

# Macromolecule : PROTEIN

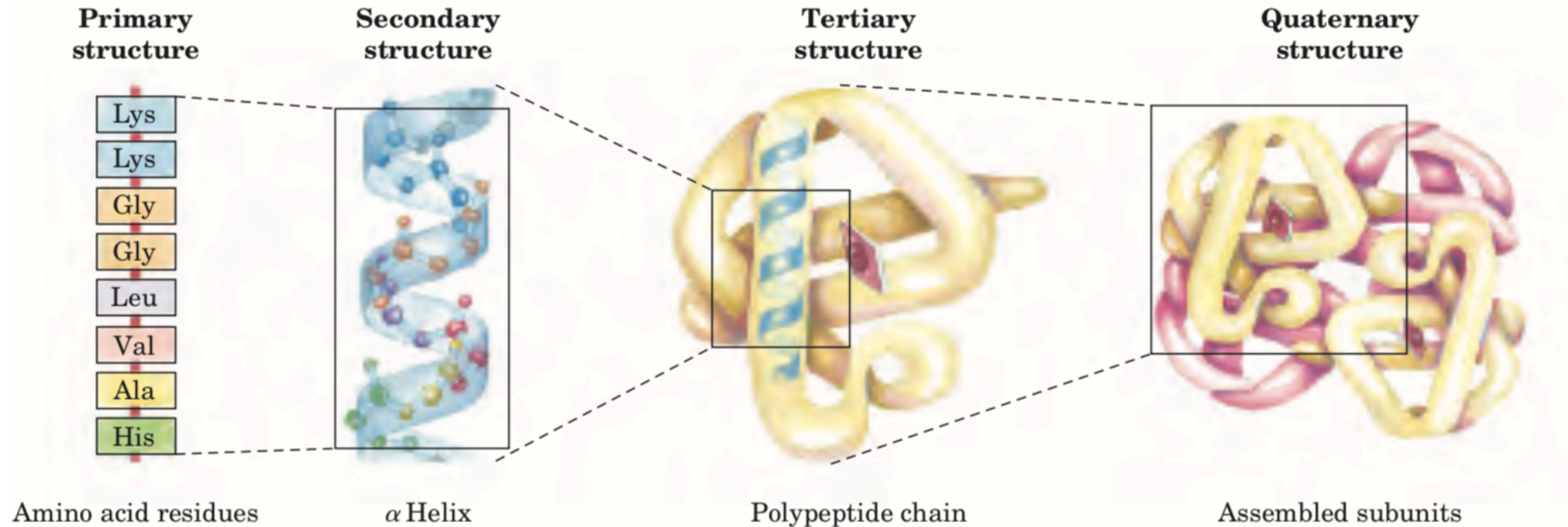
## (Part 2 of 2)

Presented by Lucia Dhiantika Witasari

# Overview

1. Amino acid (Part 1)
2. Peptide bond (Part 1 )
- 3. Protein structure**
- 4. Protein functions**

# Protein Structure



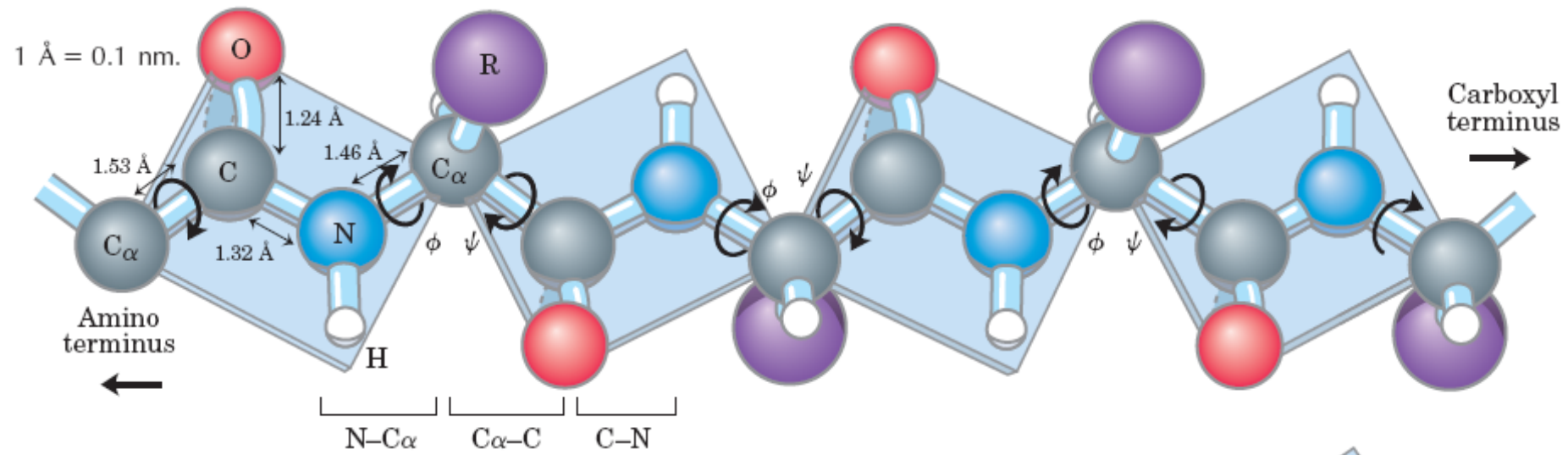
**FIGURE 3-16 Levels of structure in proteins.** The *primary structure* consists of a sequence of amino acids linked together by peptide bonds and includes any disulfide bonds. The resulting polypeptide can be coiled into units of *secondary structure*, such as an  $\alpha$  helix. The he-

lix is a part of the *tertiary structure* of the folded polypeptide, which is itself one of the subunits that make up the *quaternary structure* of the multisubunit protein, in this case hemoglobin.

- **Primary structure** is the *sequence* of amino acid residues → A description of all covalent bonds (mainly peptide bonds and disulfide bonds) linking amino acid residues in a polypeptide chain.
- **Secondary structure** refers to particularly stable arrangements of amino acid residues giving rise to recurring structural patterns.
- **Tertiary structure** describes all aspects of the three-dimensional folding of a polypeptide.
- When a protein has two or more polypeptide subunits, their arrangement in space is referred to as **quaternary structure**.

# PRIMARY STRUCTURE

## Peptide Bonds Are rigid and Planar



In a pair of linked amino acids, six atoms (C $\alpha$ , C, O, N, H, and C $\alpha$ ) lie in a plane.

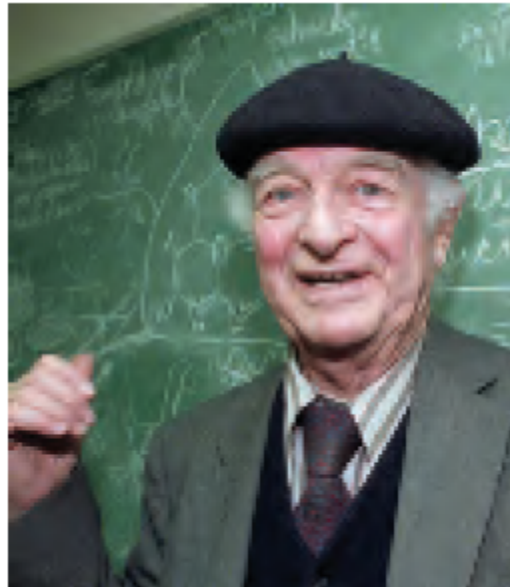
The N-C $\alpha$  and C $\alpha$ -C bonds → can rotate

The peptide C-N bond → not free to rotate.

primary structure is linear polymers → sequences of amino acids.

# SECONDARY STRUCTURE

- **The Alpha Helix Is a Coiled Structure Stabilized by Intrachain Hydrogen Bonds**
- **Beta Sheets Are Stabilized by Hydrogen Bonding Between Polypeptide Strands**



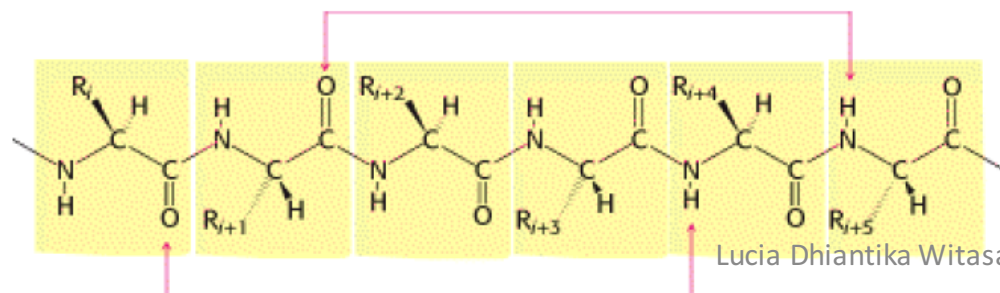
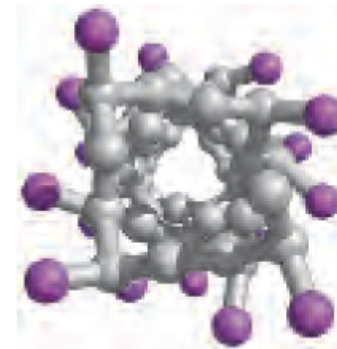
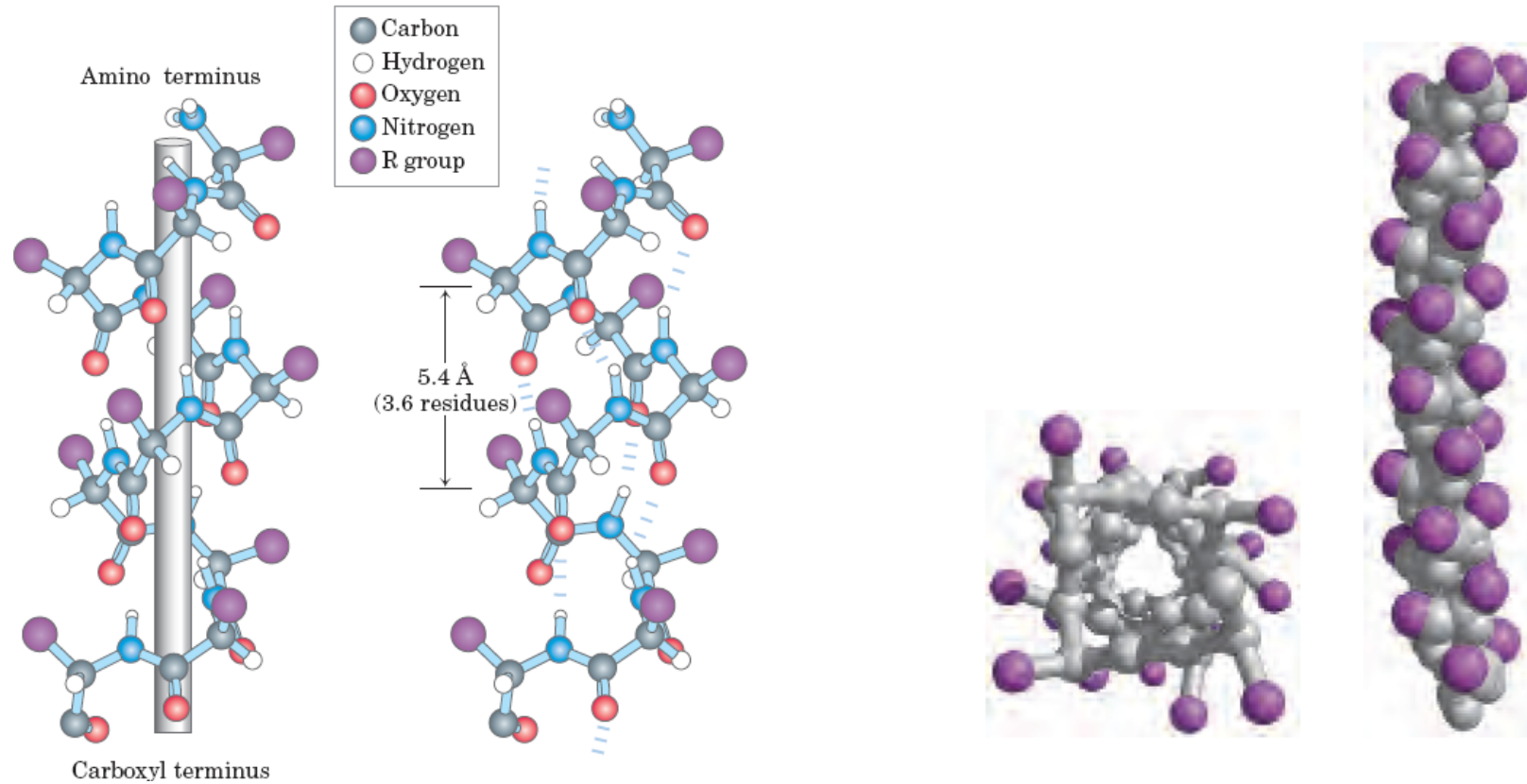
Linus Pauling, 1901–1994



Robert Corey, 1897–1971

# The $\alpha$ -HELIX structure

The Alpha Helix Is a Coiled Structure Stabilized by Intrachain Hydrogen Bonds

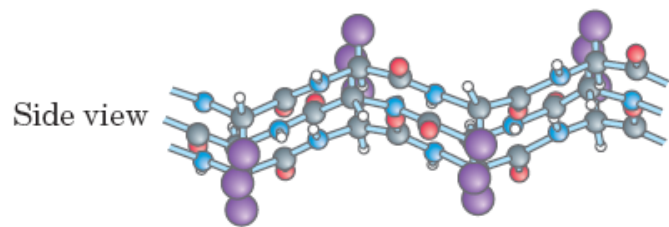
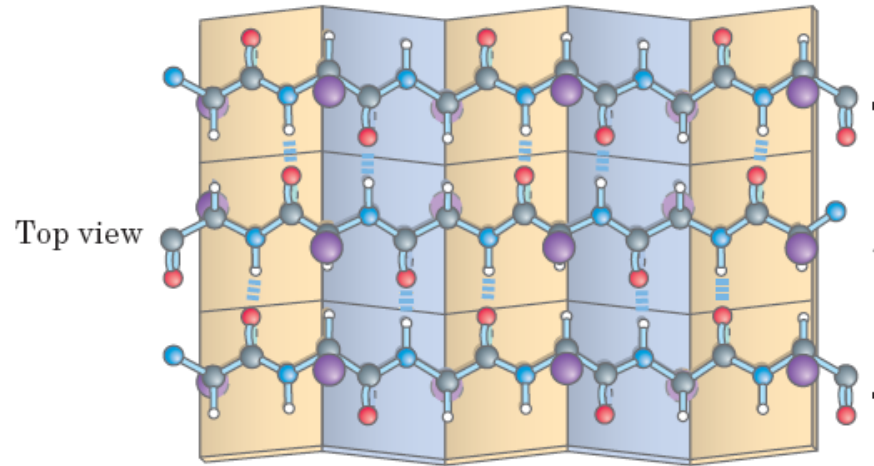


In the  $\alpha$  helix, the CO group of residue  $n$  forms a hydrogen bond with the NH group of residue  $n+4$ .

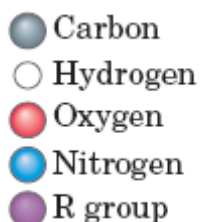
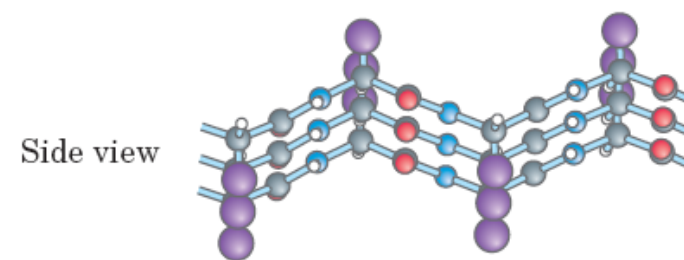
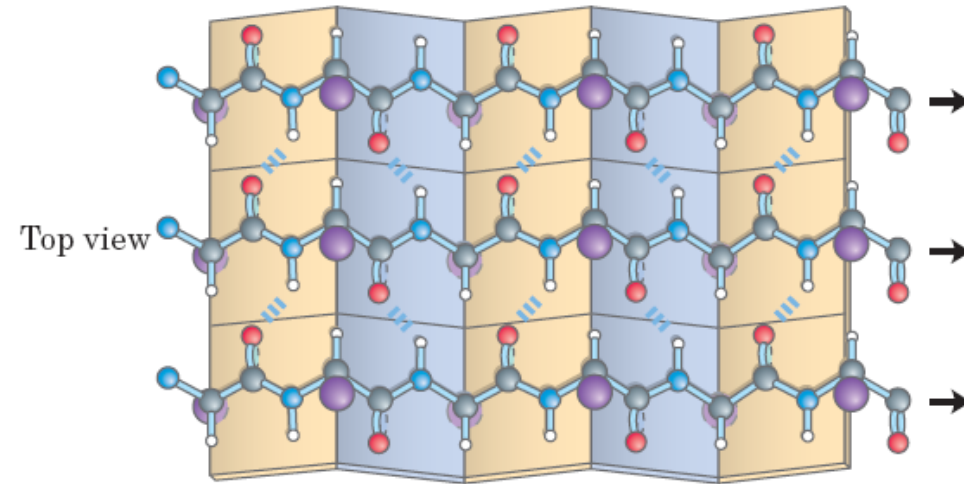
# The $\beta$ -SHEETS Structure

interchain hydrogen bonding

(a) Antiparallel



(b) Parallel



**hydrogen bonds are formed between adjacent segments of polypeptide chain.**



# TERTIARY STRUCTURE

- The overall three-dimensional arrangement of all atoms in a protein
- specific bend-producing residues → Pro, Thr, Ser, and Gly.
- Proteins with significant primary sequence similarity, and/or with demonstrably similar structure and function, are said to be in the same **protein family**.
- Two or more families with little primary sequence similarity sometimes make use of the same major structural motif and have functional similarities; these families are grouped as **superfamilies**

# Tertiary contd..

- **Fibrous proteins, having polypeptide chains arranged in long strands or sheets**
  - consist largely of a single type of secondary structure
  - the structures that provide support, shape, and external protection to vertebrates
- **Globular proteins, having polypeptide chains folded into a spherical or globular shape.**
  - contain several types of secondary structure
  - most enzymes and regulatory proteins

# Organization of proteins based on motifs

- All  $\alpha$
- All  $\beta$
- $\alpha/\beta$

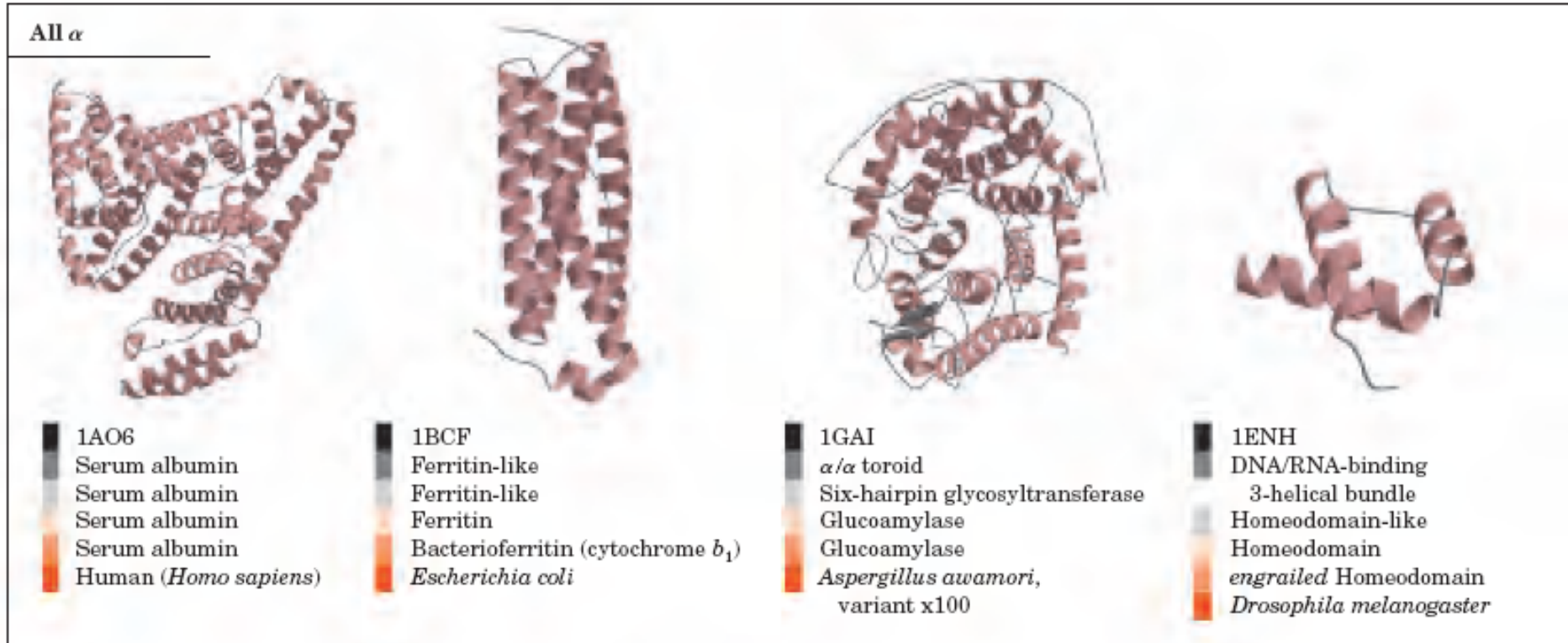
in which the  $\alpha$  and  $\beta$  segments are interspersed or alternate

- $\alpha + \beta$

in which the  $\alpha$  and  $\beta$  regions are somewhat segregated

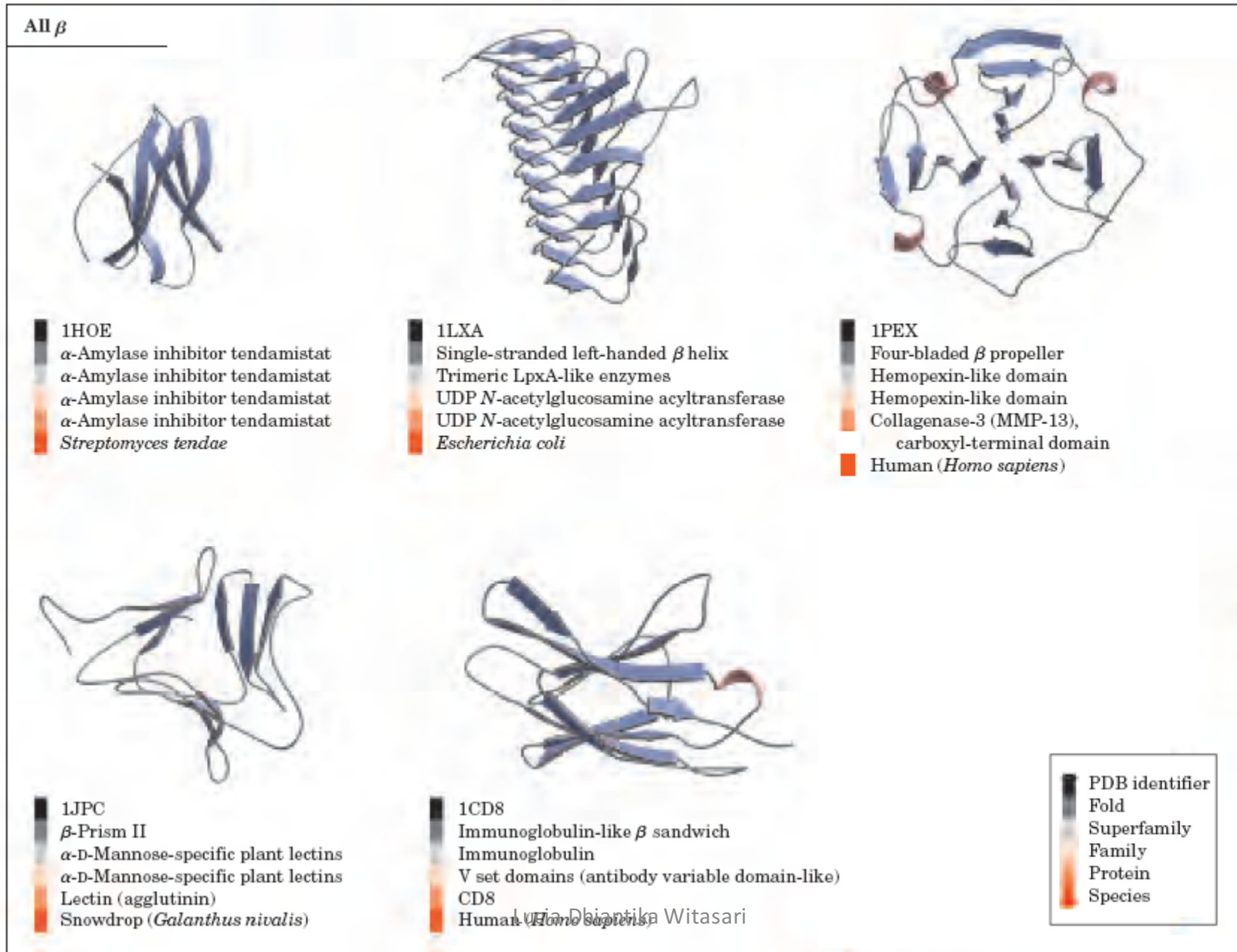
**domains exhibiting similar folding patterns are said to have the same motif even though their constituent *helices and sheets may differ* in length.**

# All $\alpha$

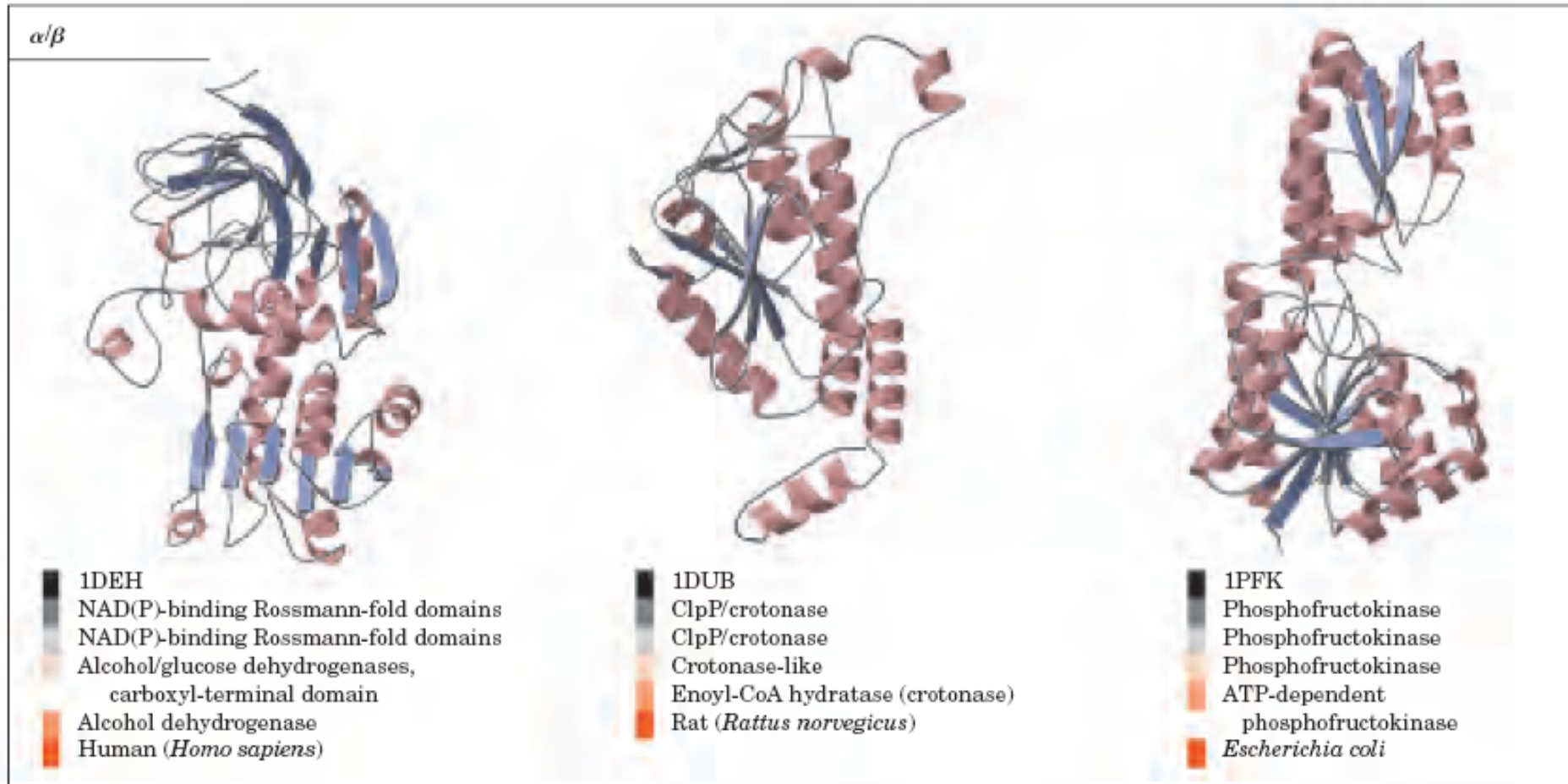


- The top two levels of organization, **class and fold**, are **purely structural**.
- Below the fold level, categorization is based on evolutionary relationships.

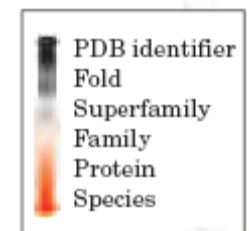
# All $\beta$

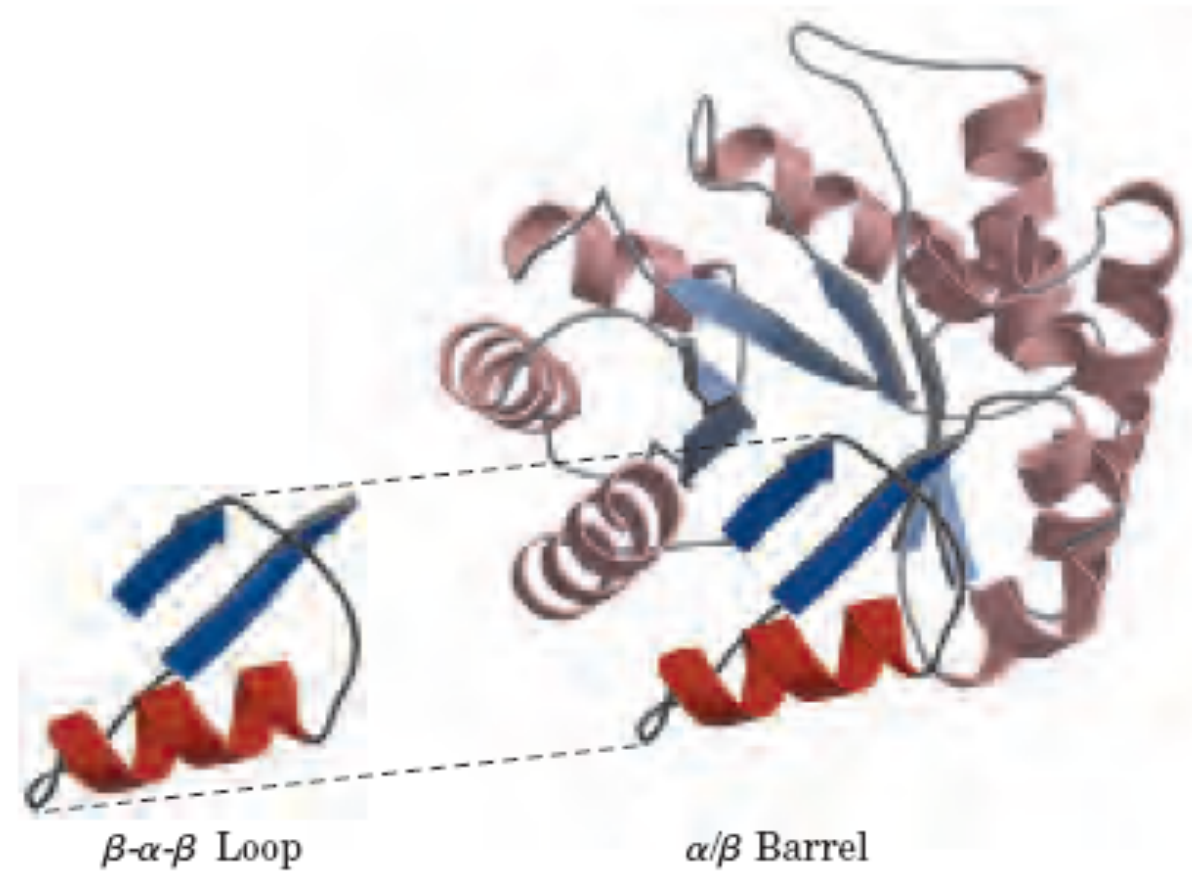


# $\alpha/\beta$



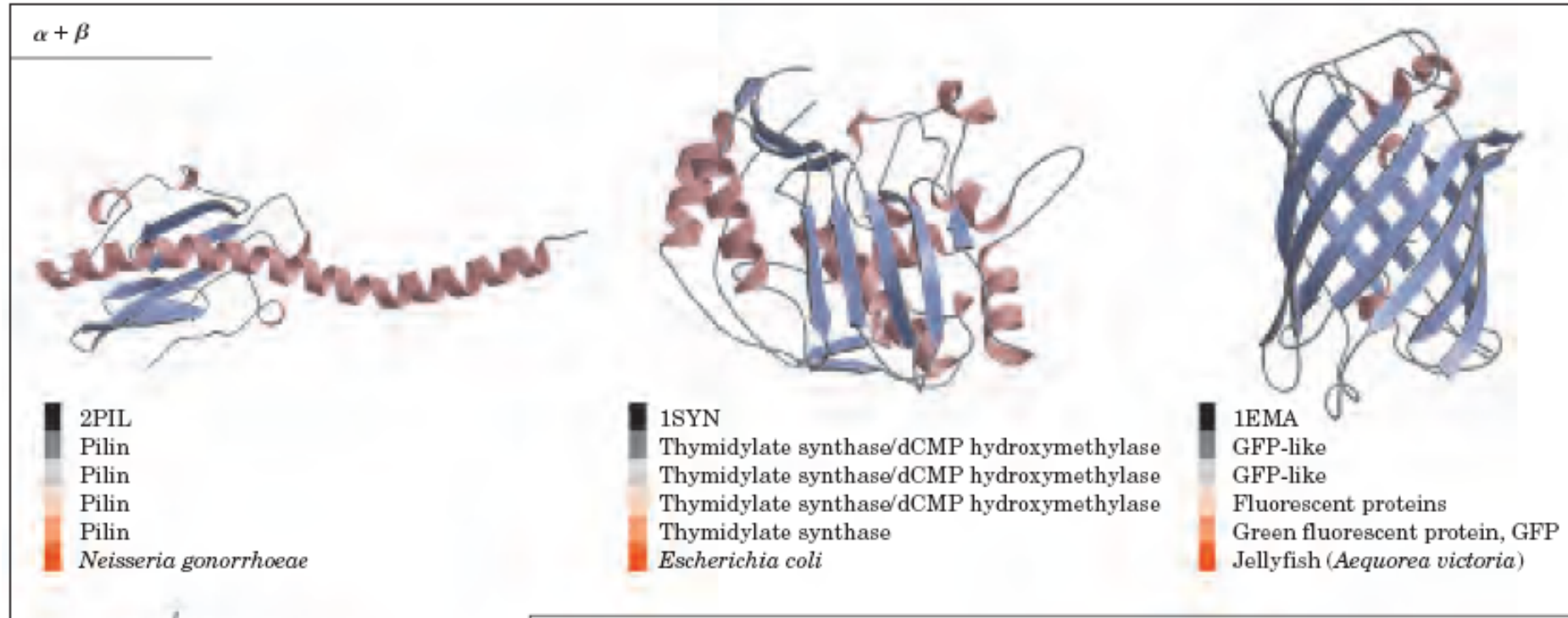
- The  $\alpha / \beta$  barrel is a common motif constructed from repetitions of the simpler  $\beta$ - $\alpha$ - $\beta$  *loop motif*.



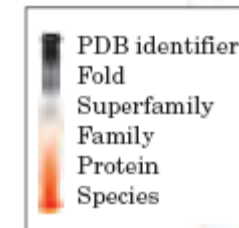


**a domain of the pyruvate kinase (a glycolytic enzyme) from rabbit**

$\alpha + \beta$



the  $\alpha$  and  $\beta$  regions are somewhat segregated

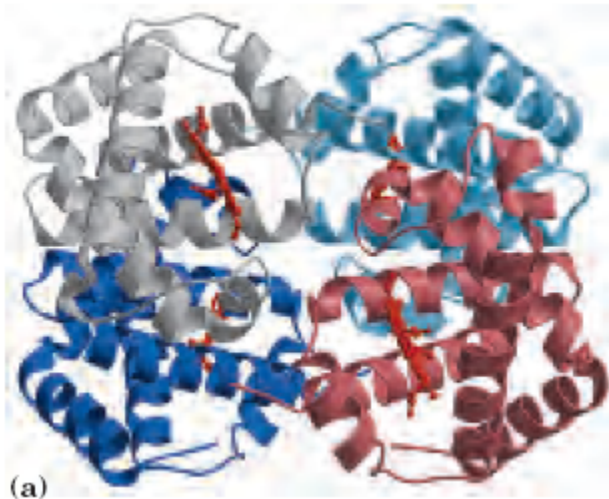




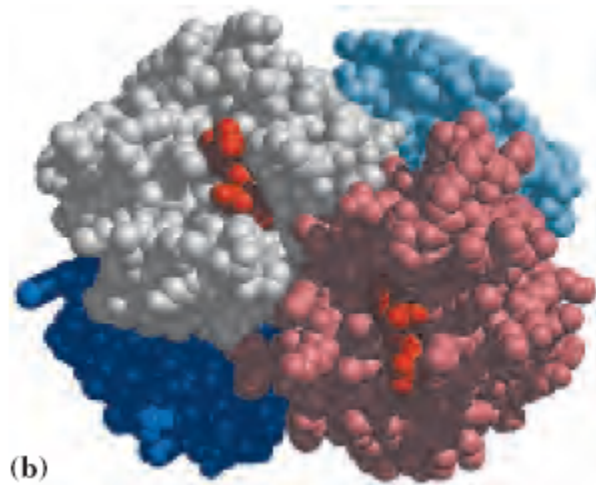
# QUATERNARY STRUCTURE

- Some proteins contain two or more separate polypeptide chains, or subunits, which may be identical or different.
- Quaternary structure results from interactions between the subunits of multisubunit (multimeric) proteins or large protein assemblies.

# Quaternary structure of deoxyhemoglobin.



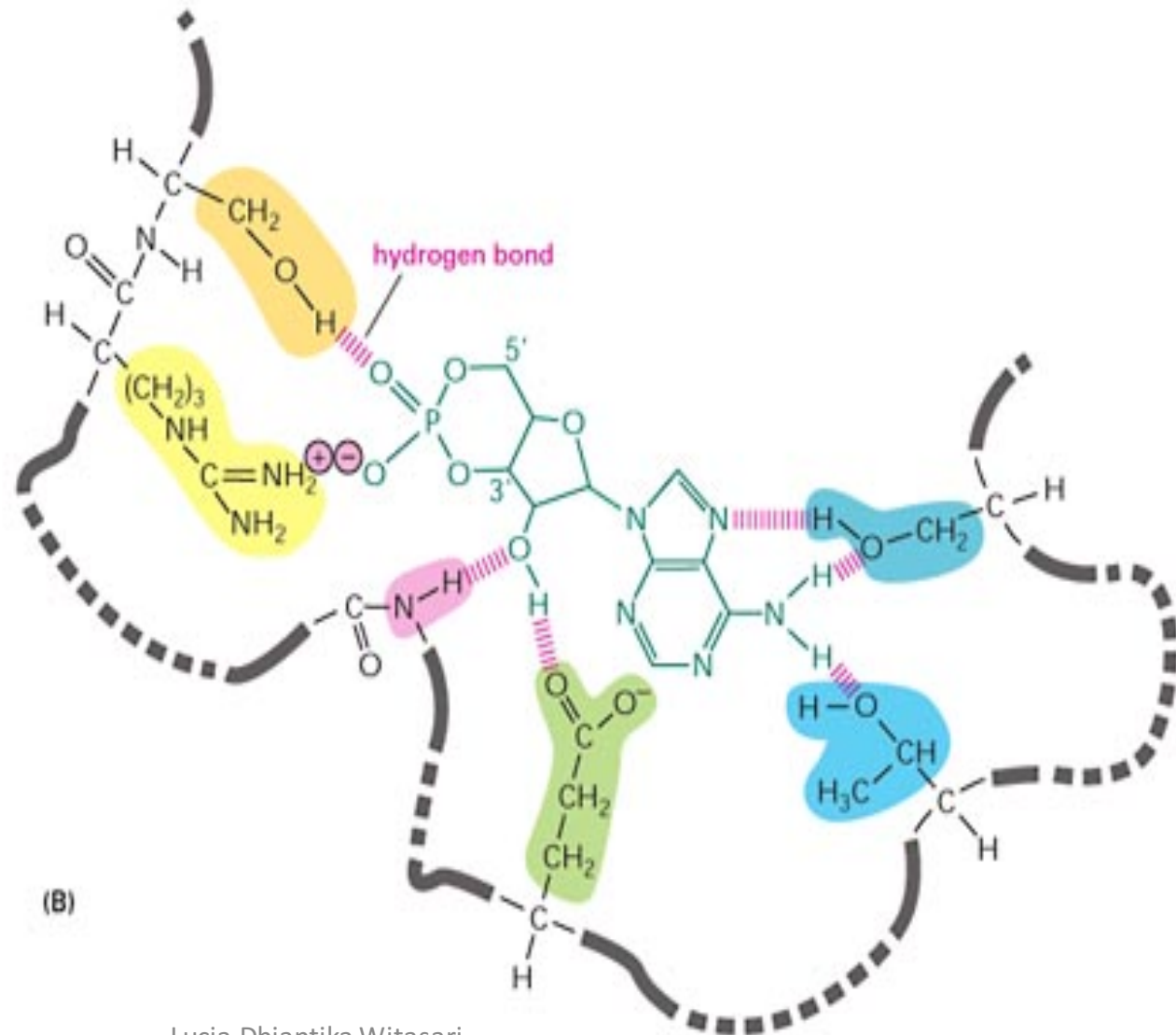
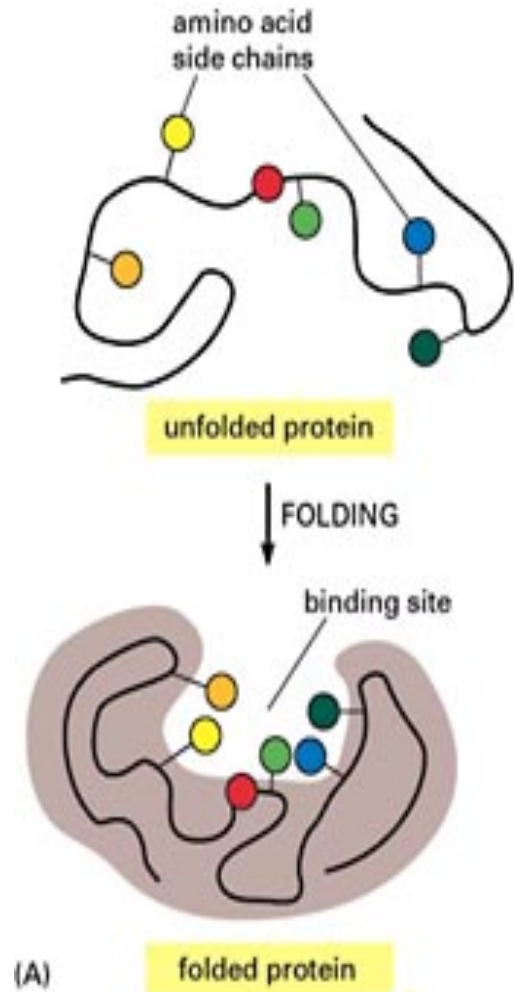
- The  $\alpha$  subunits are shown in gray and light blue
- the  $\beta$  subunits in pink and dark blue



# Protein Quaternary Structures Range from Simple Dimers to Large Complexes

- A multisubunit protein = a **multimer** → two to hundreds of subunits.
- A multimer with just a few subunits is often called an **oligomer**.
- If a multimer is composed of a number of **nonidentical subunits**, the overall structure of the protein can be **asymmetric** and quite complicated.
- most multimers have **identical subunits** or repeating groups of nonidentical subunits, usually in **symmetric** arrangements.
- Some multimeric proteins have a repeated unit consisting of a single subunit or a group of subunits referred to as a **protomer**.

# PROTEIN FOLDING



# Death by Misfolding: The Prion Diseases

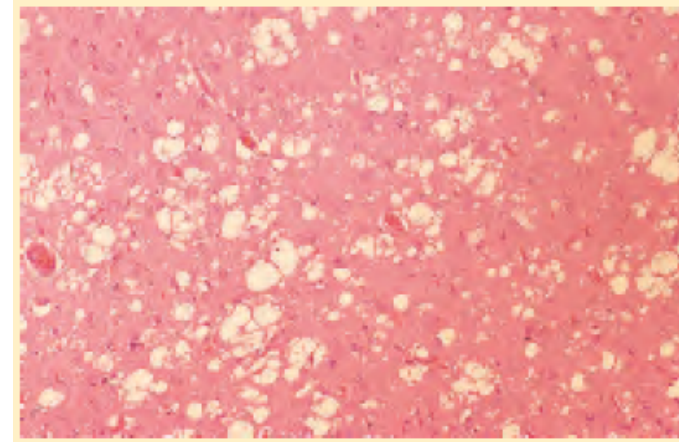
**Stanley Prusiner**

The infectious agent has been traced to a single protein (*Mr 28,000*), **Prion** (from *proteinaceous infectious only*) protein (*PrP*).

Prion protein is a normal constituent of brain tissue in all mammals. → molecular signaling function.

Illness occurs only when the normal cellular PrP, or PrPC, occurs in an altered conformation called PrPSc (Sc denotes scrapie)

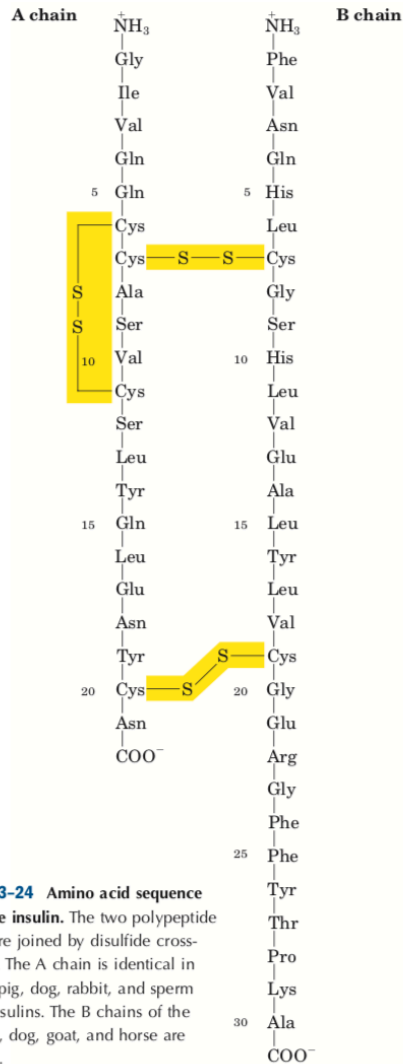
The interaction of PrPSc with PrPC converts the latter to PrPSc, initiating a domino effect in which more and more of the brain protein converts to the disease-causing form.



**A mutation in the gene encoding PrP produces a change in one amino acid residue → the conversion of PrPC to PrPSc**

- What is it that makes one protein an enzyme, another a hormone, another a structural protein, and still another an antibody? How do they differ chemically?
- **The Function of a Protein Depends on Its Amino Acid Sequence**
  - proteins with different functions always have different amino acid sequences.
  - 
  - thousands of human genetic diseases have been traced to the production of defective proteins. Perhaps one-third of these proteins are defective because of a single change in their amino acid sequence; hence, if the primary structure is altered, the function of the protein may also be changed.
  - comparing functionally similar proteins from different species → these proteins often have similar amino acid sequences.

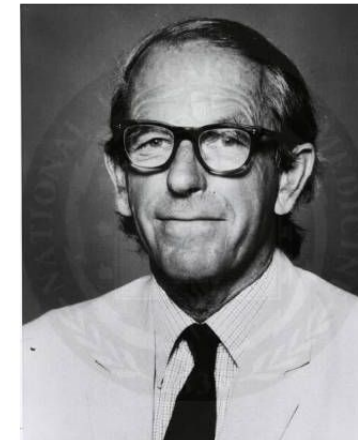
# The Amino Acid Sequences of Millions of Proteins Have Been Determined



**FIGURE 3-24** Amino acid sequence of bovine insulin. The two polypeptide chains are joined by disulfide cross-linkages. The A chain is identical in human, pig, dog, rabbit, and sperm whale insulins. The B chains of the cow, pig, dog, goat, and horse are identical.

## Frederick Sanger

- Discovered DNA sequencing by chain termination method
- Nobel Prize 1 (1958)
  - Complete amino acid sequence of insulin
- Nobel Prize 2 (1980)
  - For DNA sequencing



# PROTEIN FUNCTION



# Most Enzymes Are Proteins

Their catalytic activity depends on the integrity of their native protein conformation.

What will happen if an enzyme is denatured or dissociated into its subunits or is broken down into its component amino acids ?

**TABLE 6–3** International Classification of Enzymes

<i>No.</i>	<i>Class</i>	<i>Type of reaction catalyzed</i>
1	Oxidoreductases	Transfer of electrons (hydride ions or H atoms)
2	Transferases	Group transfer reactions
3	Hydrolases	Hydrolysis reactions (transfer of functional groups to water)
4	Lyases	Addition of groups to double bonds, or formation of double bonds by removal of groups
5	Isomerases	Transfer of groups within molecules to yield isomeric forms
6	Ligases	Formation of C—C, C—S, C—O, and C—N bonds by condensation reactions coupled to ATP cleavage

Note: Most enzymes catalyze the transfer of electrons, atoms, or functional groups. They are therefore classified, given code numbers, and assigned names according to the type of transfer reaction, the group donor, and the group acceptor.

<i>Enzyme</i>	<i>Substrate</i>
Catalase	H <sub>2</sub> O <sub>2</sub>
Carbonic anhydrase	HCO <sub>3</sub> <sup>−</sup>
Acetylcholinesterase	Acetylcholine
β-Lactamase	Benzylpenicillin
Fumarase	Fumarate
RecA protein (an ATPase)	ATP

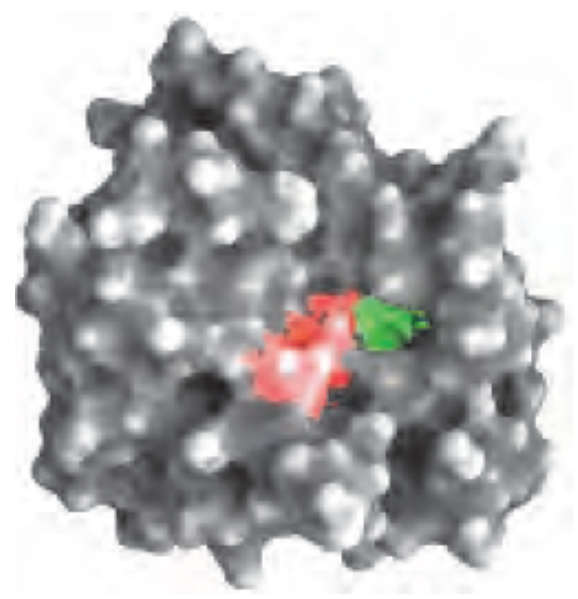
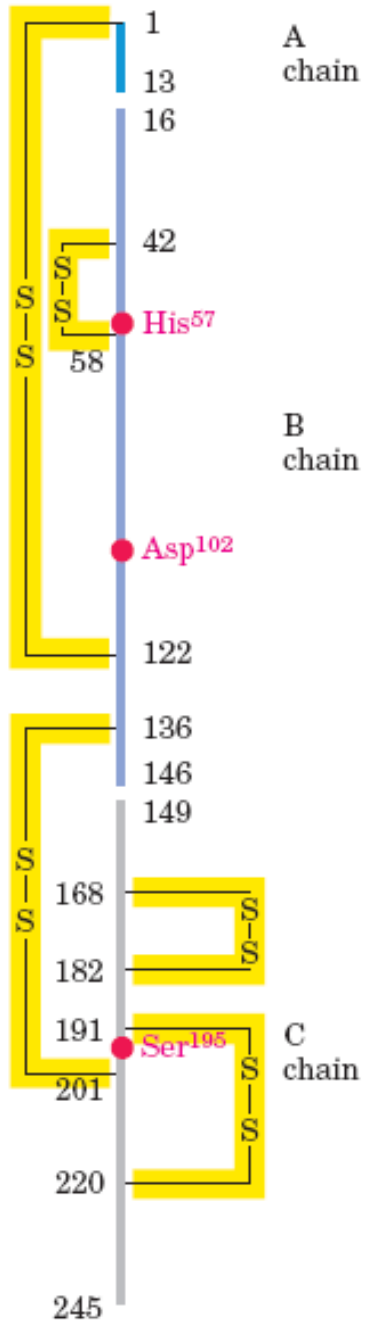
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# Bovine pancreatic chymotrypsin

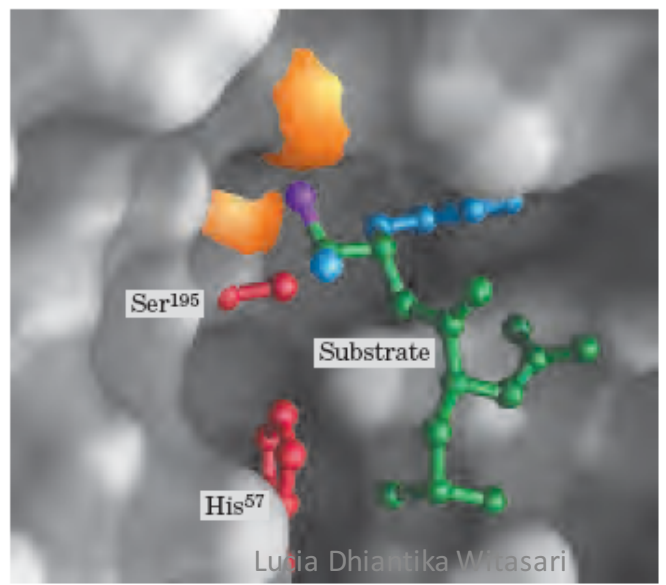
*(Mr 25,191)*

- *Is a protease*, an enzyme that catalyzes the hydrolytic cleavage of peptide bonds.
- specific for Trp, Phe, Tyr.

# Chymotrypsin structure

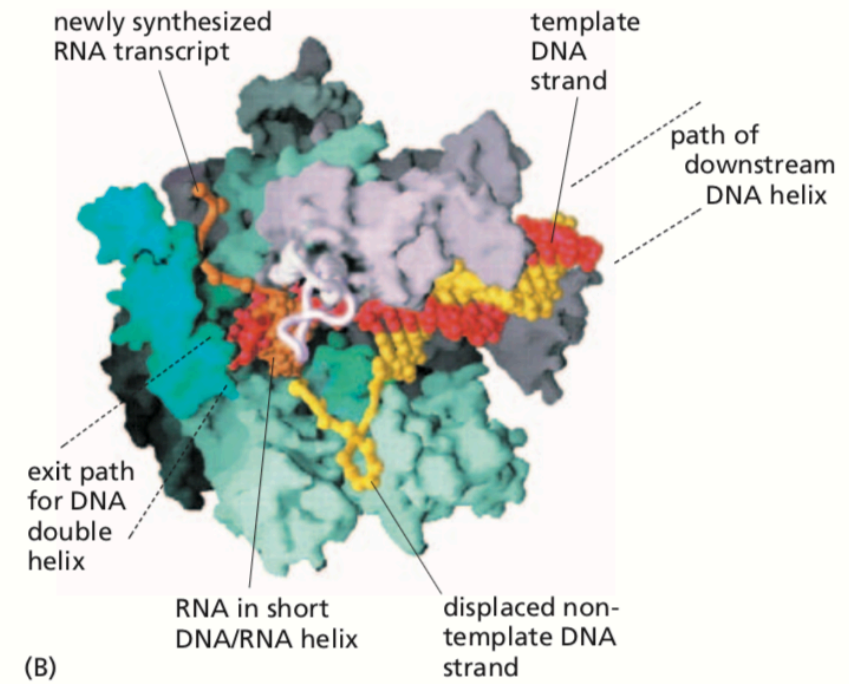
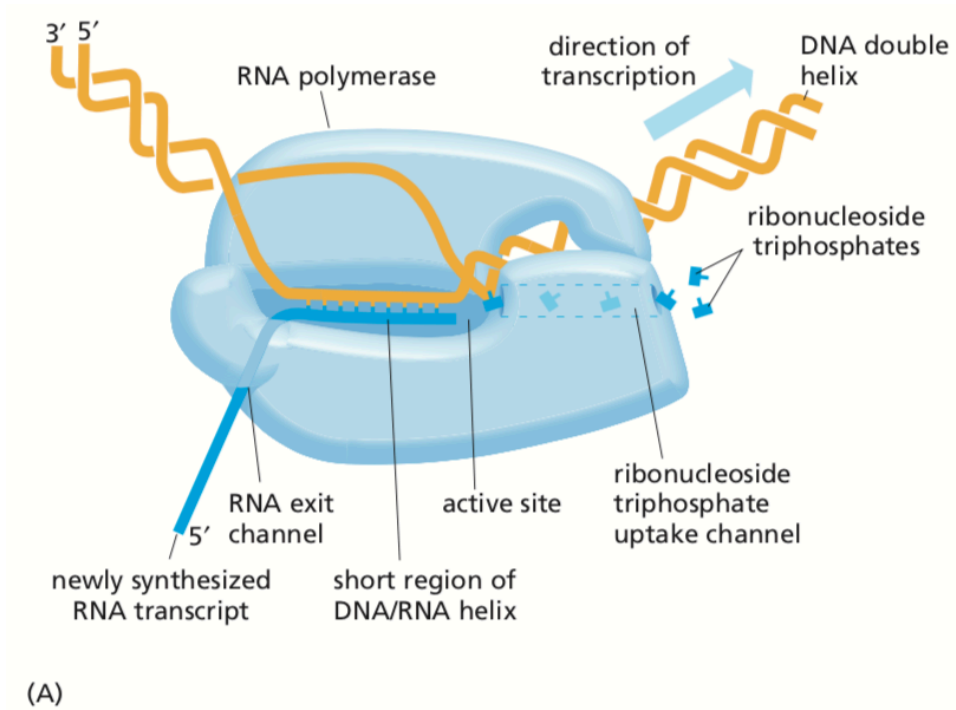
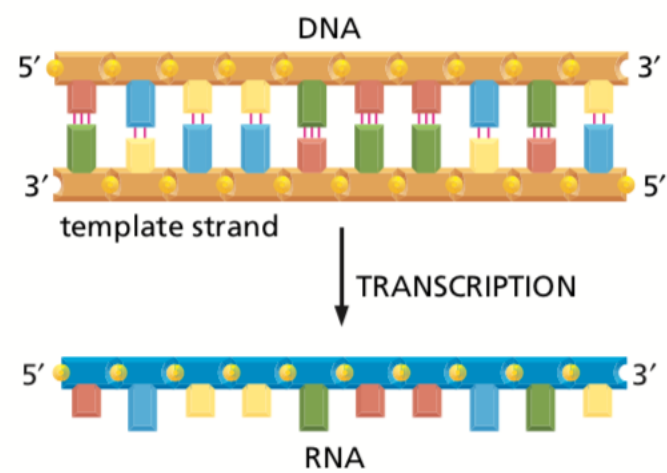


(c)



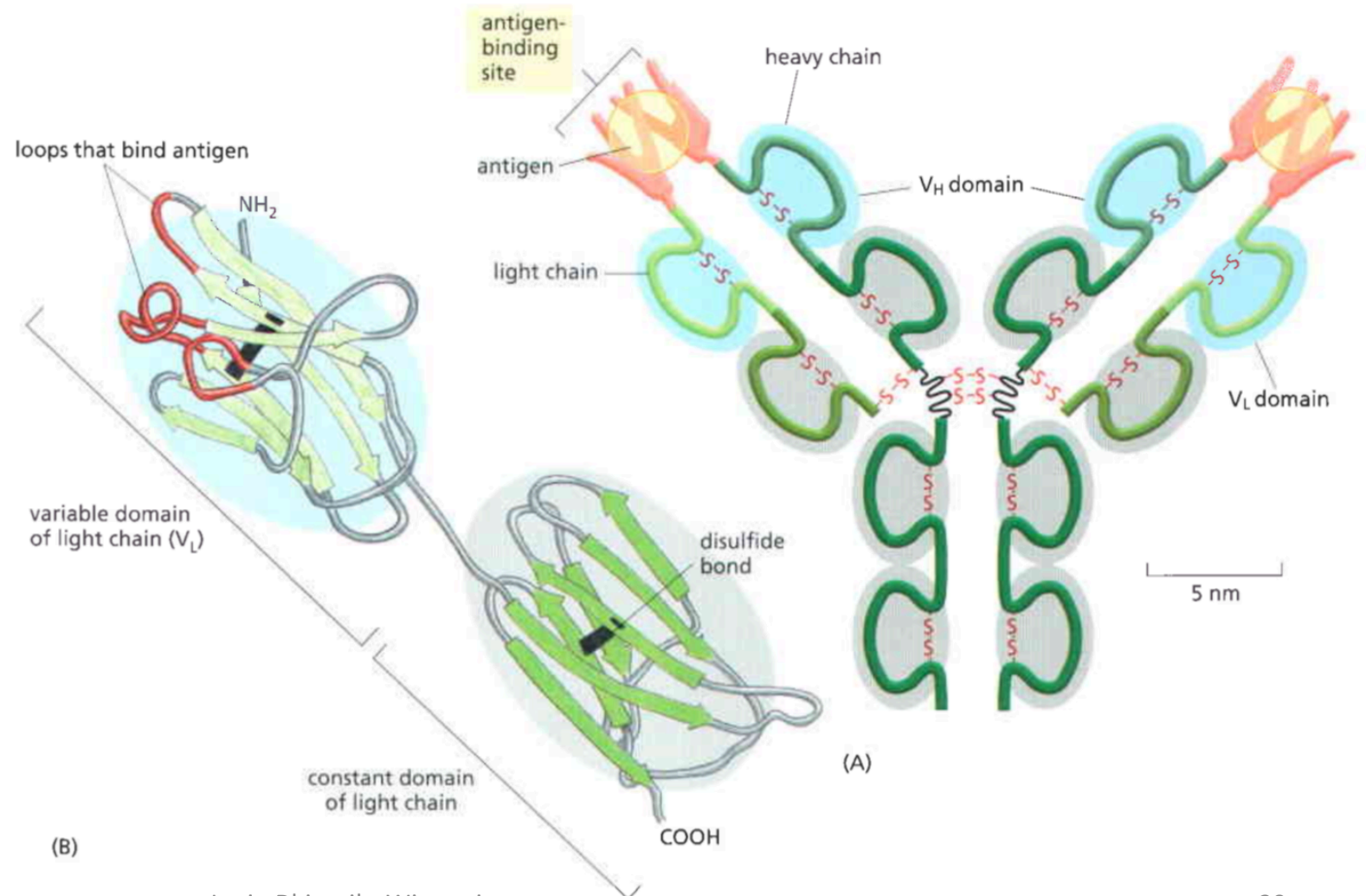
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# RNA polymerase

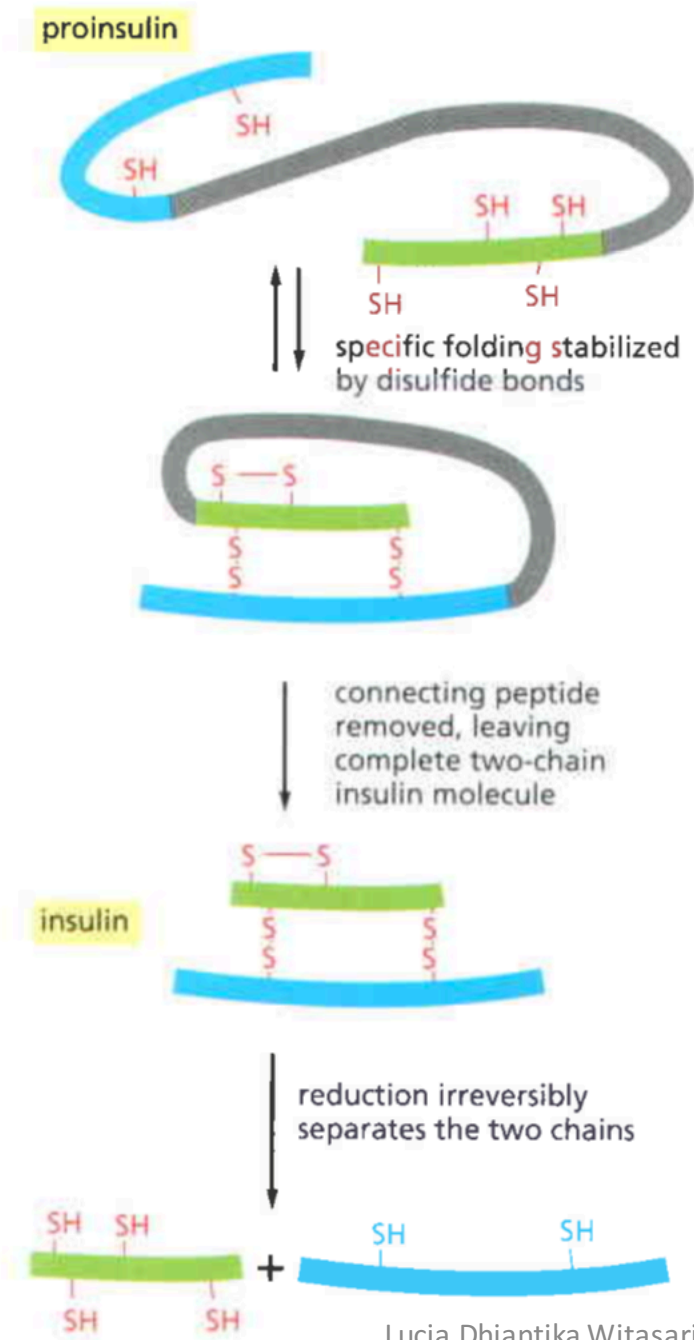


# Antibody or immunoglobulin

Antibody is protein produced by immune system in response to foreign molecule (antigen



# Hormone



**Figure 3–35 Proteolytic cleavage in insulin assembly.** The polypeptide hormone insulin cannot spontaneously re-form efficiently if its disulfide bonds are disrupted. It is synthesized as a larger protein (*proinsulin*) that is cleaved by a proteolytic enzyme after the protein chain has folded into a specific shape. Excision of part of the proinsulin polypeptide chain removes some of the information needed for the protein to fold spontaneously into its normal conformation. Once insulin has been denatured and its two polypeptide chains have separated, its ability to reassemble is lost.

# Protein Denaturation

- **Loss of Protein Structure Results in Loss of Function**  
→ denaturation
- Most proteins can be denatured by heat, which affects the weak interactions in a protein (primarily hydrogen bonds)

The very heat-stable proteins of thermophilic bacteria have evolved to function at the temperature of hot springs (~100 C). Why??



# What else?

Proteins can be denatured by :

- **extremes of pH,**
- by certain **miscible organic solvents** such as alcohol or acetone,
- by certain solutes such as **urea and guanidine hydrochloride,**
- by **detergents.**

**no covalent bonds in  
the polypeptide chain are broken**

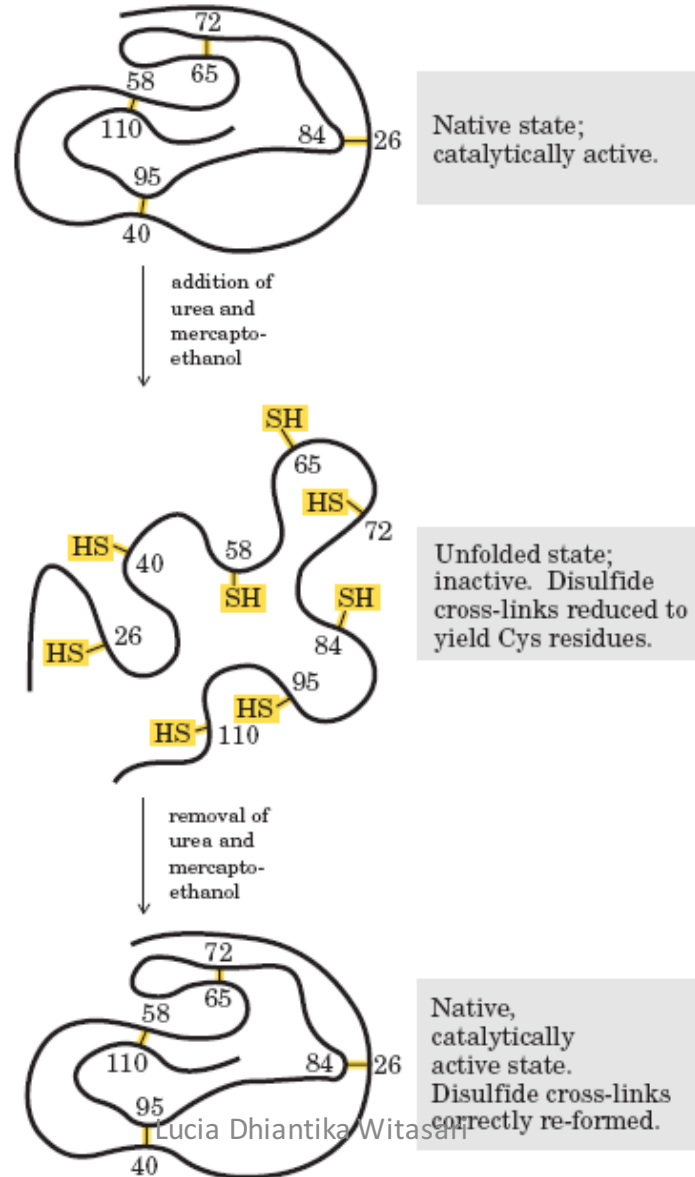
- extremes of pH alter the **net charge** on the protein, causing electrostatic repulsion and the disruption of some **hydrogen bonding**.
- Organic solvents, urea, and detergents act primarily by disrupting the **hydrophobic interactions** that make up the stable core of globular proteins;

# Denaturation of some proteins = reversible or irreversible?

- Certain globular proteins denatured by heat, extremes of pH, or denaturing reagents will regain their native structure and their biological activity...

if returned to conditions in which the native conformation is stable → **renaturation.**

# Renaturation of unfolded, denatured ribonuclease



# Recommended video for learning

- <https://www.youtube.com/watch?v=wvTv8TqWC48>
- <https://www.youtube.com/watch?v=qBRFIMcxZNM>
- <https://www.youtube.com/watch?v=2BsnnhMC0Ms>

## References

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