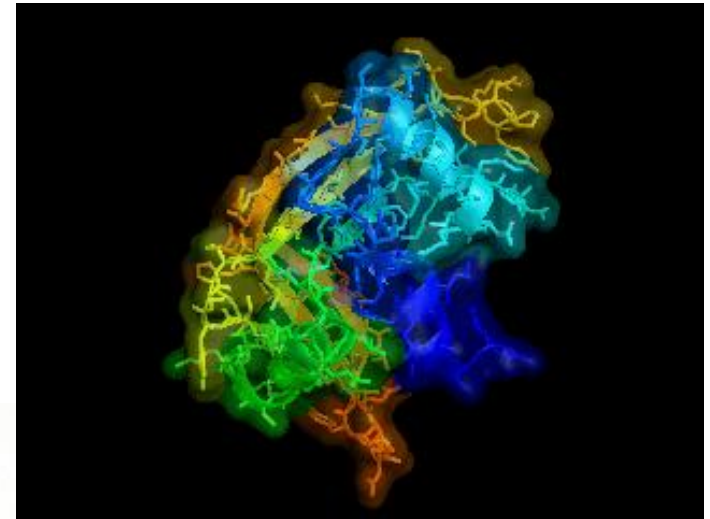
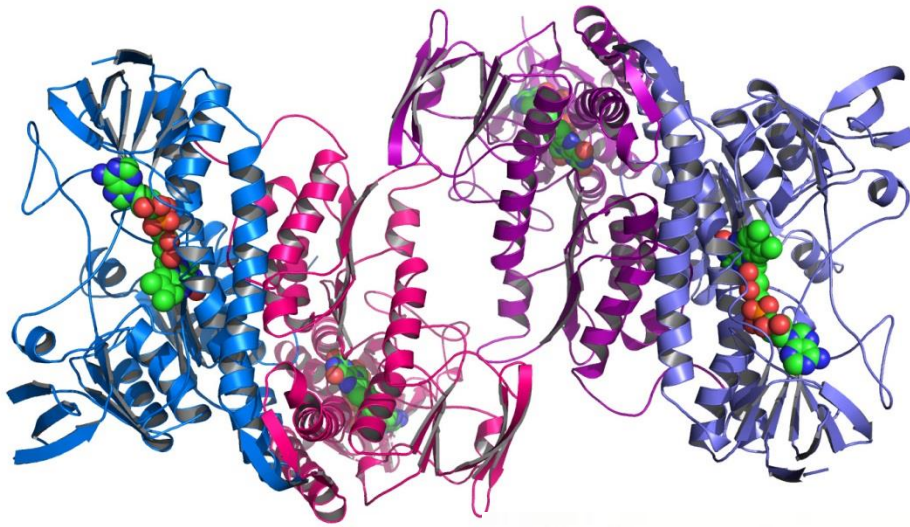


Chapter 9: Proteins



Molecular Biology

replication

C DNA

C RNA

transcription

translation

protein

■ general
■ special

general transfer: occurs normally in cells

special transfer: occurs only in the laboratory in specific conditions

unknown transfer: never known to occur

Proteins

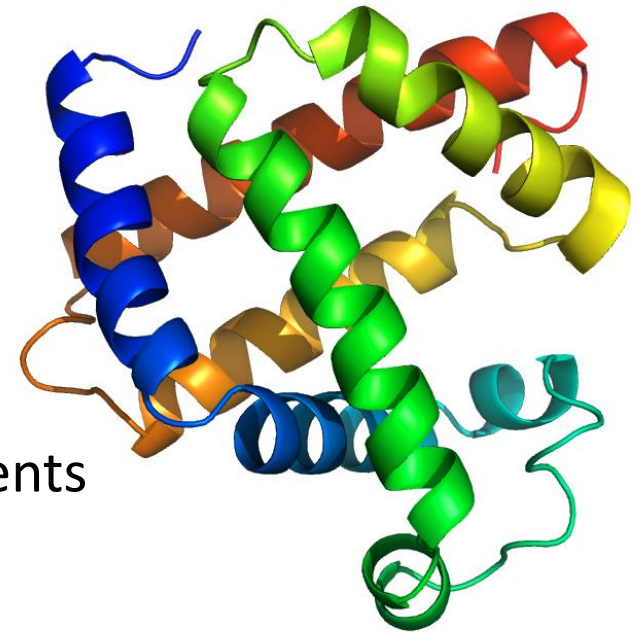
protein: information-carrying biopolymer

biopolymer: biomolecule made of many parts

Proteins are composed of long chains of amino acids in a precise sequence.

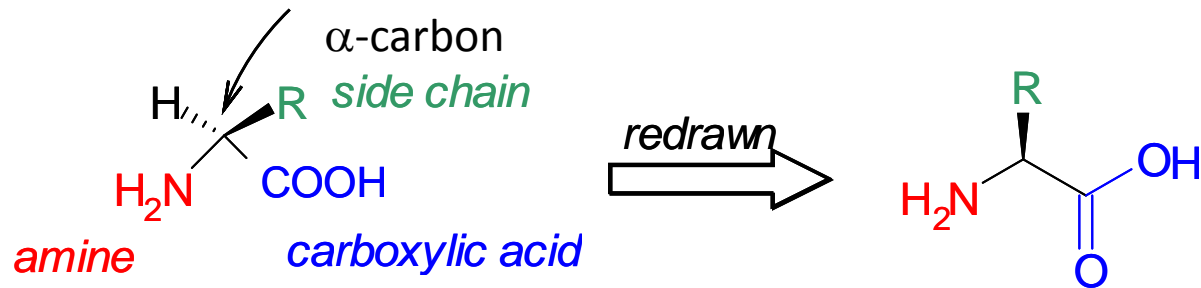
Proteins are used for:

- **Structure** of bodies
- **Catalysis** of reactions
- **Movement** of muscle tissue
- **Transport** of metals or other elements
- **Hormones** to move information
- **Storage** of energy
- **Regulation** of gene expression



Amino Acids

amino acid: an amine, a carboxylic acid, and a side chain



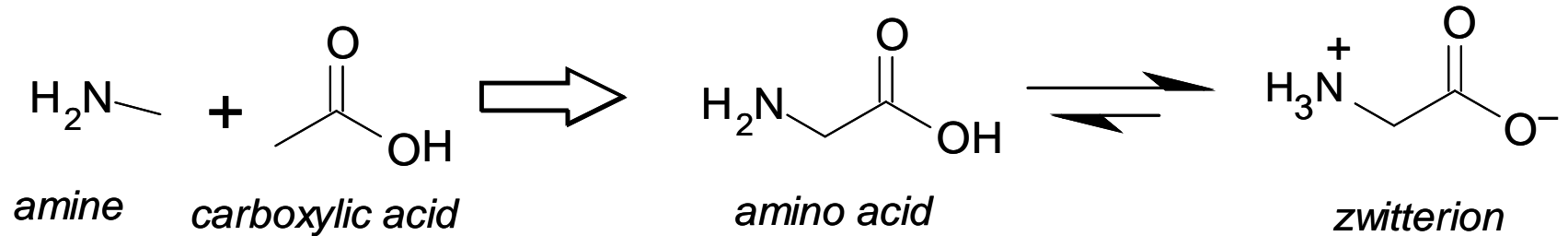
alpha amino acid: amine – carbon – carboxylic acid

There are 20 common amino acids, 10 of which are classified as “essential”.



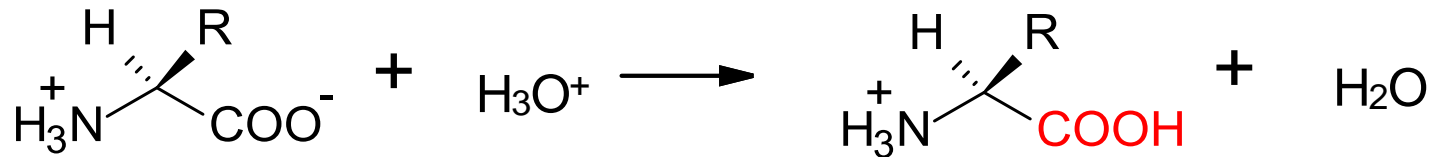
Ionization

Amino acids are always ionized.

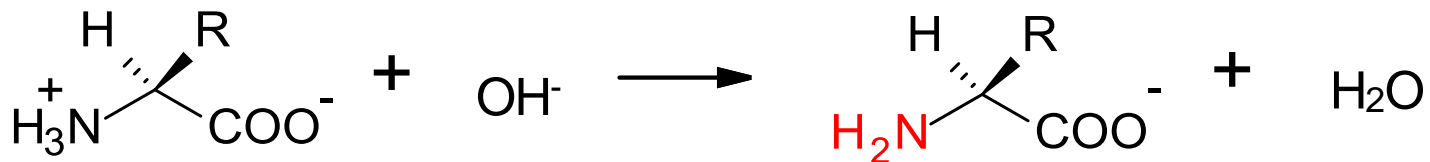


zwitterion: contains charges but is overall neutral.

At pH = 2 (acidic):



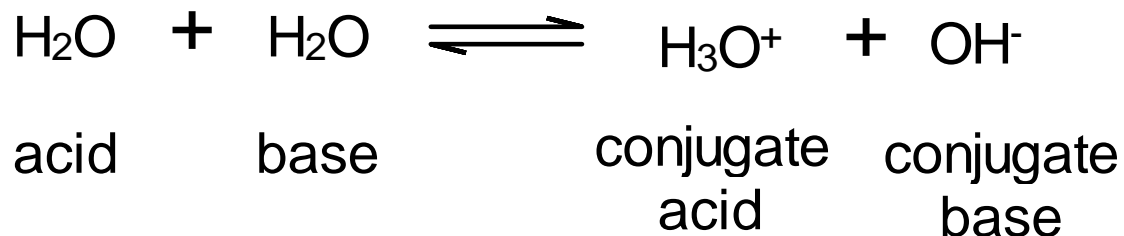
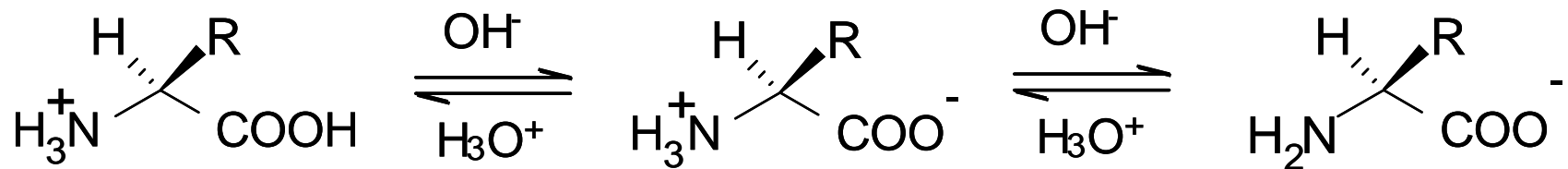
At pH = 10 (basic):



Amphiprotism

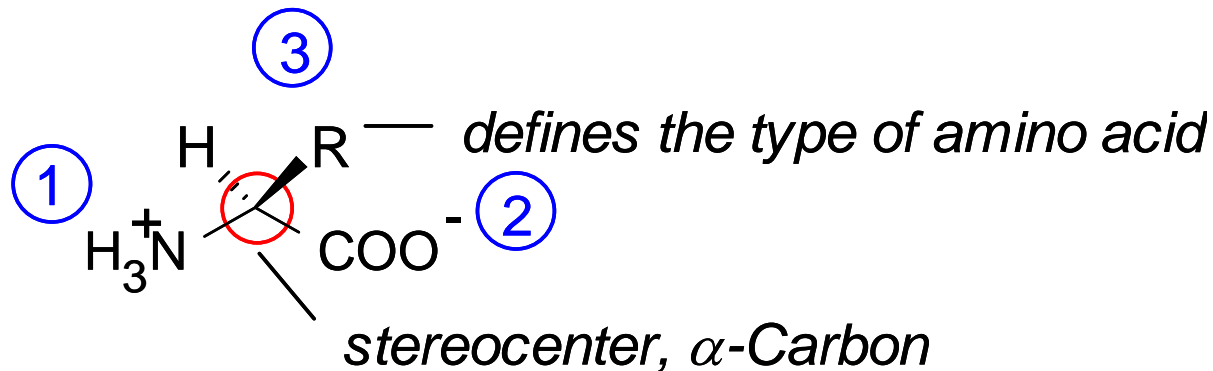
isoelectric point (pI): the pH at which
positive charges = negative charges

For most amino acids: around pH = 6.



Stereochemistry

The α -carbon is always a **stereocenter**
(with two exceptions).



All amino acids exhibit S-stereochemistry,
except for glycine (no stereocenter)
and cysteine (R-isomer).

Abbreviations

Amino acids are classified by “R” – the organic group bonded to the α -carbon.

Abbreviations are three- and one-letter, usually derived from the name.

Protein structures use line-angle drawings or letter abbreviations.

The List

NAME	3-LETTER	1-LETTER	NAME	3-LETTER	1-LETTER
Alanine	Ala	A	Methionine	Met	M
Cysteine	Cys	C	Asparagine	Asn	N
Aspartic Acid	Asp	D	Proline	Pro	P
Glutamic Acid	Glu	E	Glutamine	Gln	Q
Phenylalanine	Phe	F	Arginine	Arg	R
Glycine	Gly	G	Serine	Ser	S
Histidine	His	H	Threonine	Thr	T
Isoleucine	Ile	I	Valine	Val	V
Lysine	Lys	K	Tryptophan	Trp	W
Leucine	Leu	L	Tyrosine	Tyr	Y

* Non-intuitive abbreviations

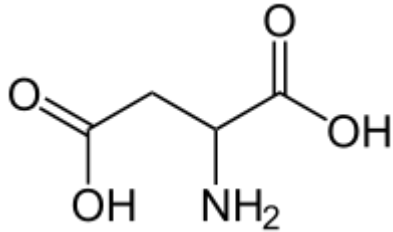
Categories

Amino acids are categorized by their side chains' structural properties and chemical behavior.

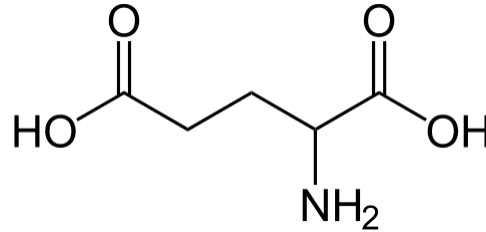
- **acidic:** contains either carboxylic acid or phenol
- **basic:** contains amine
- **aromatic:** contains aromatic groups
- **aliphatic :** comprised of alkyl chains
- **polar:** contains an amide or alcohol
- **sulfur:** contains a thiol or sulfide
- **twisty:** flexible/inflexible

Acidic Amino Acids

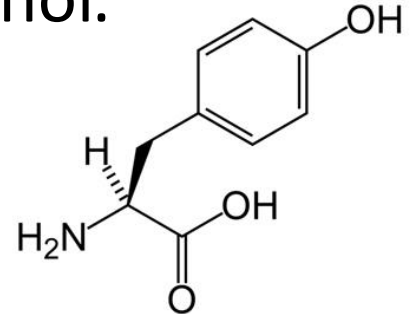
Contain either a carboxylic acid or a phenol.



aspartic acid



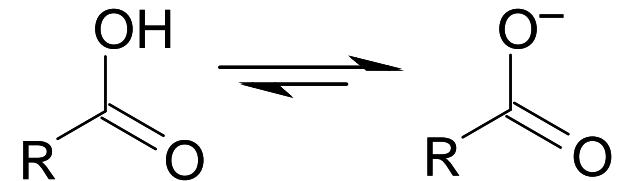
glutamic acid



tyrosine

With a $\text{pK}_a = 5$, at $\text{pH} = 7$ aspartate and glutamate dominate 100 to 1.

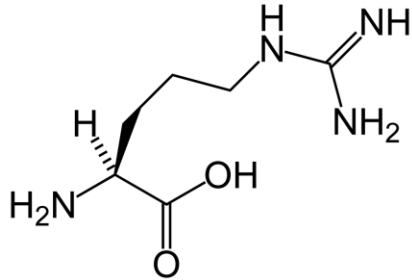
At $\text{pH} = 7$ (blood stream):



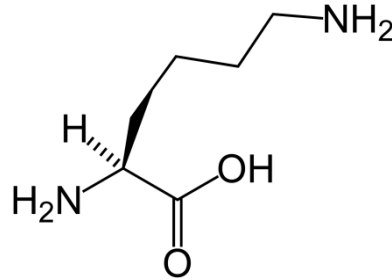
Tyrosine has a $\text{pK}_a = 10$, thus is found primarily in the protonated phenol structure.

Basic Amino Acids

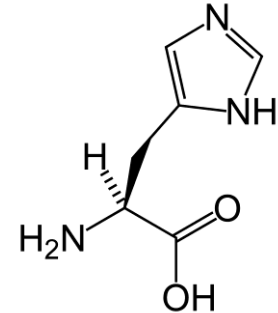
Contain an amine group in their side chain.



arginine

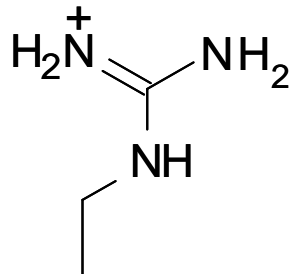


lysine

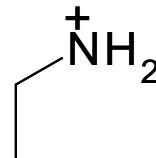


histidine

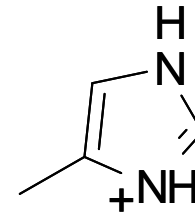
Only certain amine groups in arginine and histidine are protonated.



Arg



Lys



His

$[BH^+]/[B]$

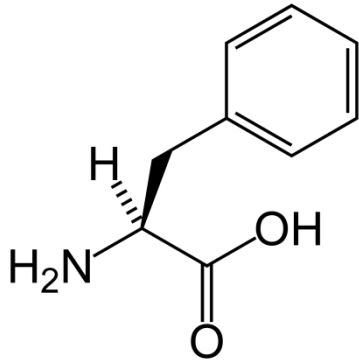
100,000 : 1

1,000 : 1

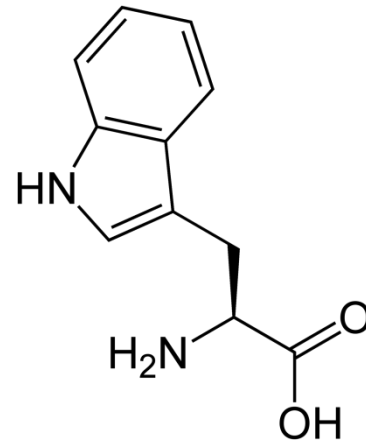
1 : 1

Aromatic Amino Acids

Contain aromatic rings.



phenylalanine



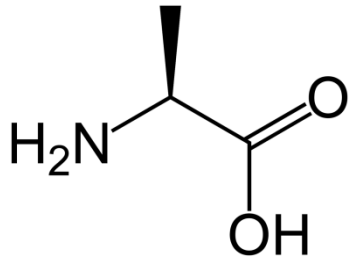
tryptophan

The aromatic systems allow transfer of charge (electrons) and use as neurotransmitters.

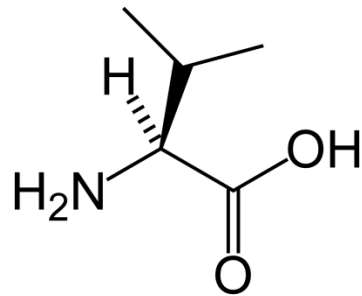
Aromatic amino acids are also classified as nonpolar with hydrophobic ends (the side chains).

Aliphatic Amino Acids

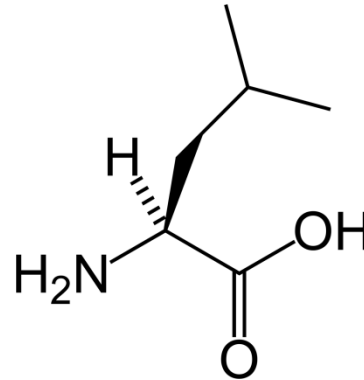
Contain alkyl side chains.



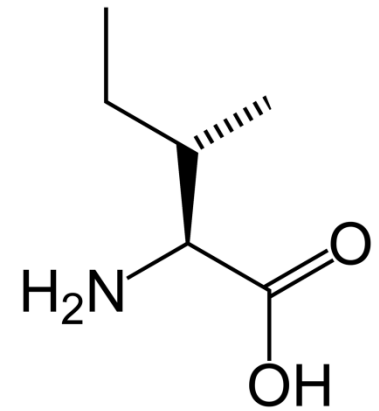
alanine



valine



leucine



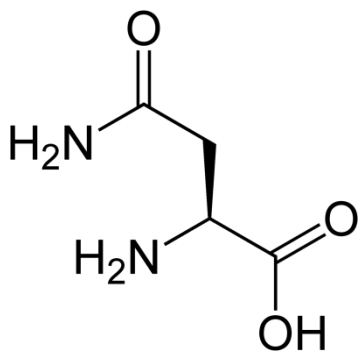
isoleucine

All aliphatic amino acids are nonpolar.

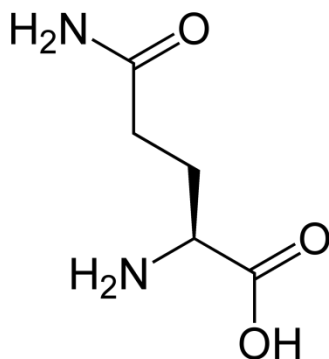
Alkyl side chains are very stable and therefore mostly unreactive.

Polar Amino Acids

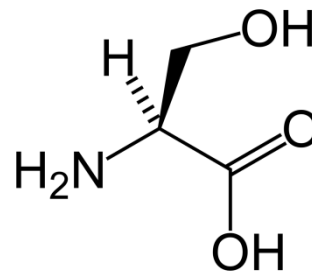
Contain either amide or alcohol functional groups.



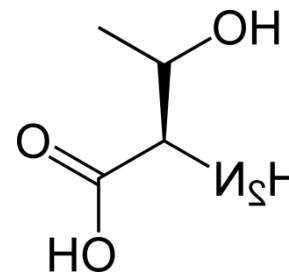
asparagine



glutamine



serine

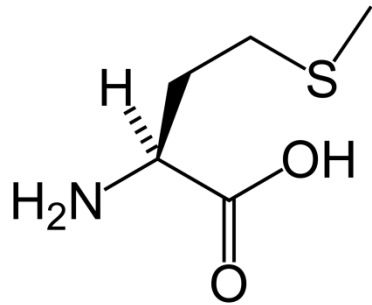


threonine

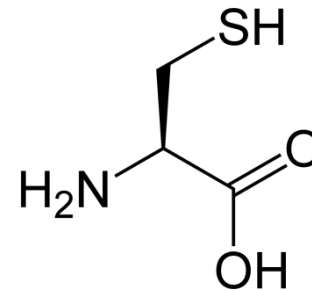
Alcohols and amides can behave as hydrogen-bond acceptors and donors.

Sulfur Amino Acids

Contain a thiol or a sulfide.

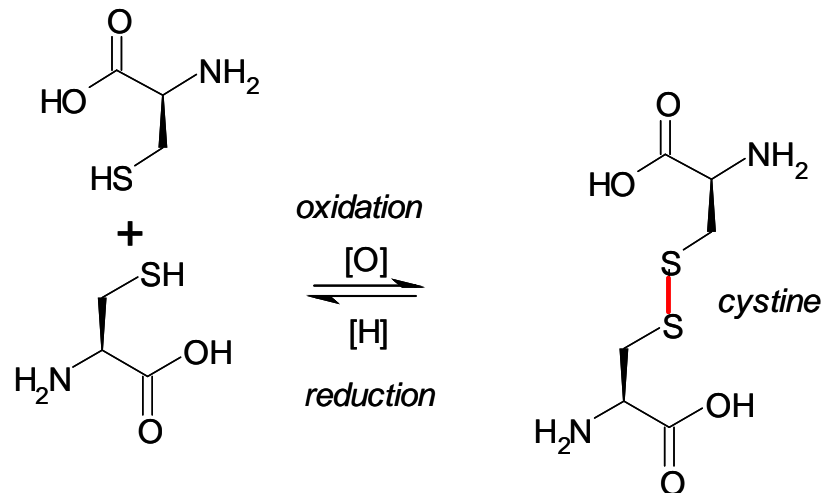


methionine



cysteine

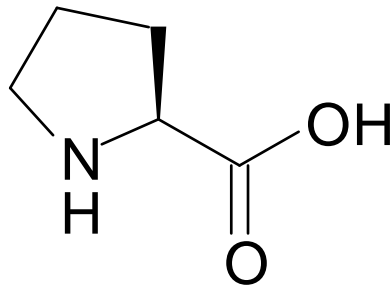
They are also classified as nonpolar.



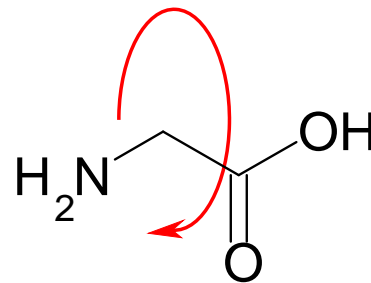
Twisty Amino Acids

Twisty amino acids do not follow the basic structure.

- glycine: has two hydrogens as its side chain (no side chain)
- proline: its side chain contains the amine group in the backbone



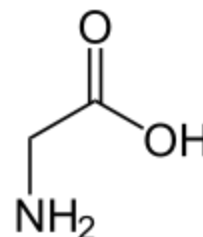
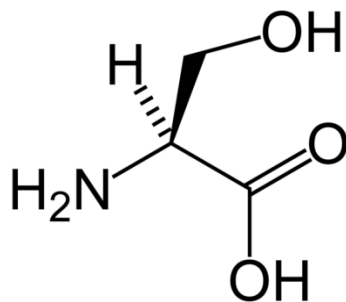
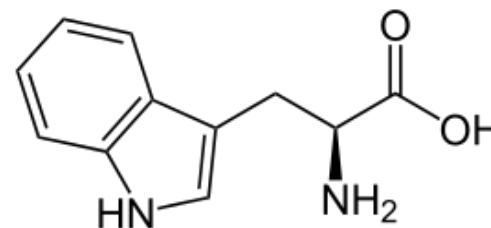
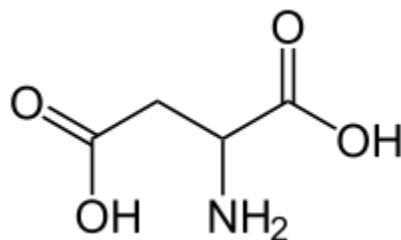
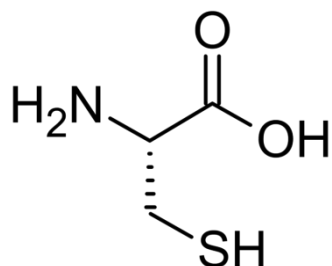
proline



glycine

Classifying Amino Acids

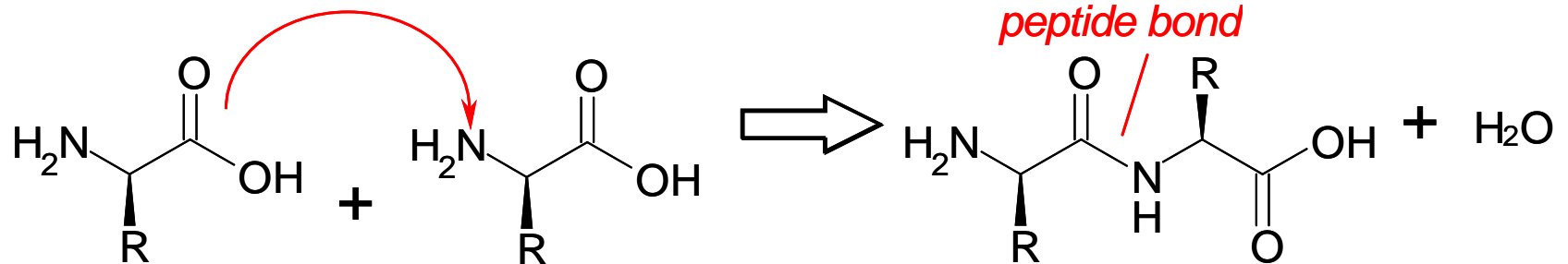
Classify the following amino acids as (1) acidic, (2) basic, (3) aromatic, (4) aliphatic, (5) polar and/or (6) nonpolar. Some may be classified multiple ways.



Proteins

Amino acids combine by forming linking amides.

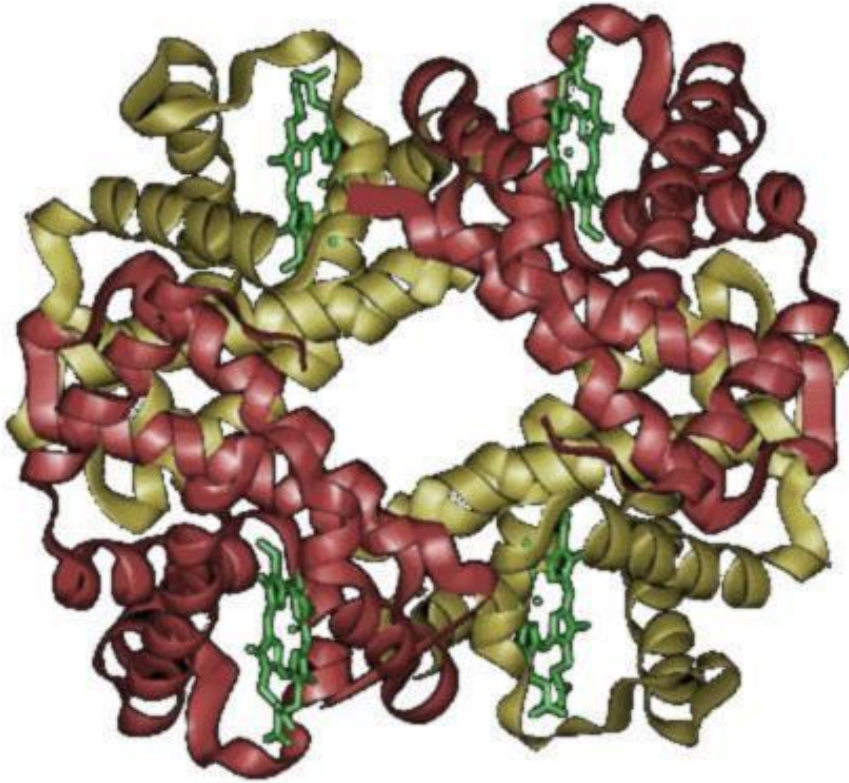
– “dehydration”



Note that:

- Water is lost.
- All stereochemistry is maintained.
- The carbonyls and the R groups *alternate*.

Hemoglobin



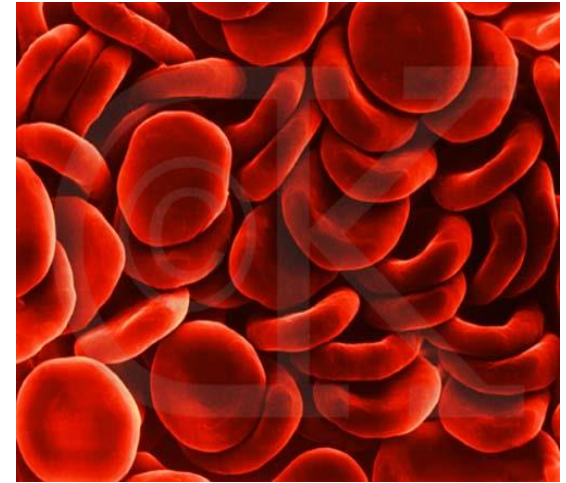
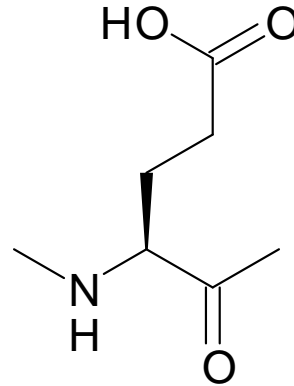
➤ hemoglobin: protein responsible for oxygen transport.

Consists of four separate polypeptide chains: two of α -hemoglobin (141 amino acids) and two of β -hemoglobin (146 amino acids).

Sickle Cell Anemia

Healthy Hemoglobin

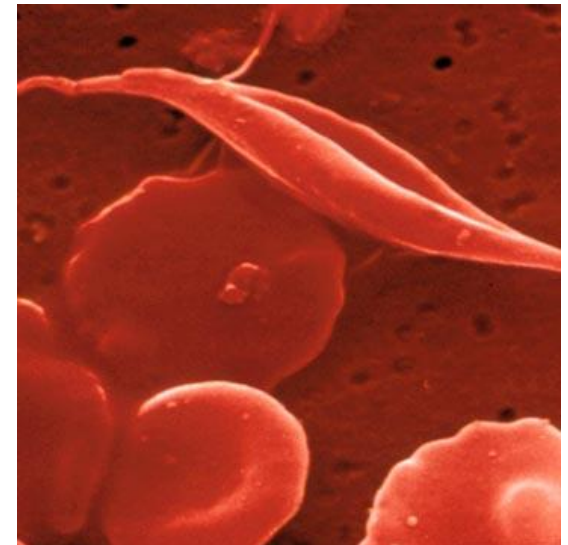
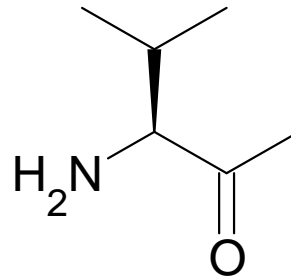
Contains glutamic acid/glutamate.



Val-His-Leu-Thr-Pro-Glu-Glu-Lys-Ser-Ala...

Mutated Hemoglobin

Contains valine.



Val-His-Leu-Thr-Pro-Val-Glu-Lys-Ser-Ala...

Order of Proteins

Amino acids must always be in a precise order for the protein to function.

For a dipeptide (protein consisting of two amino acids), there are 20^2 or 400 possible combinations.

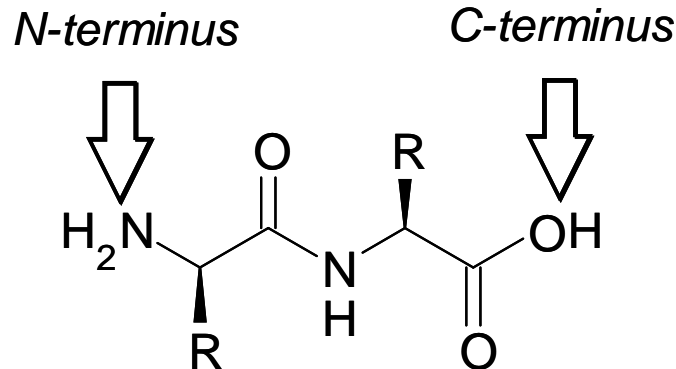
For a tripeptide (protein consisting of three amino acids), there are 20^3 or 8,000 possible combinations.

Most biological proteins contain on average 60 amino acid “residues” (polypeptide), leading to 20^{60} or 6.4×10^7 possible combinations.

Primary Structure

- primary structure: order of amino acids

Amino acids are *always* read from the N-terminus to the C-terminus.

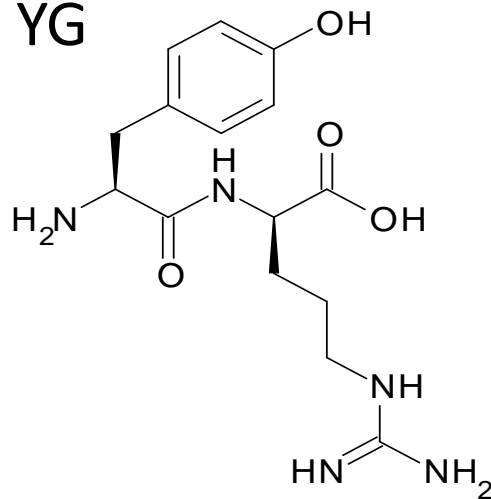


Always write the N-terminus on the *left* so that the amino acid order is correct.

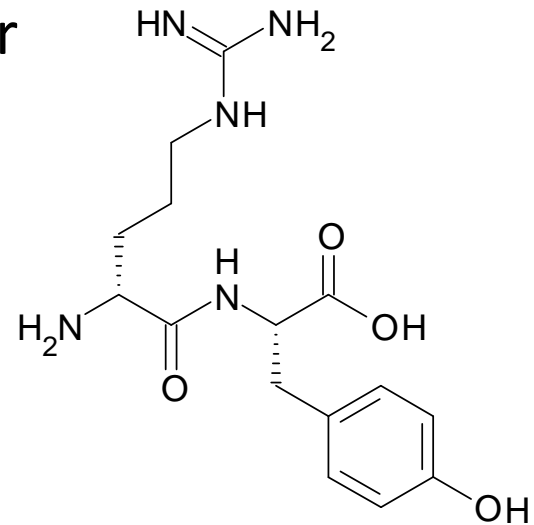
Kyotorphin

- kyotorphin: Dipeptide responsible for pain regulation in the brain.

Tyr-Arg
YG



Arg-Tyr
GY

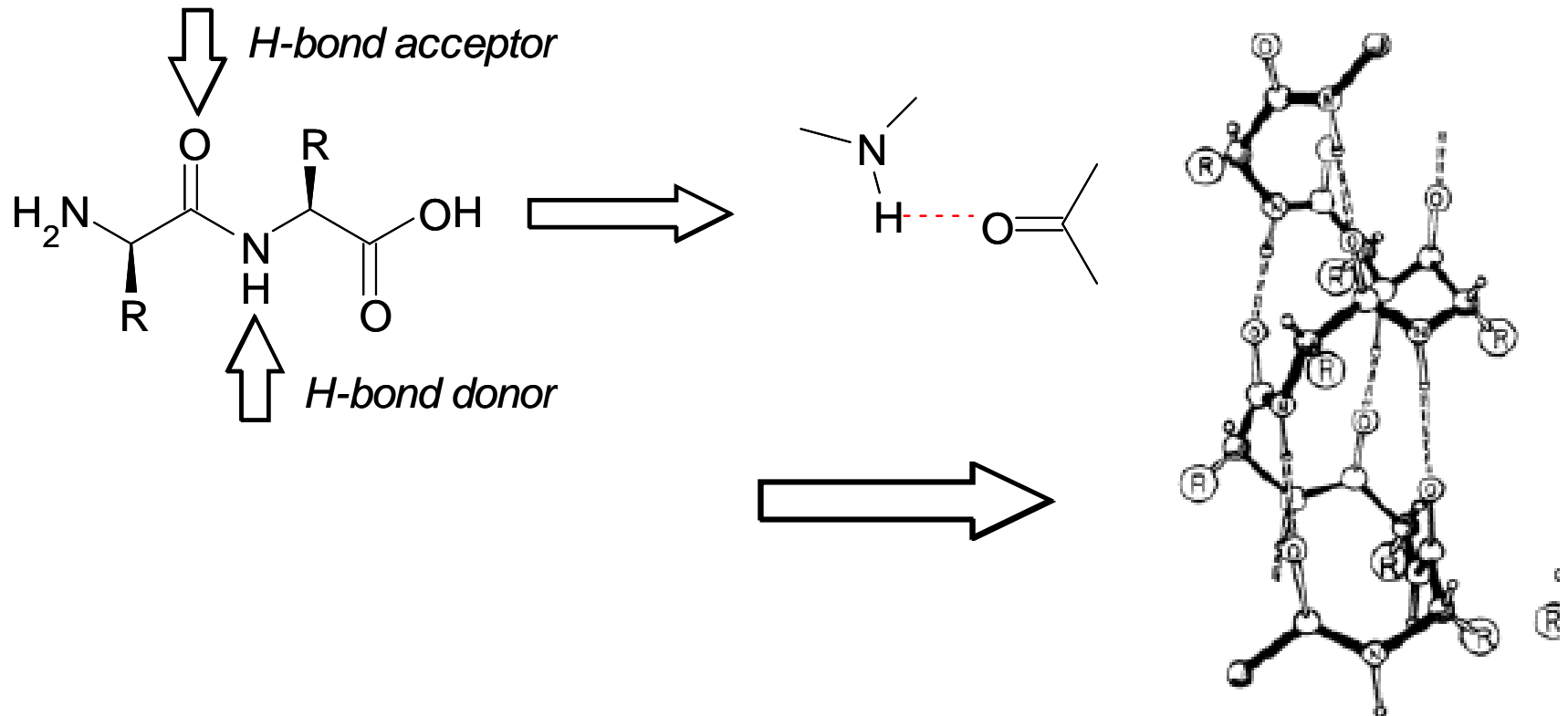


What's changed:

- N and C terminals have switched.
- Stereochemistry has inverted.
- H-bonding on the backbone has swapped.

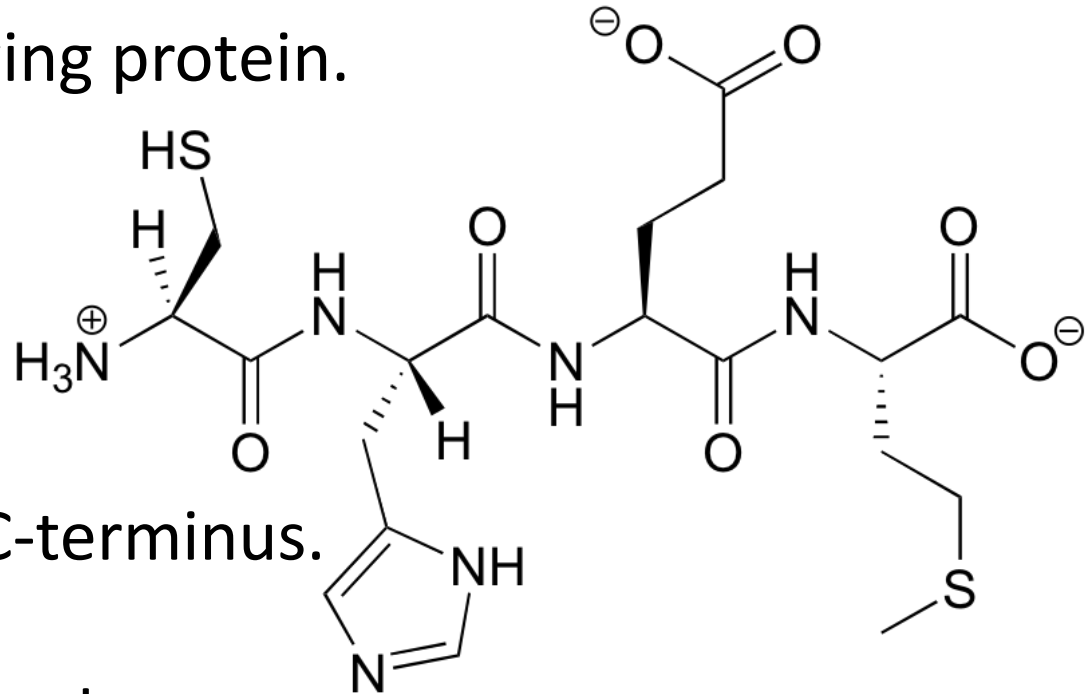
Hydrogen Bonding

The folding of a protein can be precisely ordered if it can bend in such a way to allow hydrogen bonding between the amide functional groups.



Primary Structure

Consider the following protein.



(1) Identify the N- and C-terminus.

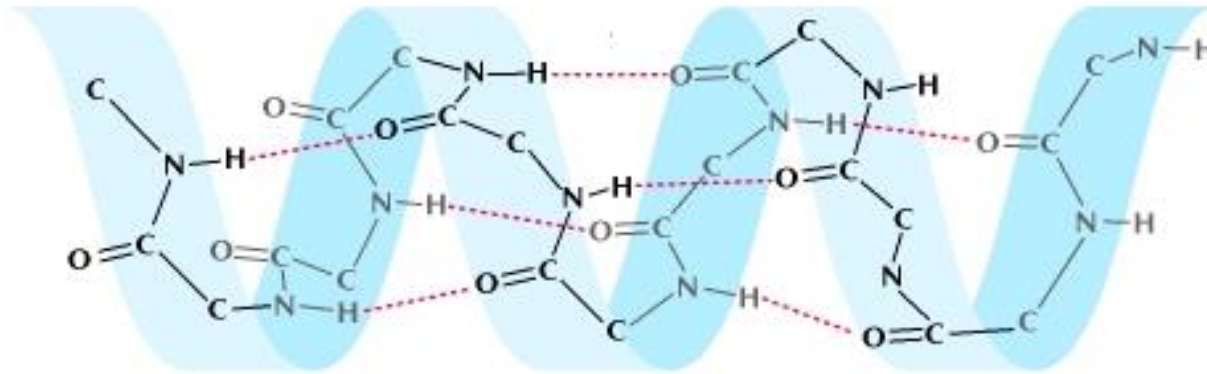
(2) Locate all peptide bonds.

(3) Count the amino acids.

(4) Classify each amino acid.

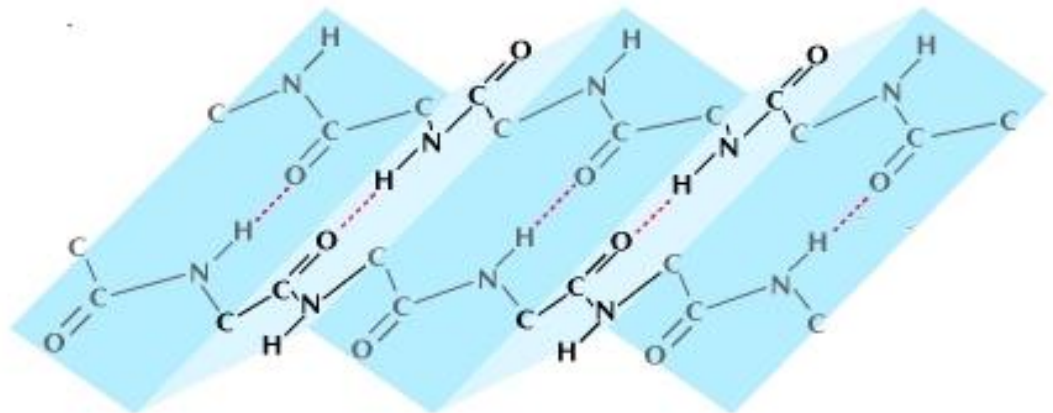
Secondary Structures

- secondary structure: hydrogen bonding on the backbone



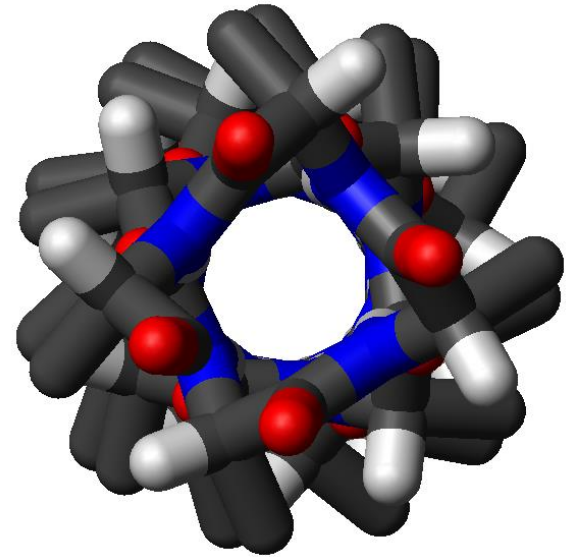
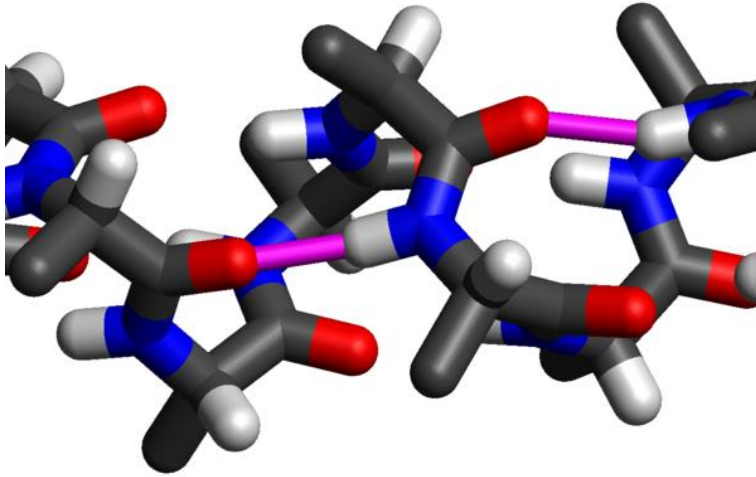
- α -helix: right-handed spiral formation

- β -sheet: strands forming into a long sheet



The α -Helix

Every fourth C=O can bond to an N-H to create a spiral.

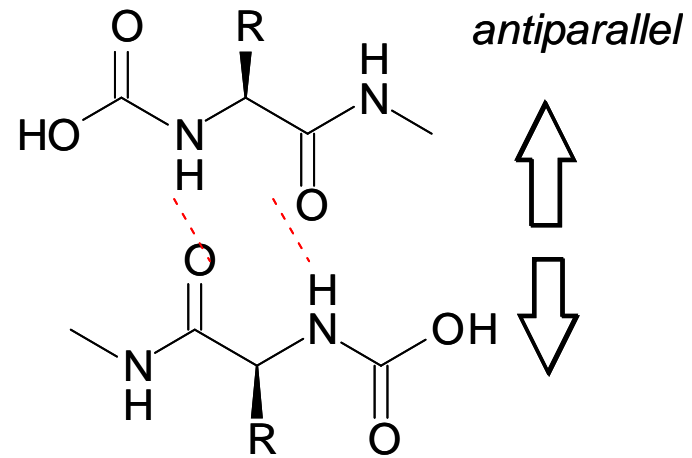
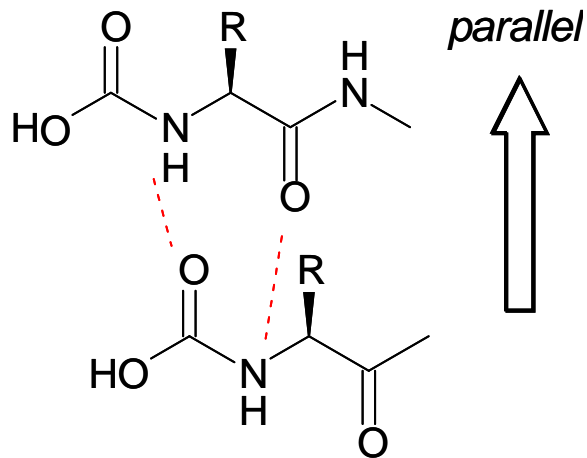


The β -sheet

β -sheets can be either *parallel* or *anti-parallel*.

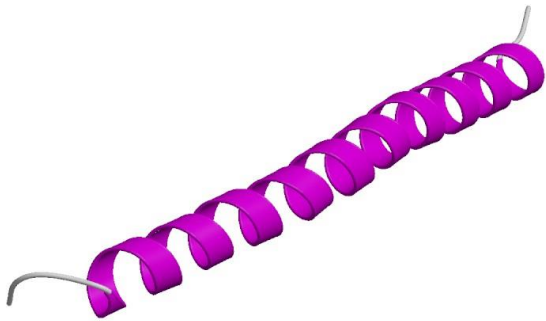
parallel: side chains point in the same direction
(all up or all down)

antiparallel: side chains point in opposite directions
(one line up, next line down)

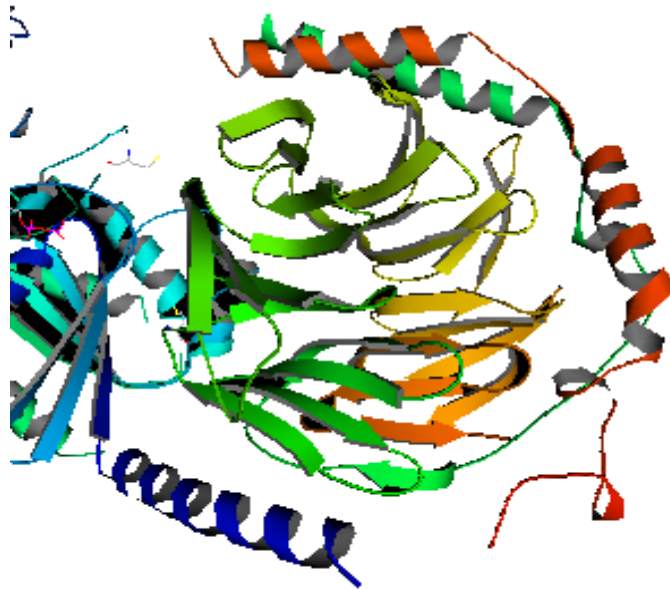
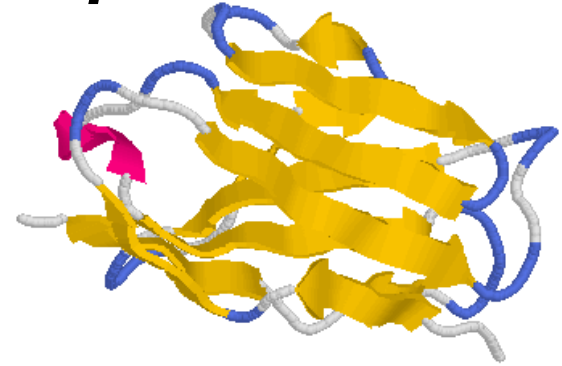


Secondary Structures

α -helix



β -sheet



Tertiary & Quaternary Structures

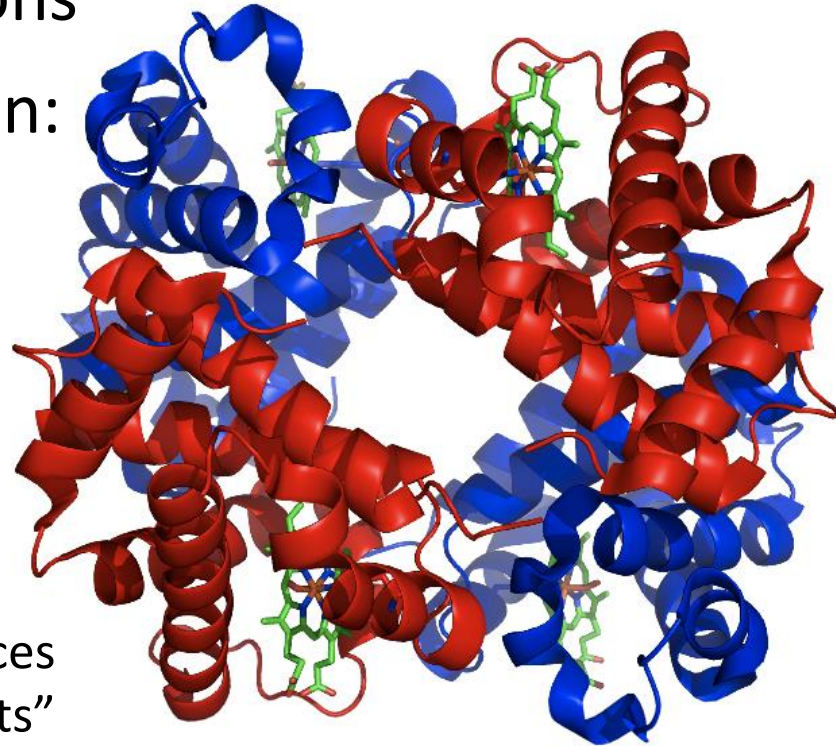
tertiary structure: formed by interactions between protein's secondary structures

quaternary structure: multiple secondary structures' interactions

Due to five sources of stabilization:

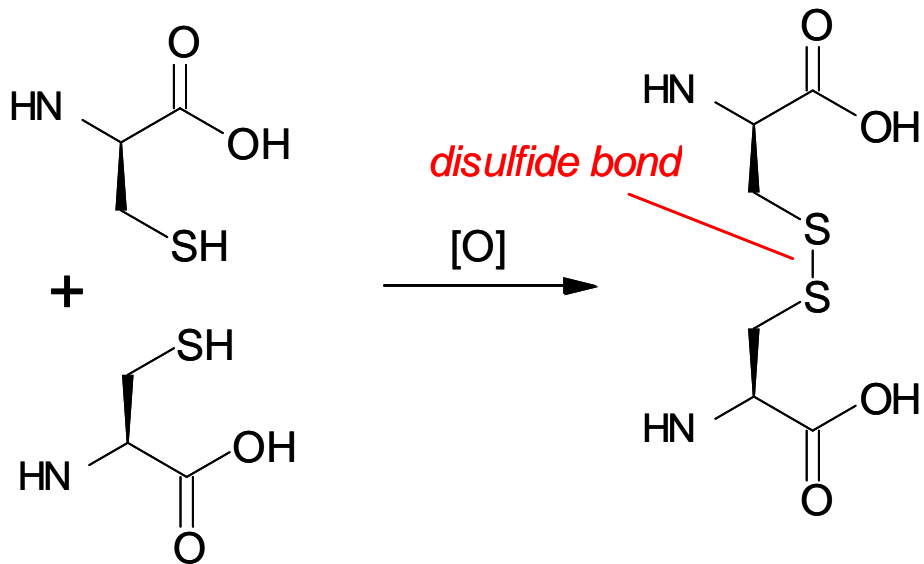
- **Covalent Bonds**
- **Hydrogen Bonding**
- **Salt Bridges**
- **Metal Ion Coordination**
- **Hydrophobic Interactions**

Hemoglobin: contains four α -helices in “quadrants”

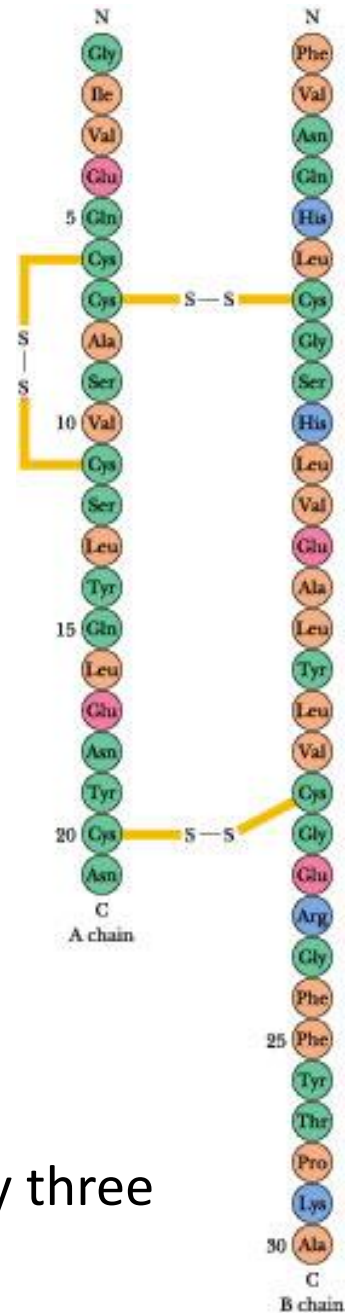


Covalent Bonds

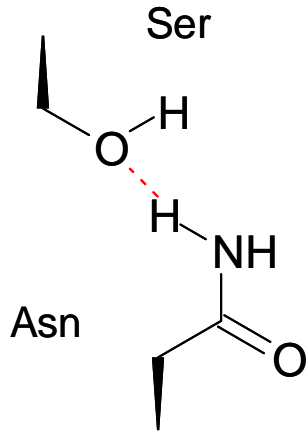
In the presence of oxygen, adjacent cysteines will oxidize their thiol groups to a disulfide.



Insulin: held together by three disulfide cross-bridges

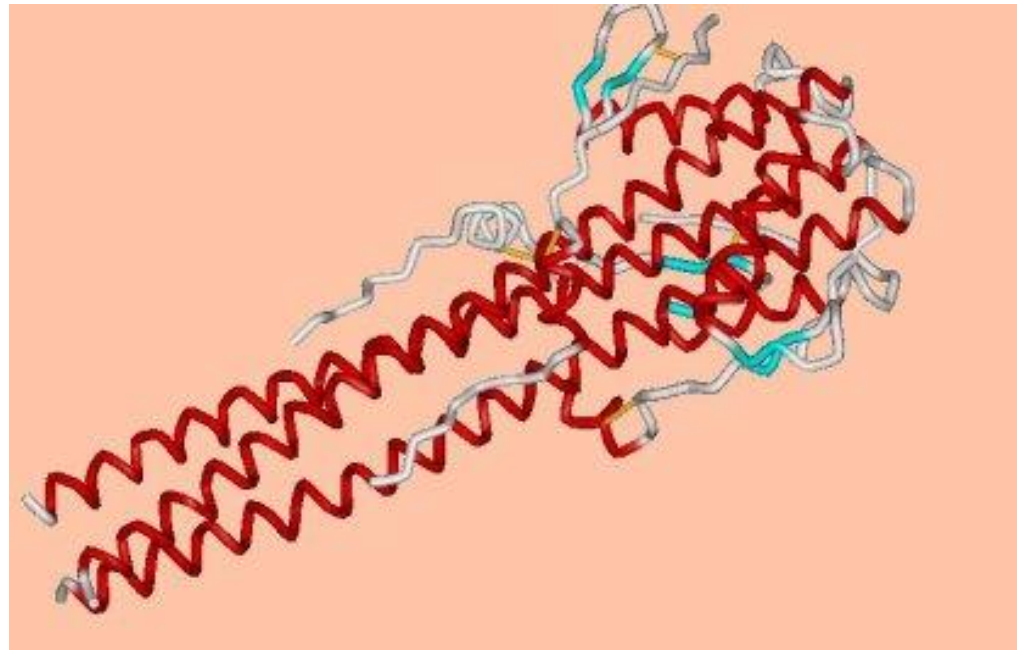


Hydrogen Bonding



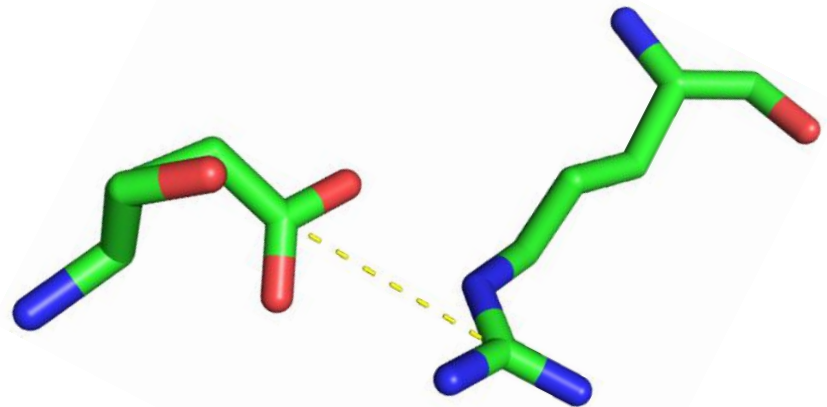
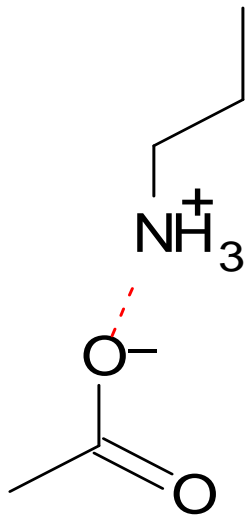
Adjacent hydrogen bond donors and acceptors can form interactions.

Human chorionic gonadotropin:
Hormone most commonly
detected by pregnancy tests



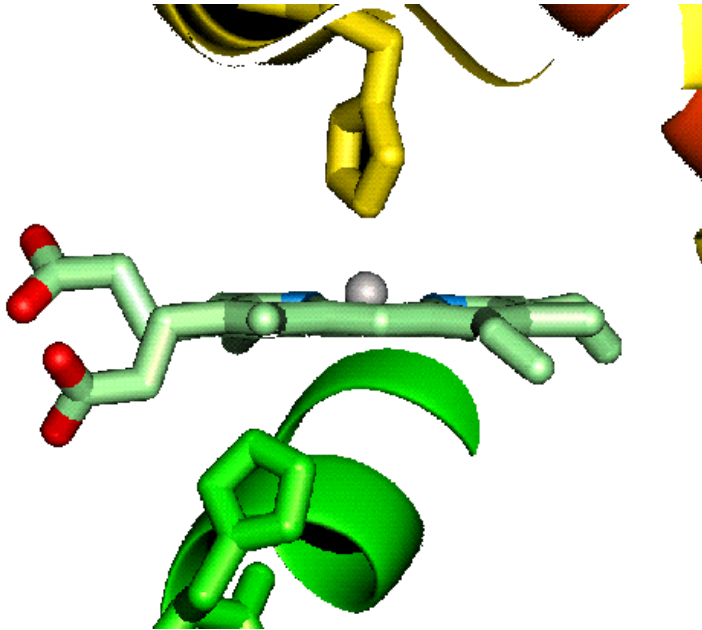
Salt Bridges

Since acidic side chains are mostly carboxylates and basic side chains are mostly ammoniums, the opposite charges form ionic interactions.

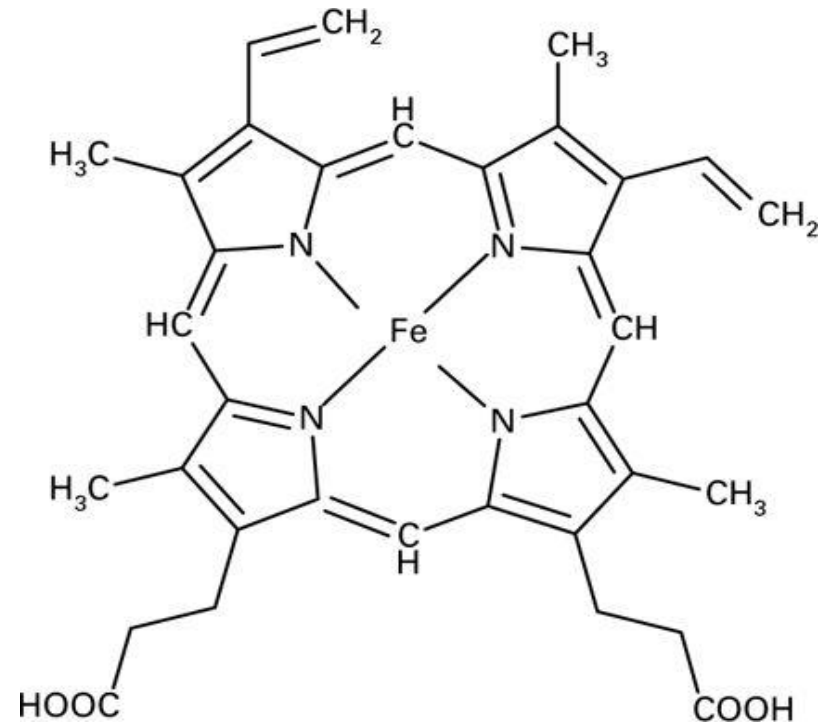


Metallic Ion Coordination

Charged salts on the sidechains can also interact with metal ions, such as Mg^{2+} or Fe^{2+}

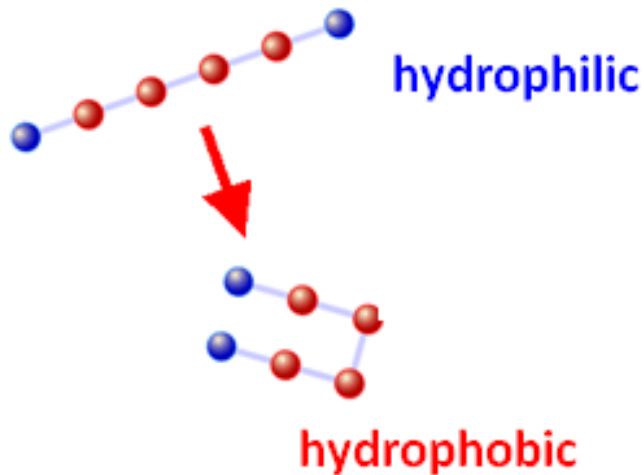


In hemoglobin, the heme form of Fe(II) is placed within the protein to move through the bloodstream.

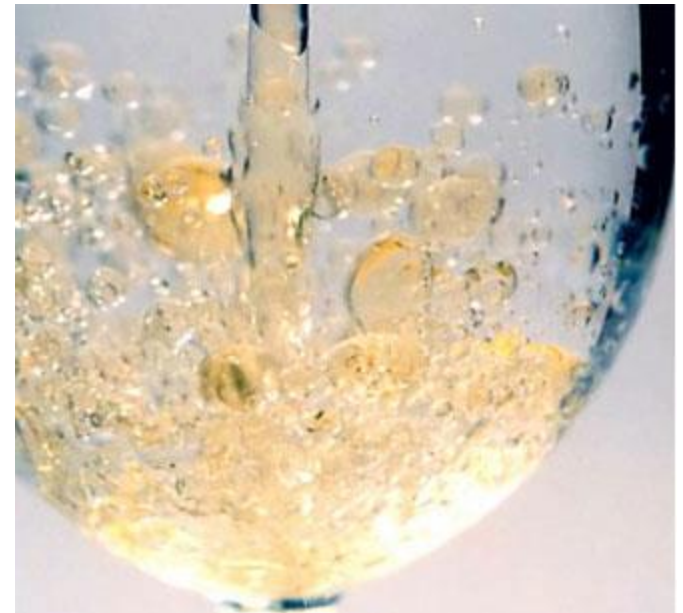


Hydrophobic Interactions

Amino acid side chains are either *hydrophilic* or *hydrophobic*.



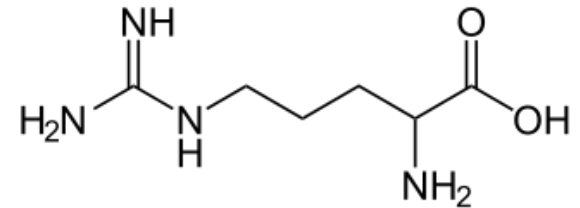
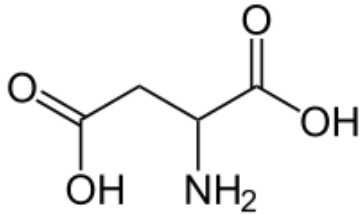
The peptide will fold itself to bend its hydrophilic side chains outside and its hydrophobic chains inside, just like oil droplets in water.



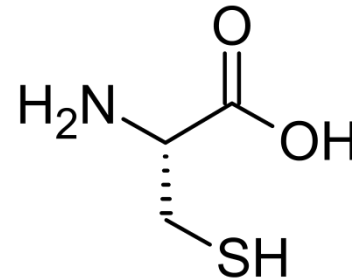
Tertiary Structures

What interactions would hold together:

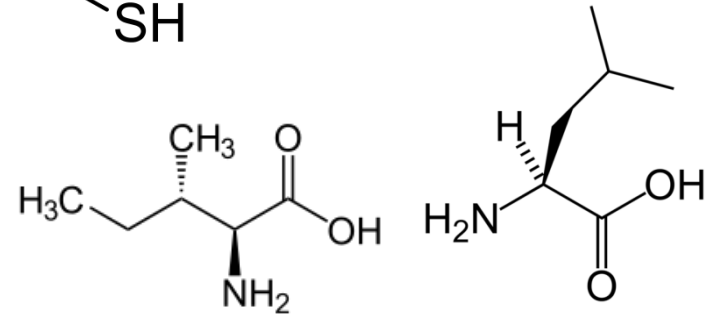
(1) aspartic acid and arginine?



(2) cystine and cystine?



(3) isoleucine and leucine?



(4) asparagine and serine?

