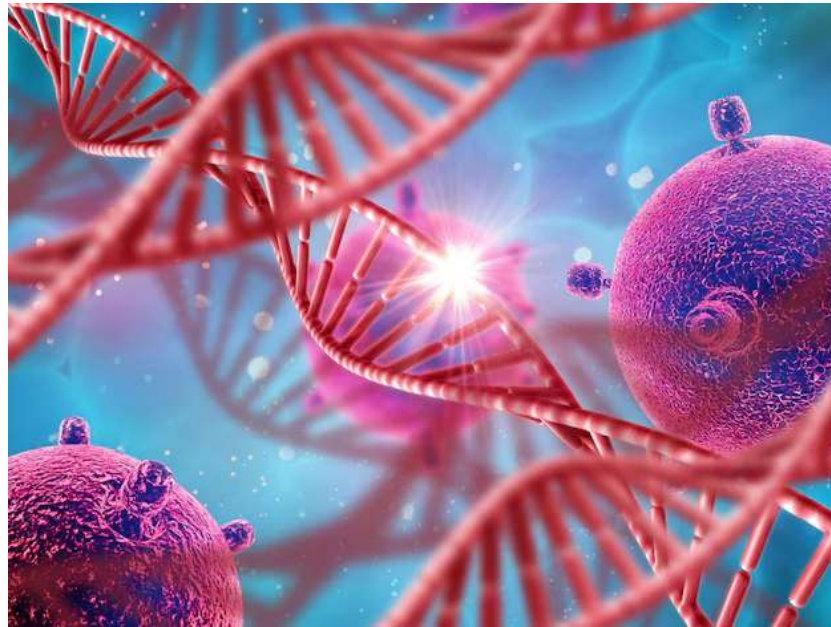


# Lecture 7

## General Biology & Cytology Course 2301130



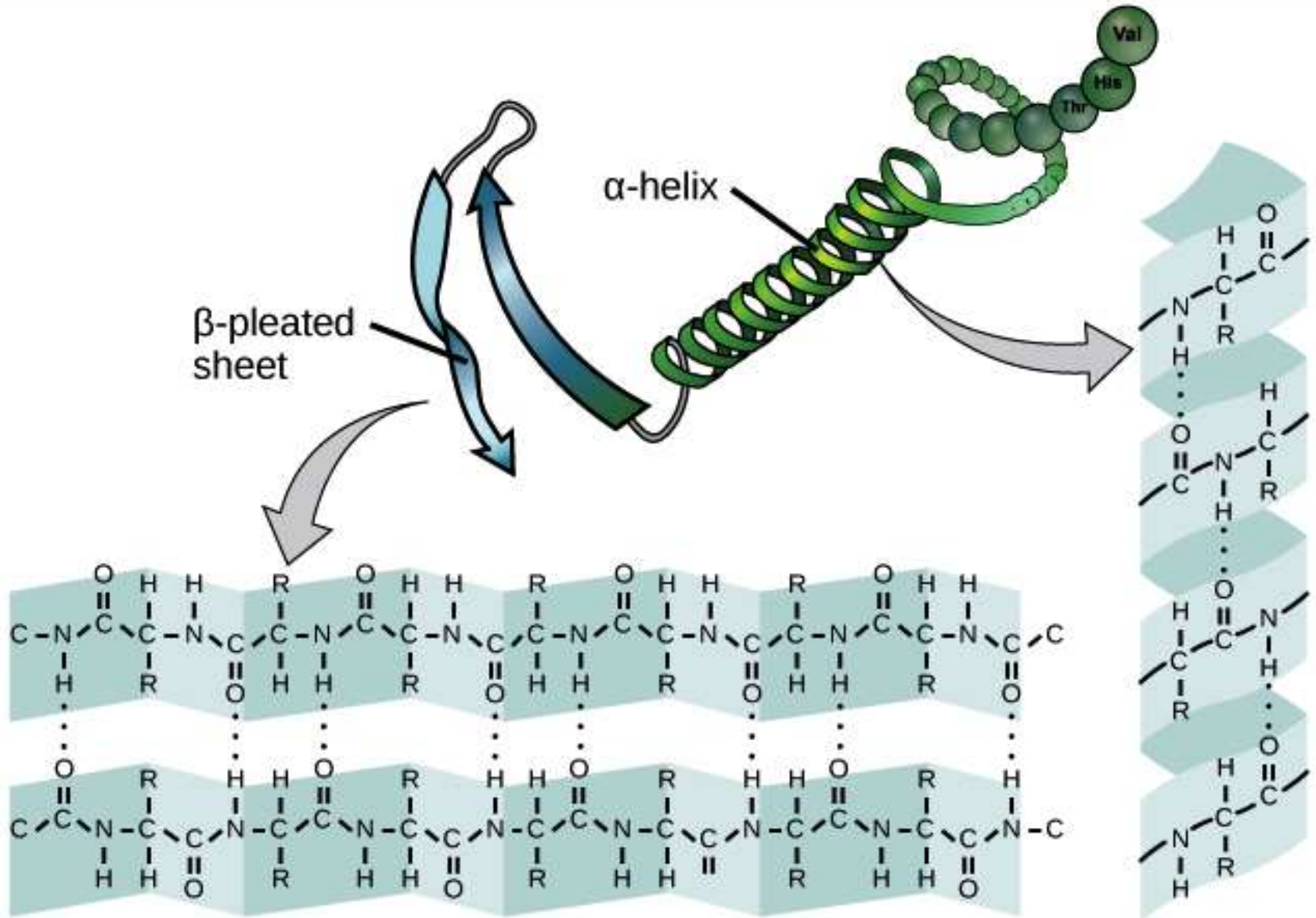
**Faculty of Dentistry, Mutah University**

**Dr. Samer Yousef Alqaraleh**

- **Secondary Structure:** refers to local folded structures that form within a polypeptide due to interactions between atoms of the backbone. (The backbone just refers to the polypeptide chain apart from the R groups — so all we mean here is that secondary structure does not involve R group atoms).

- Two common examples of secondary structures are
  - **$\alpha$  helix**
  - **$\beta$  pleated sheet**
- Both structures are held in shape by hydrogen bonds, which form between the carbonyl **O** of one amino acid and the amino **H** of another.

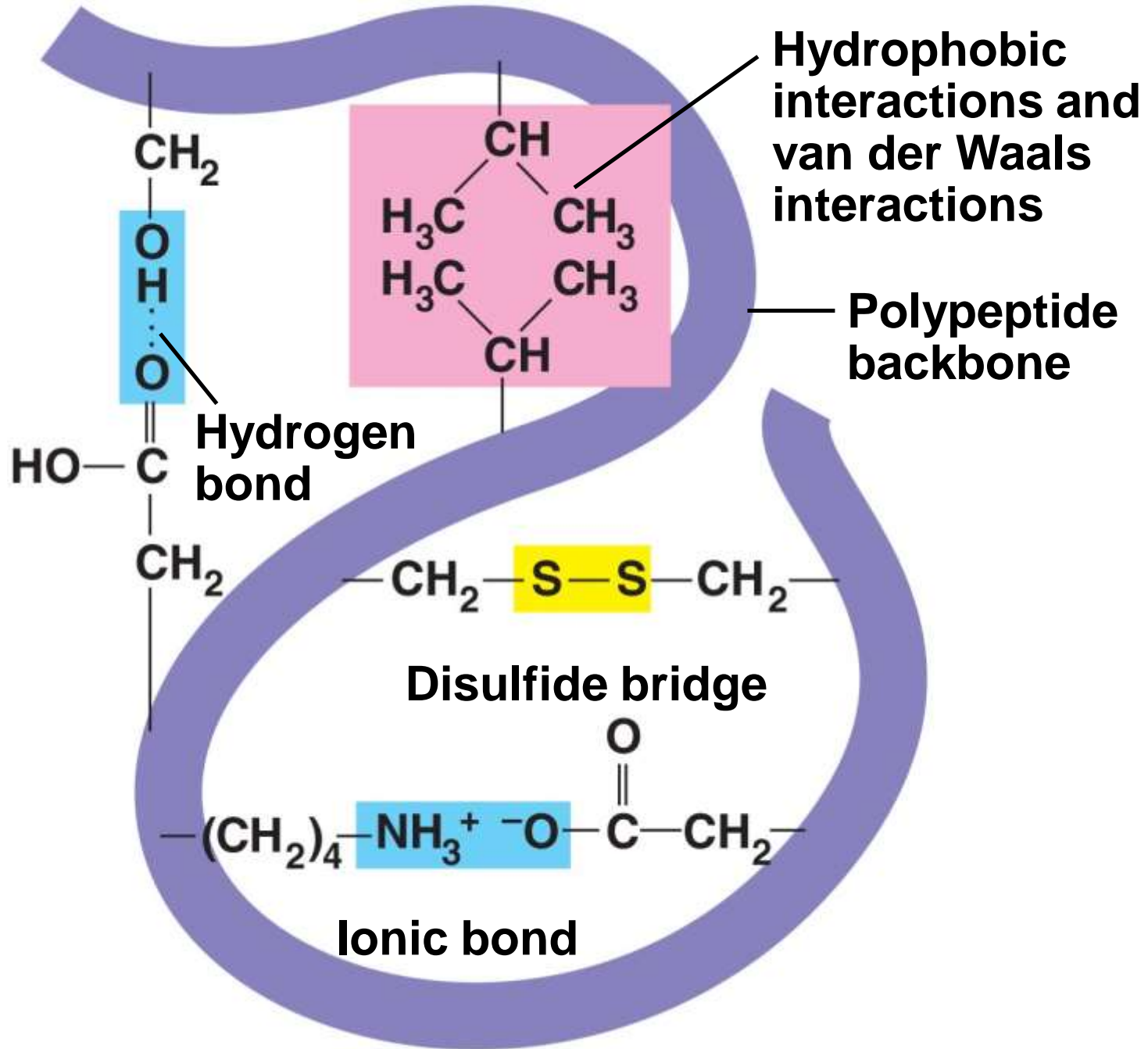
# Secondary Protein Structure



In an  **$\alpha$  helix**, the carbonyl (C=O) of one amino acid is hydrogen bonded to the amino H (N-H) of an amino acid that is four down the chain. (E.g., the carbonyl of amino acid 1 would form a hydrogen bond to the N-H of amino acid 5.) This pattern of bonding pulls the polypeptide chain into a helical structure.

**$\beta$  pleated sheet**, two or more segments of a polypeptide chain line up next to each other, forming a sheet-like structure held together by hydrogen bonds. The hydrogen bonds form between carbonyl and amino groups of backbone. The strands of a  $\beta$  pleated sheet may be **parallel**, pointing in the same direction (meaning that their N- and C-termini match up), or **antiparallel**, pointing in opposite directions (meaning that the N-terminus of one strand is positioned next to the C-terminus of the other).

- **Tertiary structure:** The overall three-dimensional structure of a polypeptide.
- Determined by interactions between R groups, rather than interactions between backbone constituents
- These interactions between R groups include hydrogen bonds, ionic bonds, **hydrophobic interactions**, and van der Waals interactions
- A special type of covalent bond that can contribute to tertiary structure: the **disulfide bond** between the sulfur-containing side chains of cysteines, are much stronger than the other types of bonds that contribute to tertiary structure.



- Many proteins are made up of a single polypeptide chain and have only three levels of structure.
- However, some proteins are made up of multiple polypeptide chains, also known as subunits.
- When these subunits come together, they give the protein its **quaternary structure**.

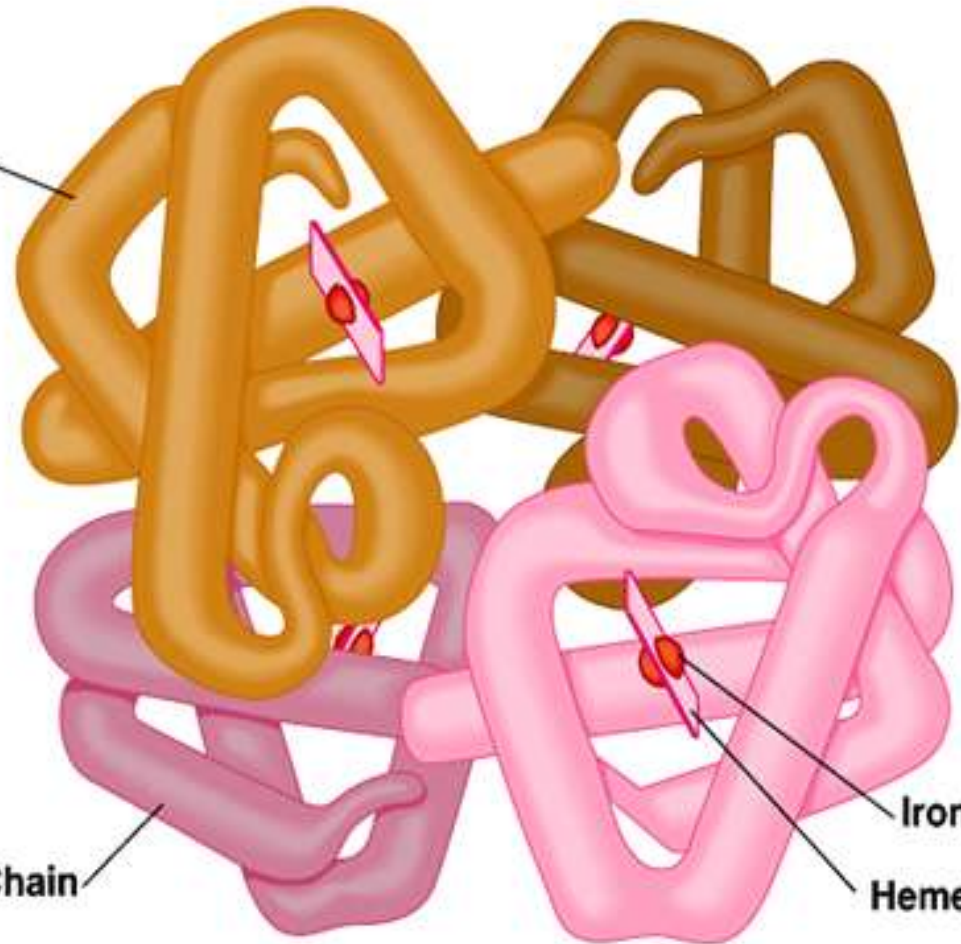
- **Quaternary structure** results when two or more polypeptide chains form one macromolecule. **Examples:**
- **Collagen** is a fibrous protein consisting of three polypeptides coiled like a rope
- **Hemoglobin** is a globular protein consisting of four polypeptides: two alpha and two beta chains.
- **DNA polymerase**, an enzyme that synthesizes new strands of DNA and is composed of ten subunits.
- In general, the same types of interactions that contribute to tertiary structure (mostly weak interactions, such as hydrogen bonding and London dispersion forces) also hold the subunits together to give quaternary structure.





Polypeptide chain

**(a) Collagen**



$\beta$  Chain

$\alpha$  Chain

Iron

Heme

**(b) Hemoglobin**

## *Sickle-Cell Disease: A Change in Primary Structure*

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- A slight change in primary structure can affect a protein's structure and ability to function
- Sickle-cell disease, an inherited blood disorder, results from a single amino acid substitution in the protein hemoglobin.

Primary structure

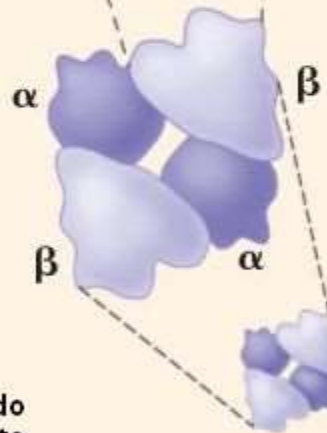
Normal hemoglobin  
Val His Leu Thr Pro Glu Glu  
1 2 3 4 5 6 7

Secondary and tertiary structures



Quaternary structure

Normal hemoglobin (top view)



Function

Molecules do not associate with one another; each carries oxygen.

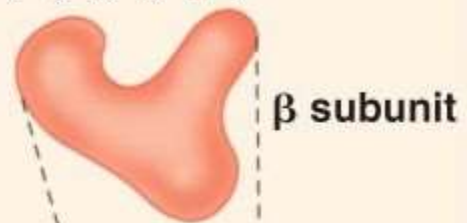


Primary structure

Sickle-cell hemoglobin  
Val His Leu Thr Pro Val Glu  
1 2 3 4 5 6 7

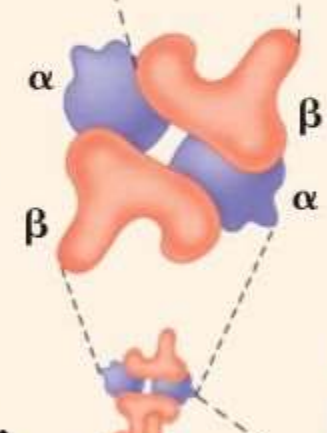
Secondary and tertiary structures

Exposed hydrophobic region



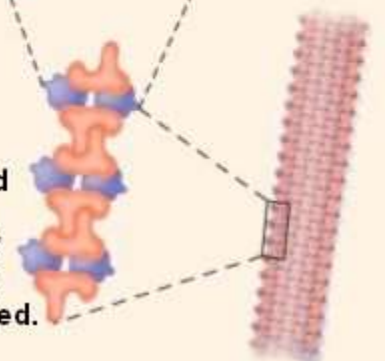
Quaternary structure

Sickle-cell hemoglobin

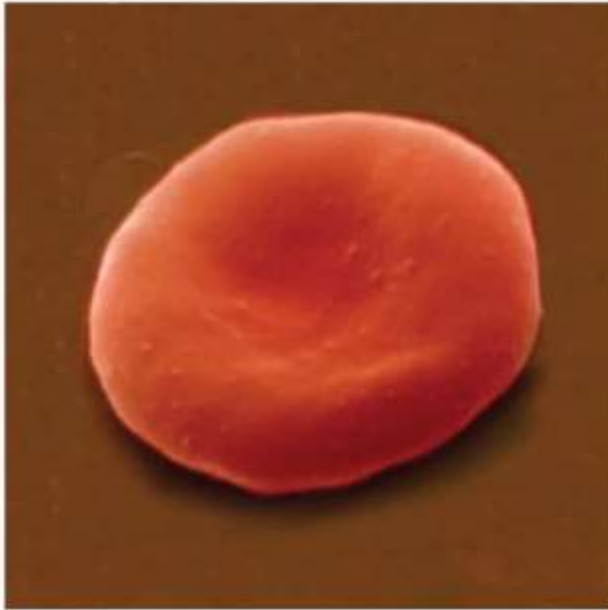


Function

Molecules interact with one another and crystallize into a fiber; capacity to carry oxygen is greatly reduced.



10  $\mu\text{m}$



**Normal red blood cells are full of individual hemoglobin molecules, each carrying oxygen.**

10  $\mu\text{m}$



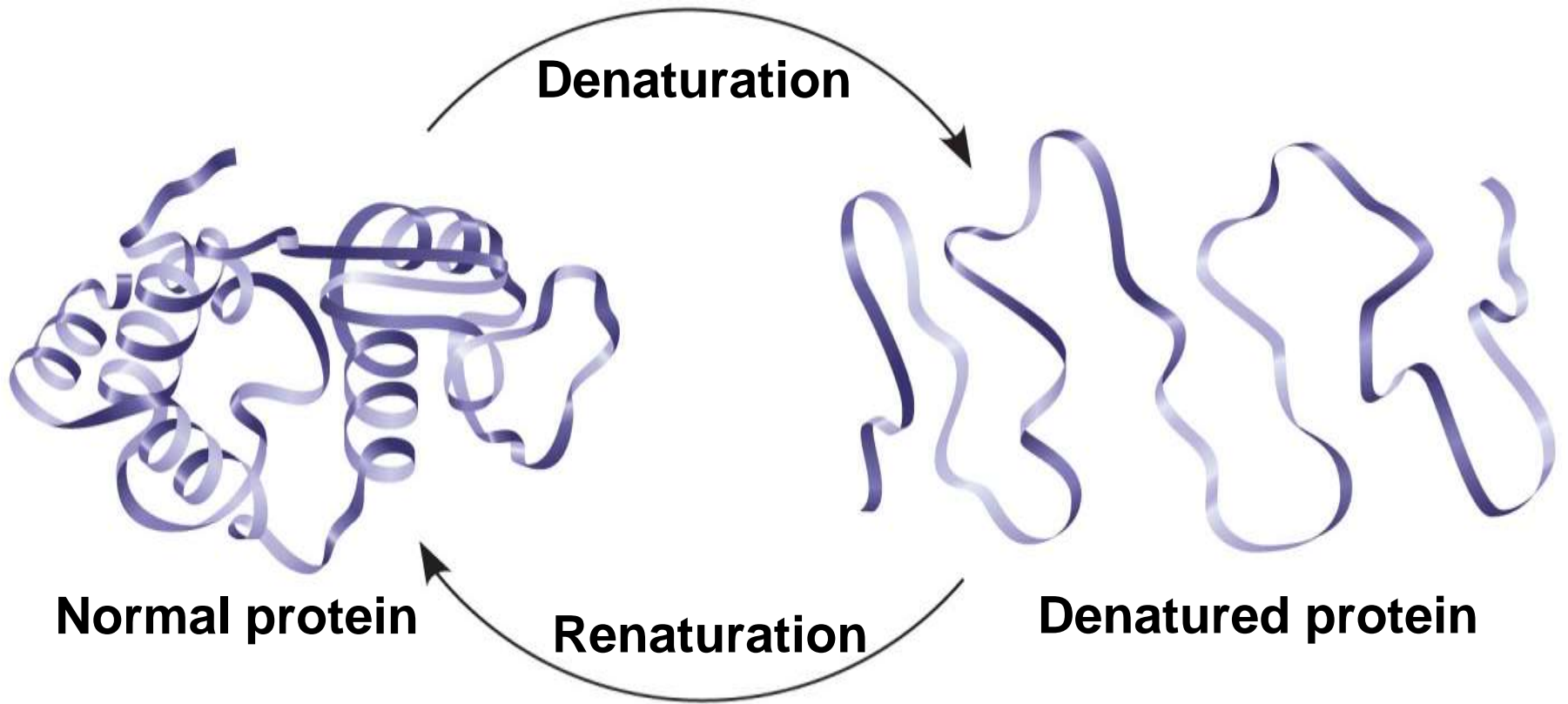
**Fibers of abnormal hemoglobin deform red blood cell into sickle shape.**

## *What Determines Protein Structure?*

- In addition to primary structure, physical and chemical conditions can affect structure
- Alterations in pH, salt concentration, temperature, Acids and bases, or other environmental factors can cause a protein to unravel
- This loss of a protein's native structure is called **denaturation**
- A denatured protein is biologically inactive

# The organized structure of protein is affected by denaturation in varied ways:

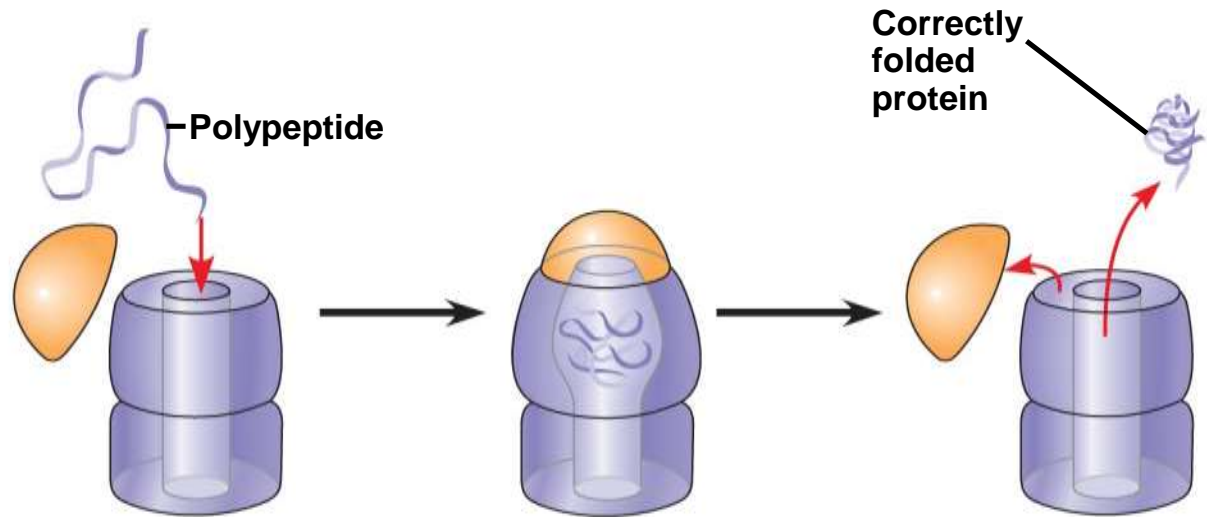
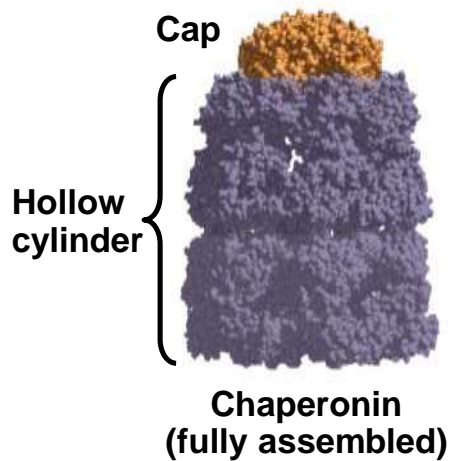
1. **In Primary Structure**: the sequence of amino acids held together by covalent peptide bonds, is not disrupted by denaturation.
2. **In Secondary Structure**: denaturation, proteins lose all regular repeating patterns such as alpha-helices and beta-pleated sheets, and adopt a random coil configuration
3. **In Tertiary structure**: denaturation involves the disruption of 3D structure.
4. **In quaternary structure**: Denaturation, protein sub-units are dissociated and/or the spatial arrangement of protein subunits is disrupted.



# *Protein Folding in the Cell*

- It is hard to predict a protein's structure from its primary structure
- Most proteins probably go through several states on their way to a stable structure
- **Chaperonins:** are protein molecules, in human mostly found in ER, that required for:
  - Correct folding.
  - Transport
  - Degradation of other proteins in vivo



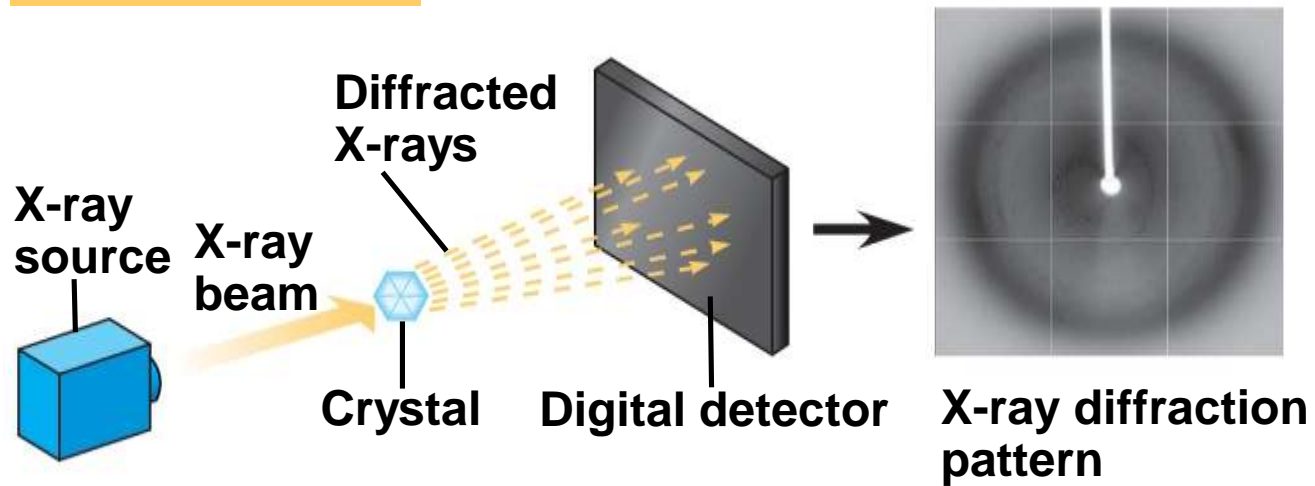


**Steps of Chaperonin Action:**

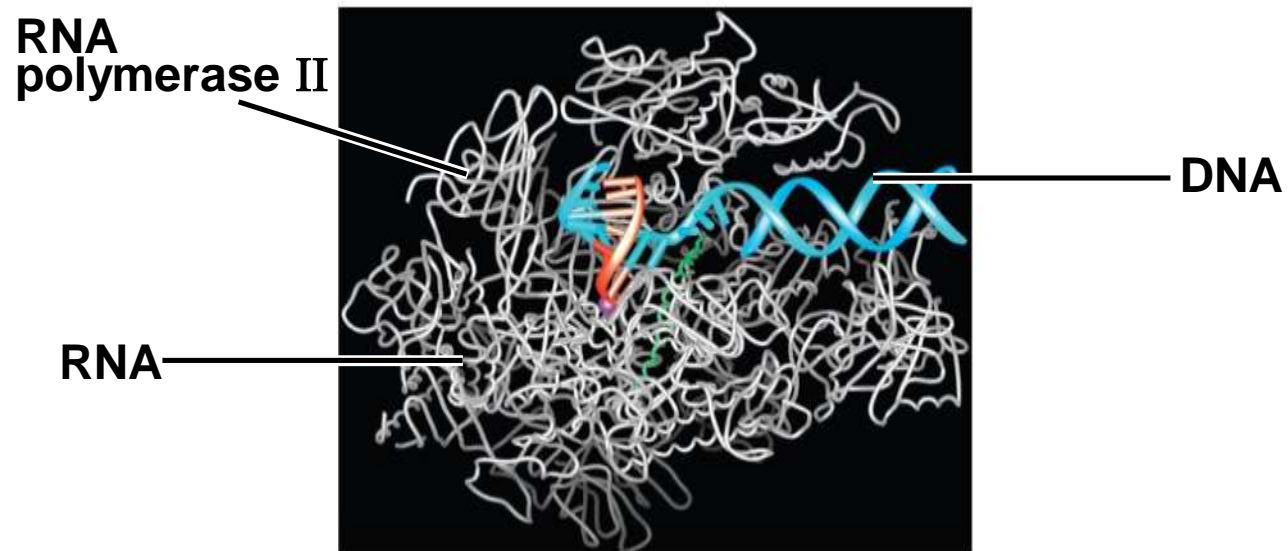
- 1 An unfolded polypeptide enters the cylinder from one end.
- 2 The cap attaches, causing the cylinder to change shape in such a way that it creates a hydrophilic environment for the folding of the polypeptide.
- 3 The cap comes off, and the properly folded protein is released.

- Scientists use **X-ray crystallography** to determine a protein's structure.
- Pauling had discovered the secondary structure of proteins using X-ray crystallography.
- Another method is nuclear magnetic resonance (**NMR**) spectroscopy, which does not require protein crystallization
- **Bioinformatics** uses computer programs to predict protein structure from amino acid sequences

## EXPERIMENT



## RESULTS



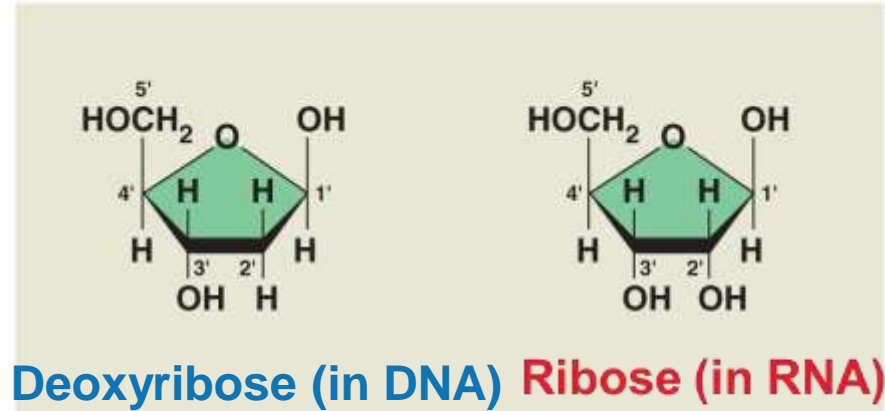
# Nucleic acids

- Store and transmit hereditary information.
- The amino acid sequence of a polypeptide is programmed by a unit of inheritance called a **gene**
- Genes are made of DNA, a **nucleic acid**
- In eukaryotic cells, DNA forms a complex with histone proteins to form chromatin, the substance of eukaryotic chromosomes.
- A chromosome may contain tens of thousands of genes. Many genes contain the information to make protein products; other genes code for RNA products. DNA controls all of the cellular activities by turning the genes “on” or “off.”

- The other type of nucleic acid, RNA, is mostly involved in protein synthesis.
- DNA molecules use an intermediary, called messenger RNA (mRNA), to communicate with the rest of the cell.
- Other types of RNA, such as rRNA, tRNA, and microRNA, are involved in protein synthesis and its regulation.
- DNA and RNA are made up of monomers known as **nucleotides**.
- The nucleotides combine with each other to form a nucleic acid, DNA or RNA.

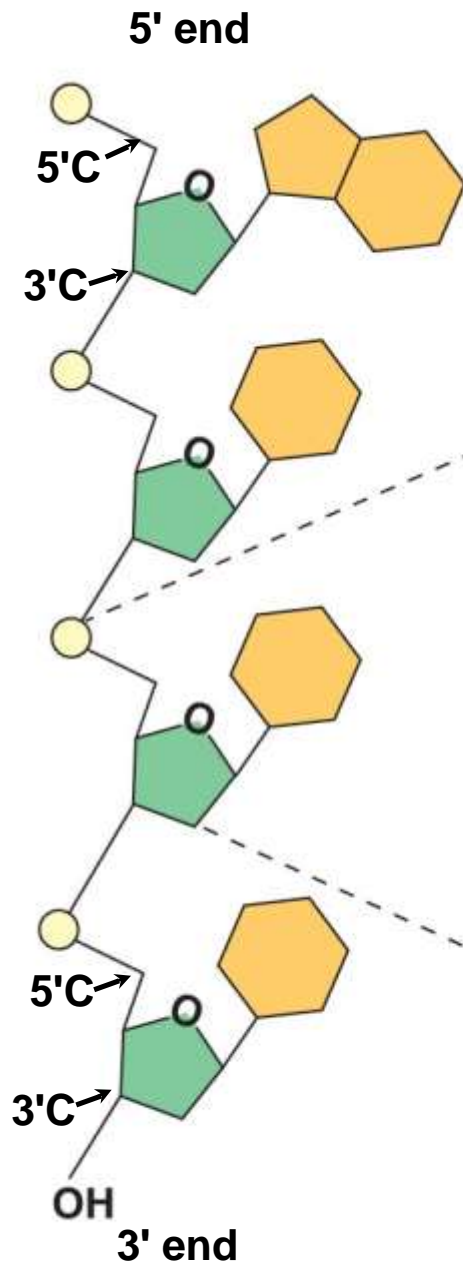
# The Roles of Nucleic Acids

- There are two types of nucleic acids:
  - **Deoxyribonucleic acid (DNA)**
  - **Ribonucleic acid (RNA)**
- DNA provides directions for its own replication
- DNA directs synthesis of messenger RNA (mRNA) and, through mRNA, controls protein synthesis
- Protein synthesis occurs in ribosomes



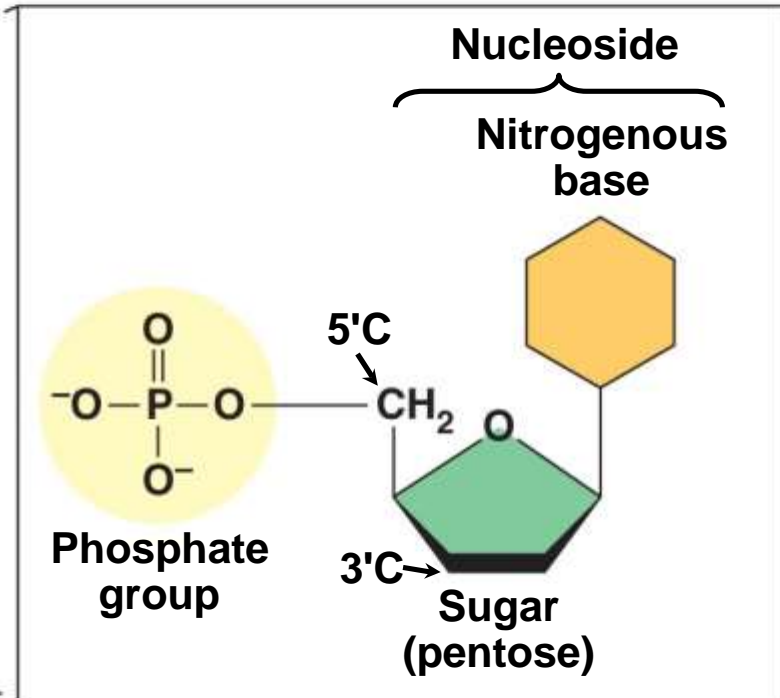
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- Nucleic acids are polymers called **polynucleotides**
  - Each polynucleotide is made of monomers called **nucleotides**
  - Each nucleotide consists of a nitrogenous base, a pentose sugar, and a phosphate group
  - The portion of a nucleotide without the phosphate group is called a ***nucleoside***



**(a) Polynucleotide, or nucleic acid**

Phosphodiester linkages are covalent bonds between the 3' carbon of one nucleotide and the 5' phosphate group of another.



**(b) Nucleotide**



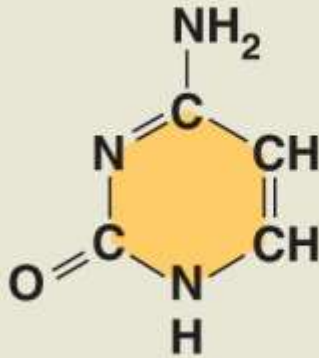
# *Nucleotide Monomers*

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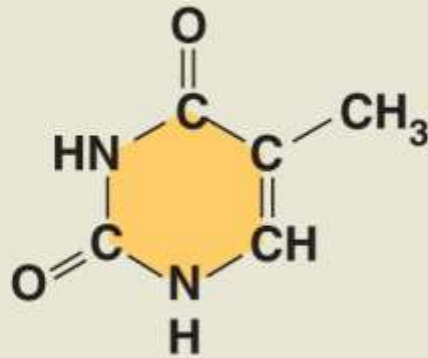
- Nucleoside = nitrogenous base + sugar
- There are two families of nitrogenous bases:
  - **Pyrimidines** (cytosine, thymine, and uracil) have a single six-membered ring
  - **Purines** (adenine and guanine) have a six-membered ring fused to a five-membered ring
- Nucleotide = nucleoside + phosphate group

## Nitrogenous bases

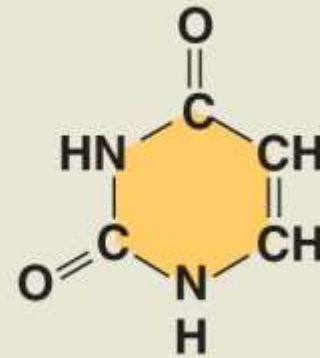
### Pyrimidines



Cytosine (C)

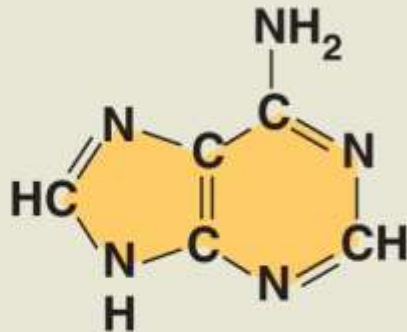


Thymine (T, in DNA)

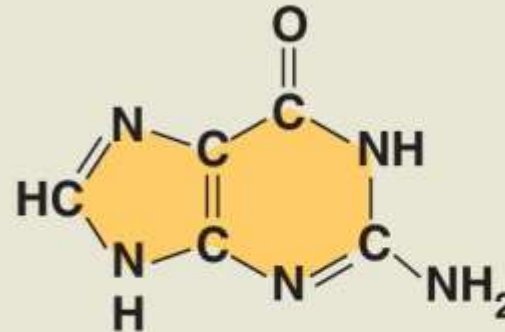


Uracil (U, in RNA)

### Purines



Adenine (A)



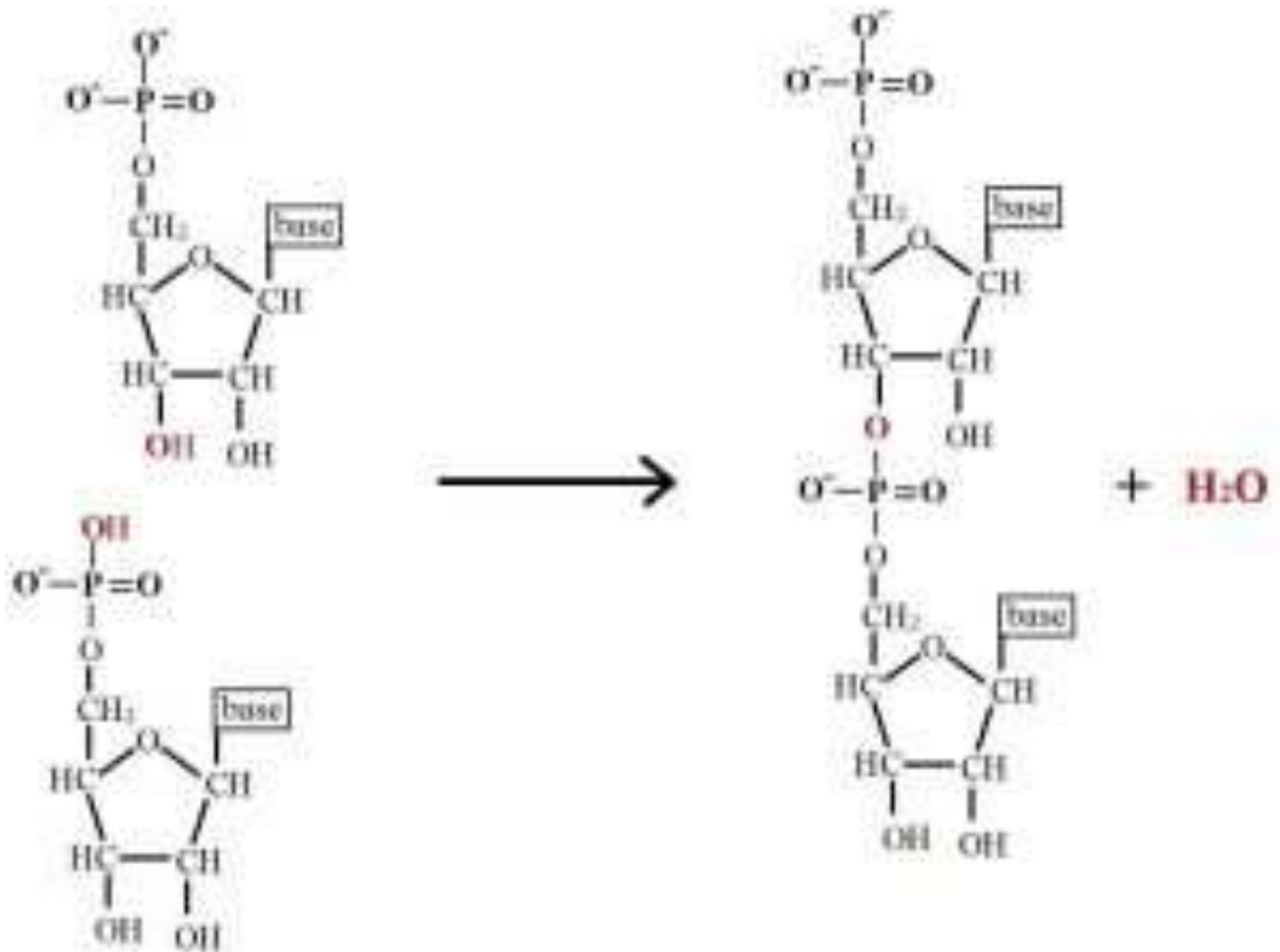
Guanine (G)

**(c) Nucleoside components: nitrogenous bases**

# *Nucleotide Polymers*

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- Nucleotide polymers are linked together to build a polynucleotide
- Adjacent nucleotides are joined by covalent bonds that form between the –OH group on the 3' carbon of one nucleotide and the phosphate on the 5' carbon on the next
- These links create a backbone of sugar-phosphate units with nitrogenous bases as appendages
- The sequence of bases along a DNA or mRNA polymer is unique for each gene

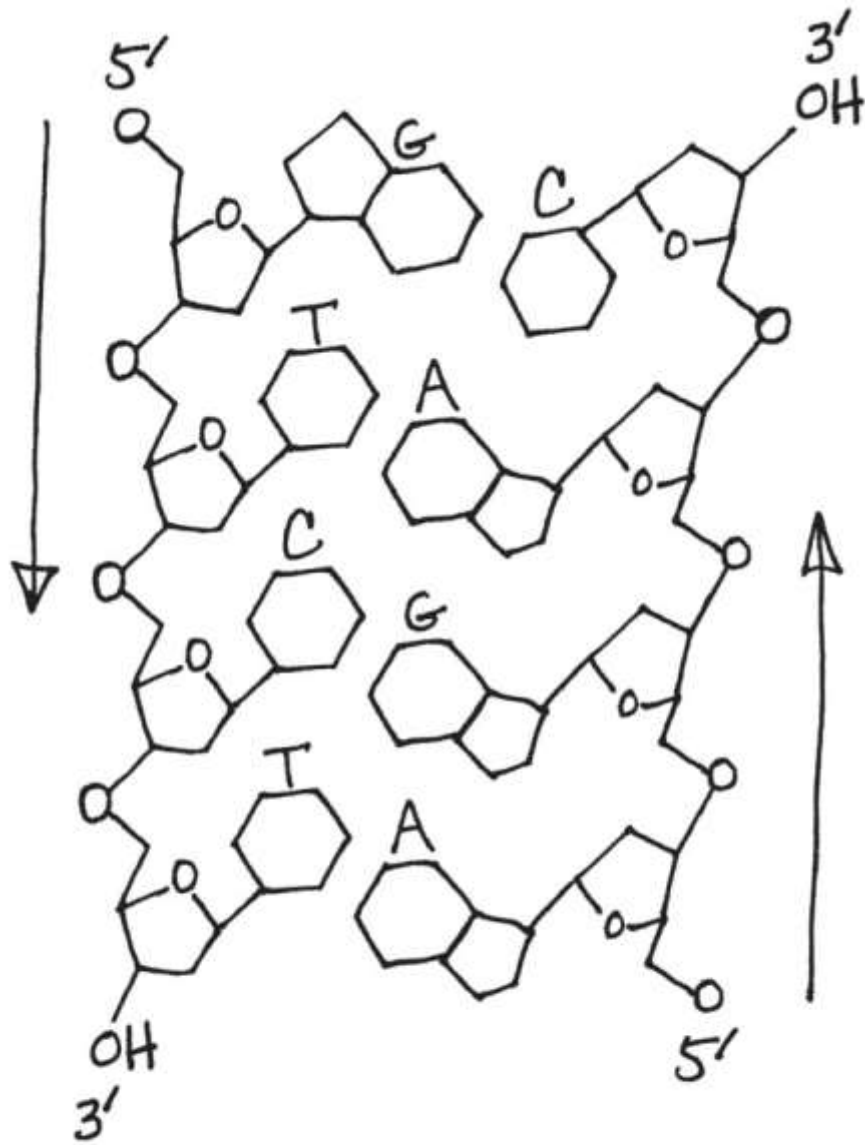


*They are formed by **dehydration synthesis reactions** when a hydroxyl group is removed from the 3' carbon of one nucleotide and a hydrogen atom is removed from the hydroxyl group attached to the 5' carbon of another nucleotide. Water is produced and a phosphodiester bond is formed.*

# The DNA Double Helix

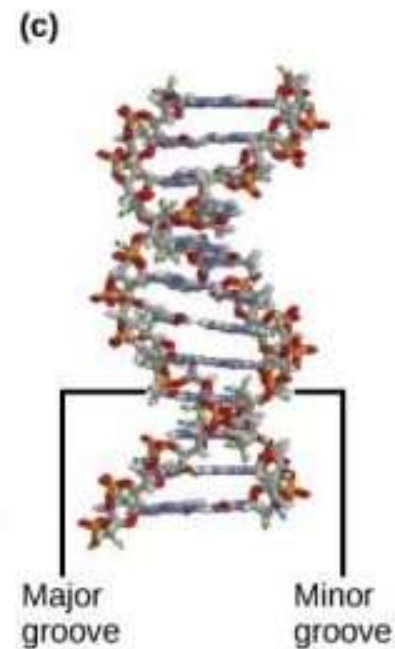
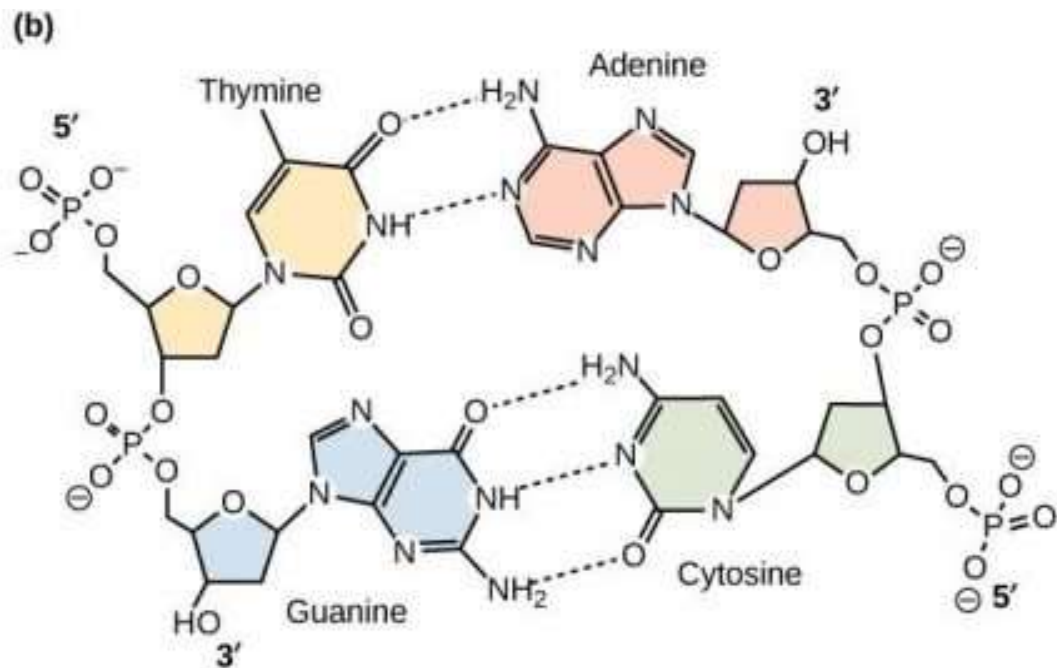
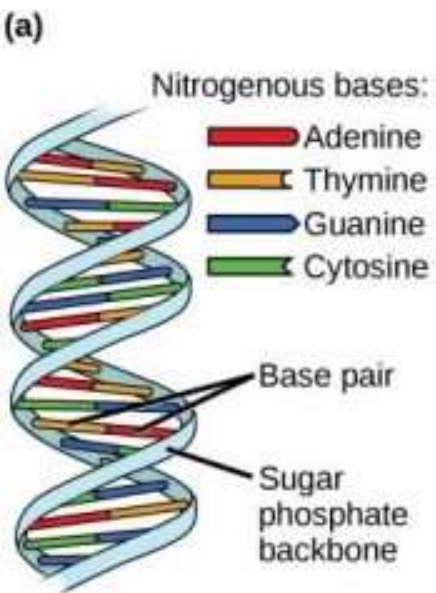
- In the 1950s, Francis Crick and James Watson worked together to determine the structure of DNA
- A DNA molecule has two polynucleotides spiraling around an imaginary axis, forming a **double helix**
- In the DNA double helix, the two backbones run in opposite 5' → 3' directions from each other, an arrangement referred to as **antiparallel**
- The nitrogenous bases in DNA pair up and form hydrogen bonds: adenine (A) always with thymine (T), and guanine (G) always with cytosine (C)

- Watson and Crick correctly proposed that DNA is made up of two strands that are twisted around each other to form a **right-handed helix**.
- Two strands of nucleotides are held together by hydrogen bonds that form between pairs of nitrogenous bases.
- The sugar and phosphate “backbone” forms the outside of the helix.
- The nitrogenous bases are stacked in the interior, like the steps of a ladder.



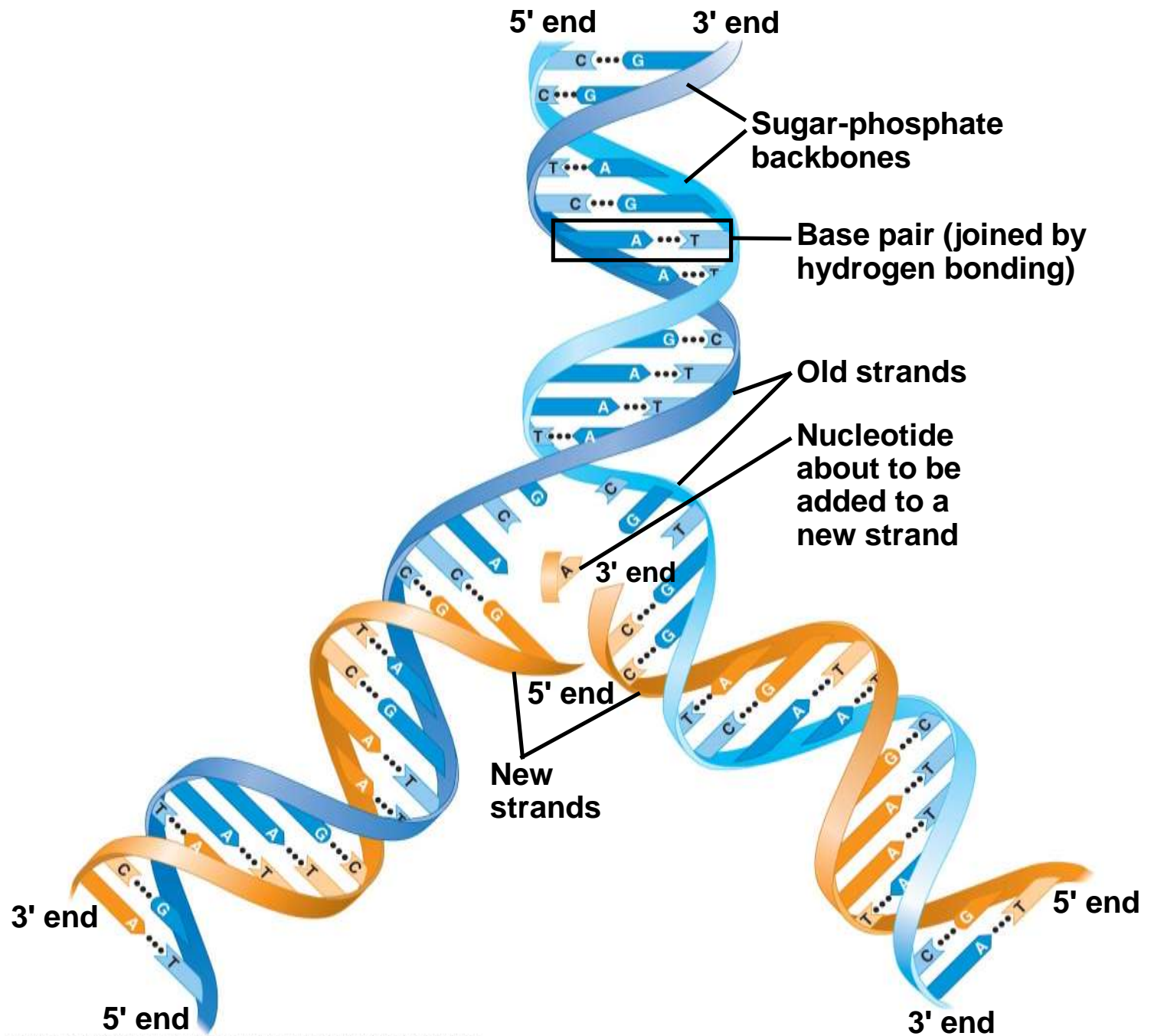
Original  
Strand

Complementary  
strand





- This is known as the base complementary rule.
- In other words, the DNA strands are complementary to each other.
- If the sequence of one strand is 5'-AATTGGCC-3', the complementary strand would have the sequence 3'-TTAACCGG-5'.
- The fact that the two strands of a DNA molecule are complementary allows DNA to replicate.
- During DNA replication, each strand is copied, resulting in a daughter DNA double helix containing one parental DNA strand and a newly synthesized strand.



# DNA and Proteins as Tape Measures of Evolution

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- The linear sequences of nucleotides in DNA molecules are passed from parents to offspring
- Two closely related species are more similar in DNA than are more distantly related species
- Molecular biology can be used to assess evolutionary kinship