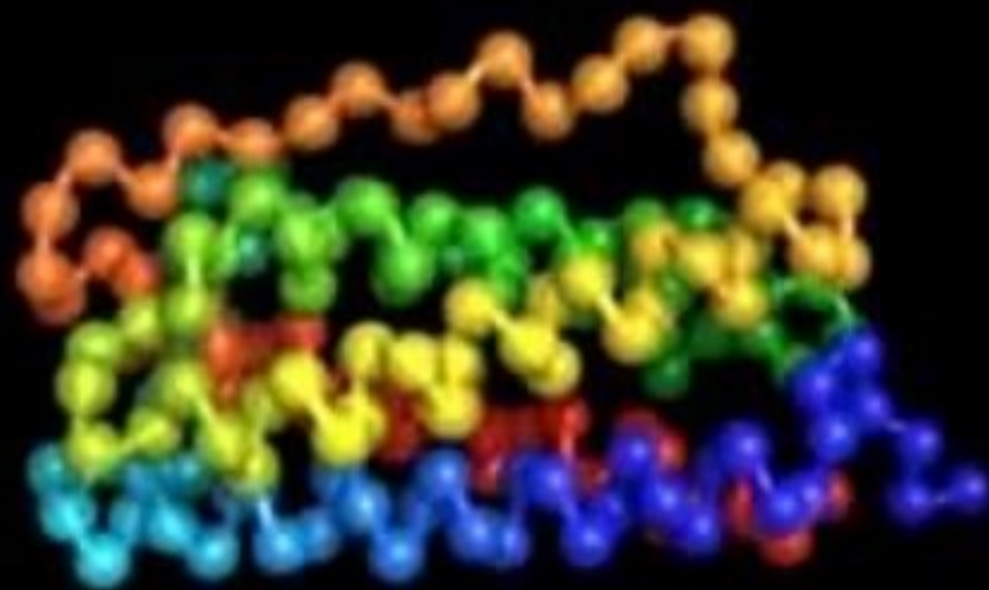


24/01/2024



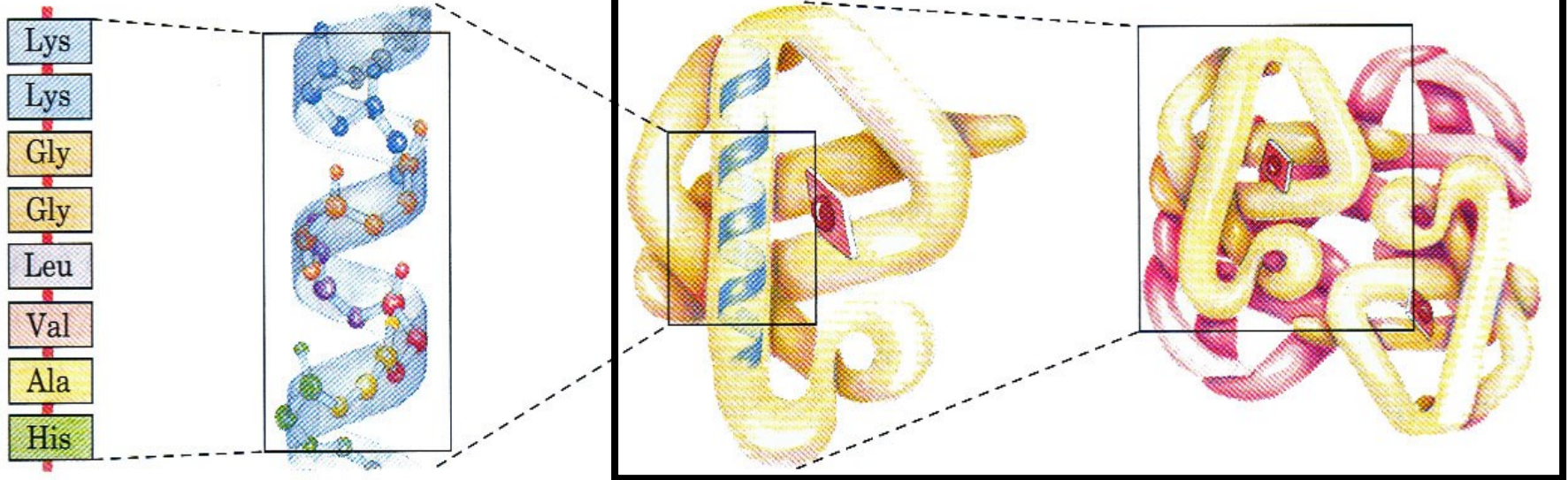
The Four Levels of Protein Structure

Primary
structure

Secondary
structure

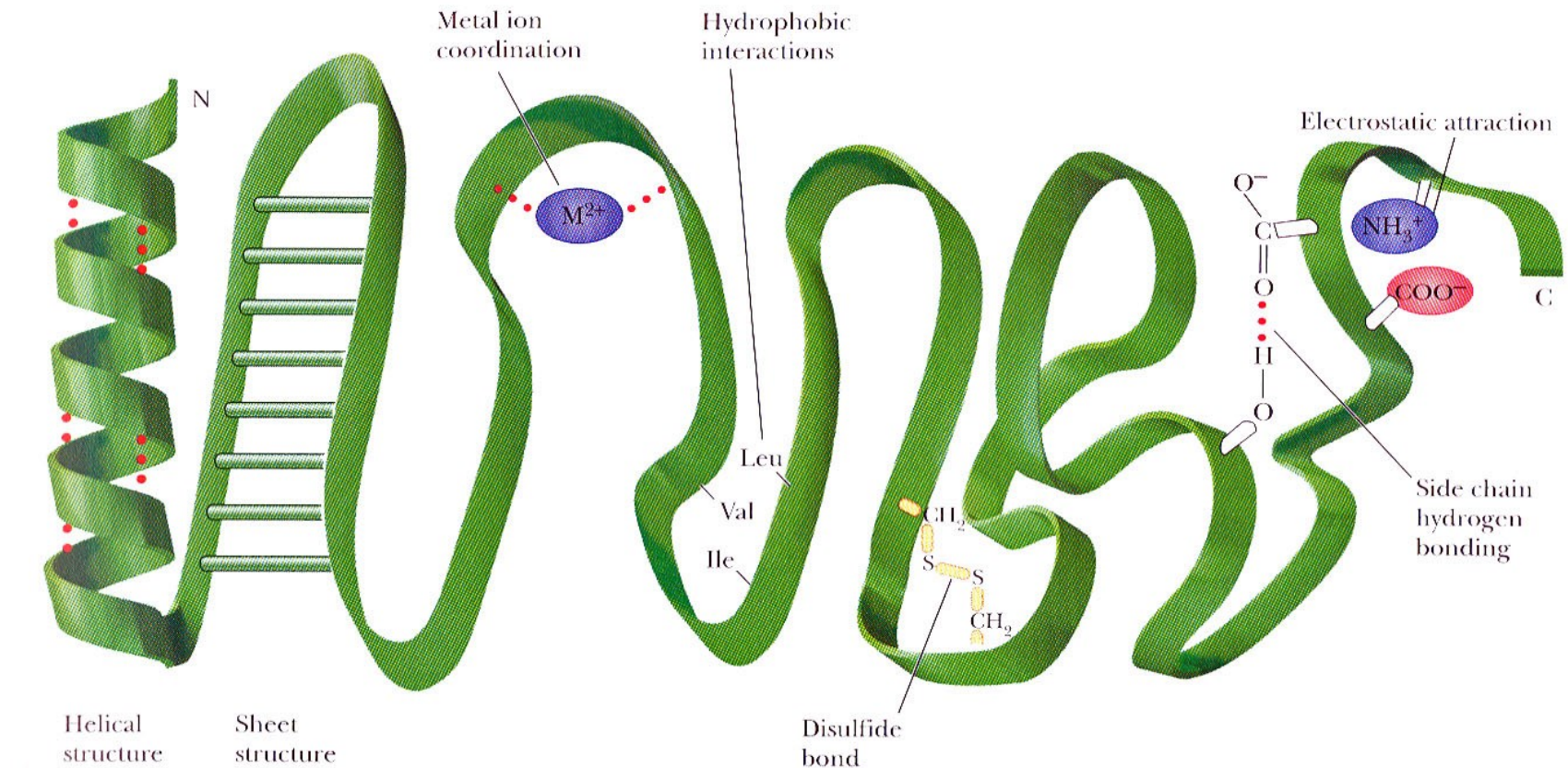
Tertiary
structure

Quaternary
structure



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

Forces that Stabilize the Tertiary Structure of Proteins



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

Two major groups of tertiary/quaternary protein structures

*Fibrous Proteins: having
polypeptide chains arranged in
long strands or sheets*

*Globular Proteins: having
polypeptide chains folded into a
spherical or globular shape*

Fibrous Proteins

- Much or most of the polypeptide chain is organized approximately parallel to a single axis (filamentous or elongated form)
- Fibrous proteins are often mechanically strong.
- Fibrous proteins are usually insoluble
- Usually play a structural role in nature - they hold things together

Fibrous Proteins

- Include the major proteins of skin and connective tissue and of animal fibers like hair and silk
- The amino acid sequence of each of these proteins favors a particular kind of secondary structure
- Include α - and β -keratins, and collagen

Secondary Structures and Properties of Fibrous Proteins

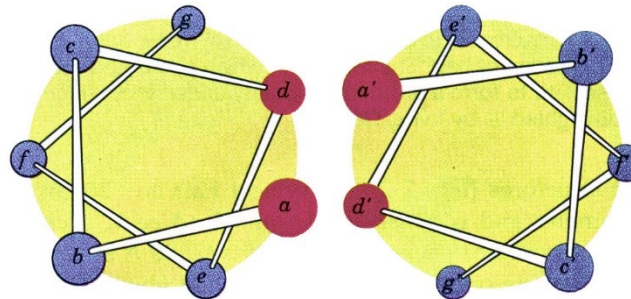
Protein	Structure	Characteristics	Examples of Occurrence
α -Keratin	α -Helix, crosslinked by disulfide bonds	Tough, insoluble protective structures of varying hardness and flexibility	α -keratin of hair, wool, feathers, and nail
β -Keratin or Fibroin	β -Conformation	Soft, flexible filaments	β -keratin or silk fibroin
Collagen	Collagen triple helix	High tensile strength, without stretch	Collagen of tendons, bone matrix

Alpha Keratin

- Found in hair, fingernails, claws, horns and beaks
- Individual molecules contain long sequences - over 300 residues in length - that are wholly α -helical

Alpha Keratin

- Pairs of these helices twine about one another in a **left-hand coiled-coil structure**
- Primary structure of helical rods consists of **7-residue repeats: (a-b-c-d-e-f-g)_n**, where **a and d are nonpolar**. Promotes association of helices! (Dimerization)



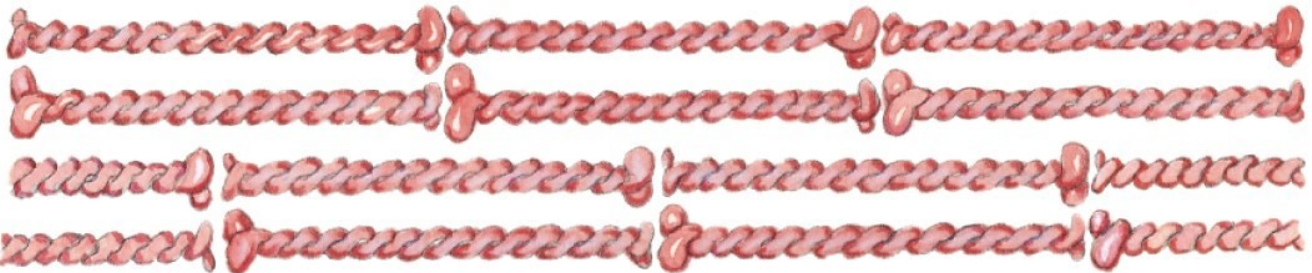
- In different tissues, α -keratin is hardened to differing degrees by the introduction of disulfide cross links

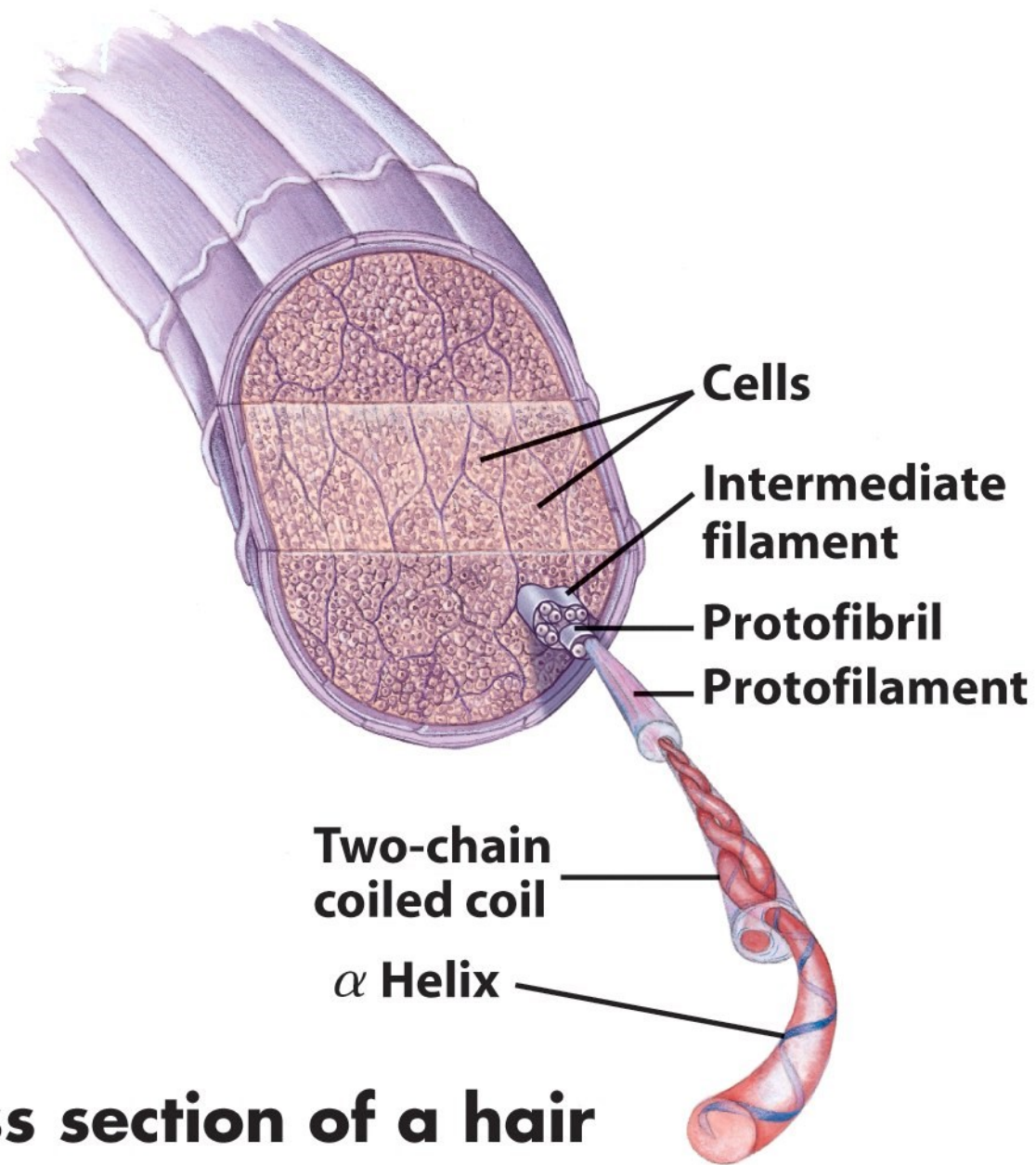
Alpha Keratin

Keratin α helix — 

Two-chain
coiled coil — 

Protofilament {  } 20–30 Å

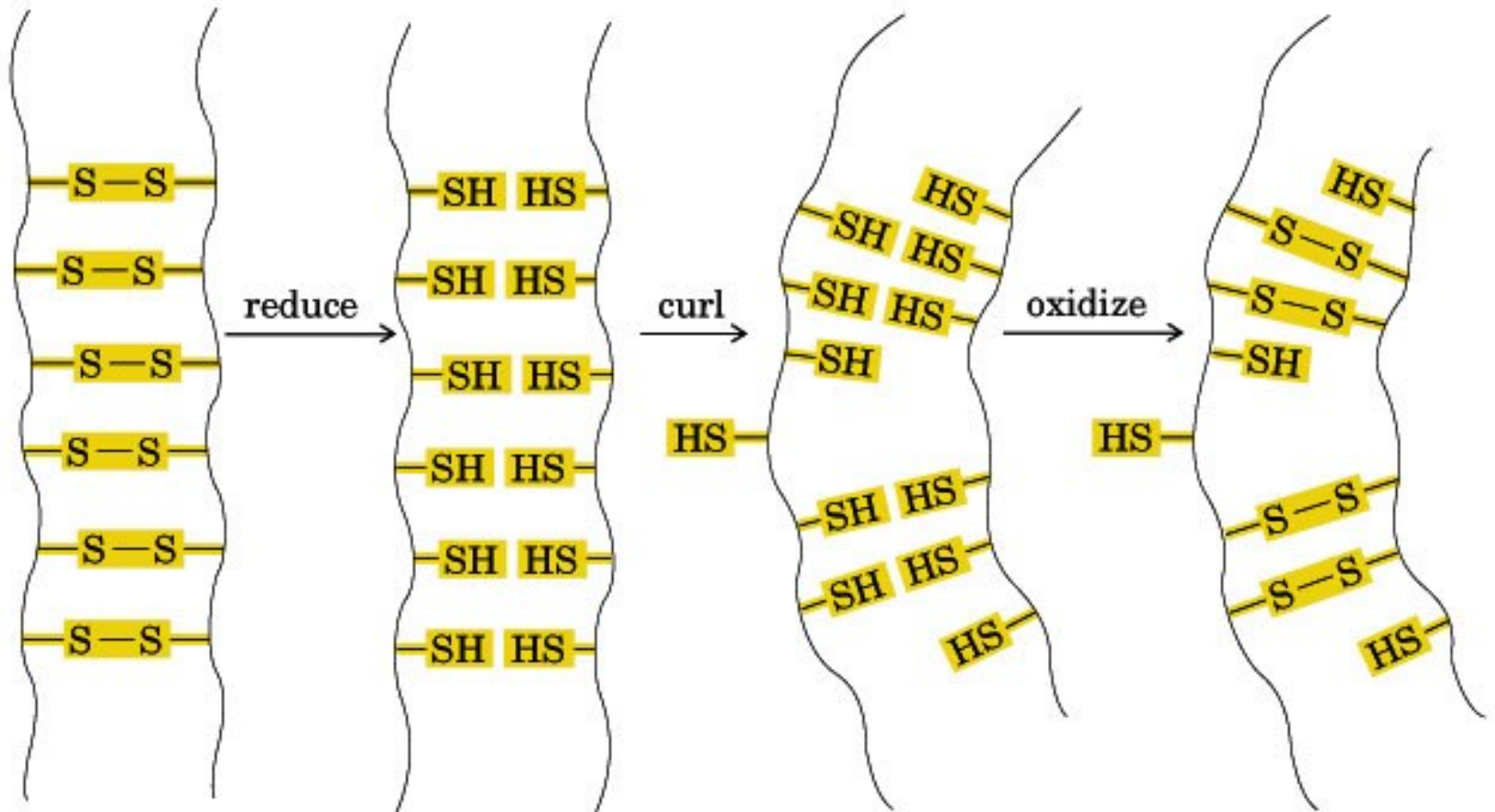
Protofibril {  }



Cross section of a hair

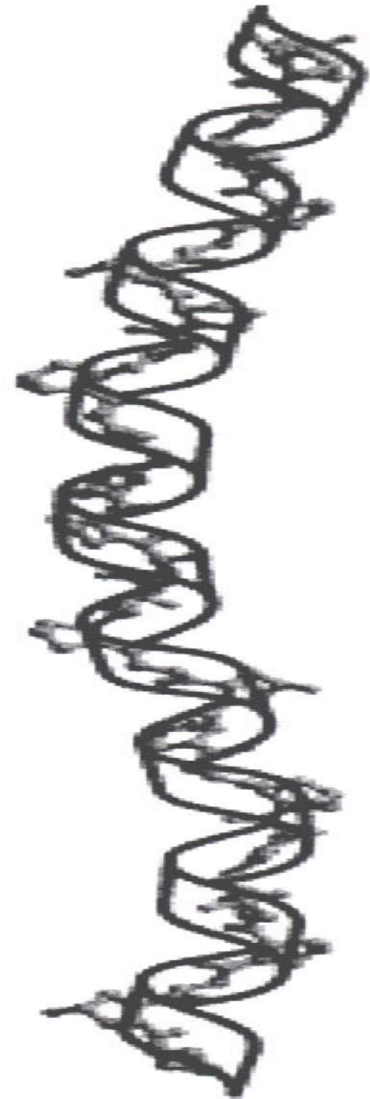
Permanent Waving

Reduction and Reoxidation of Disulfide Bonds



Collagen

- Principal component of connective tissue (tendons, cartilage, bones, teeth)
- Collagen helix is **left-handed** and has three amino acids residues per turn (**Gly-X-Pro**)

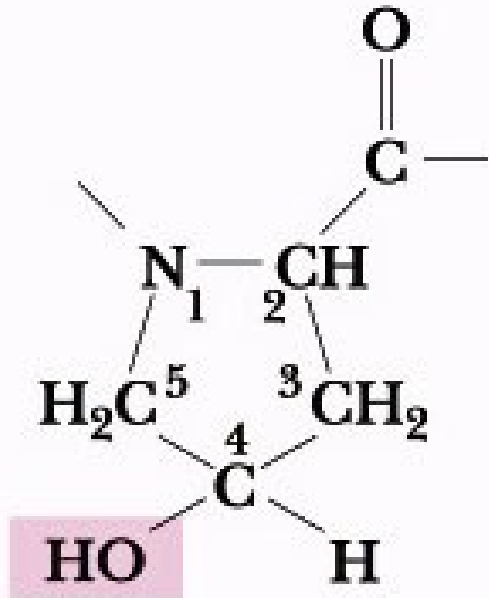


Collagen

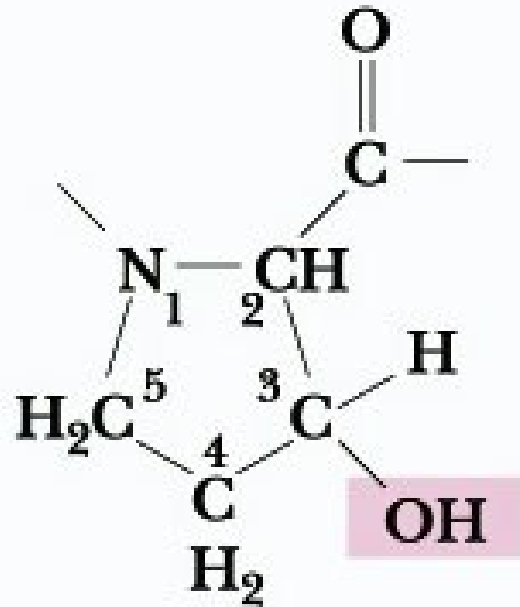
The secrets of its a.a. composition...

- Nearly one residue out of three is Gly
- Proline content is unusually high
- Unusual amino acids found:
 - 4-hydroxyproline
 - 3-hydroxyproline
 - 5-hydroxylysine
 - Pro and HyPro together make 30% of the residues

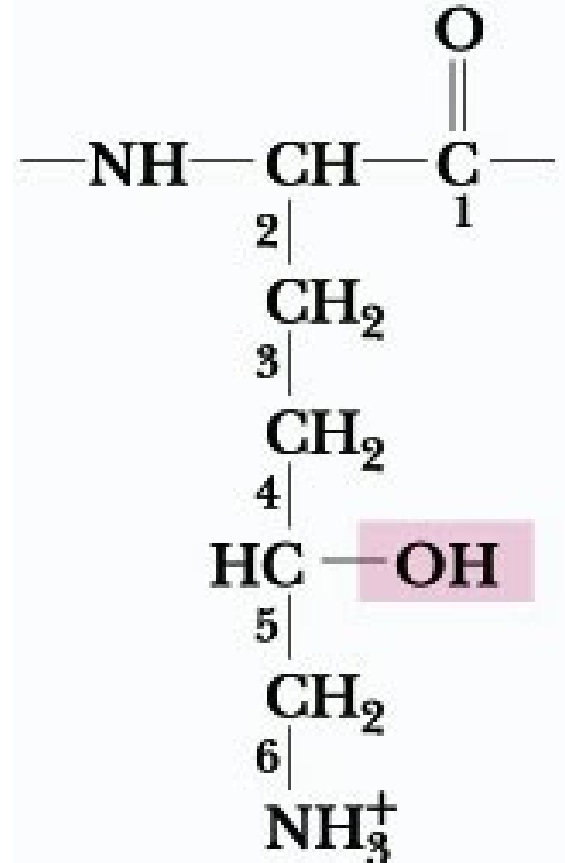
Hydroxylated Residues Found in Collagen



4-hydroxyprolyl
residue (Hyp)



3-hydroxyprolyl
residue



4-hydroxylysyl
residue (Hyl)

These hydroxylated amino acids are
synthesized post-translationally

Structure of Collagen



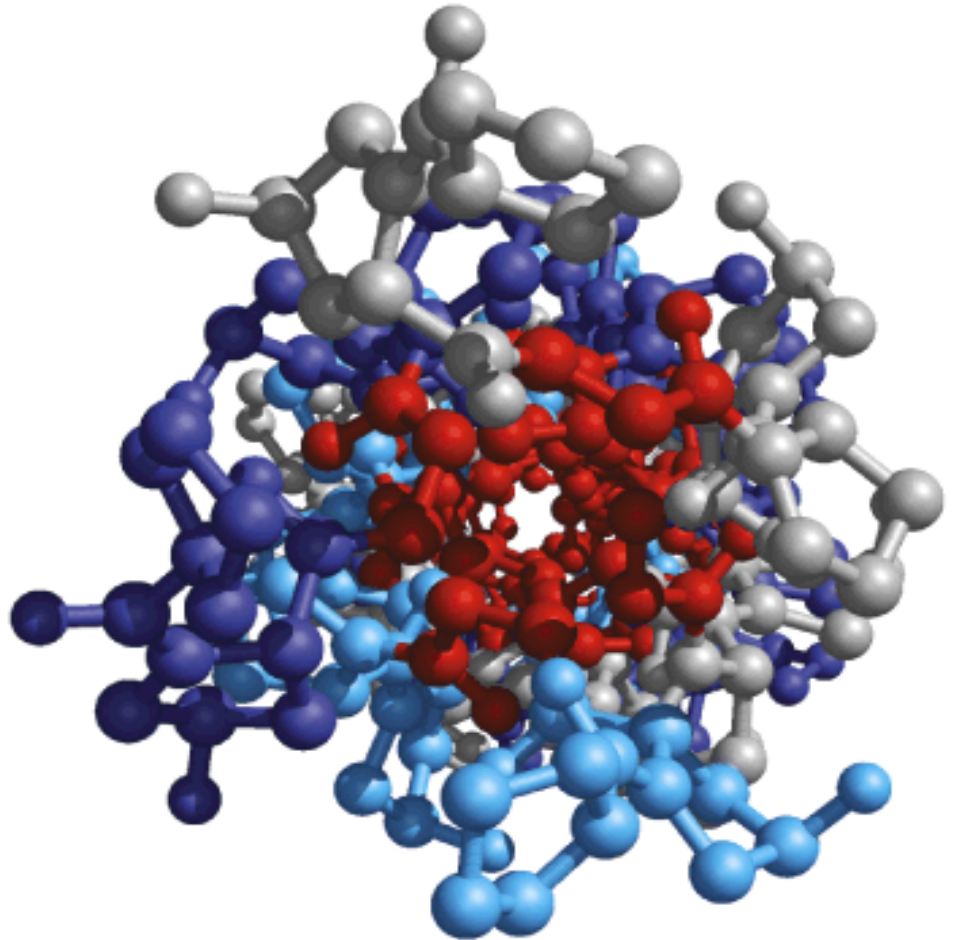
(a)



(b)



(c)



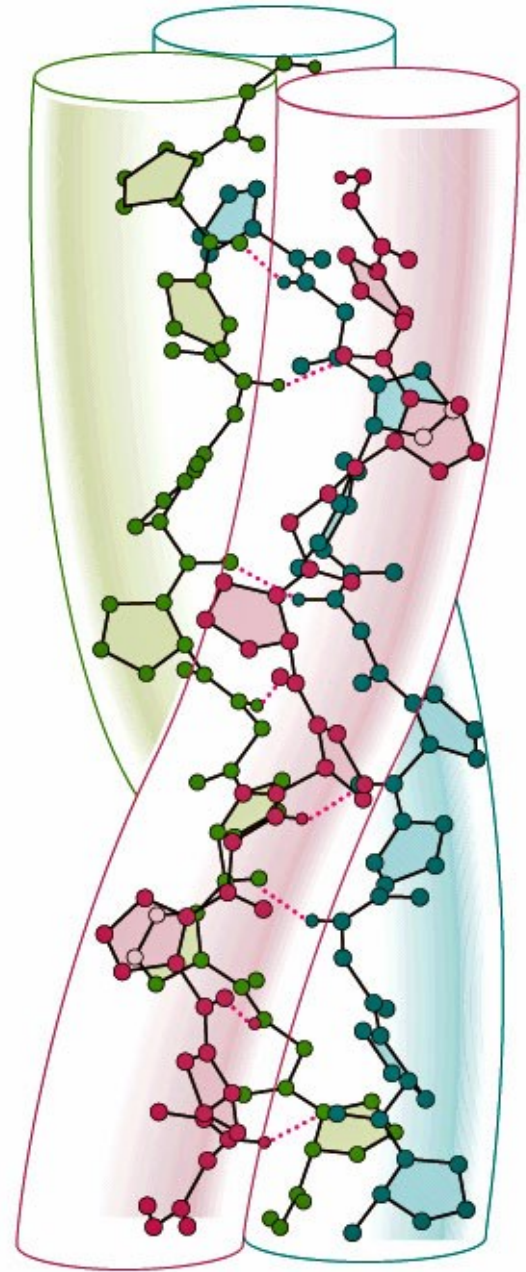
(d)

The Collagen Triple Helix

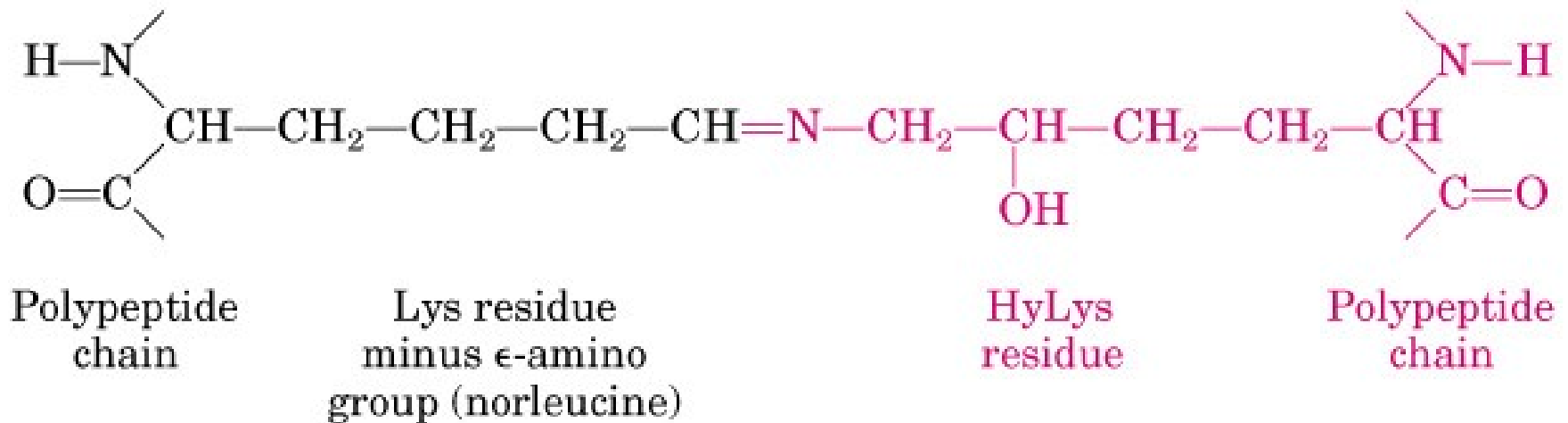
A case of structure following composition

- The unusual amino acid composition of collagen is unsuited for alpha helices OR beta sheets
- But it is ideally suited for the collagen triple helix: three intertwined helical strands
- Much more extended than alpha helix, with a rise per residue of 2.9 Å
- 3.3 residues per turn
- Long stretches of Gly-Pro-(Pro/HyP)

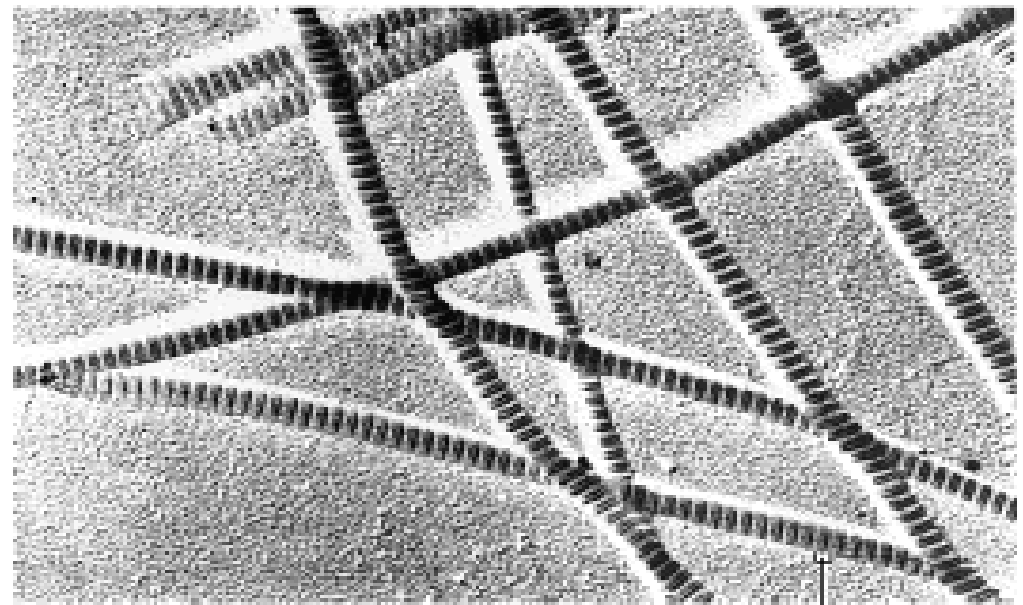
Collagen Triple Helix



Formation of Lys-Lys Cross-Links in Collagen



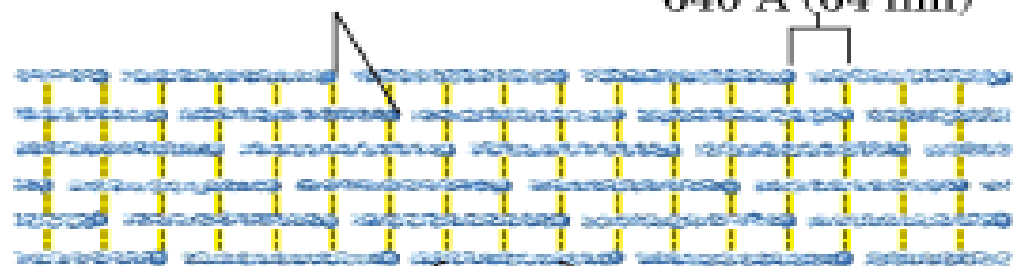
Structure of Collagen Fibrils



250
nm

Heads of collagen
molecules

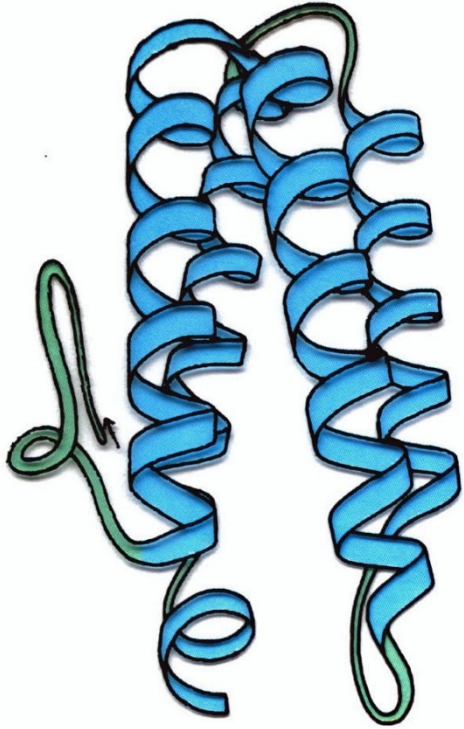
Cross-striations
640 Å (64 nm)



Section of collagen
molecule

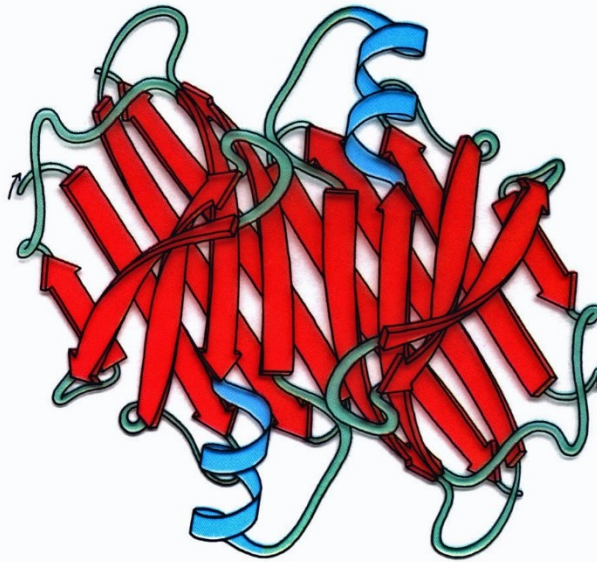
Globular Proteins

Structural diversity reflects functional diversity in Globular proteins



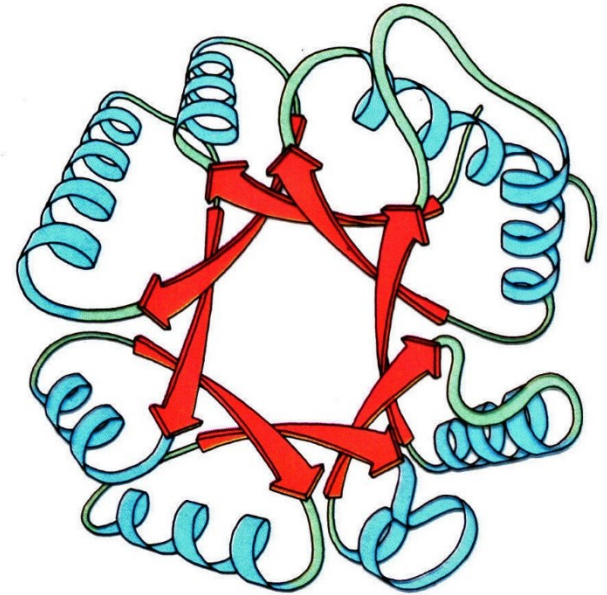
myohemerythrin

Predominantly
 α -helix



prealbumin

Predominantly
 β -sheet



pyruvate kinase

Mixed α -helix
and β -sheet

TABLE 4-2 Approximate Amounts of α Helix and β Conformation in Some Single-Chain Proteins

<i>Protein (total residues)</i>	<i>Residues (%)</i> *	
	α Helix	β Conformation
Chymotrypsin (247)	14	45
Ribonuclease (124)	26	35
Carboxypeptidase (307)	38	17
Cytochrome c (104)	39	0
Lysozyme (129)	40	12
Myoglobin (153)	78	0

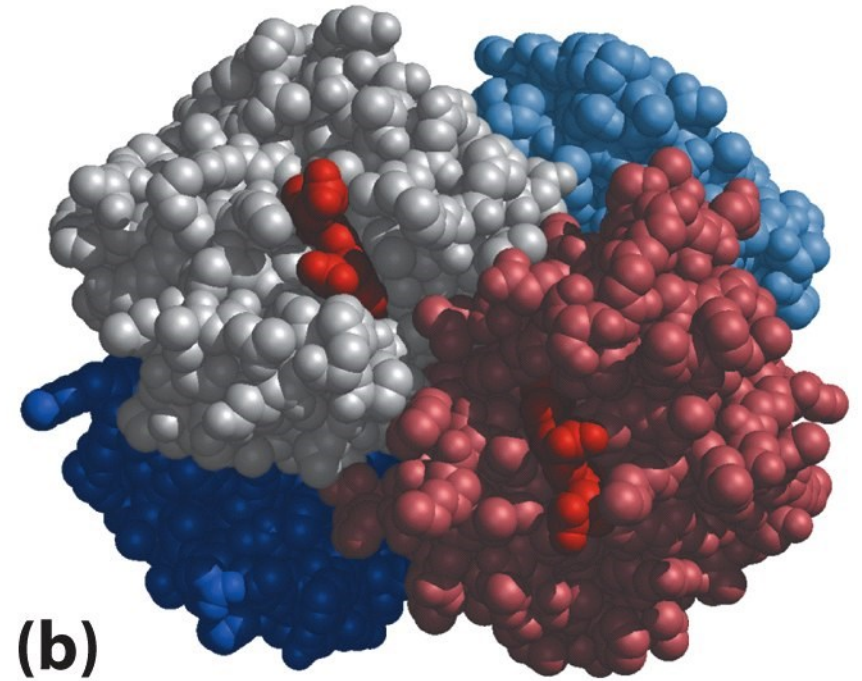
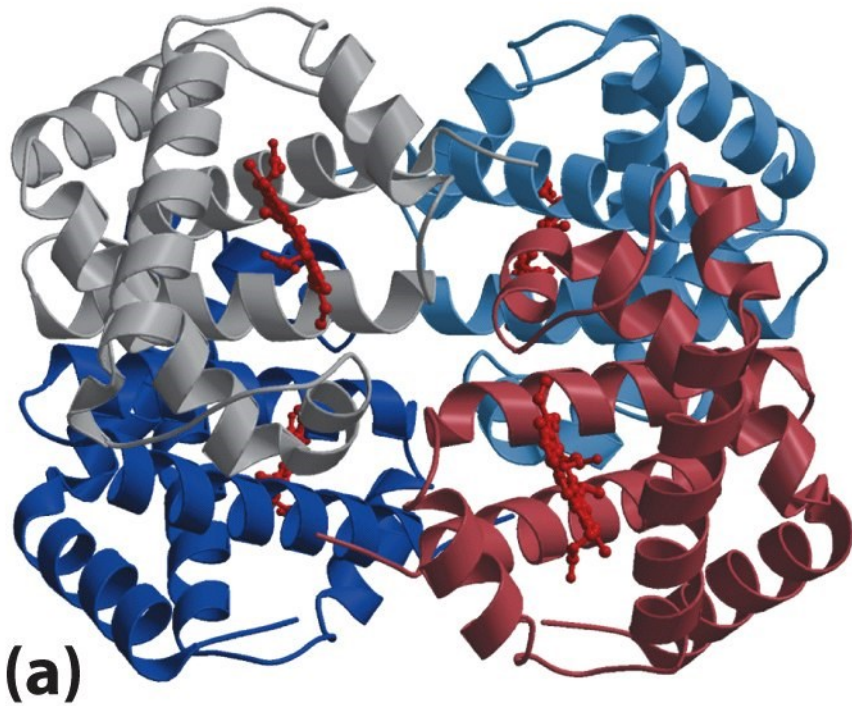
Source: Data from Cantor, C.R. & Schimmel, P.R. (1980) *Biophysical Chemistry*, Part I: *The Conformation of Biological Macromolecules*, p. 100, W. H. Freeman and Company, New York.

*Portions of the polypeptide chains that are not accounted for by α helix or β conformation consist of bends and irregularly coiled or extended stretches. Segments of α helix and β conformation sometimes deviate slightly from their normal dimensions and geometry.

Protein Structure Determination

- As of September of 2006, scientists around the globe had catalogued the structures of about 33,000 proteins and other biological macromolecules.
- These structures, known to atomic resolution, are deposited in and accessed from the RCSB Protein Data Bank (<http://www.rcsb.org/pdb>).

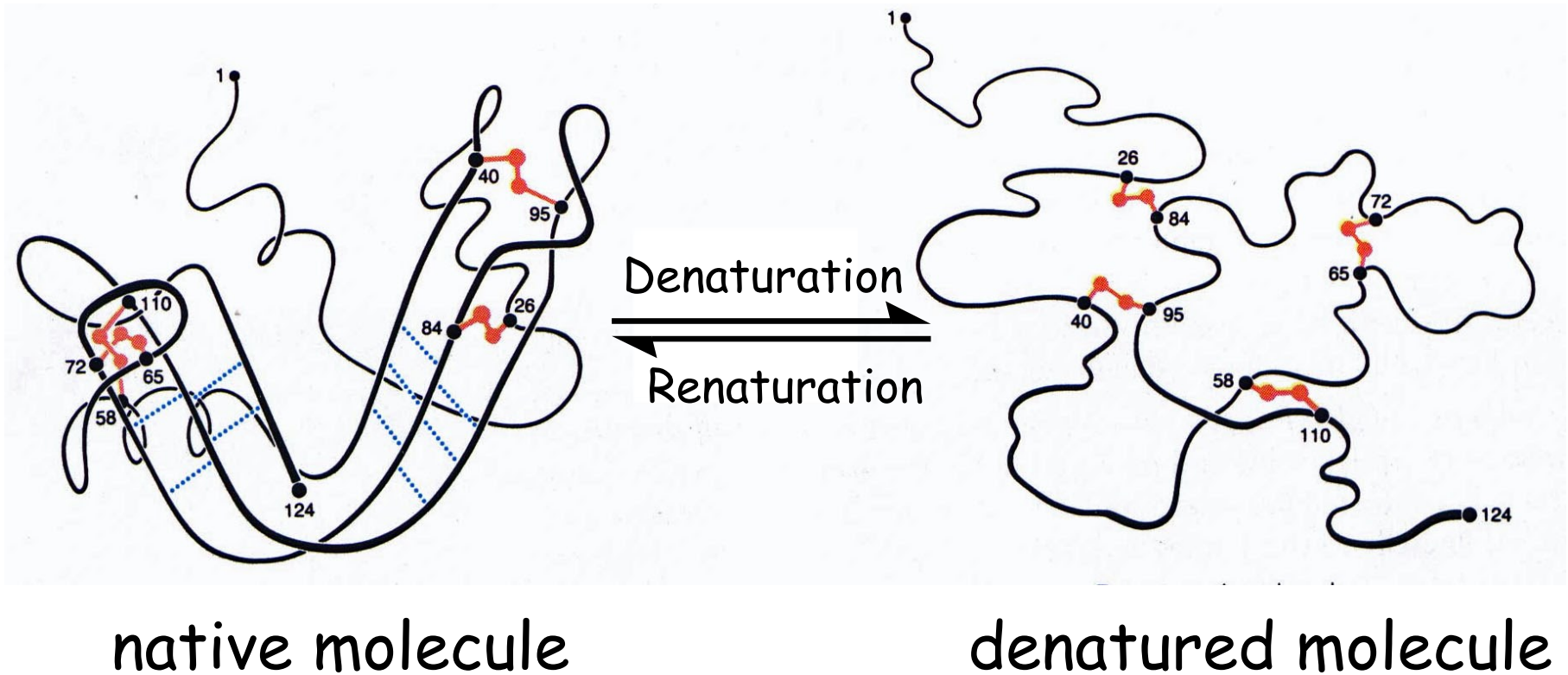
Protein quaternary structures range from simple dimers to larger complexes



*Tetrameric structure
of deoxyhemoglobin*

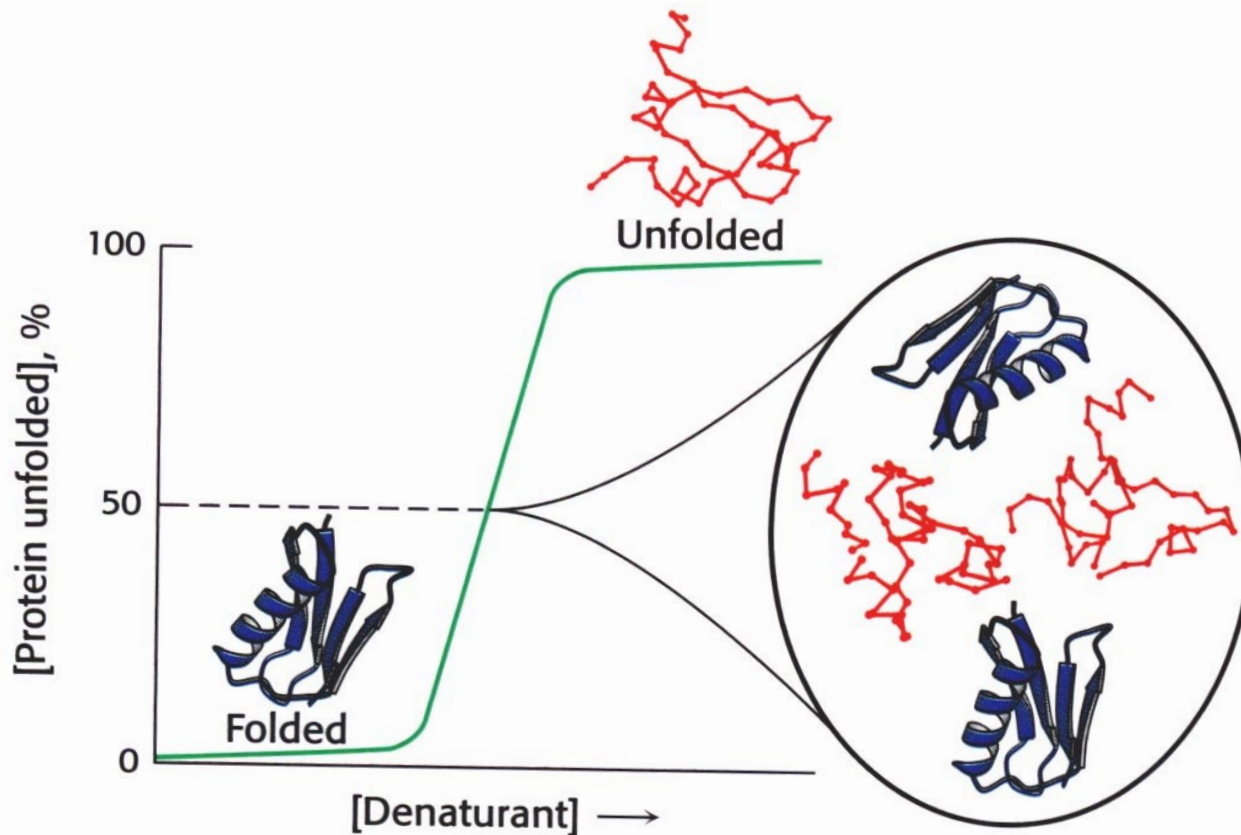
29/01/2024

Protein Unfolding or Denaturation



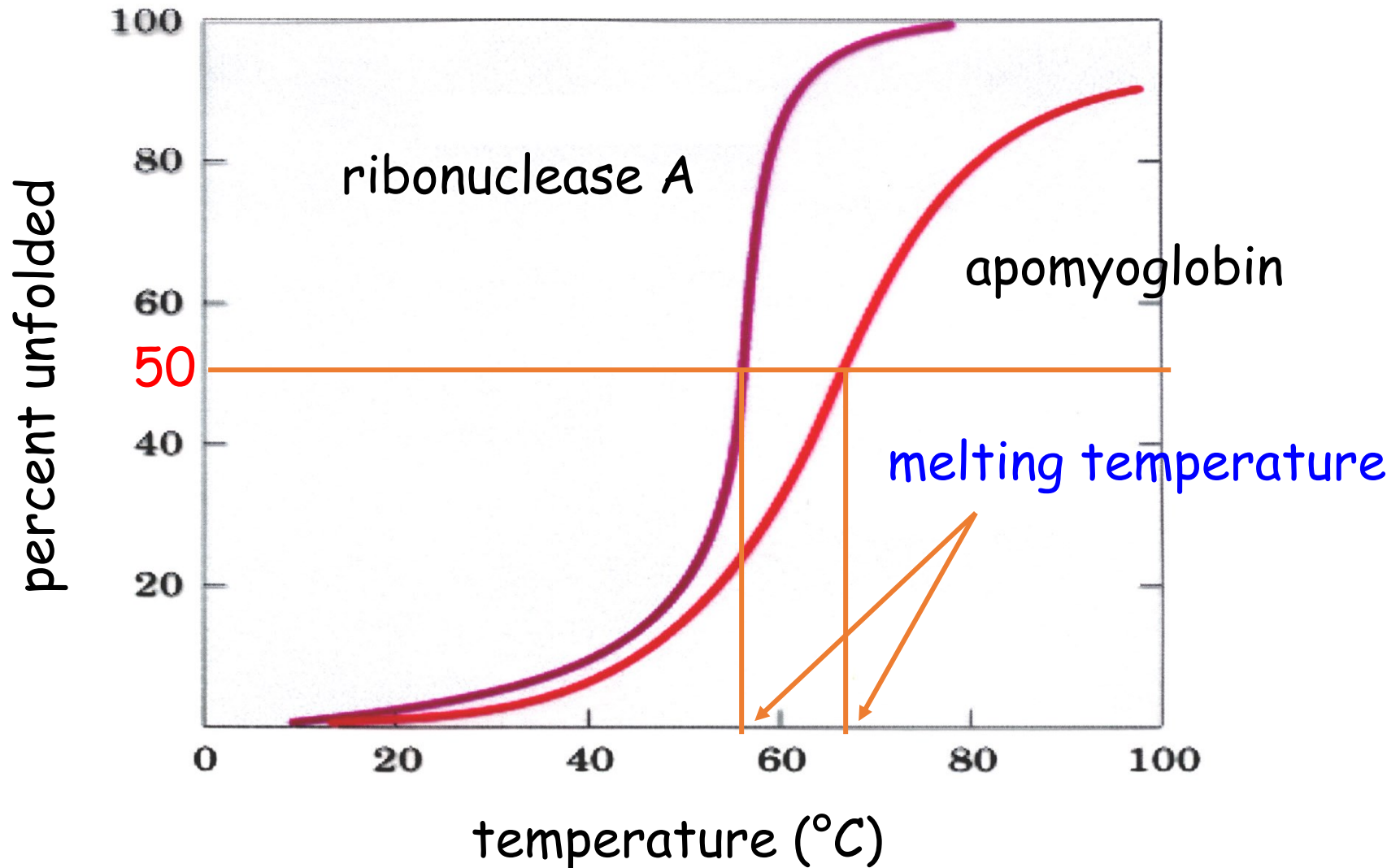
Protein folding can be a **reversible** or an **irreversible** process.

Protein Unfolding or Denaturation

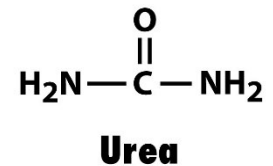
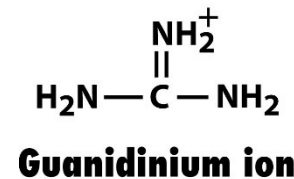
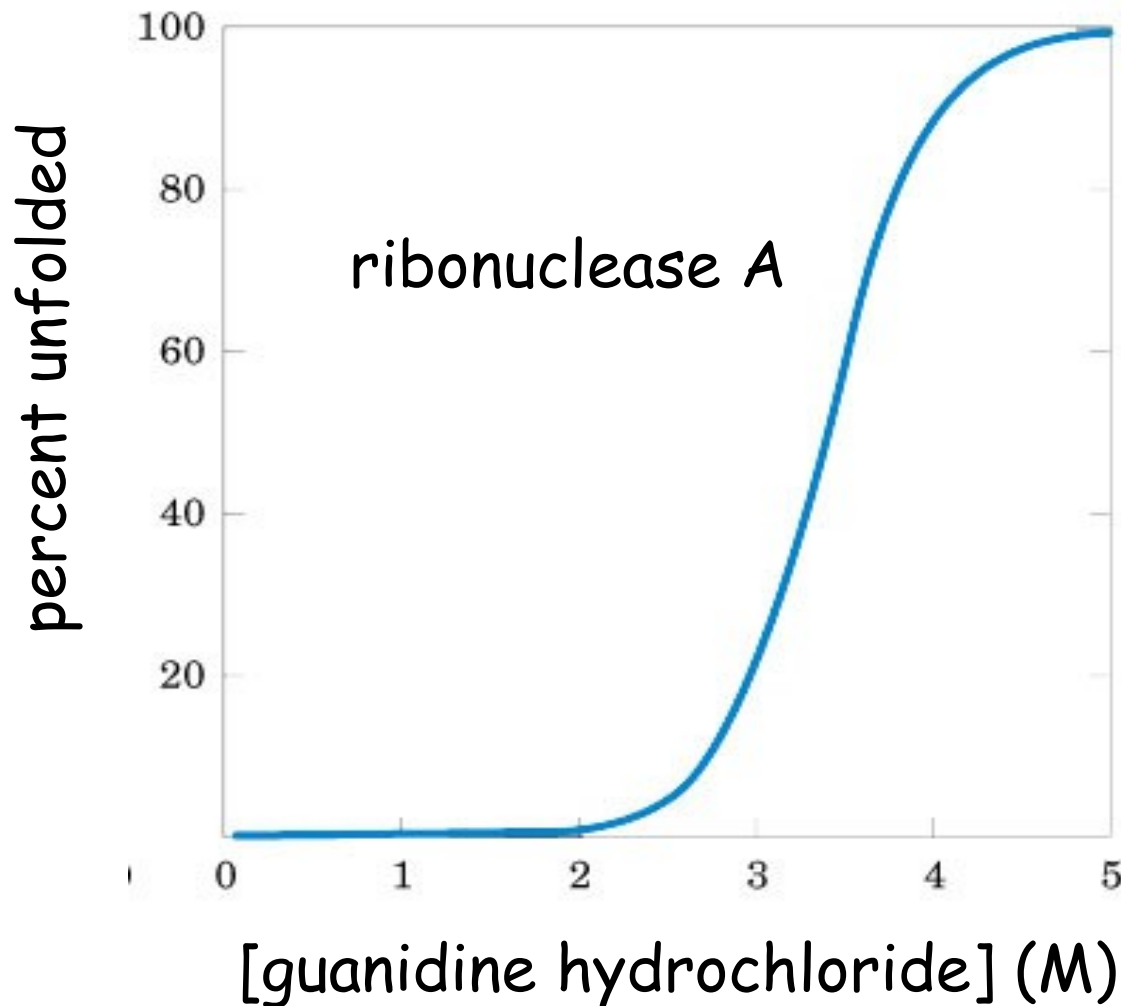


Denaturants: **temperature** (heating or cooling), **pH** (acid or base), **chemical** (urea, guanidine hydrochloride, organic solvents)

Protein Unfolding: Thermal Denaturation



Protein Denaturation - Chemical Denaturants: Urea or Guanidine Hydrochloride



Unnumbered figure pg 159 Fundamentals of Biochemistry, 2/e
© 2006 John Wiley & Sons

Intro

- **Enzymes are proteins that accelerate, or catalyze chemical reactions.** In these reactions, the molecules at the beginning of the process are called **substrates** and the enzyme converts these into different molecules: the **products**. Almost all processes in the cell need enzymes in order to occur at significant rates.
- **Enzymes are usually named according to the reaction they catalyze.** Typically the suffix -ase is added to the name of the substrate (e.g., lactase is the enzyme that cleaves lactose) or the type of reaction (e.g., DNA polymerase forms DNA polymers).

Intro

- Like all catalysts, enzymes work by **providing an alternative path of lower activation energy** for a reaction and dramatically accelerating its rate. Some enzymes can make their conversion of substrate to product occur many **millions of times faster**.
- Enzymes are like any catalyst: are not consumed in chemical reactions, nor do they alter the equilibrium of a reaction. However, enzymes do differ from most other catalysts by **being much more specific**.
- Enzyme activity can be affected by other molecules. **Inhibitors** are molecules that decrease enzyme activity, and **activators** are molecules that increase activity. Drugs and poisons are often enzyme inhibitors.

General properties of enzymes

- 1. Higher reaction rates:** 10^6 to 10^{12} times faster than uncatalyzed reactions and several magnitude faster than chemically catalyzed reactions.
- 2. Milder reaction conditions:** physiological conditions. Many chemically catalyzed reactions need high temperature and high pressure.
- 3. Greater reaction specificity:** rarely have side products.
- 4. Capacity for regulation:** the activity of enzymes can be regulated through cofactors, inhibitors etc.

General properties of enzymes

Table 11-1 Catalytic Power of Some Enzymes

Enzyme	Nonenzymatic Reaction Rate (s^{-1})	Enzymatic Reaction Rate (s^{-1})	Rate Enhancement
Carbonic anhydrase	1.3×10^{-1}	1×10^6	7.7×10^6
Chorismate mutase	2.6×10^{-5}	50	1.9×10^6
Triose phosphate isomerase	4.3×10^{-6}	4300	1.0×10^9
Carboxypeptidase A	3.0×10^{-9}	578	1.9×10^{11}
AMP nucleosidase	1.0×10^{-11}	60	6.0×10^{12}
Staphylococcal nuclease	1.7×10^{-13}	95	5.6×10^{14}

Source: Radzicka, A. and Wolfenden, R., *Science* **267**, 91 (1995).

Table 11-1 Fundamentals of Biochemistry, 2/e

© 2006 John Wiley & Sons

Naming of enzymes

Class	Reaction type	Important subclasses
1 Oxidoreductases	<p>○ = Reduction equivalent</p> <p>A_{red} + B_{ox} ⇌ A_{ox} + B_{red}</p>	Dehydrogenases Oxidases, peroxidases Reductases Monooxygenases Dioxygenases
2 Transferases	<p>A-B + C ⇌ A + B-C</p>	C ₁ -Transferases Glycosyltransferases Aminotransferases Phosphotransferases
3 Hydrolases	<p>A-B + H₂O ⇌ A-H + B-OH</p>	Esterases Glycosidases Peptidases Amidases
4 Lyases ("synthases")	<p>A + B ⇌ A-B</p>	C-C-Lyases C-O-Lyases C-N-Lyases C-S-Lyases
5 Isomerases	<p>A ⇌ Iso-A</p>	Epimerases <i>cis trans</i> Isomerases Intramolecular transferases
6 Ligases ("synthetases")	<p>B + A + XTP ⇌ A-B + XDP</p> <p>X = A, G, U, C</p>	C-C-Ligases C-O-Ligases C-N-Ligases C-S-Ligases