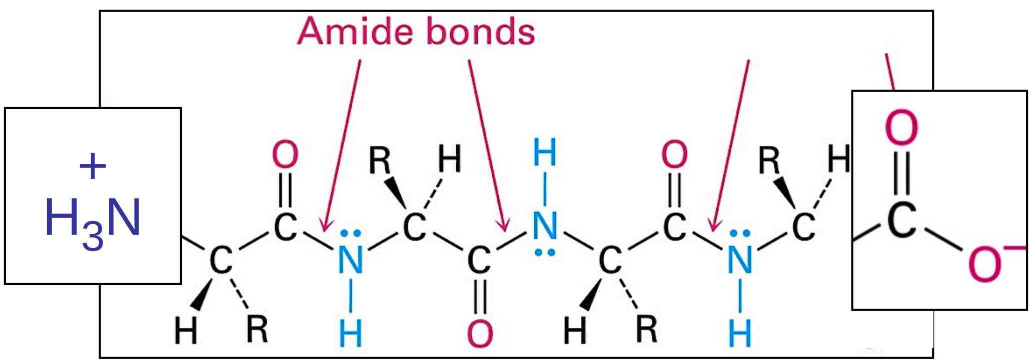


Peptides

•Peptides have amino acids joined together *via* amide bonds (also known as peptide bonds)

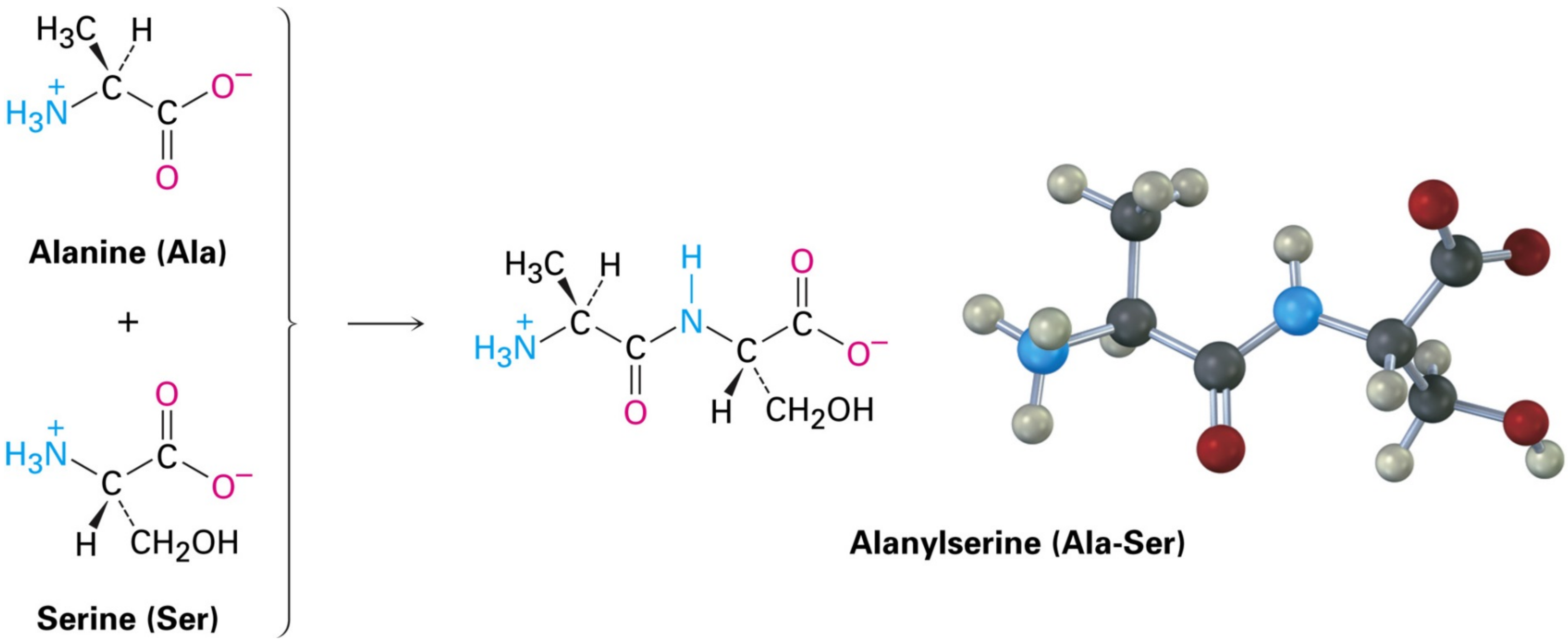
•An amino group from one amino acid residue condenses with a carboxyl group of a second amino acid residue to form a bond with loss of water and so on

starts at the N-terminus (left)

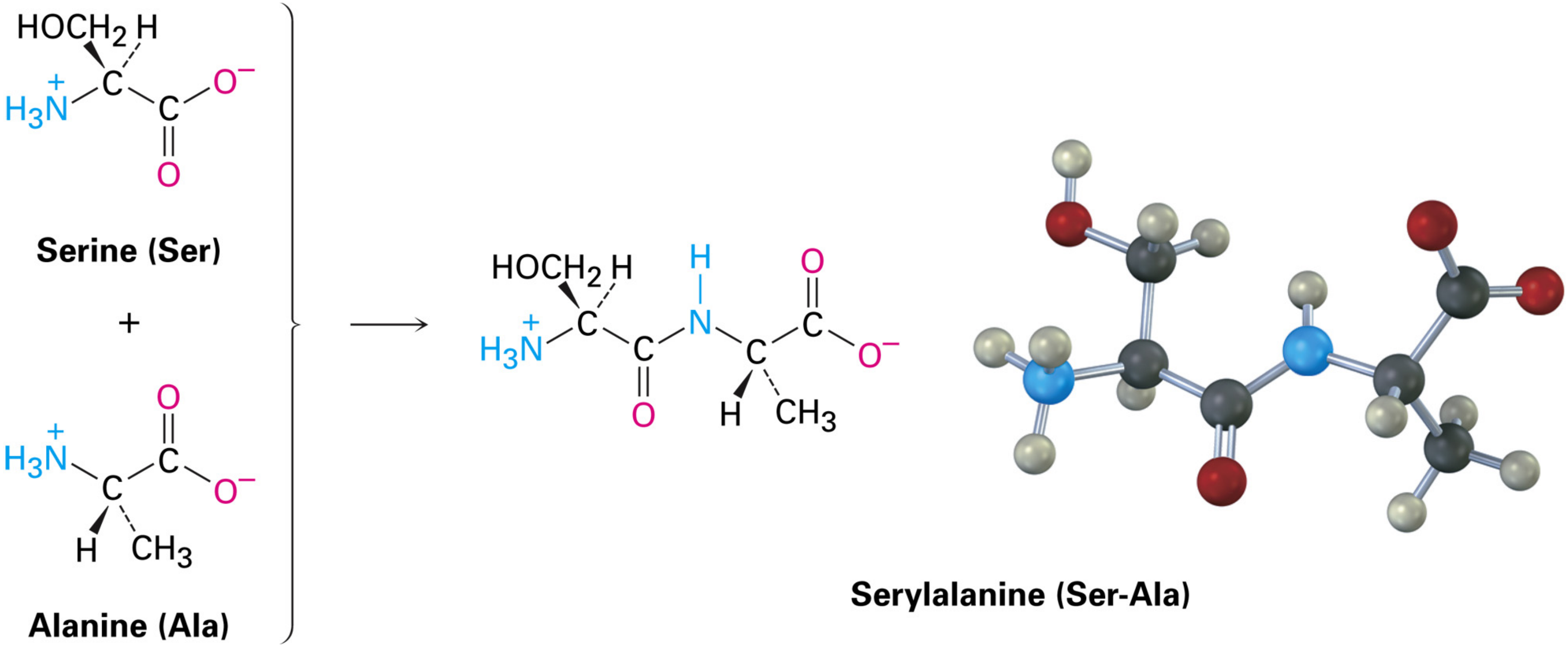


ends at the C-terminus (right)

Peptides

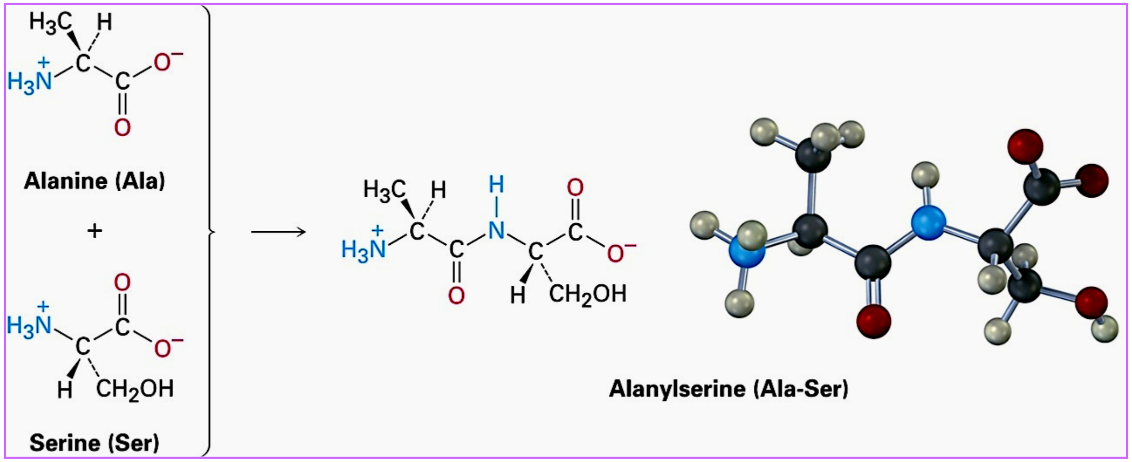


Peptides

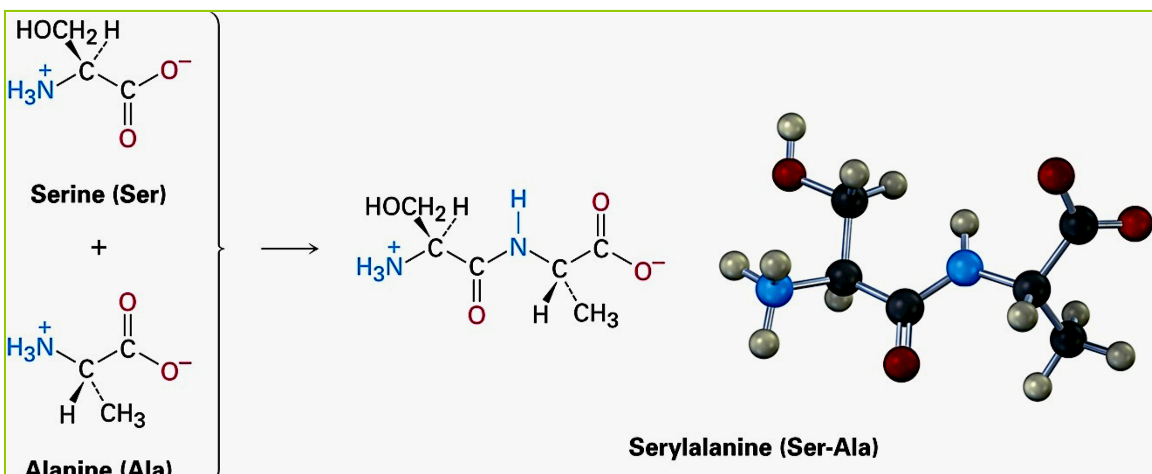


•By convention the peptide is written with the N-terminal amino acid (contains free NH_3^+) on the left and C-terminal amino acid (free COO^-) on the right

Peptide sequence gives unique chemistry



these are two <u>different</u> peptides



Proteins are long peptides with 3D shape

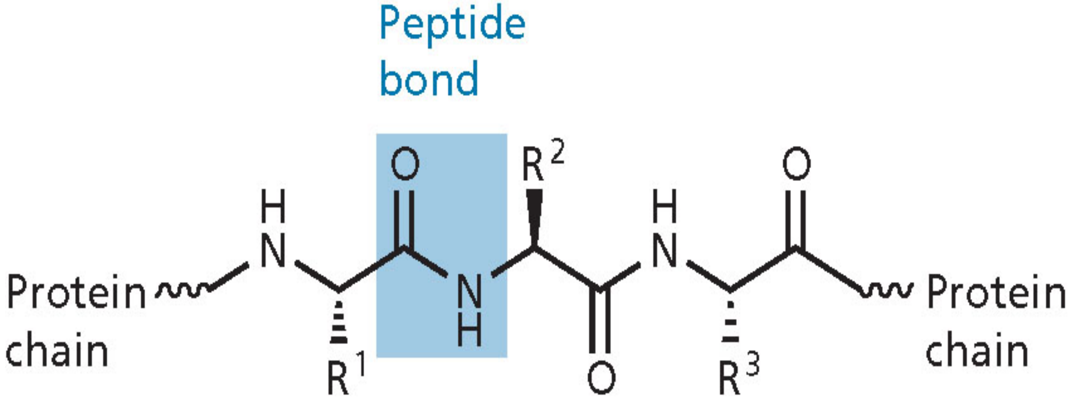
- Proteins are polypeptides
- They include receptors and enzymes and are important for virtually all biological functions
- Fibrous proteins include collagens in tendons and connective tissues and myosin in muscle tissue - are polypeptides with chains arranged side by side in long filaments, making them tough and insoluble in water
- Globular proteins are usually coiled and compact, roughly spherical and water soluble – often mobile in cells
- Most of the ~3000 enzymes (catalyse reactions) are globular proteins

Protein structure

- Proteins have 4 levels of structure - primary, secondary, tertiary and quaternary

primary structure

- The linear sequence in which amino acids are **covalently** linked *via* **amide bonds (peptide bonds)** from N (free NH_2) to C-terminus (free CO_2H) (gene product)



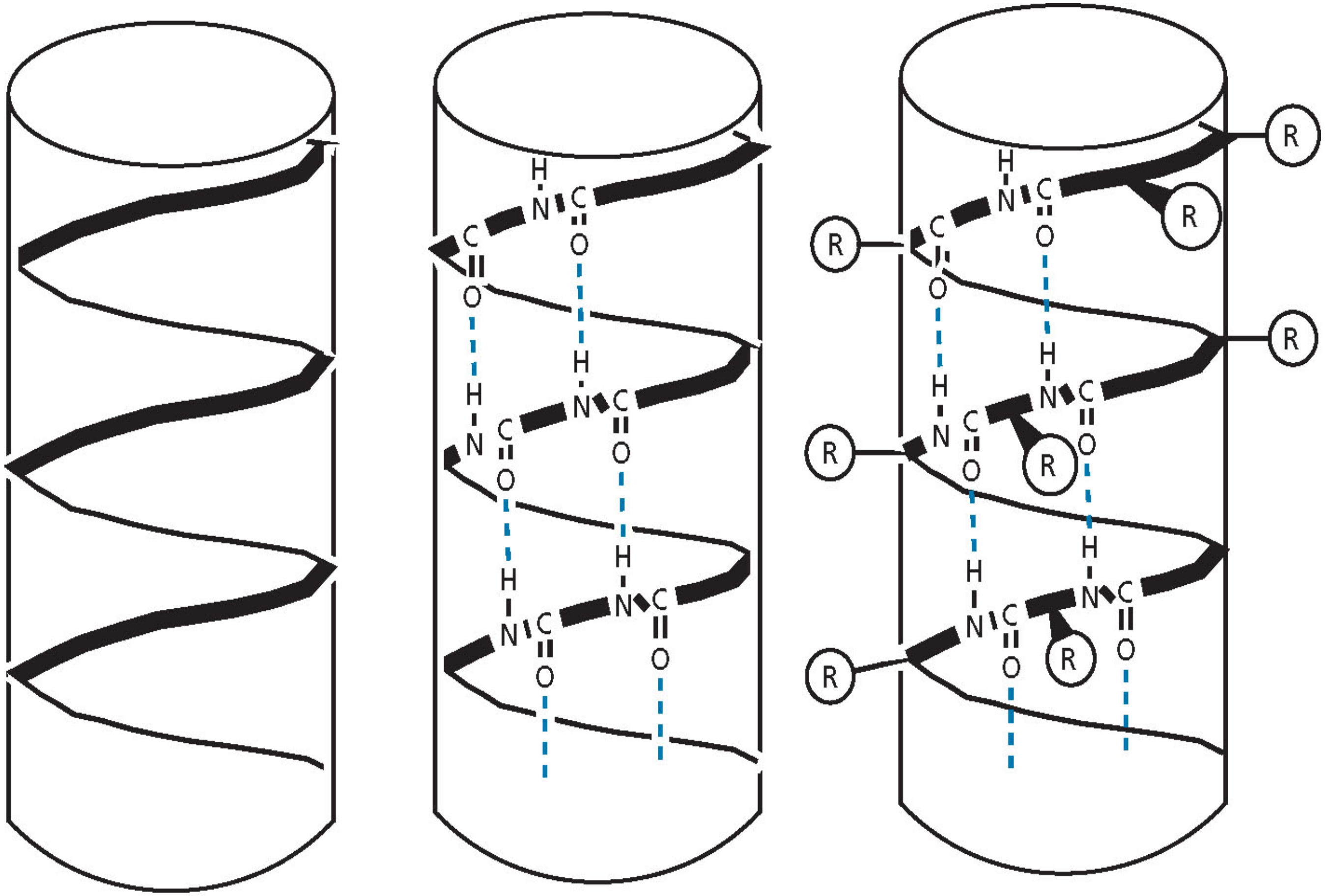
Protein structure

secondary structure

- the secondary structure of proteins consists of regions of ordered structures taken up by the protein chain
- includes the alpha helix and the beta-pleated sheet

Protein structure – α-helix

secondary structure

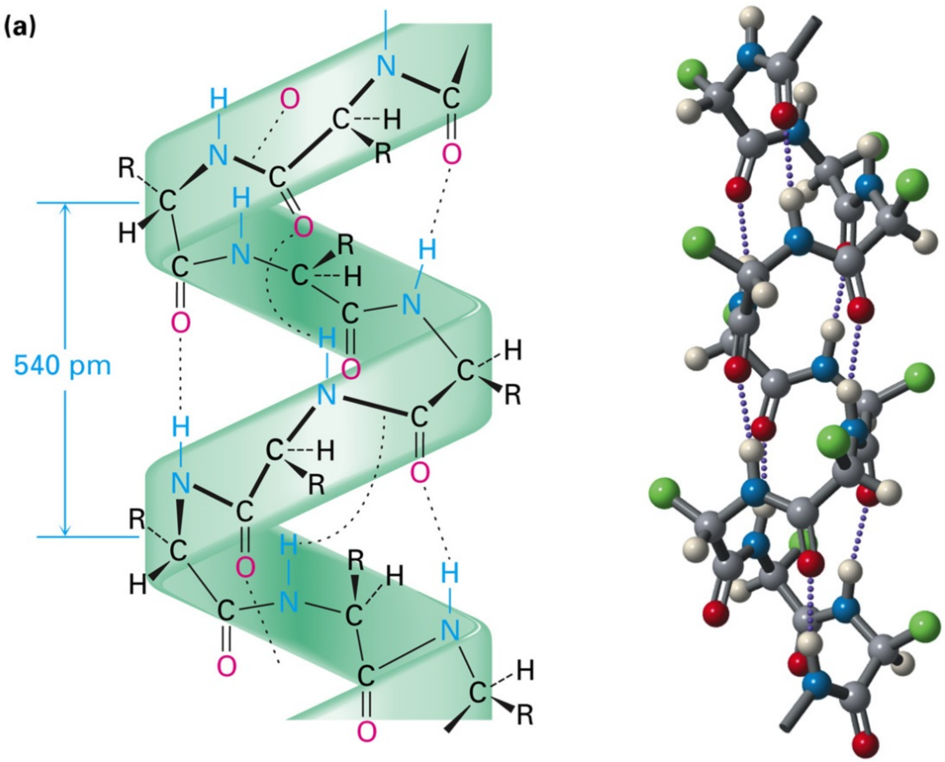


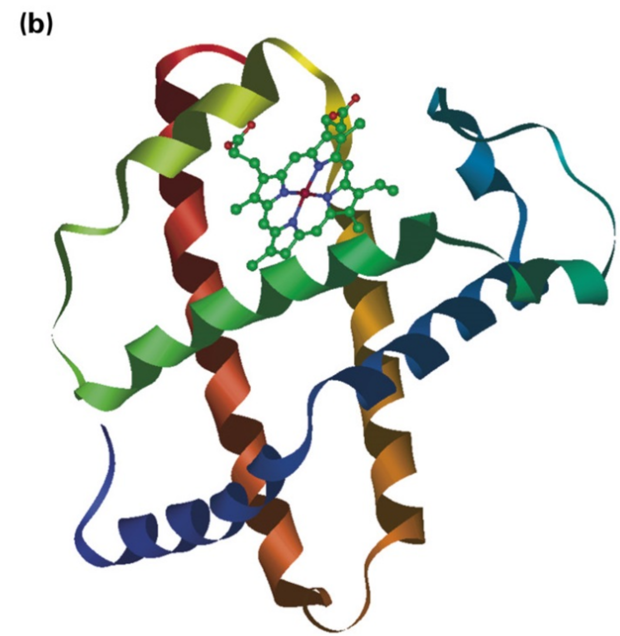
α-Helical backbone

Hydrogen bonding between peptide bonds

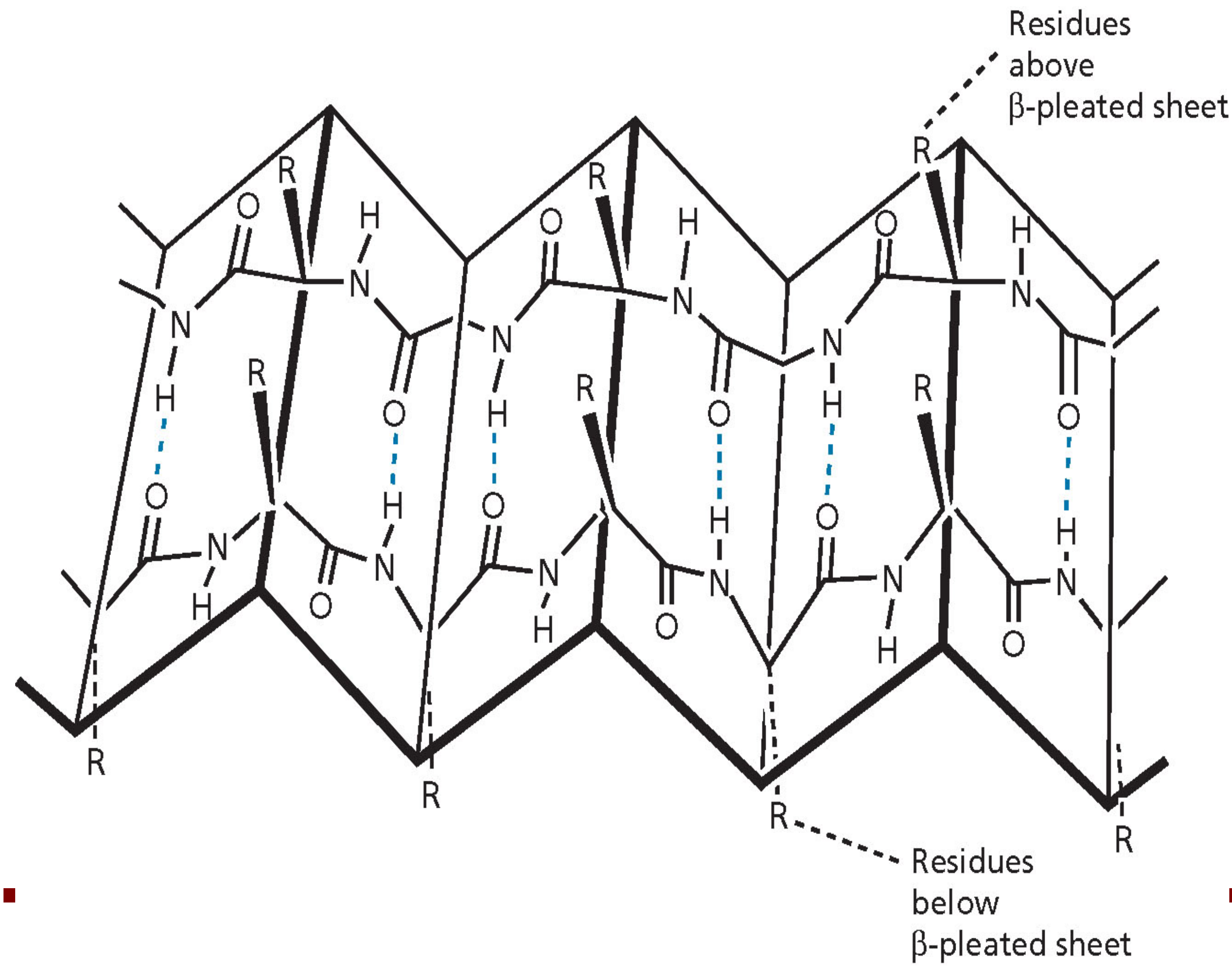
Position of residues

Protein structure α-helix

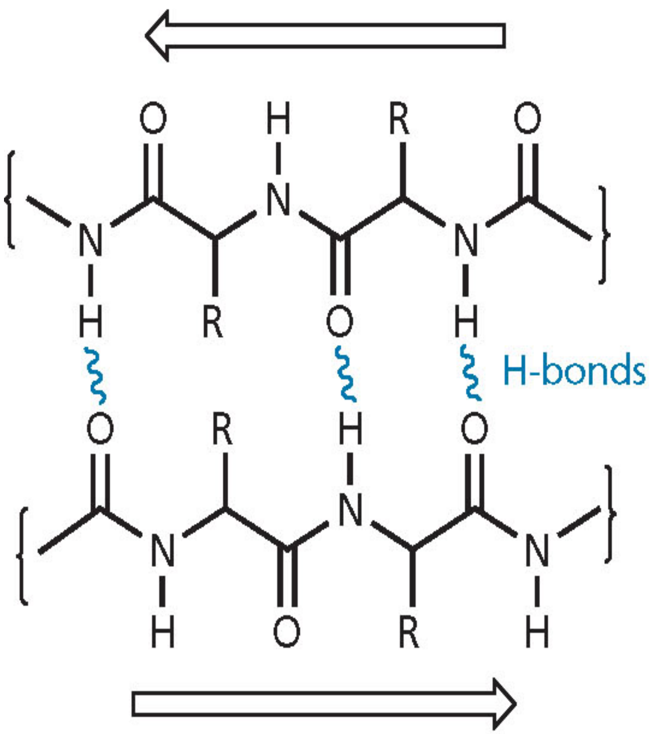




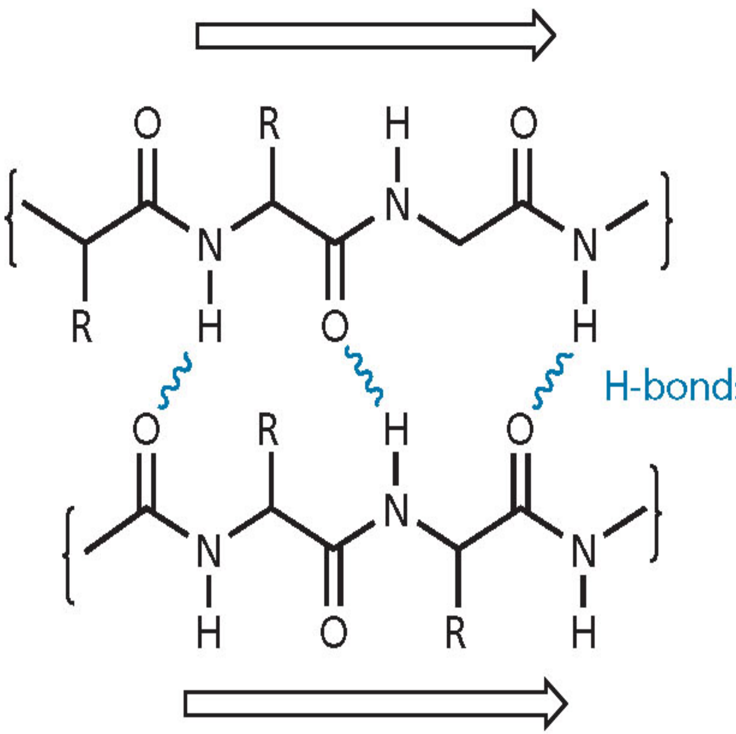
Protein structure β-pleated sheet
secondary structure



Protein structure β-pleated sheet
secondary structure

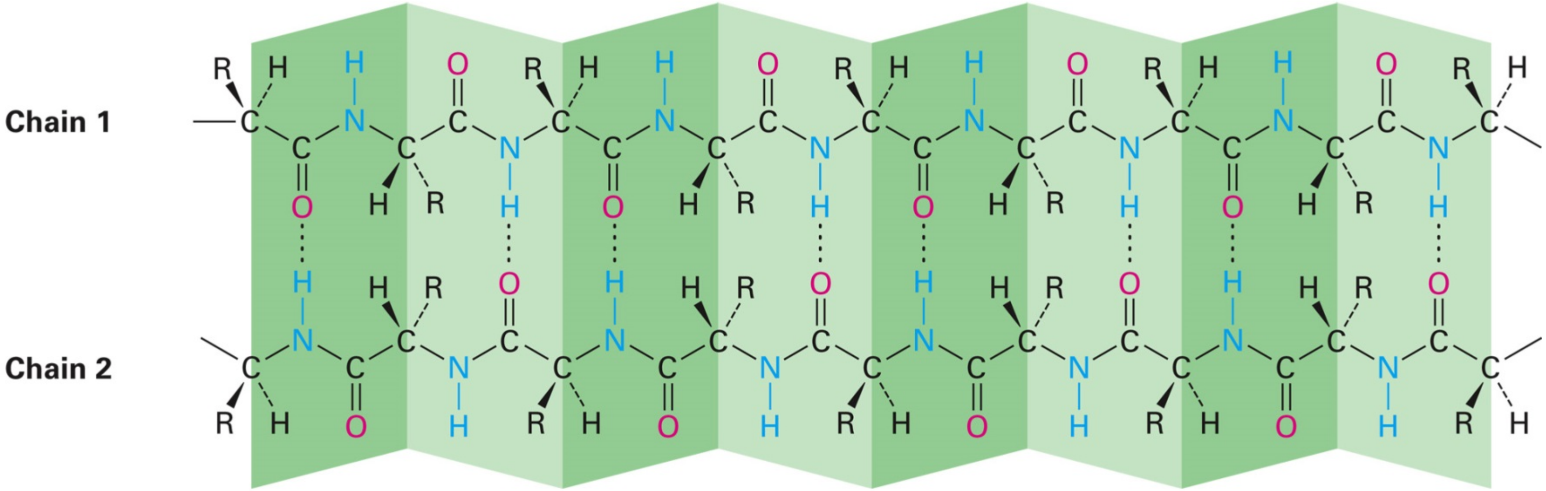


Antiparallel β-sheet

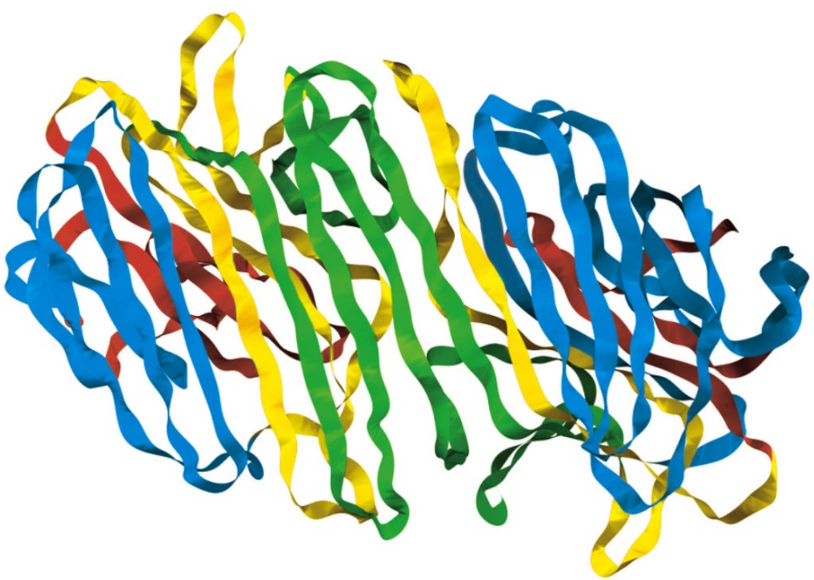


Parallel β-sheet

(a)



(b)

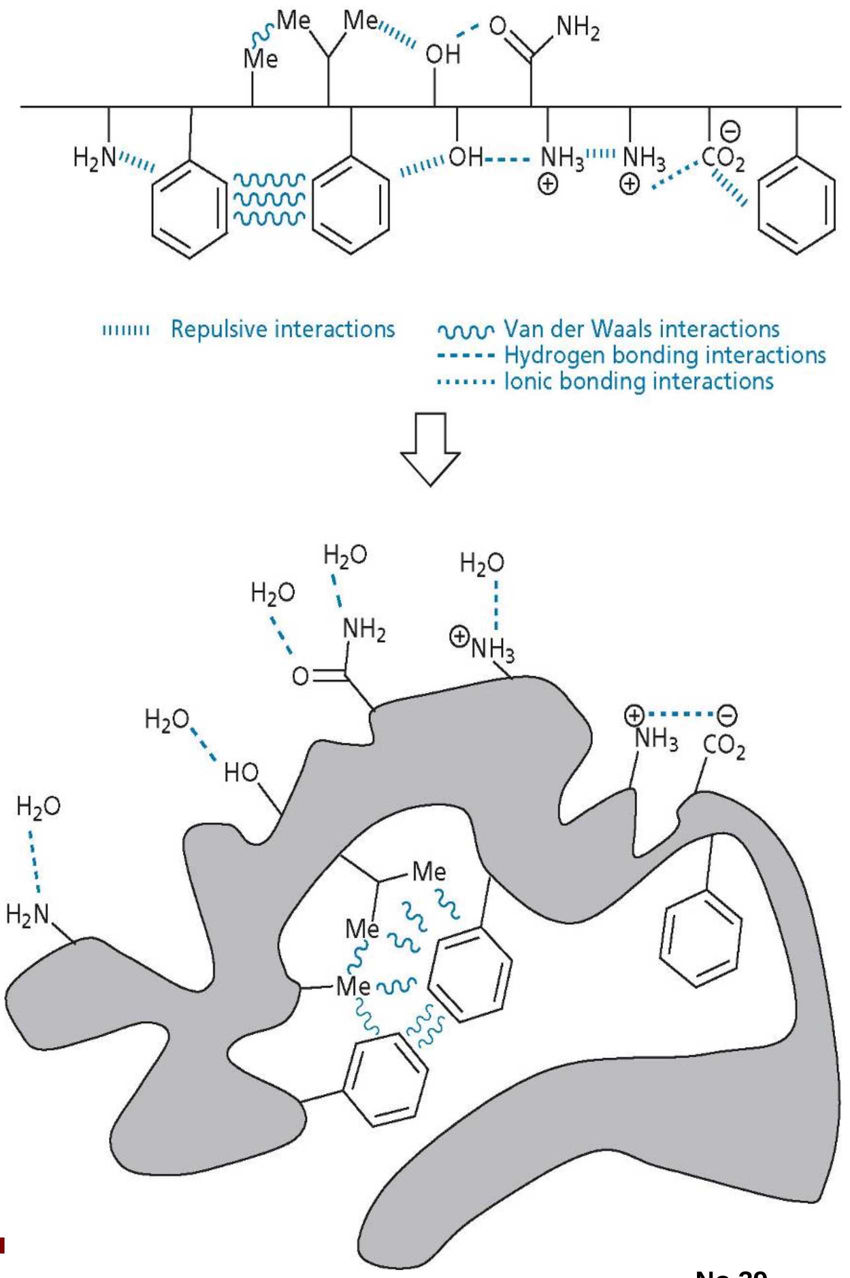


Protein structure

tertiary structure

- overall 3D shape of protein - crucial to function
- the overall protein shape/folding occurs spontaneously and arises from primary structure
- this automatic folding even takes place as proteins are being synthesised in the cell on ribosomes

Protein structure

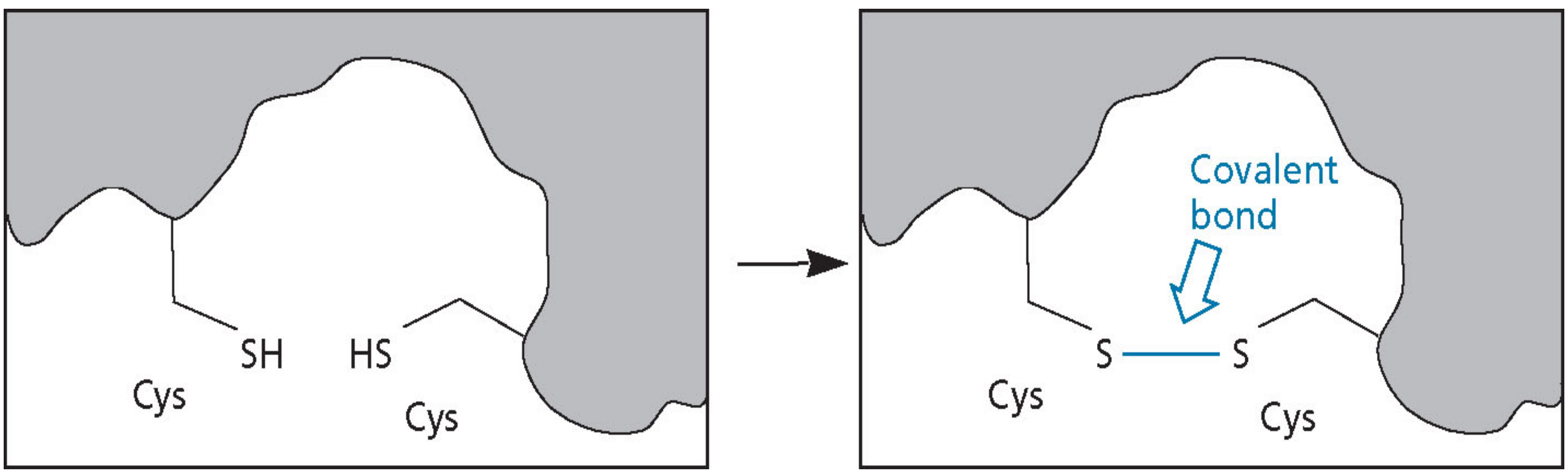


tertiary structure

- Proteins twist and turn to minimise unfavourable interactions and enhance favourable interactions to give tertiary structure.
- In water, proteins fold to give hydrophilic (water loving) groups external and hydrophobic (water hating) groups interior

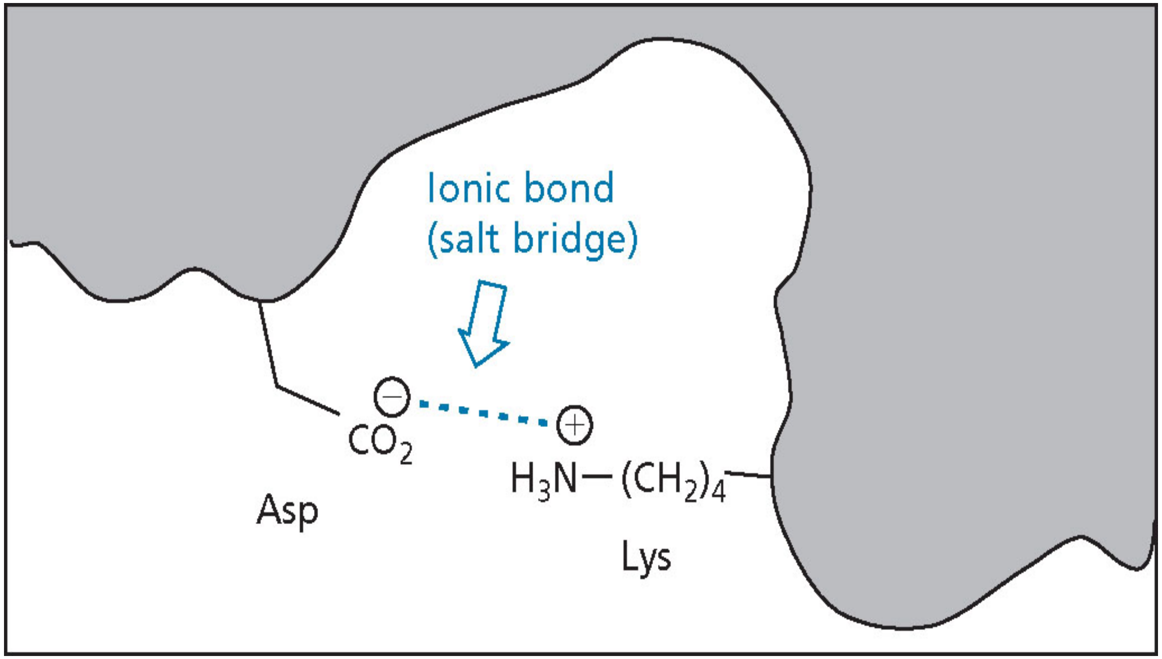
Tertiary structure of proteins cont'd

- Disulfide bonds between 2 cysteines (cystine)
- Two cysteines may be far apart but brought together by protein folding



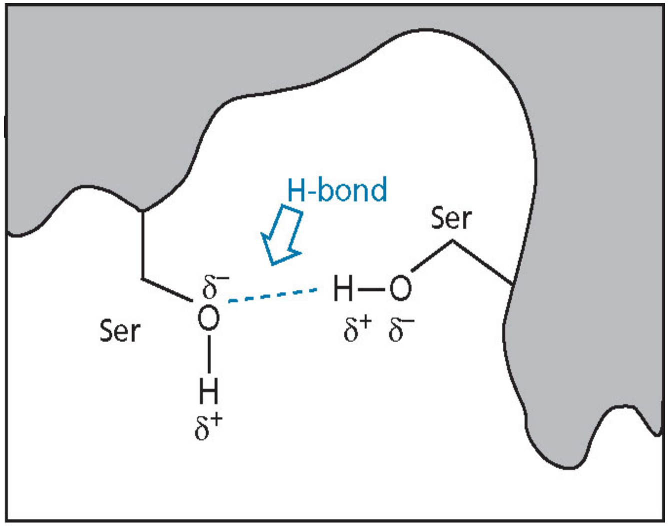
Tertiary structure of proteins cont'd

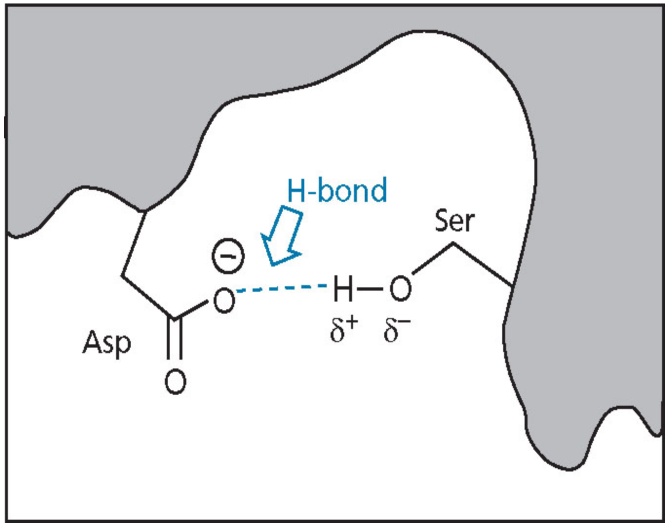
- Ionic bonds



Tertiary structure of proteins cont'd

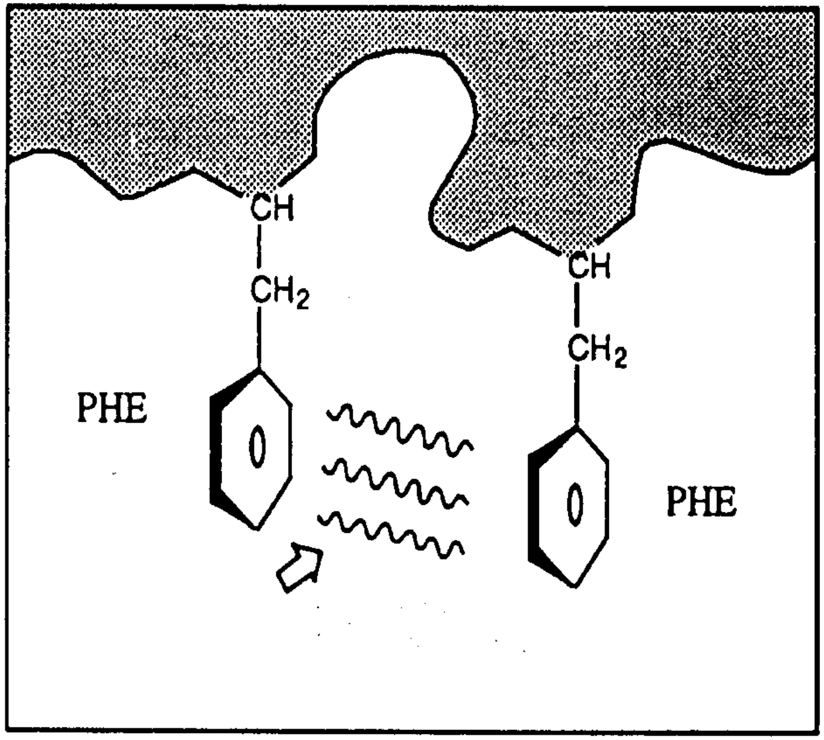
- Hydrogen bonds

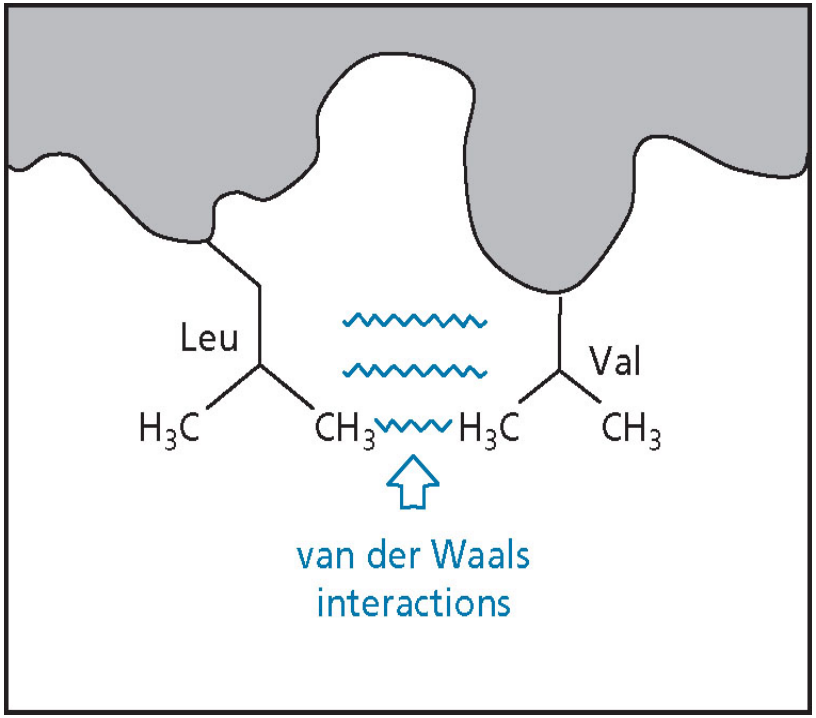


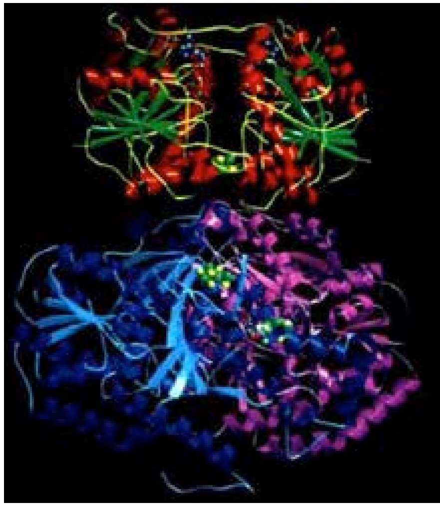


Tertiary structure of proteins cont'd

- van der Waals forces of non-polar groups







1º structure: the amino acid sequence (*i.e.* the gene product).

3º structure: the overall 3D shape caused by twisting of the polypeptide to accommodate aqueous solvent effects.

2º structure: regular oriented arrays of peptide units.

4º structure: stable non-covalent aggregates of multiple polypeptide chains

hydrophobic interactions, H-bonding and electrostatic interactions

both tertiary & quaternary structure are critical for function