

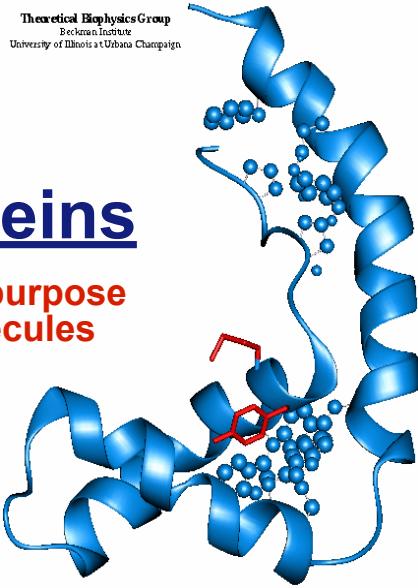


Theoretical Biophysics Group  
Beckman Institute  
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# Proteins

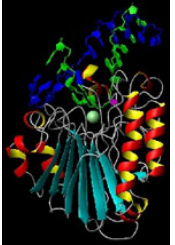
Multi-purpose molecules



# Proteins

**Most structurally & functionally diverse group**

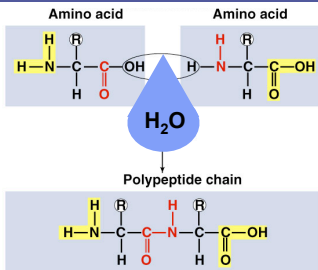
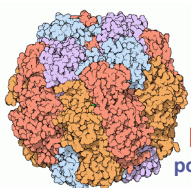
- Proteins are involved functionally in almost everything:
  - Enzymatic proteins** - Speed up chemical reactions
    - Pepsin, DNA polymerase
  - Structural Proteins** - Support
    - Keratin, collagen
  - Transport Proteins** - Transporation & Carrying
    - Hemoglobin, aquaporin
  - Signaling Proteins** - Send signals to coordinate activities
    - Insulin, adrenalin
  - Receptor Proteins** - Respond to external stimuli
  - Defense Proteins** - Disease Protection
    - Antibodies
  - Contractile & Motor Proteins** - Movement
    - Actin & myosin
  - Storage Proteins** - Storing amino acids
    - Ovalbumin, casein



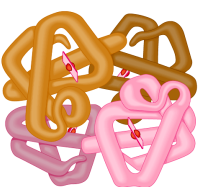
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# Proteins

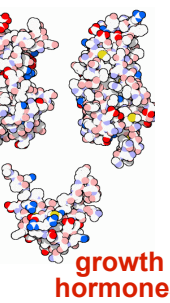
- Structure**
  - monomers = **amino acids**
    - 20 different amino acids
  - polymer = **polypeptide**
    - Proteins** consist of one or more polypeptide chains folded & bonded together
    - Can be very large macromolecules
    - Have complex 3-D shapes

**Hemoglobin** - 4 polypeptide chains



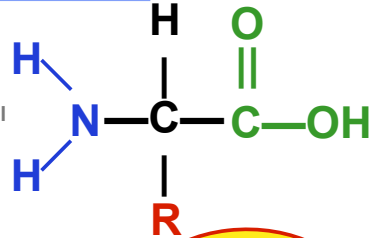
**Rubisco** - 16 polypeptide chains




**growth hormones**

# Amino acids

- Structure**
  - central  $\alpha$  carbon**
    - Only glycine has no asymmetrical carbon since its R group is an H.
  - amino group**
  - carboxyl group (acid)**
  - R group (side chain)**
    - variable group
    - different for each amino acid
    - confers unique chemical properties to each amino acid
      - Each becomes like a different letters of an alphabet
      - With 20 letters you can make many words (proteins)



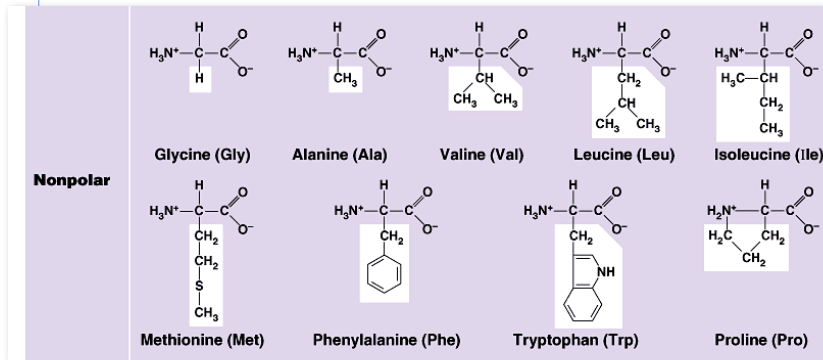
Oh, I get it!  
amino =  $\text{NH}_2$   
acid =  $\text{COOH}$



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## Effect of different R groups.

### ■ nonpolar & hydrophobic side chains

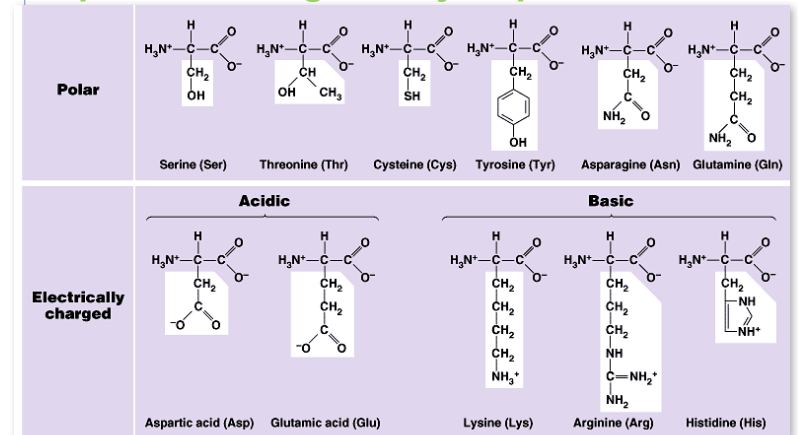


Why are these nonpolar & hydrophobic?

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## Effect of different R groups

### ■ polar or charged & hydrophilic

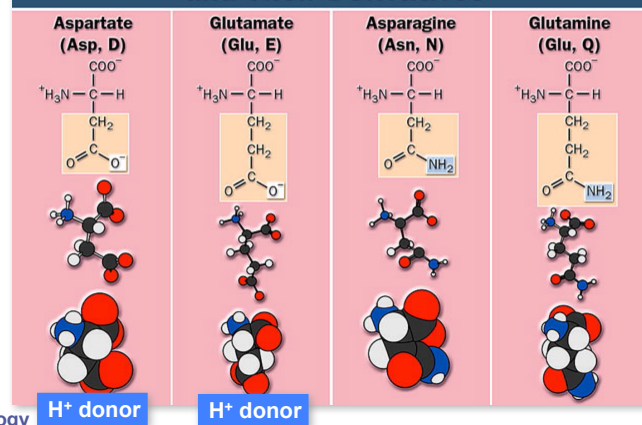


Why are these polar or charged & hydrophilic?

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## Ionizing in cellular waters - side chains that gain a full negative charge

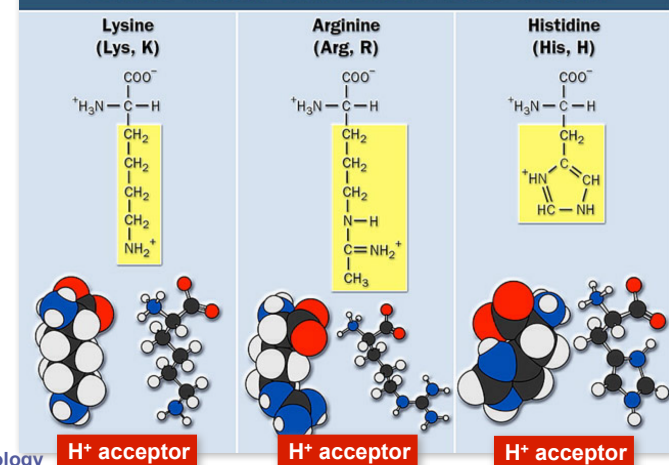
### Amino Acids with Acidic Side Chains and Their Derivatives



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## Ionizing in cellular waters - side chains that gain a full positive charge

### Amino Acids with Basic Side Chains

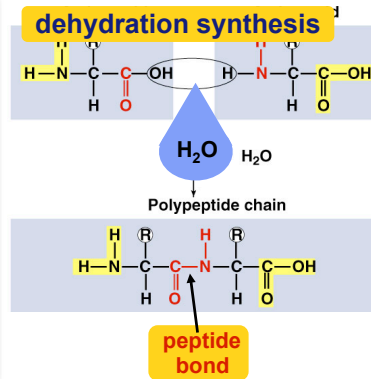
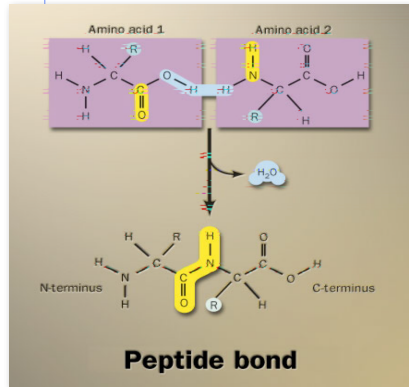


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## Building proteins involves building polymers of amino acids called **polypeptides**

### ■ **Peptide bonds**

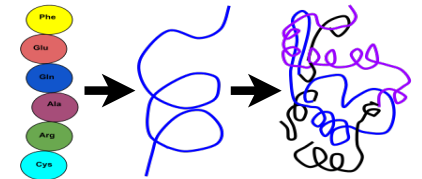
- ◆ **covalent** bond between  $\text{NH}_2$  (amine) of one amino acid &  $\text{COOH}$  (carboxyl) of another
- ◆ Creates a  $\text{C}-\text{N}$  bond between monomers (amino acids)



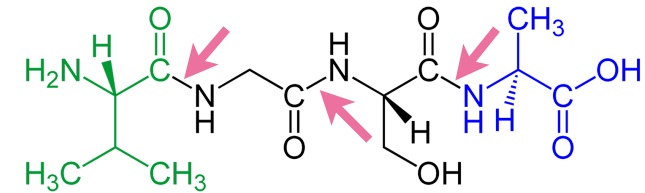
## Sample polypeptide

### ■ **Proteins are made up of ONE or MORE polypeptides**

- ◆ Polypeptides fold up into 3D shapes.
- ◆ One of more folded up polypeptides may come together to form a final functional protein



- Where are the peptide bonds in this sample polypeptide?



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## Sulfur containing R groups of amino acids

### ■ Can form **disulfide bridges**

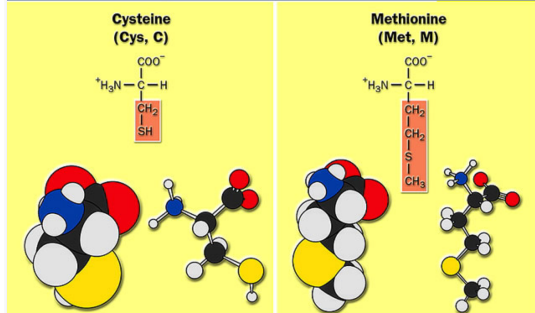
- ◆ **covalent** cross links between sulfhydryl functional groups
- ◆ stabilizes 3-D structures of folded up chains of amino acids

**R-S - S-R**

You wondered why perms smell like rotten eggs?



### Amino Acids with Sulfur-containing Side Chains

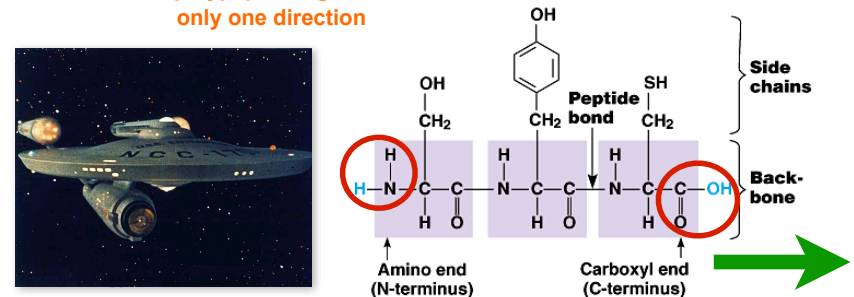


## Building proteins

### ■ Polypeptide chains have direction

- ◆ **N-terminus** =  $\text{NH}_2$  end
- ◆ **C-terminus** =  $\text{COOH}$  end
- ◆ repeated sequence (N-C-C) is the polypeptide backbone
- polypeptides grow in only one direction

Polypeptides 'grow' in one direction: From the N to the C terminal.

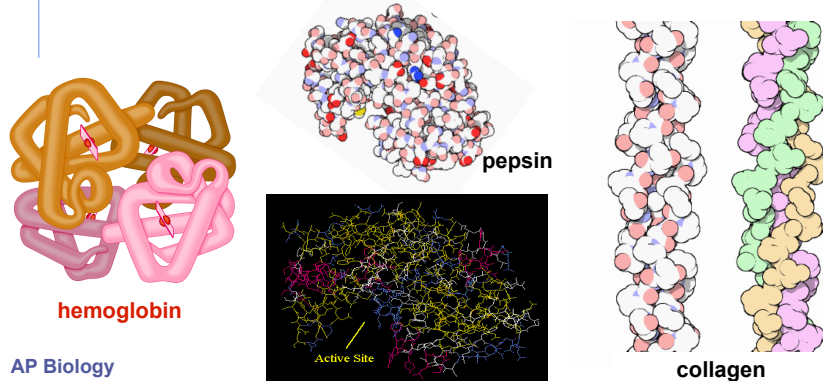


## Protein structure & function

### Function depends on structure

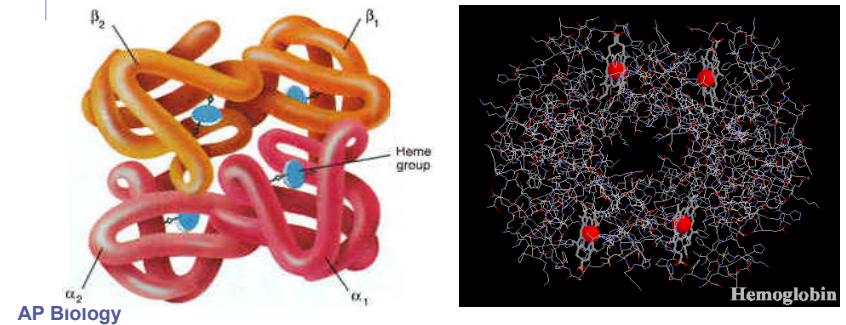
#### 3-D structure

- twisted, folded, coiled into unique shape



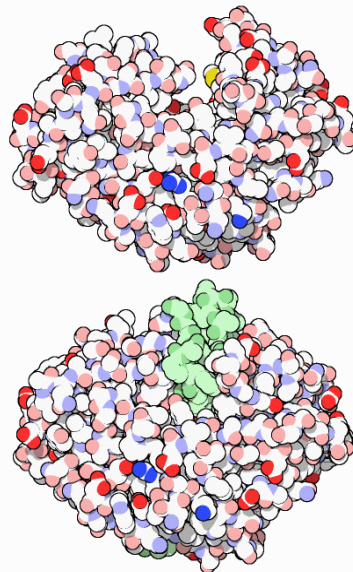
## Form fits function

- Hemoglobin is the protein found in **red blood cells**.
- It is composed of **four polypeptide chains**, two alpha chains and two beta chains, each with a ring-like '**heme**' group (of Cs and Ns) containing an iron atom at its center.
- Oxygen binds reversibly** to these iron atoms and is transported through blood through an ion-induced dipole intermolecular force.



## Form fits function

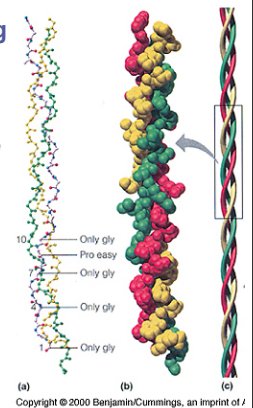
- Pepsin is the first in a series of enzymes in our **digestive system** that digest proteins.
- In the stomach, protein chains bind in the deep **active site** groove of pepsin, seen in the upper illustration and are **broken into smaller pieces**.
  - Then, a variety of proteases and peptidases in the intestine finish the job.
- The small fragments--amino acids and dipeptides--are then **absorbed by cells for use as metabolic fuel or construction of new proteins**.



## Form fits function

### The most plentiful protein in bodies.

- About 1/4 of all of the protein in your body is collagen.
- Collagen is a **major structural protein**, forming molecular cables that strengthen the tendons and vast, resilient sheets that support the skin and internal organs. Bones and teeth are made by adding mineral crystals to collagen.
- Collagen **provides structure to our bodies**, protecting and supporting the softer tissues and connecting them with the skeleton.

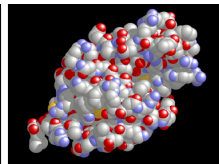
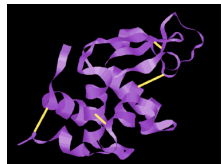




## Primary (1°) structure of Proteins

### Order of amino acids in chain

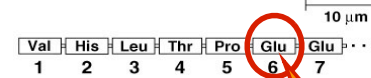
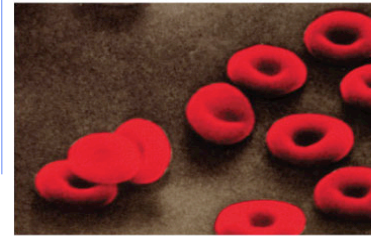
- amino acid sequence determined by the genes (DNA)
- slight change in amino acid sequence can affect protein's structure & its function
  - even just one amino acid change can make all the difference!



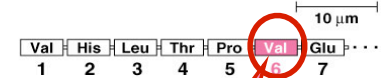
lysozyme: enzyme in tears & mucus that kills bacteria

## Sickle cell anemia

Just 1 wrong out of 146 amino acids!



(a) Normal red blood cells and the primary structure of normal hemoglobin



(b) Sickled red blood cells and the primary structure of sickle-cell hemoglobin

I'm Glutamic Acid & hydrophilic!

But I'm Valine & hydrophobic!

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## Sickle cell anemia

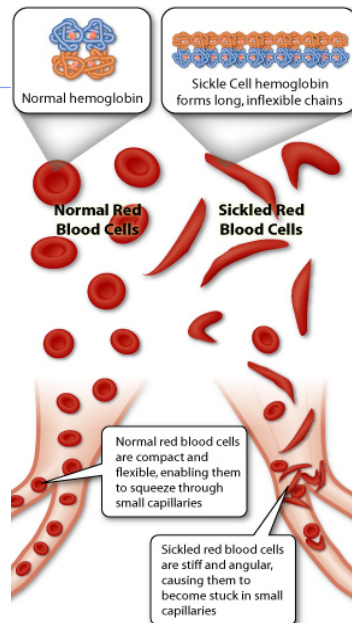
**Non-polar Val** is now stuck facing the aqueous solution but does not interact with polar water molecules unlike polar Glu.

The non-polar Valines from adjacent polypeptide chains will **stick together**, excluded from water.

Instead of being separate proteins inside the red blood cell, **hemoglobins now stick together** forming **crystal-like chains** that can **carry O<sub>2</sub> less efficiently** & **distort the outer shape of the cell**.

Sickle shaped cells can form **clots** in the circulatory system.

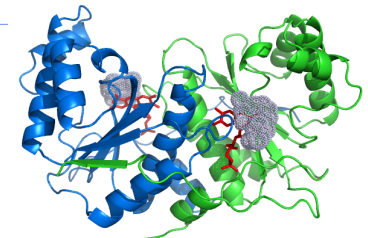
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## Secondary (2°) structure of Proteins

### "Local folding"

- folding along short sections of polypeptide backbone
- interactions between adjacent amino acids
  - Caused by **Hydrogen Bonding** between the **partially charged H** of the backbone amino acid's amino group and **partially negative O** of the backbone amino acid's carboxyl group
    - weak bonds between polypeptide backbone (not a.a. side chains!)
- Hydrogen bonding forms sections of 3-D structures
  - $\alpha$ -helixes**
  - $\beta$ -pleated sheets**
- One polypeptide can have both in different regions



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## Secondary (2°) structure

### 3-D structures

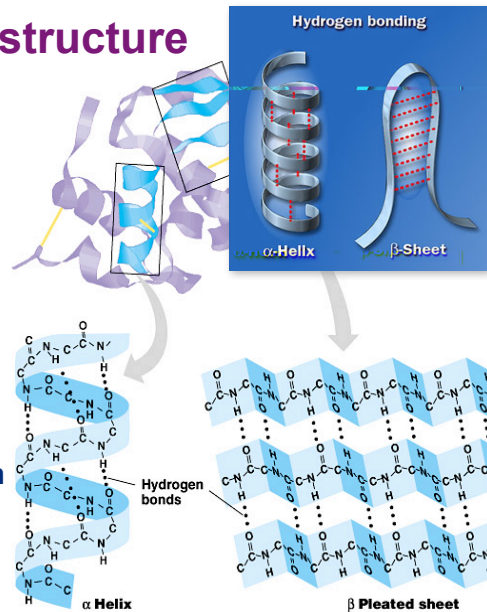
#### α-helix

- Coils with H-bonds between every fourth a.a.

#### β-pleated sheet

- Two or more regions of polypeptide chain lying side by side with H-bonds between backbone

- One polypeptide can have both in different regions



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## Tertiary (3°) structure

### “Whole molecule folding”

- interactions between distant amino acid side chains!

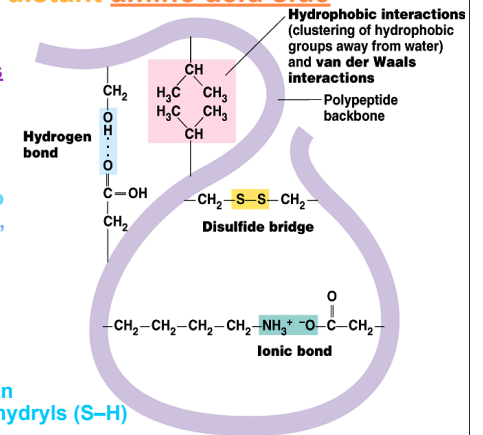
#### hydrophobic interactions

- cytoplasm is water-based
- non-polar amino acids cluster together away from water due to **hydrophobic exclusion**, Experiencing **London Dispersion Forces**

#### H bonds & ionic bonds

#### Disulfide bridges

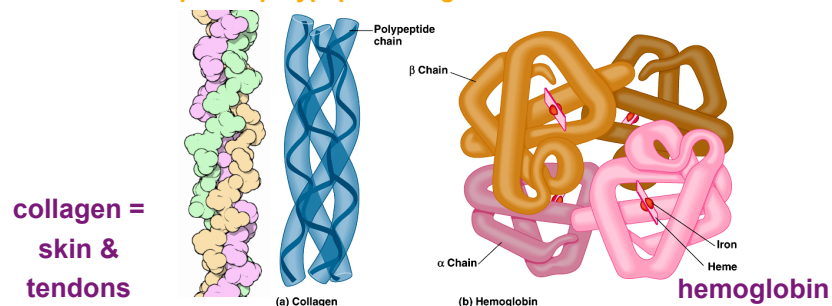
- covalent bonds between sulfurs in R group **sulphydryls (S-H)**
- anchors 3-D shape



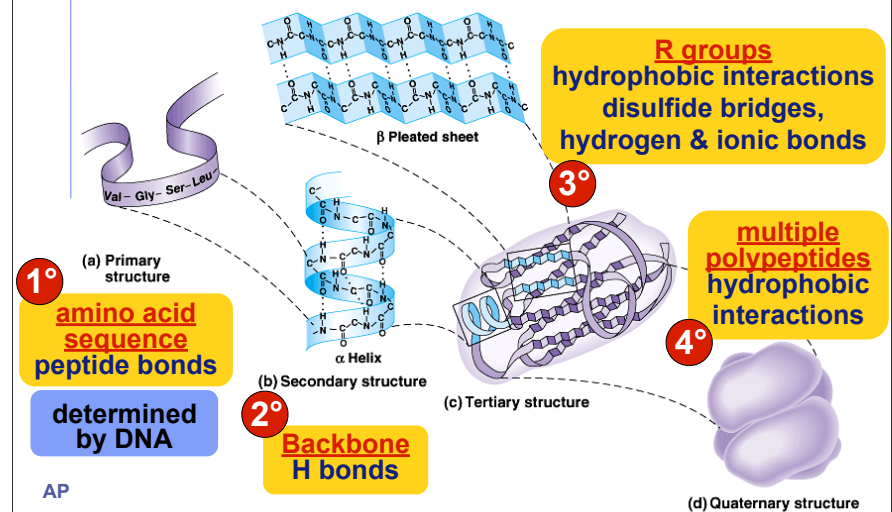
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## Quaternary (4°) structure

- More than one polypeptide chain** bonded together
- Proteins can be made up of more than one polypeptide chain
  - For these, the protein is not functional until all polypeptides are assembled
    - hydrophobic interactions & van der Waals Interactions help hold polypeptides together



## Protein structure (review)



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## Protein denaturation

In Biology,  
size doesn't matter  
like SHAPE does!



### ■ Unfolding a protein

- ◆ conditions that disrupt intermolecular forces like Hydrogen bonds, ionic attractions, dipole-ion and dipole-dipole attractions etc..

1. temperature increases

2. pH changes

- proton concentrations alterations

3. Salinity changes

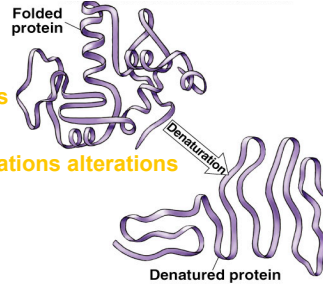
- positive & negative ion concentrations alterations

- ◆ alter 2° & 3° structure

- alter 3-D shape

- ◆ destroys functionality

- some proteins can return to their functional shape after denaturation under proper conditions, but many cannot.

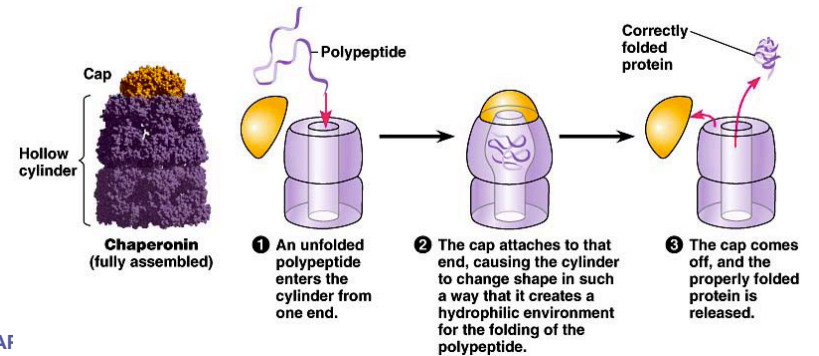


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## Chaperonin proteins

### ■ Guide protein folding

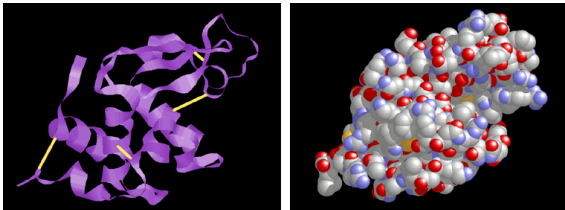
- ◆ provide shelter for folding polypeptides
- ◆ keep the new protein segregated from cytoplasmic influences



## Protein models

### ■ Protein structure visualized by

- ◆ X-ray crystallography
- ◆ extrapolating from amino acid sequence
- ◆ computer modeling



lysozyme

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admire  
Let's build ~~X~~ those Proteins!



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2007-2008