BCH 101

Amino acids/Proteins

BY

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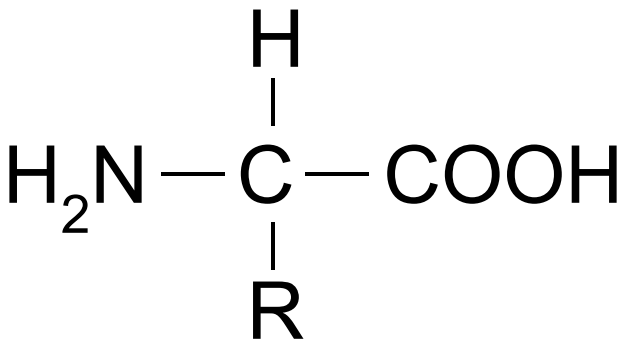
Protein - More than an Energy Source

Proteins / polypeptides - chains formed by the condensation/combination of 20 different α - amino acids.

- Polypeptides - may be di-, tri -, etc; up to 10 a.a.
- Proteins - longer than 10 a.a. units; ie. MW>10,000

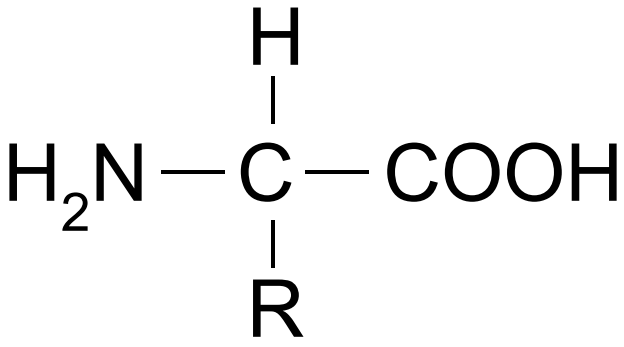
Amino Acids - Protein building blocks

An amino acid is a compound having both a carboxyl group(-COOH) and an amino group(-NH_2).



All amino acids from protein have the -NH_2 attached at the C α to the –COOH (as well as the H- & R-).

All naturally occurring α-amino acids, except glycine (R=H), are chiral and the 'L' stereoisomer.



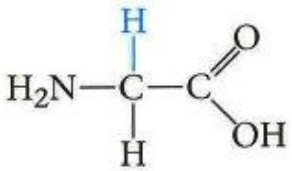
There are 20 α-amino acids in naturally occurring protein. By convention the -NH_2 is placed ‘to the left’.

Each aa has a ‘common’ name often ending in ‘-ine’.

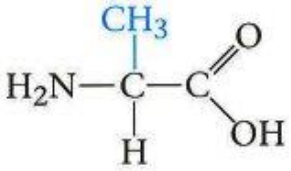
There are ~150 other physiologically important amino acids, GABA (a neurotransmitter).

Amino Acids - 1

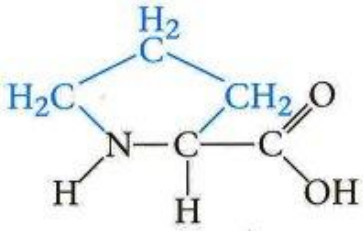
Nonpolar R Groups
(hydrophobic)



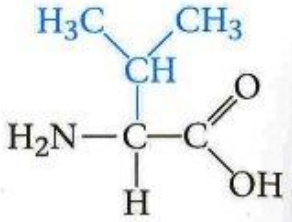
Glycine (gly)



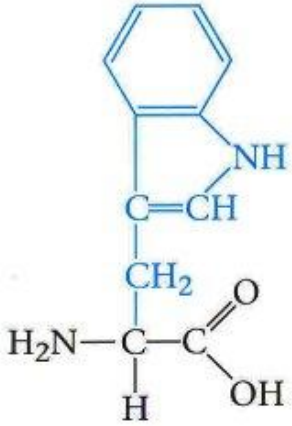
Alanine (ala)



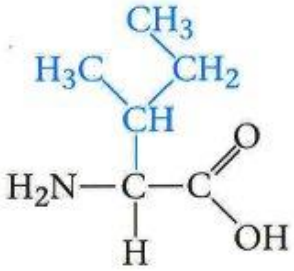
Proline (pro)



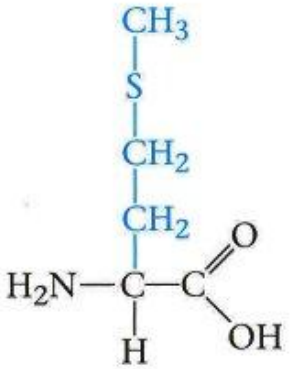
Valine (val)



Tryptophan (trp)

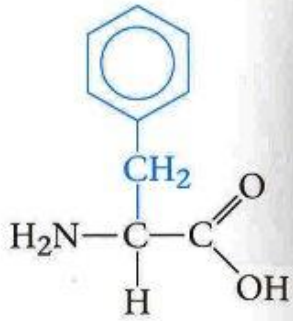


Isoleucine (ile)



Methionine (met)

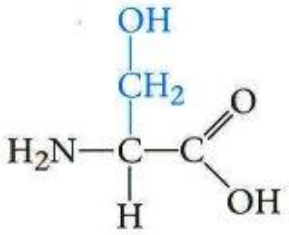
Leucine (leu)



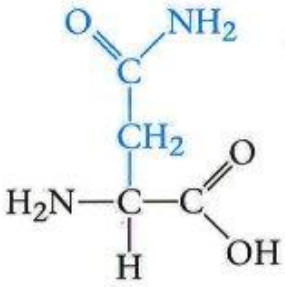
Phenylalanine (phe)

Amino Acids - 2

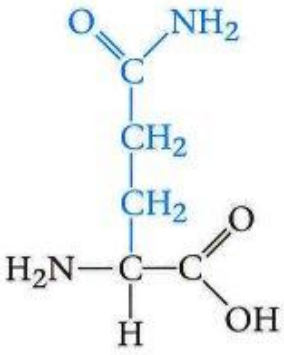
Polar R Groups
(hydrophilic)



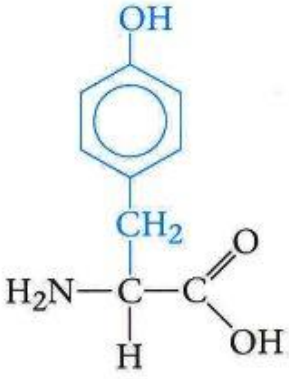
Serine (ser)



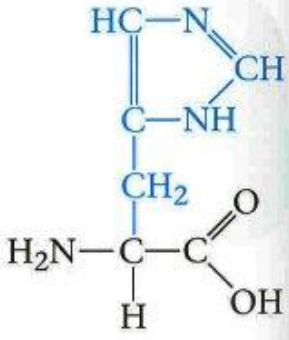
Asparagine (asn)



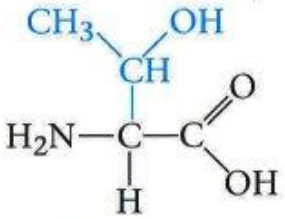
Glutamine (gln)



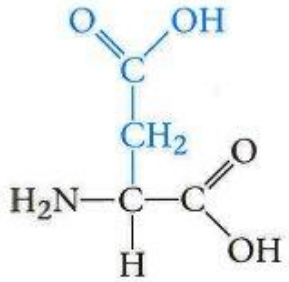
Tyrosine (tyr)



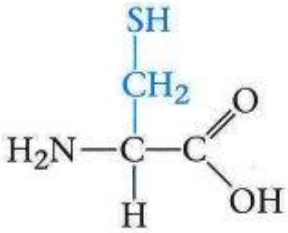
Histidine (his)



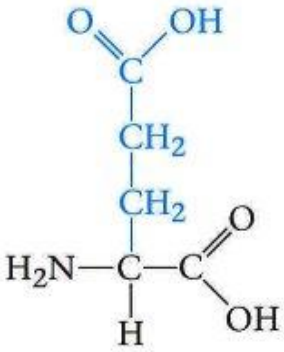
Threonine (thr)



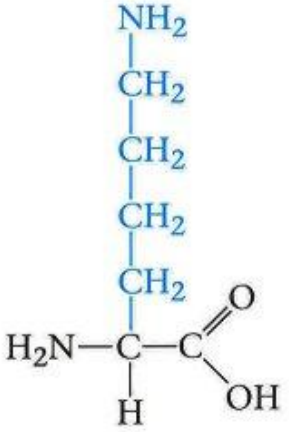
Aspartic acid (asp)



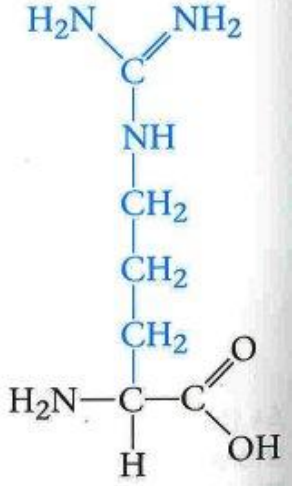
Cysteine (cys)



Glutamic acid (glu)



Lysine (lys)



Arginine (arg)

Amino acids

- Contain both an acidic functional group (COOH) and a basic one (-NH_2), NH or N
- Thus reactions are highly pH dependent

Condensation and Hydrolytic Reactions

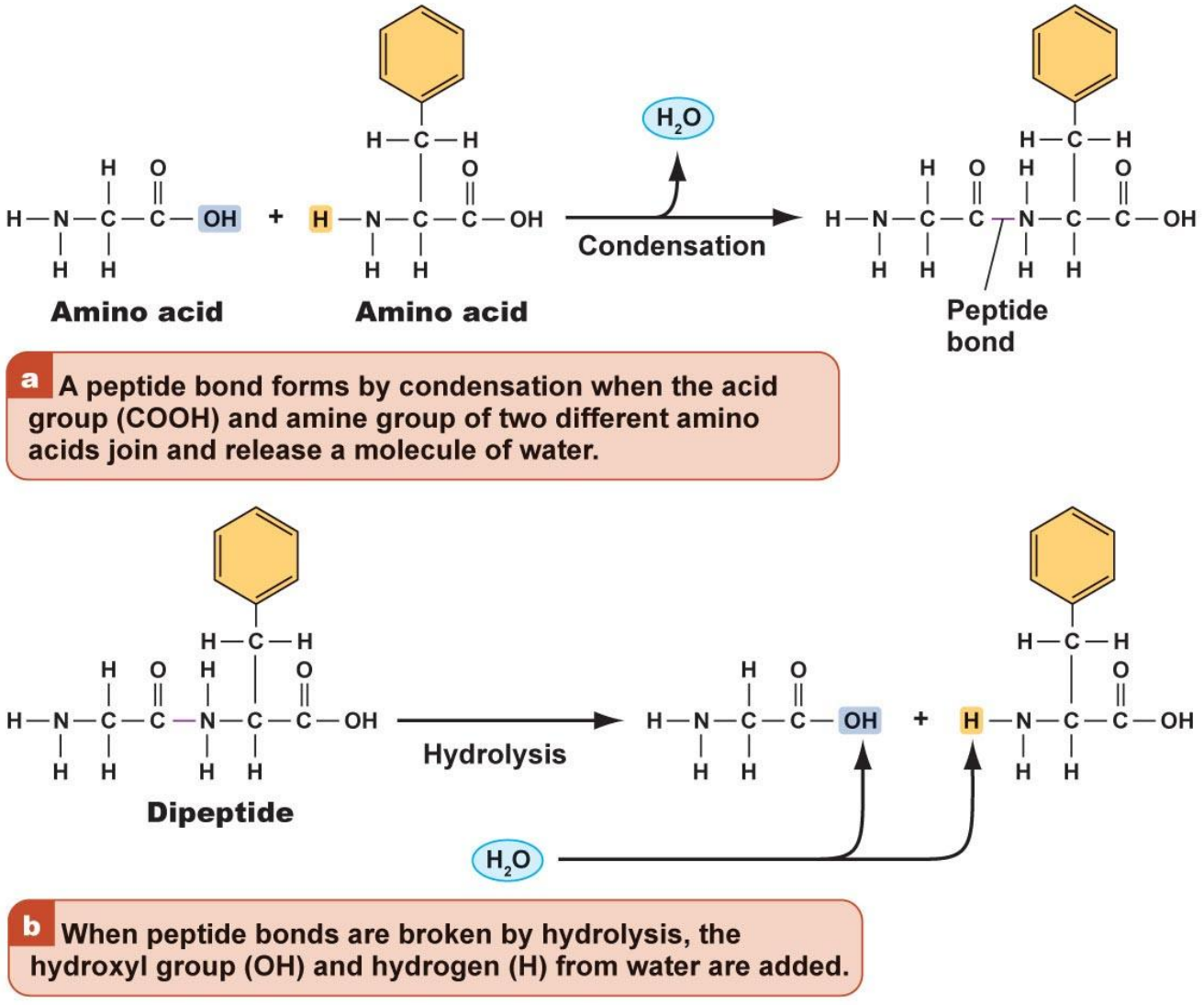
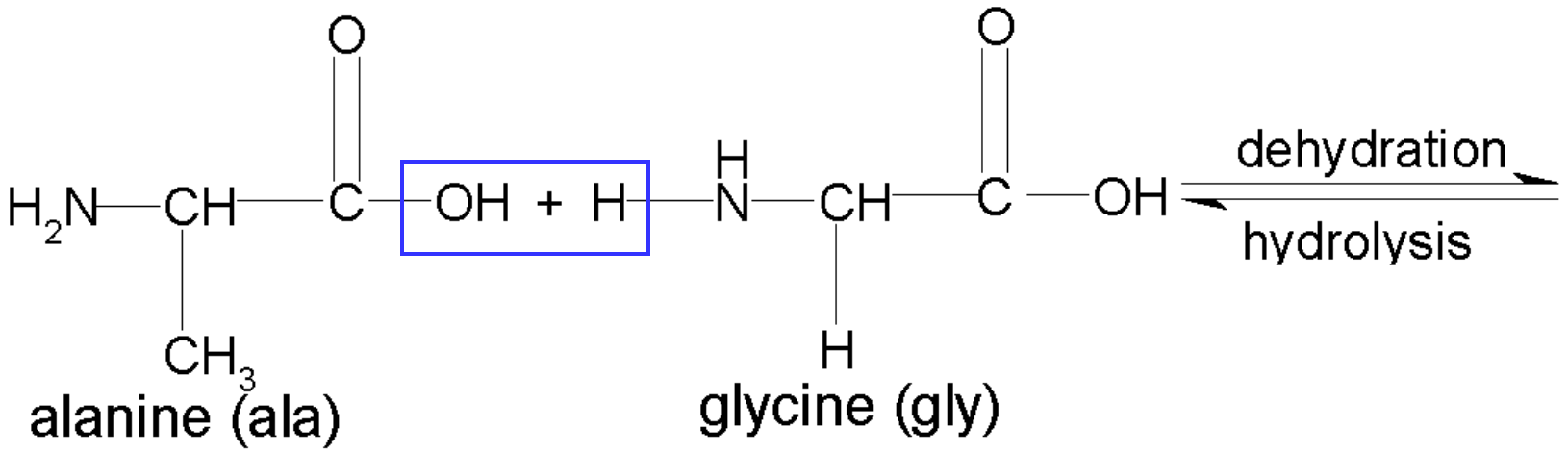


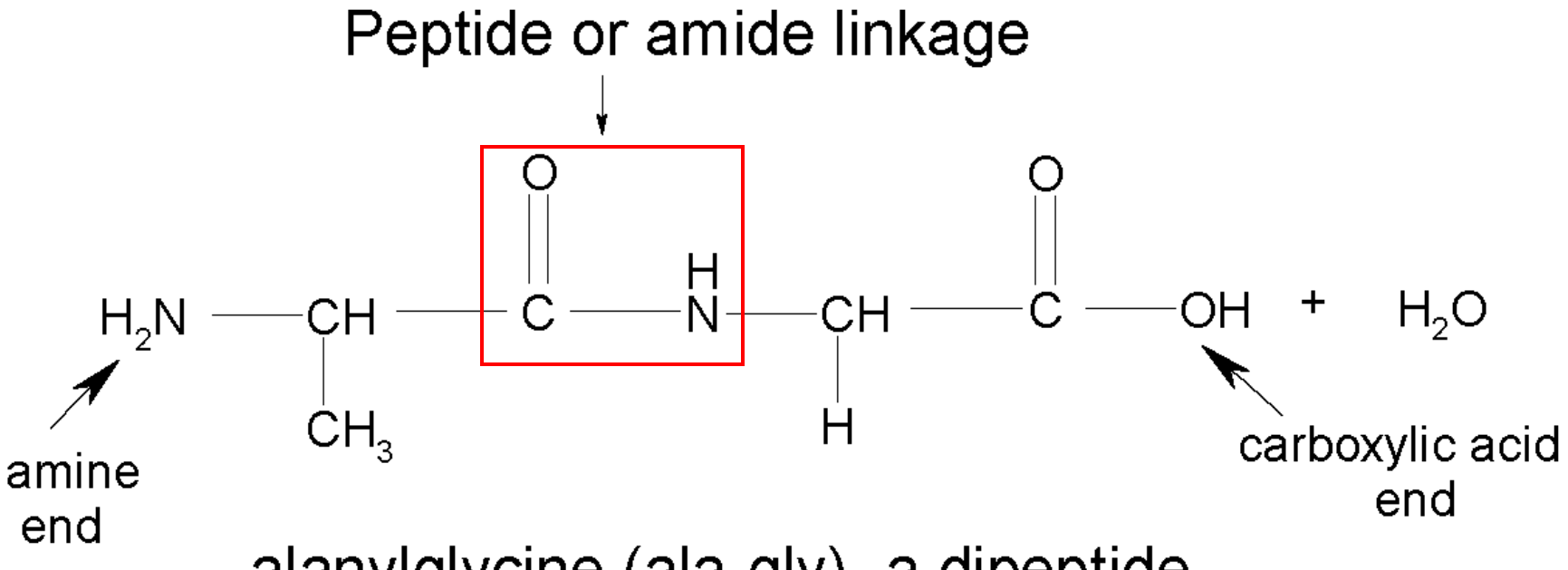
Figure 6.3

pH dependent properties

- Zwitterionic structures contain both N-H+ and COO-.
- At low pH, protonate COO-.
- At higher pH : lose H on N
- Isoelectric pH: differs for each amino acid (due to structural differences)

Peptides – Buildup/Breakdown





Essential, Nonessential, and Conditional

- Essential – must be consumed in the diet
- Nonessential – can be synthesized in the body
- Conditionally essential – cannot be synthesized due to illness or lack of necessary precursors
  - Premature infants lack sufficient enzymes needed to create arginine

Table 6.1

The Mighty Twenty

Essential Amino Acids	Nonessential Amino Acids
Histidine (His)[a]	Alanine (Ala)
Isoleucine (Ile)	Arginine (Arg)[b]
Leucine (Leu)	Asparagine (Asn)
Lysine (Lys)	Aspartic acid (Asp)
Methionine (Met)	Cysteine (Cys)[b]
Phenylalanine (Phe)	Glutamic acid (Glu)
Threonine (Thr)	Glutamine (Gln)[b]
Tryptophan (Trp)	Glycine (Gly)[b]
Valine (Val)	Proline (Pro)[b]
	Serine (Ser)
	Tyrosine (Tyr)[b]

[a] Histidine was once thought to be essential only for infants. It is now known that small amounts are also needed for adults.

[b] These amino acids can be "conditionally essential" if there are either inadequate precursors or inadequate enzymes available to create these in the body.

Dipeptides

- Consider the 2 amino acids glycine (G) and alanine (A).
- How many dipeptides can be made if these are randomly mixed?
- GG, AA, GA and AG
- N terminal on LHS; C terminal on RHS

Tripeptides

- Consider amino acids Glycine (G), Alanine (A) and Phenylalanine (P)
- How many different tripeptides are possible if each amino acid must be present?

Possible tripeptides

- 3 choices for the N-terminal amino acid
- 2 choices for middle
- 1 choice for the C terminal amino acid
- Thus 3 x2 x1 =6 choices if each aa must be present.
- But total number possible is 3 x3x3 =27; includes AAA, PPP, GGG etc

Levels of Protein Structure

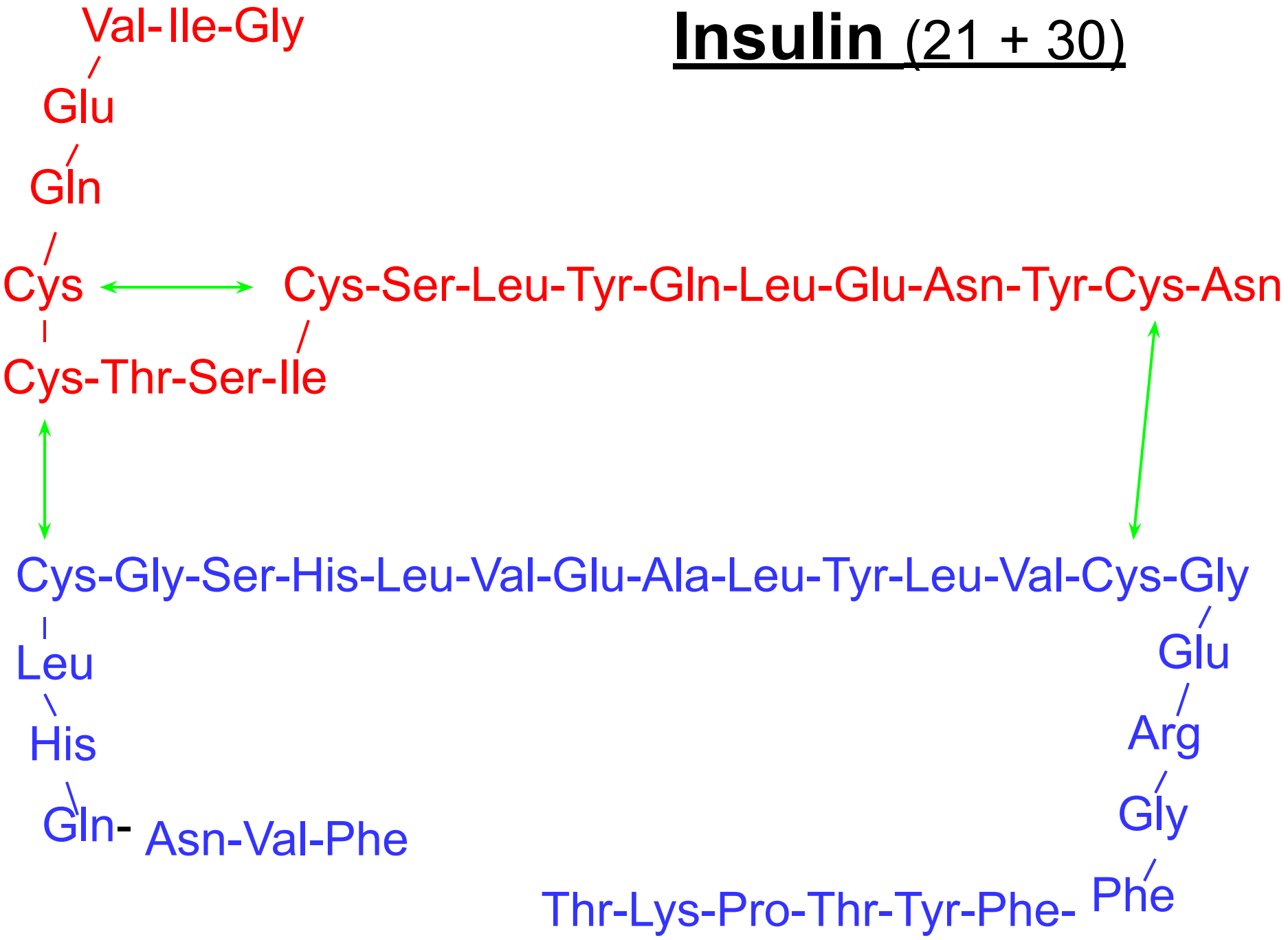
Primary structure - the sequence of amino acids in the peptide chain and the location of the disulfide bridges.

Secondary structure - a description of the conformation/ shape of the backbone of the protein.

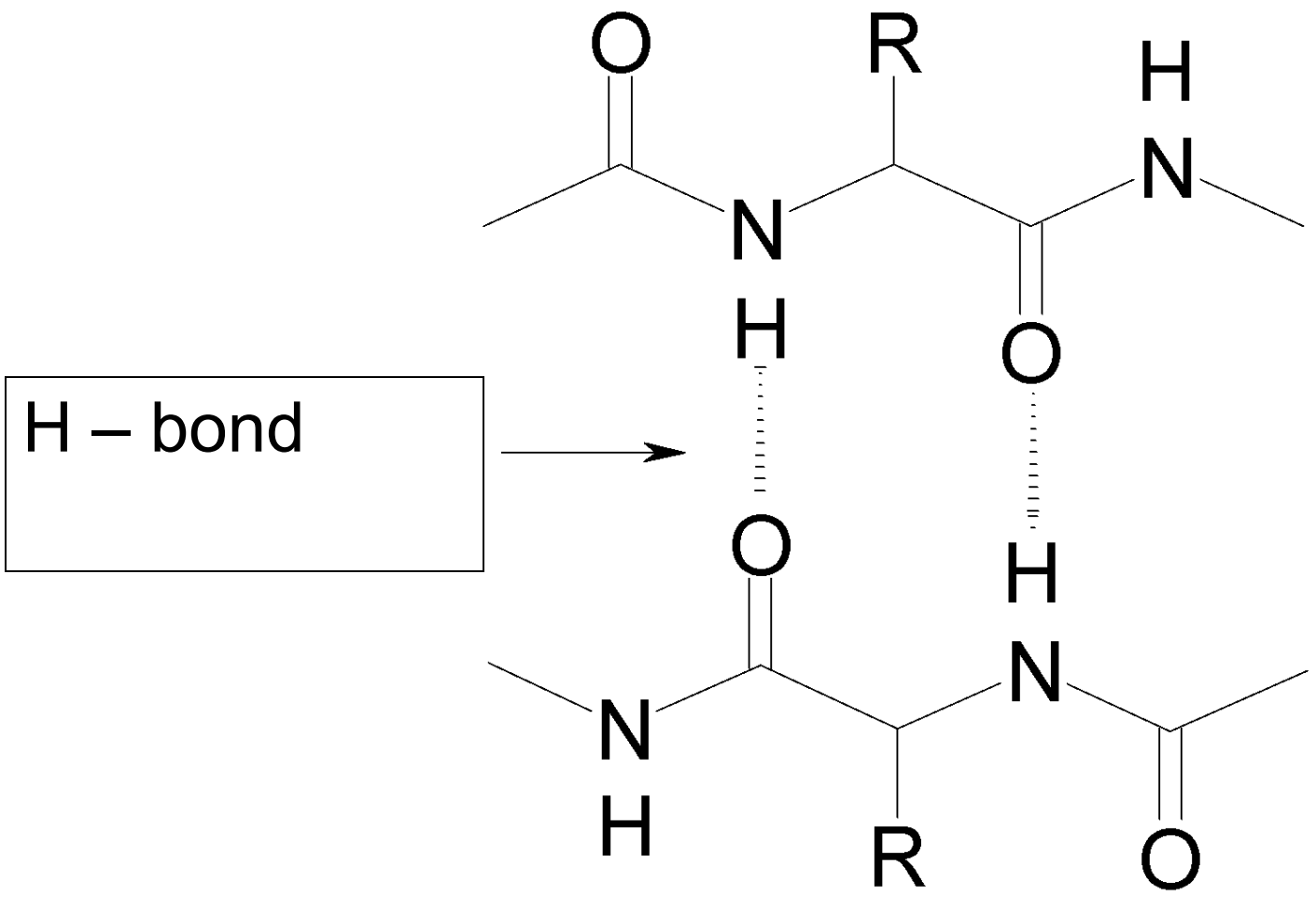
Tertiary structure - a description of the 3D structure of the entire polypeptide.

If the protein has more than one chain it can have a quaternary structure.

Insulin (21 + 30)

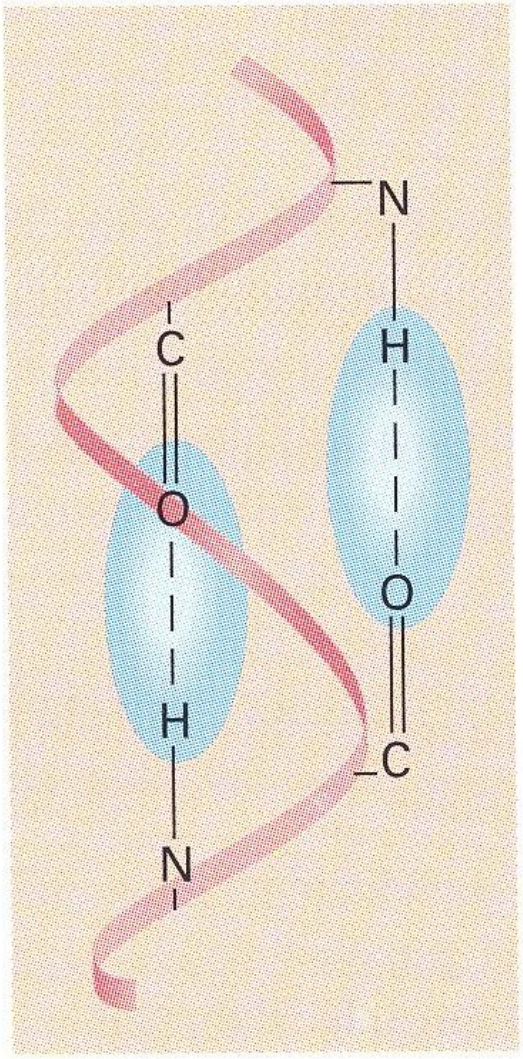


Secondary (2^0) Structure - sheets

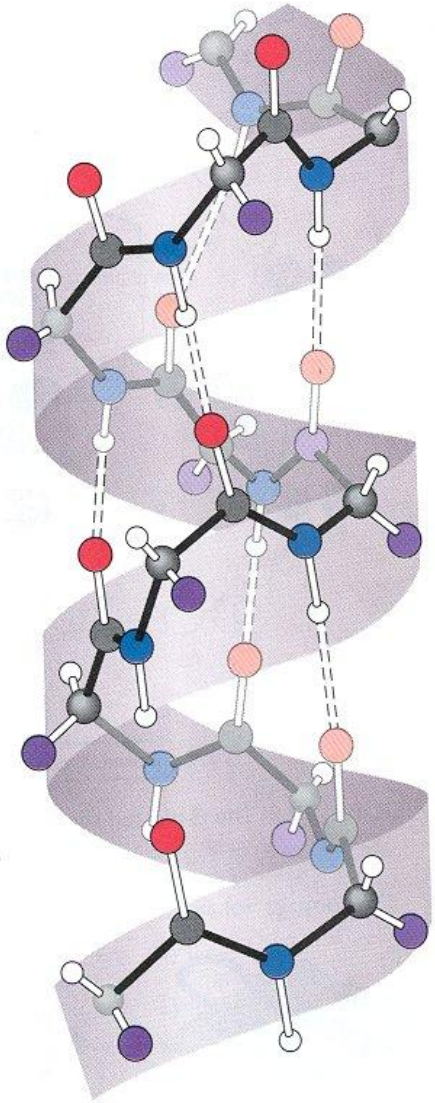


sheets/strands, eg. fingernails, silk

Secondary Structure(2^0) - the α-Helix



H-bonding - intramolecular



Tertiary Structure of Proteins

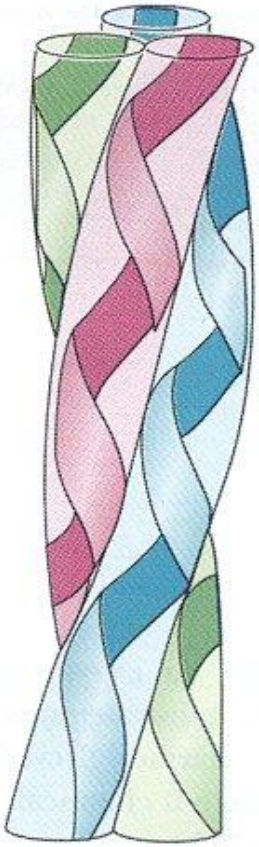
- Arises from weaker attractive forces (non polar dispersion forces) between hydrophobic parts of the same chain that are widely separated in the primary structure, but close in space
- “intramolecular”
- Results in chain twisting and folding

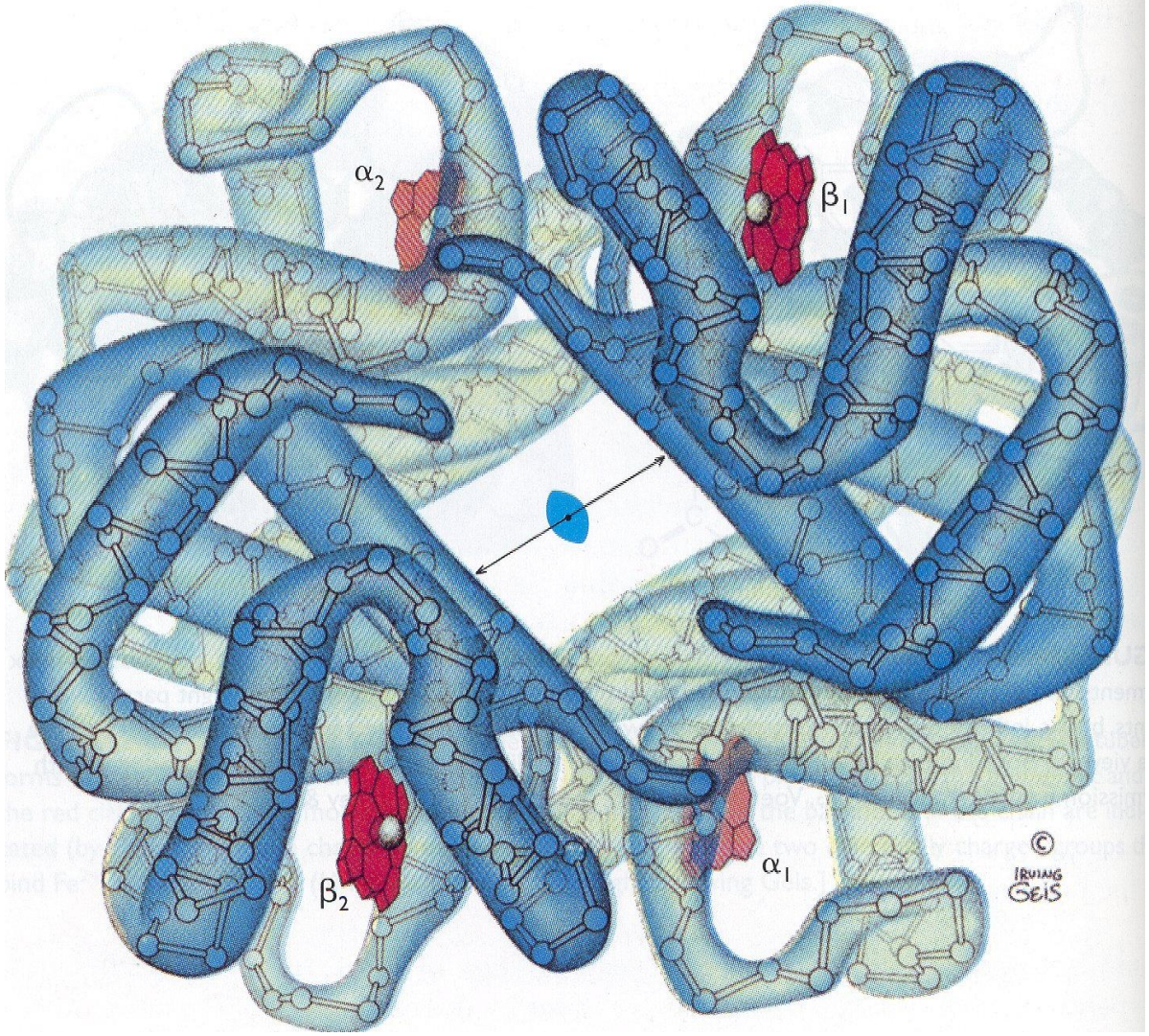
Tertiary structure of protein: braids and globs

- Collagen-a fibrous protein (precursor of gelatin) has a triple helix structure-some elasticity due to interchain interactions
- Hemoglobin (a globular protein)

Tertiary Structure (3^0) - braids & globs

collagen



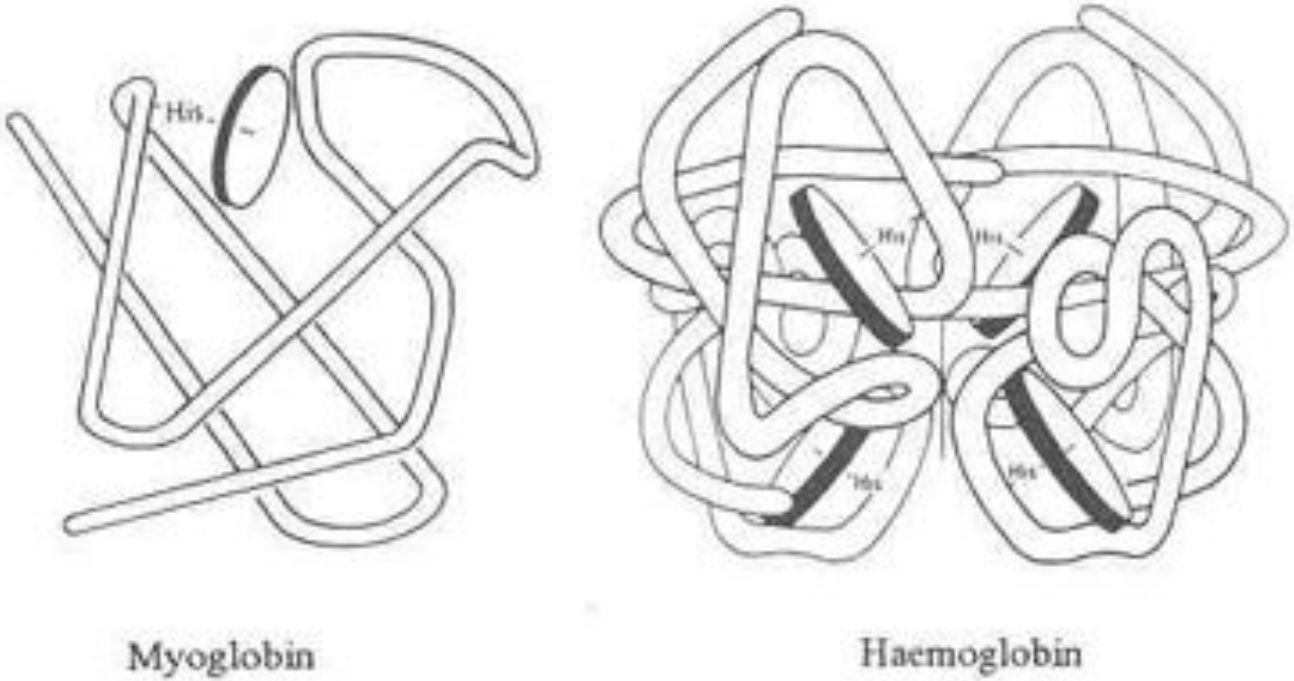


hemoglobin

Hemoglobin(H) and Myoglobin (M)

- H has 4 polypeptide chains : carries O_2, CO_2 and H^+ in the blood, and possesses quaternary structure
- M has a single chain of 153 amino acids: carries O_2 from the blood vessels to the muscles and stores it until needed.
- Both have Fe II containing heme unit in each chain that binds O_2.

Myoglobin Structure



Myoglobin Haemoglobin

Figure 3 Myoglobin versus haemoglobin

To summarize

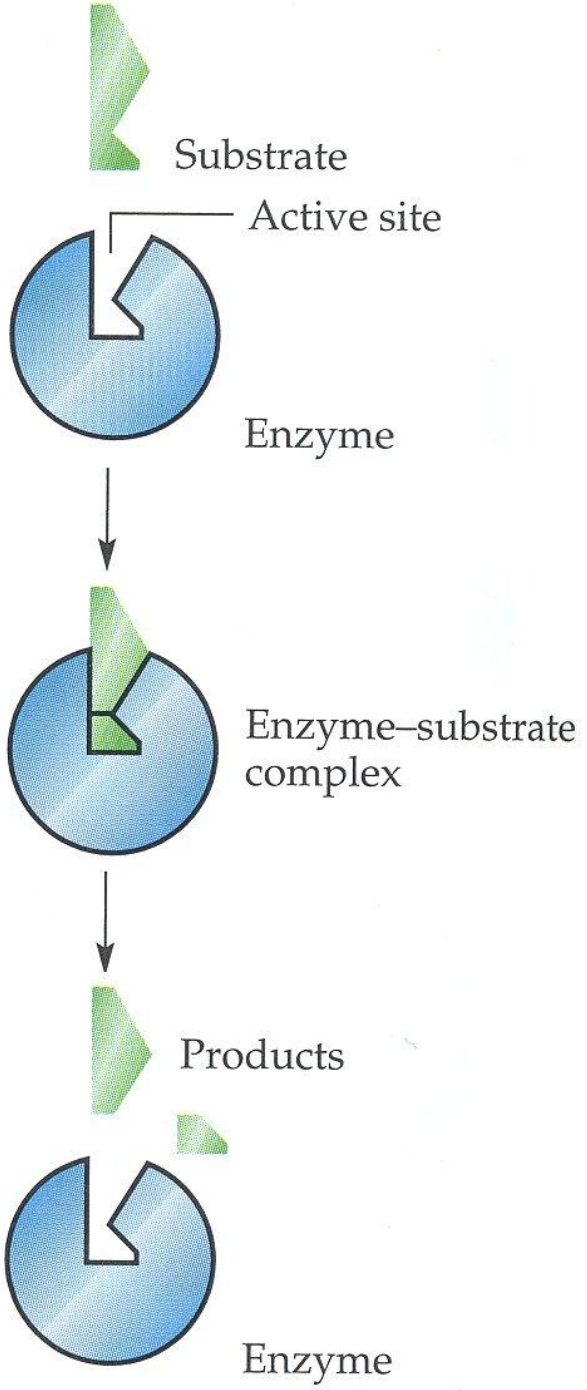
- Myoglobin cannot have quaternary structure since it has only one polypeptide chain
- Hemoglobin has 4 polypeptide chains and possesses quaternary structure

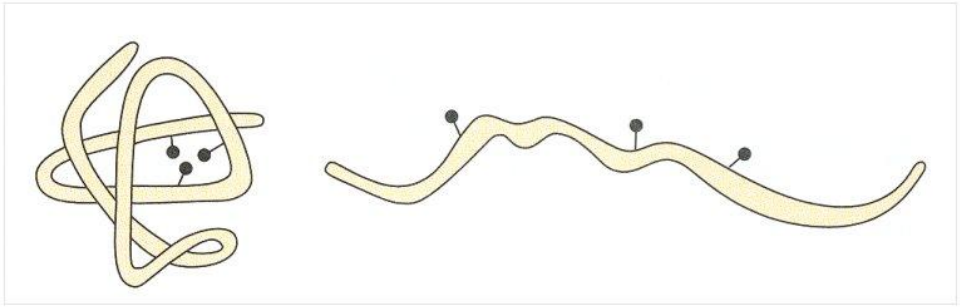
Enzyme structure

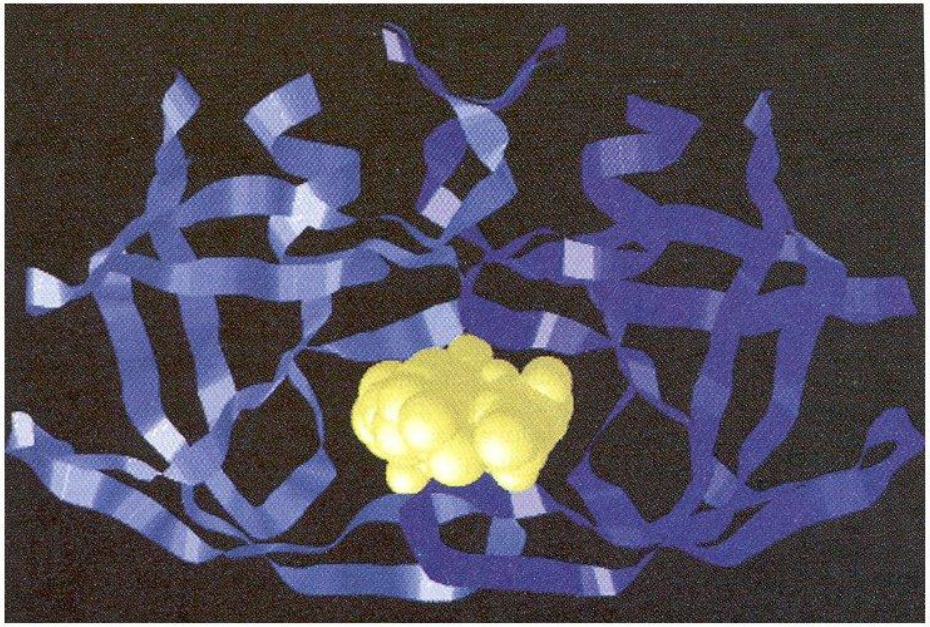
- Many enzymes are proteins and their specific binding properties to a substrate depend on their overall molecular shape or "conformation"

Lock and key mechanism for activity

Active Site of Enzymes







Denaturation -

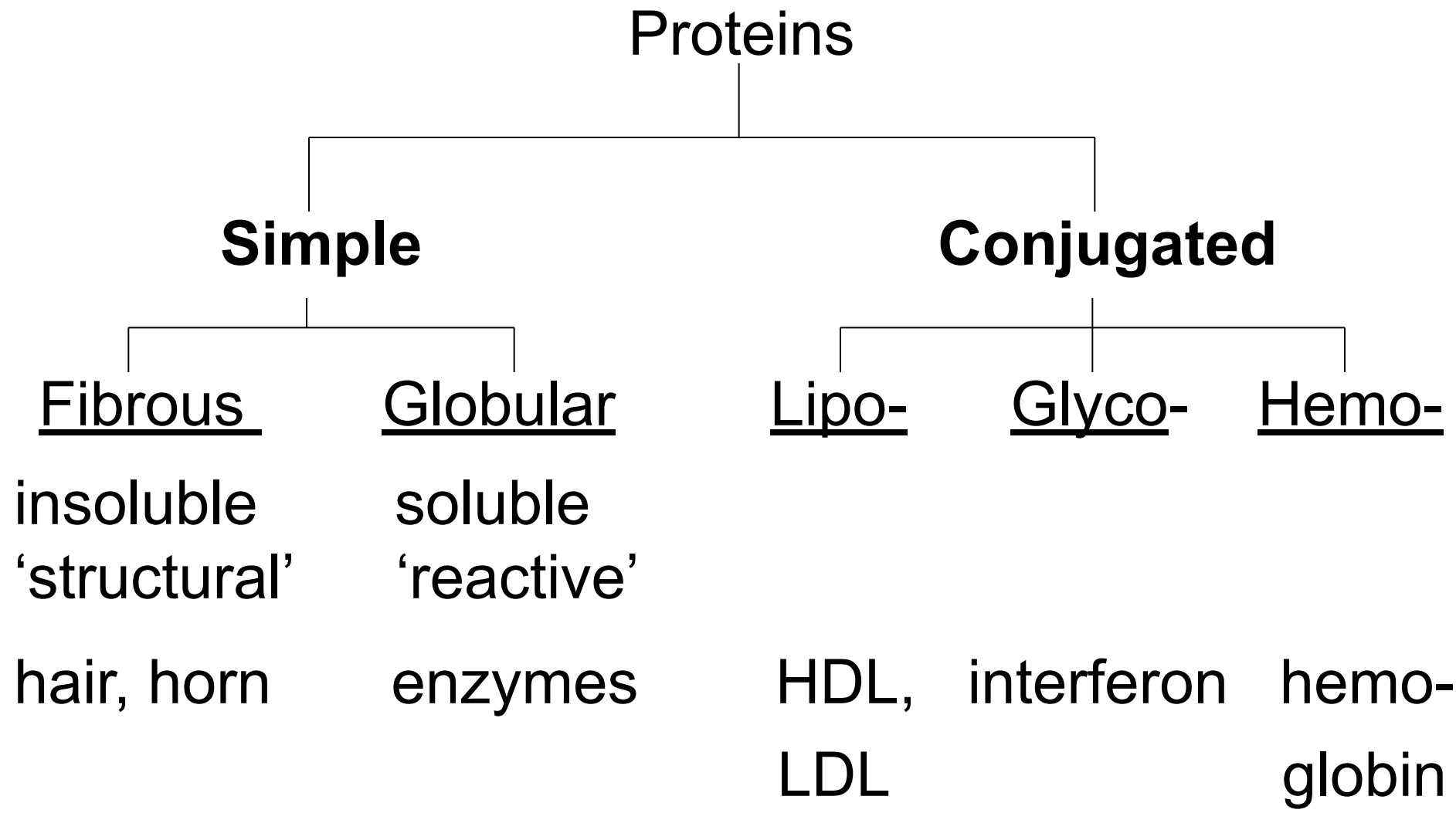
any physical or chemical process that changes the protein structure and makes it incapable of performing its normal function.

Whether denaturation is reversible depends on the protein and the extent of denaturation.

<u>Examples:</u>

- heating egg whites (irreversible)
- ‘permanent’ waving of hair (reversible)

Proteins by Structure



Proteins by Structure

Fibrous

Collagens	Elastins	Keratins	Myosins
bones	lungs	hair/feathers	muscles
tendons	ligaments	horn/nails	
cartilage			

Proteins by Structure

Globular

Albumins

egg whites

Globulins

antibodies(γ-globulin)

enzymes

Proteins by Function

Enzymes	- the biological catalysts
Contractile	- muscle
Hormones	- insulin, growth hormone
Neurotransmitters	- endorphins
Storage	- store nutrients, eg. seeds, casein in milk
Transport	- hemoglobin
Structural	- collagen, keratins
Protective	- antibodies
Toxins	- snake venom, botulinum

(Non)Essential Amino Acids

The essential amino acids (10) are those that our bodies cannot synthesize. We must obtain them from our dietary intake.

They are:

histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, valine (and arginine in infants).

The non-essential a.a.(10) can be synthesized in our bodies from breakdown products of metabolism.

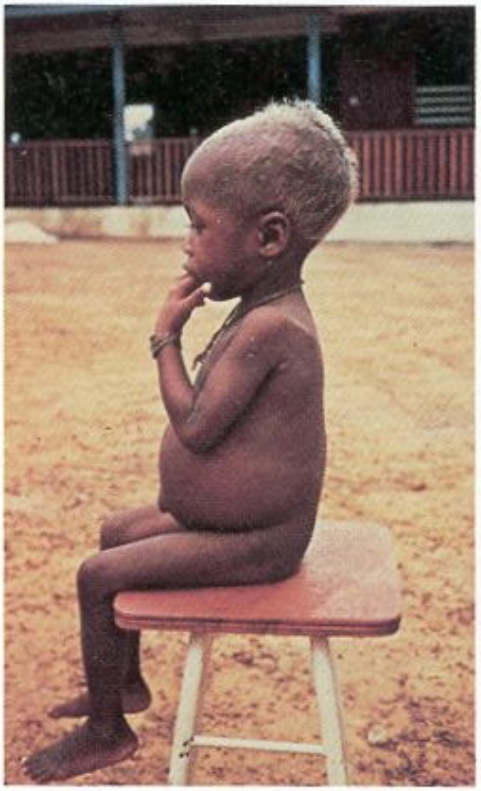
Vegetarian Diets

- Main challenge is to get enough high quality protein with the correct balance of essential amino acids

Protein Content (approx.%) of Foods

cheese	30
peanuts	27
chicken	21
fish	18
beef	18
soy	17
wheat	13
beans	7
rice	8
peas	7
milk	6
corn	4
cassava	3
potatoes	2

Malnourished - the inability to obtain sufficient complete protein, ie. essential amino acids, <u>for the body to function properly.</u>



Symptoms - extreme emaciation, bloated abdomen, lack of pigmentation, mental apathy, eventual death, eg. no antibodies, muscle breakdown, capacity of brain diminished (increases from ~350g at birth to full size(~1200g) by 2 yrs).

1 of every 8 people on Earth suffers malnutrition severe enough to stunt physical and mental growth.

Glycolipids

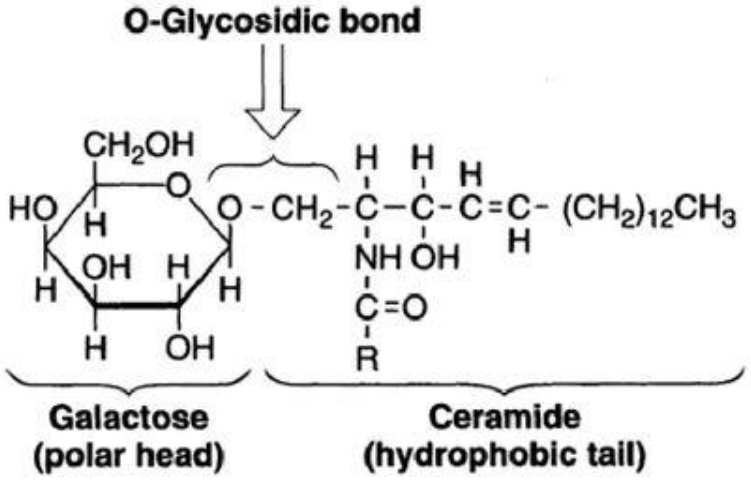
- Glycolipids are derivatives of ceramides with carbohydrate directly attached to ceramide
- In contrast to sphingomyelin they do not have a phosphocholine group

Glycoprotein – Function

- Glycoproteins serve **many functions** in the body.
- Some glycoproteins **provide structure** e.g. **collagens**.
- Some glycoproteins are involved in immunity e.g. **immunoglobulins** (such as IgG).
- **Mucins** are secreted into mucus of the respiratory and digestive tracts where the specific mucins can retain water thus allowing mucus to **serve as an effective lubricant.**
- Specific glycoproteins present on the surface of red blood cells **determine blood group type**

Glycolipid structure — cerebrosides

- The carbohydrate component is linked by an O-glycosidic bond to ceramide
- Cerebrosides contain a single sugar (Glu or Gal) or few sugars; they are abundant in brain and myeline sheath



Galactocerebroside
(a glycosphingolipid)

Roles of glycolipids

- Glycolipids have important roles in cell interactions, growth, and development
- They are very antigenic (e.g., blood group antigens);
- act as surface receptors for some toxins and viruses;
- and undergo major changes during cell transformation

❑ What is Glycoprotein ?:

- Glycoproteins are proteins that contain oligosaccharide chains (glycans) covalently attached to polypeptide side-chains.
- This process is known as glycosylation.
- The carbohydrate is attached to the protein during the following modifications: Co-translational modification & Post-translational modification.
- In proteins that have segments extending extracellularly, the extracellular segments are often glycosylated.

Functions Served by Glycoproteins

Function	Glycoproteins
Structural molecule	Collagens
Lubricant and protective agent	Mucins
Transport molecule	Transferrin, ceruloplasmin
Immunologic molecule	Immunoglobulins, histocompatibility antigens
Hormone	Chorionic gonadotropin, thyroid-stimulating hormone (TSH)
Enzyme	Various, eg, alkaline phosphatase
Cell attachment-recognition site	Various proteins involved in cell-cell (eg, sperm-oocyte), virus-cell, bacterium-cell, and hormone-cell interactions