Protein Types

Proteins

- Made through the process of translation
- Consist a long chain of amino acids each linked to its neighbor through a peptide bond
- Each protein has a unique amino acid sequence that directs how the protein will fold
- Are folded into a unique conformation that facilitate the protein's function

Proteins

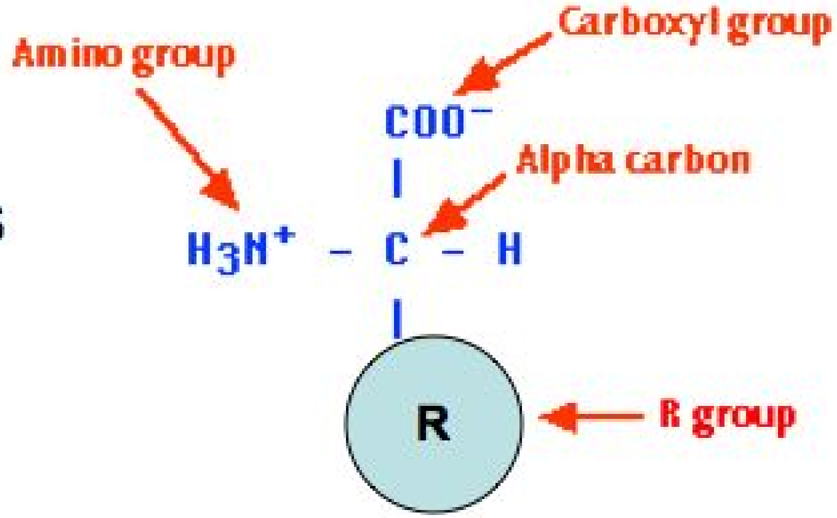
- Proteins begin to fold as they are being synthesized
- Molecular chaperones help guide the folding of the proteins

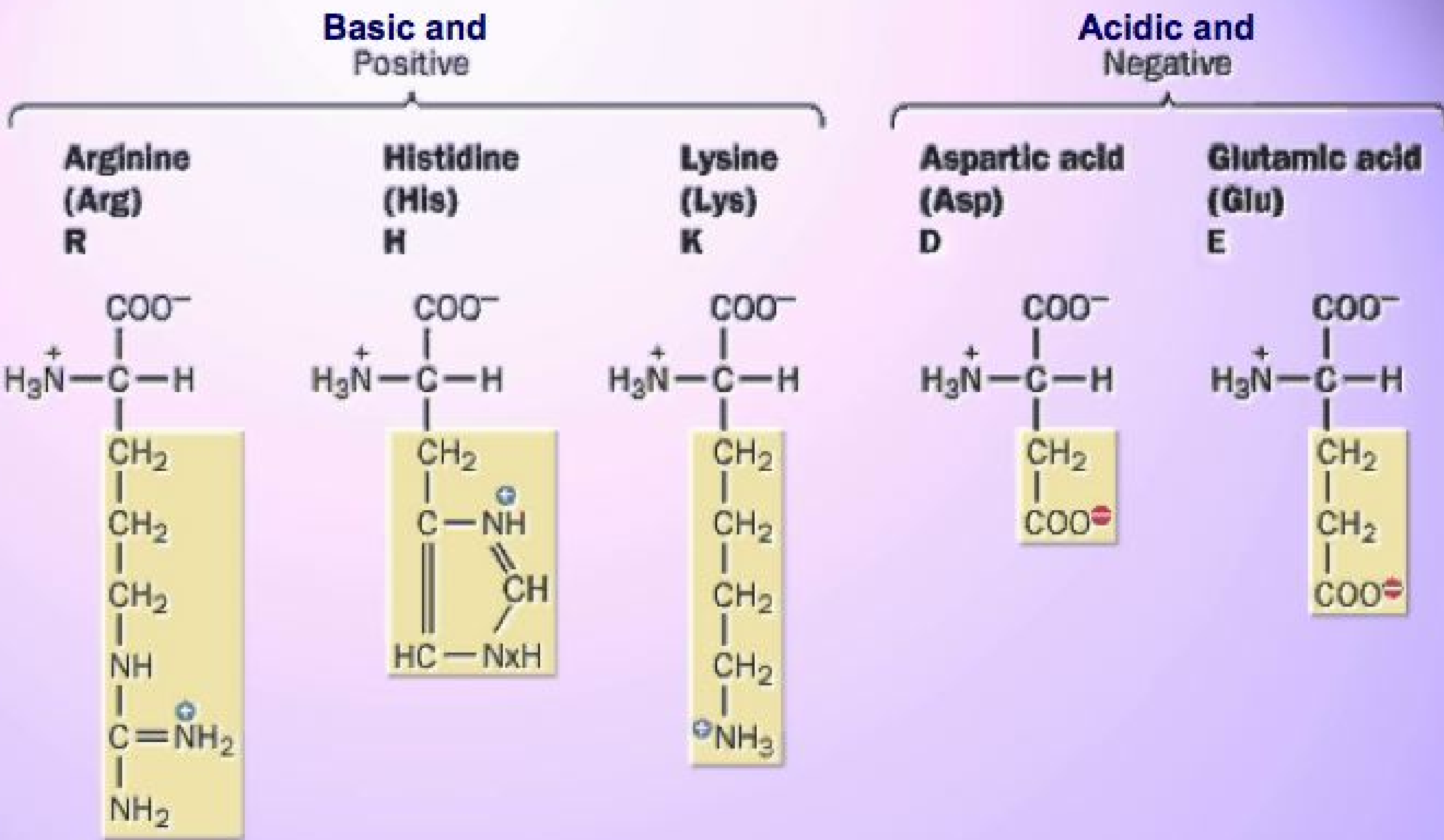
Amino Acids

- Amino acids are the building blocks of proteins
- 20 different amino acids are used to synthesize proteins
- The **shape** and other properties of each protein is dictated by the precise sequence of amino acids in it
- Humans must include adequate amounts of 9 amino acids in their diet. These "essential" amino acids cannot be synthesized from other precursors

Amino Acids

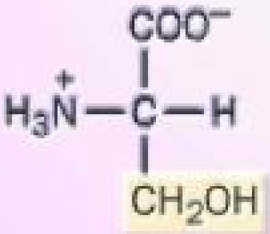
- Each amino acid consists of an **alpha carbon atom** to which is attached
  - a hydrogen atom
  - an amino group
  - a carboxyl group
  - one of 20 different "R" groups



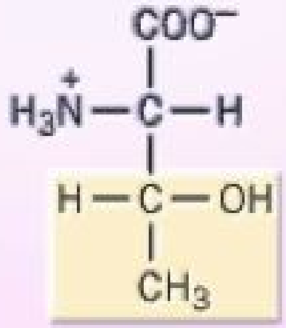


Amino acids with electrically charged side chains

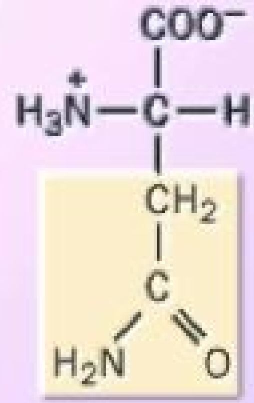
Serine
(Ser)
S



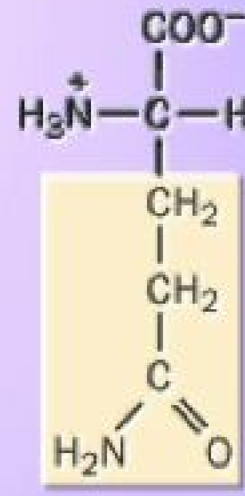
Threonine
(Thr)
T



Asparagine
(Asn)
N

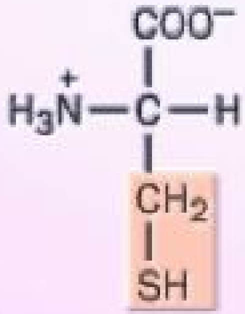


Glutamine
(Gln)
Q

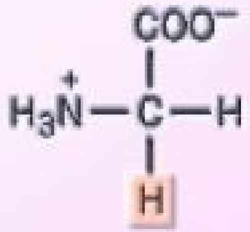


Amino acids with polar but uncharged side chains

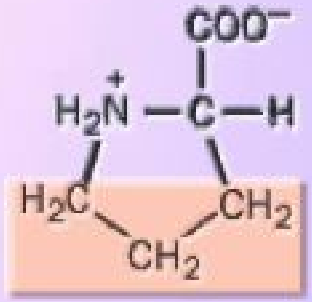
Cysteine
(Cys)
C



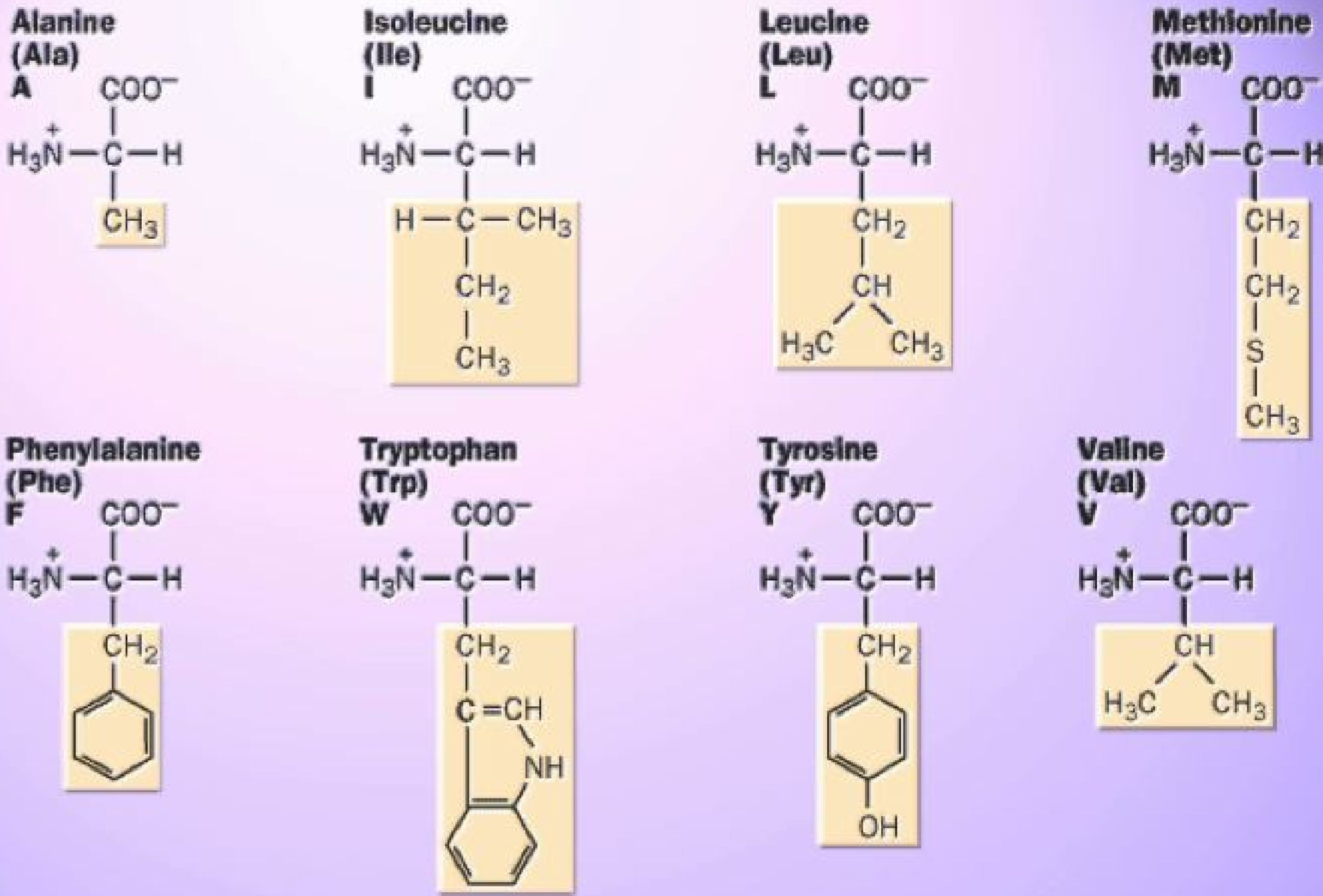
Glycine
(Gly)
G



Proline
(Pro)
P



Special cases



Amino acids with hydrophobic side chains

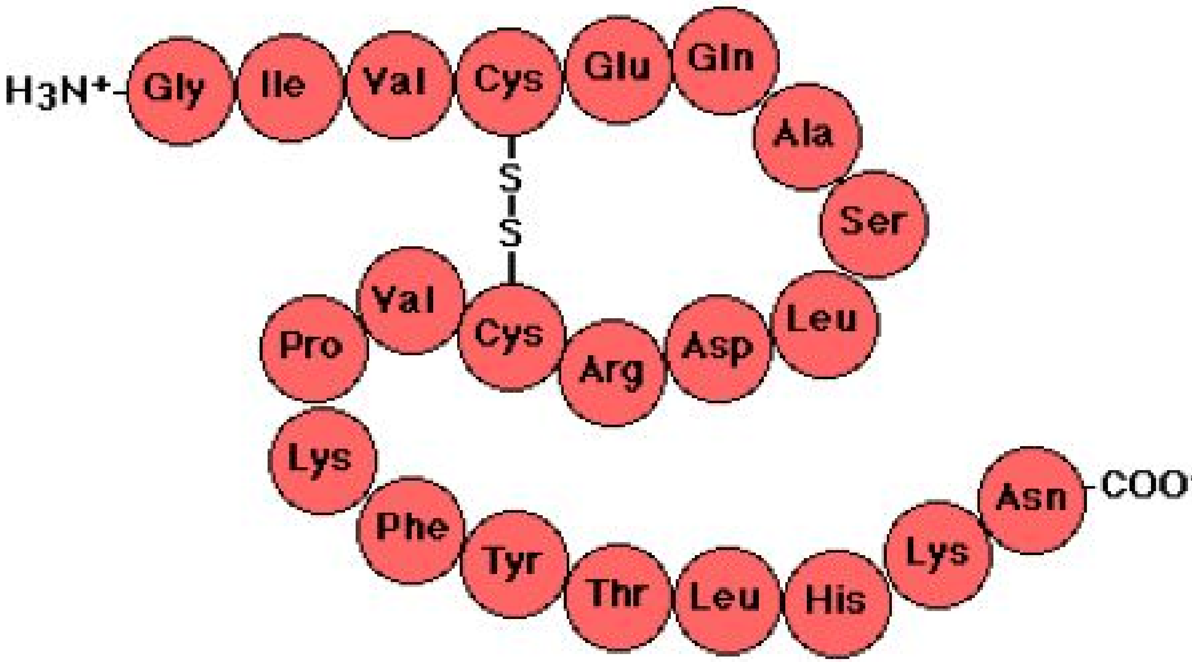
Proteins fold into the conformation of lowest energy

- Based on the interactions between and among the amino acids, each protein has a unique 3-D structure
- The final folded structure, or conformation, is the one in which free energy is minimized
- The structure or shape of the protein can change once it interacts with other cellular components
- The shape of a protein is crucial to the function of the protein

Four levels of organization

- Primary Structure
  - Amino acid sequence
- Secondary Structure
  - Stretches of the molecule form alpha and β-sheets
- Tertiary Structure
  - Full 3-D shape of the protein
- Quaternary Structure
  - 3-D relationship of different subunits or proteins of a multi-subunit protein or multi-protein complex

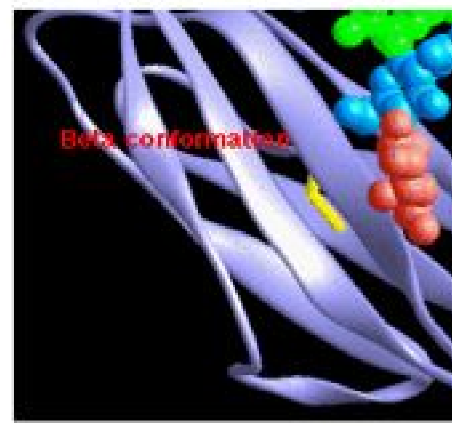
Primary Structure



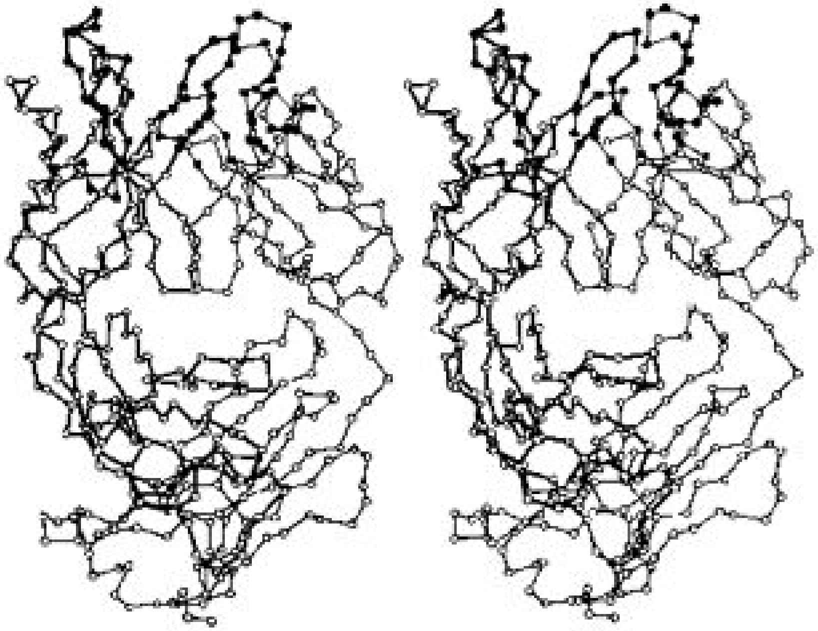
Secondary Structure

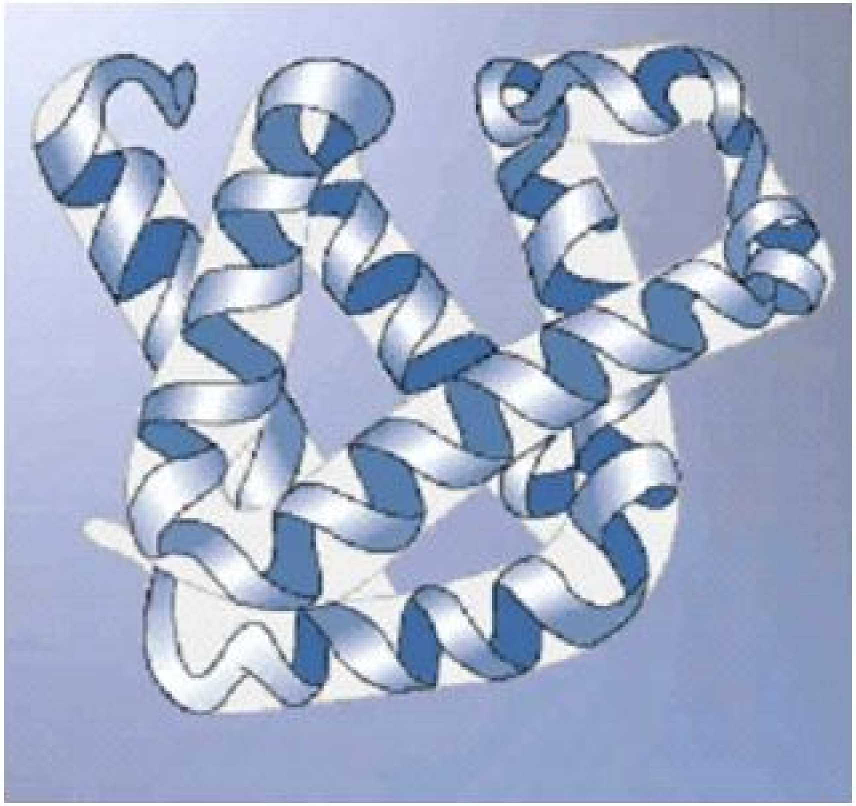
- Alpha helix
  - The R groups of the amino acids all extend to the outside.
  - The helix makes a complete turn every 3.6 amino acids.
  - The helix is right-handed; it twists in a clockwise direction.

- β-sheet
  - consists of pairs of chains lying side-by-side
  - stabilized by hydrogen bonds between the chains
  - The chains are often "anti-parallel"; the N-terminal to C-terminal direction of one being the reverse of the other.

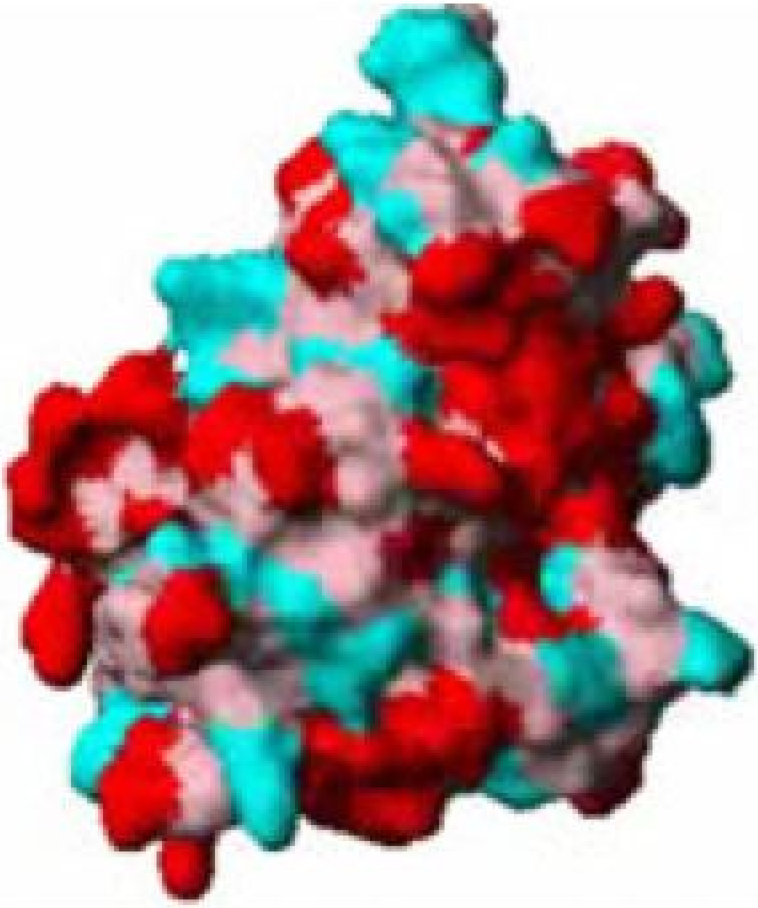


Tertiary Structure





Quaternary Structure



Chaperones

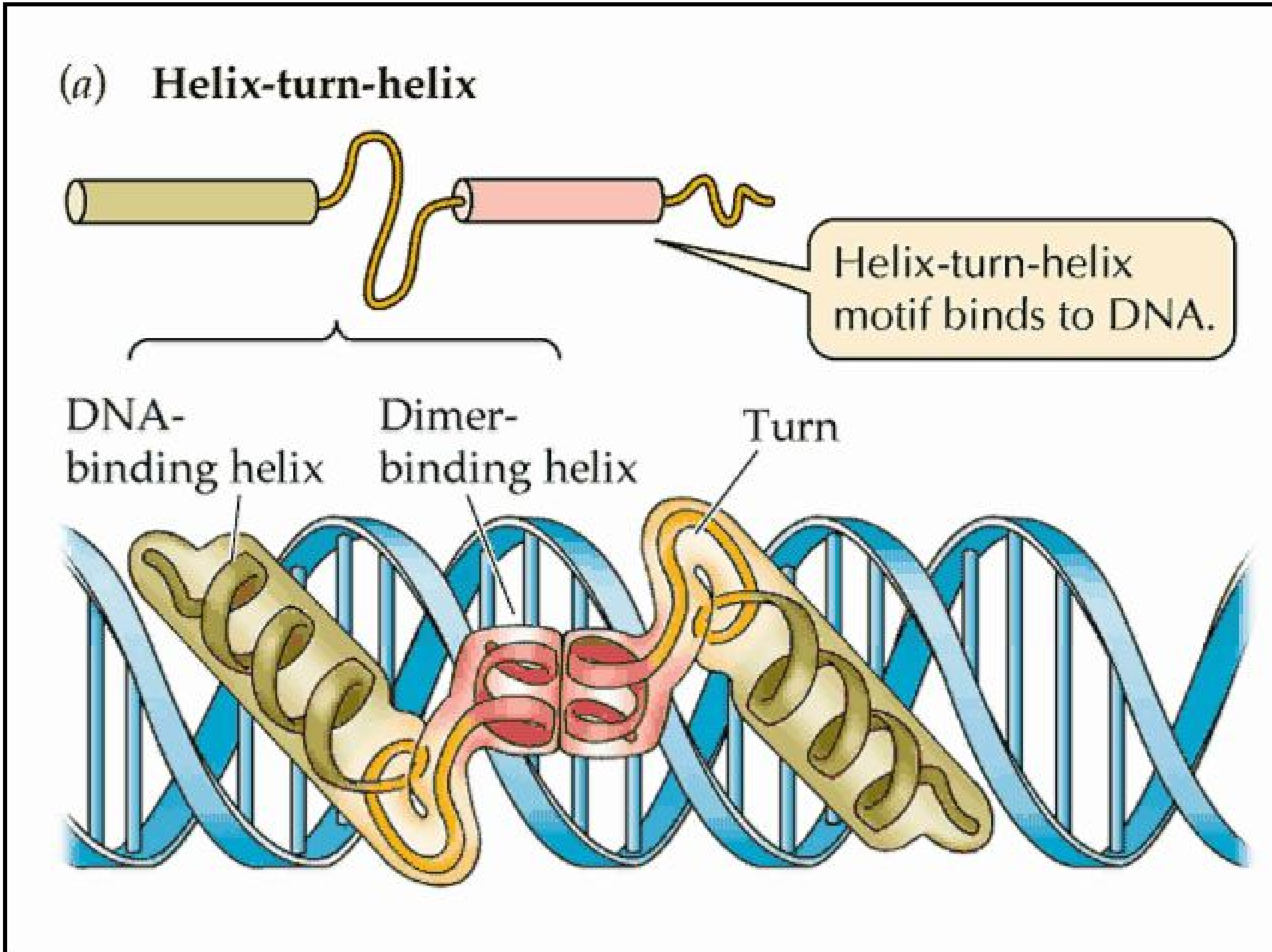
- Although the three-dimensional (tertiary) structure of a protein is determined by its primary structure, it may need assistance in achieving its final shape
- As a protein is being synthesized, it emerges (N-terminal first) from the ribosome and the folding process begins
- However, the emerging protein finds itself surrounded by the watery cytosol and many other proteins
- As hydrophobic amino acids appear, they must find other hydrophobic amino acids to associate with. Ideally, these should be their own, but there is the danger that they could associate with nearby proteins instead — leading to aggregation and a failure to form the proper tertiary structure
- To avoid this problem, the cells of all organisms contain molecular chaperones that stabilize newly-formed protein while they fold into their proper structure
- Most (~80%) newly-synthesized proteins are stabilized by molecular chaperones that bind briefly to their surface until they have folded properly
- The chaperones use the energy of ATP to do this work

Folding motifs

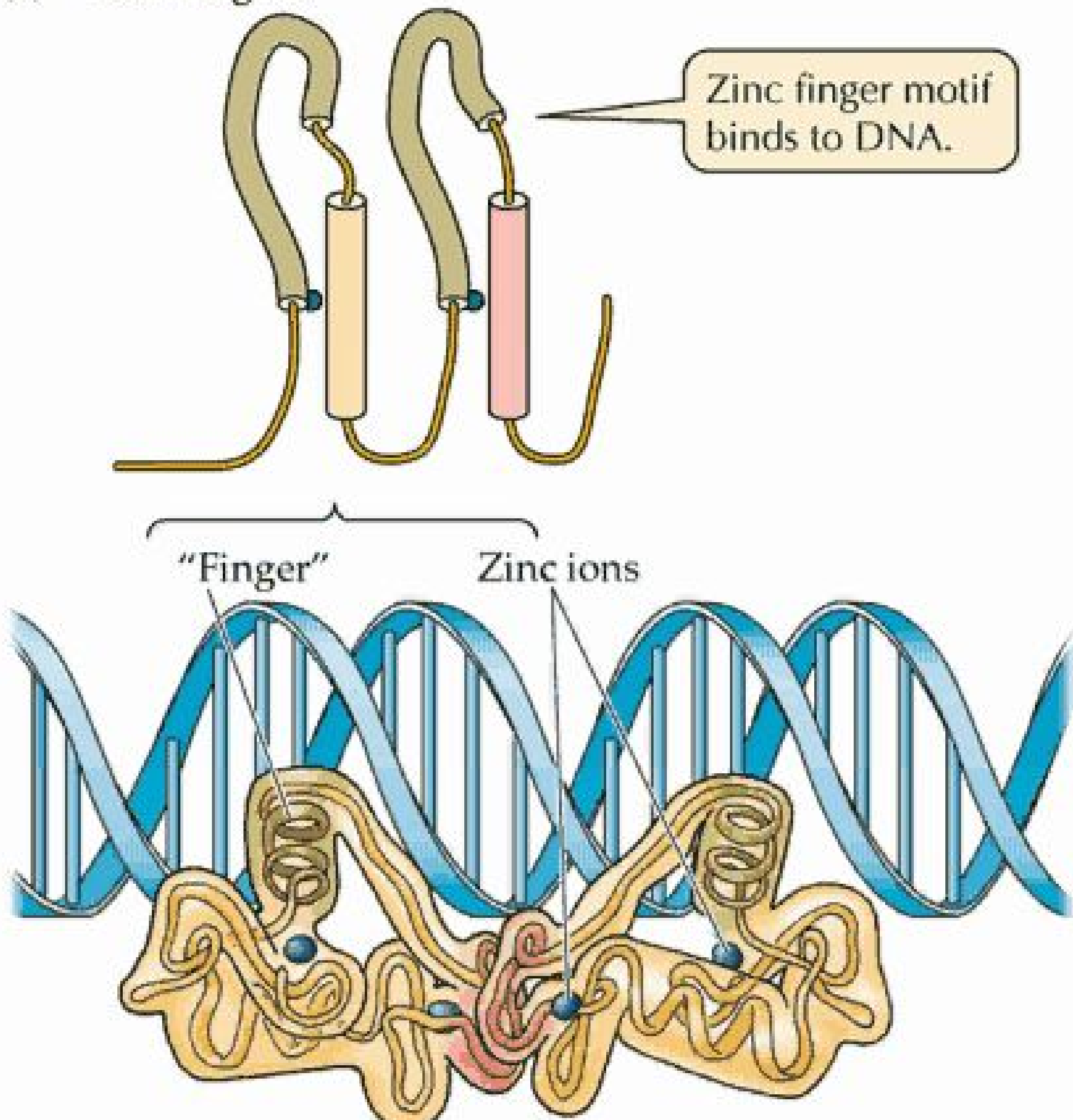
- Regular combinations of secondary structure. The next slides give examples of some of these motifs. These motifs are the start of tertiary structure.
- In combination these motifs give the proteins their tertiary structure and will result in a functional or in the case of a mutant motif a nonfunctional protein.

Example of motifs

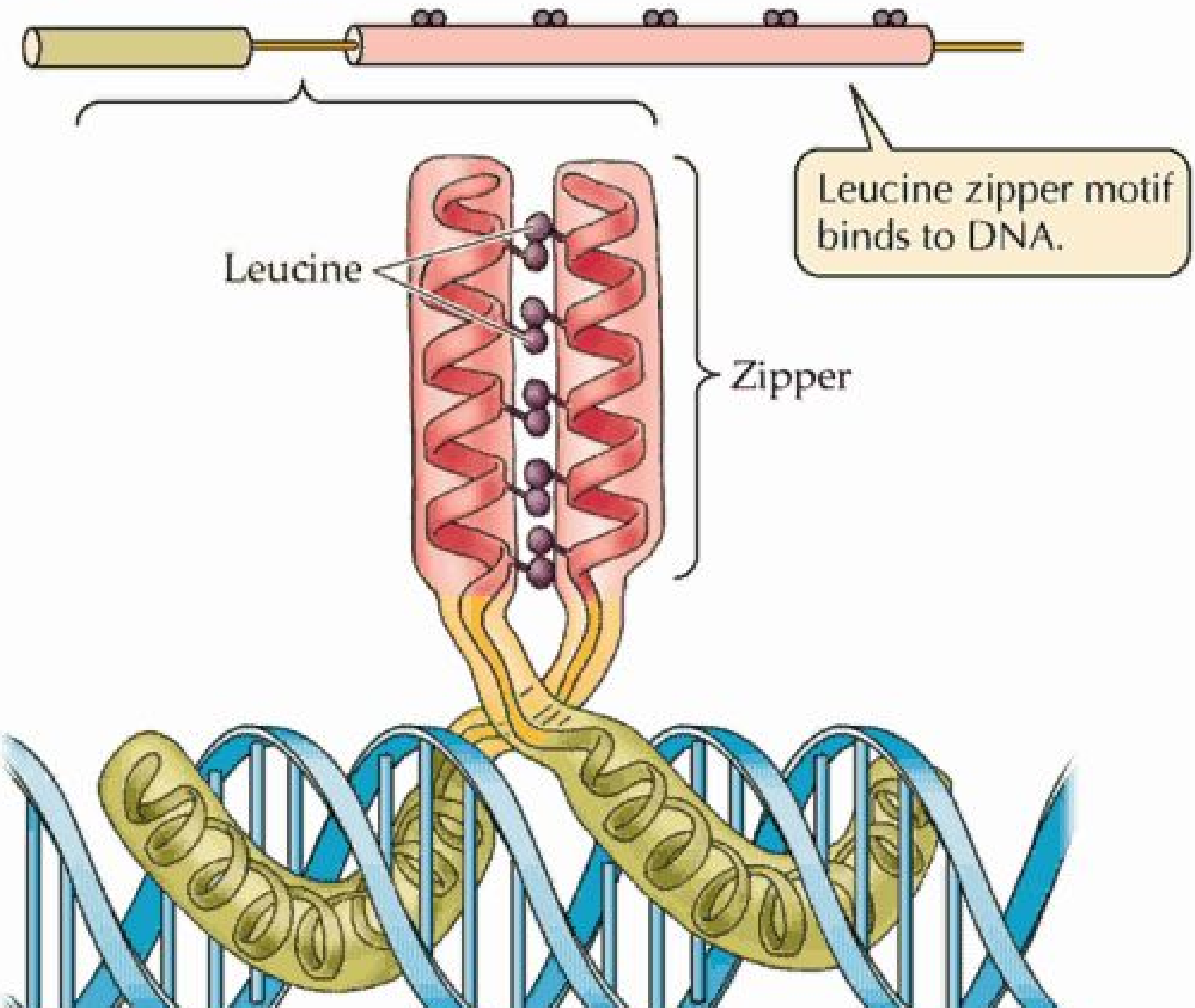
- Helix-loop-helix--- this is a Ca2+ binding motif (AKA EF hand)
- Zinc fingers---composed of alpha helix and 2 beta sheets. Found in proteins that bind to DNA and RNA.
- Coiled coil--Alpha helixes that are intertwined. This is seen in some structural proteins Collagen is a good example


(a) Helix-turn-helix
Helix-turn-helix motif binds to DNA.
DNA-binding helix
Dimer-binding helix
Turn

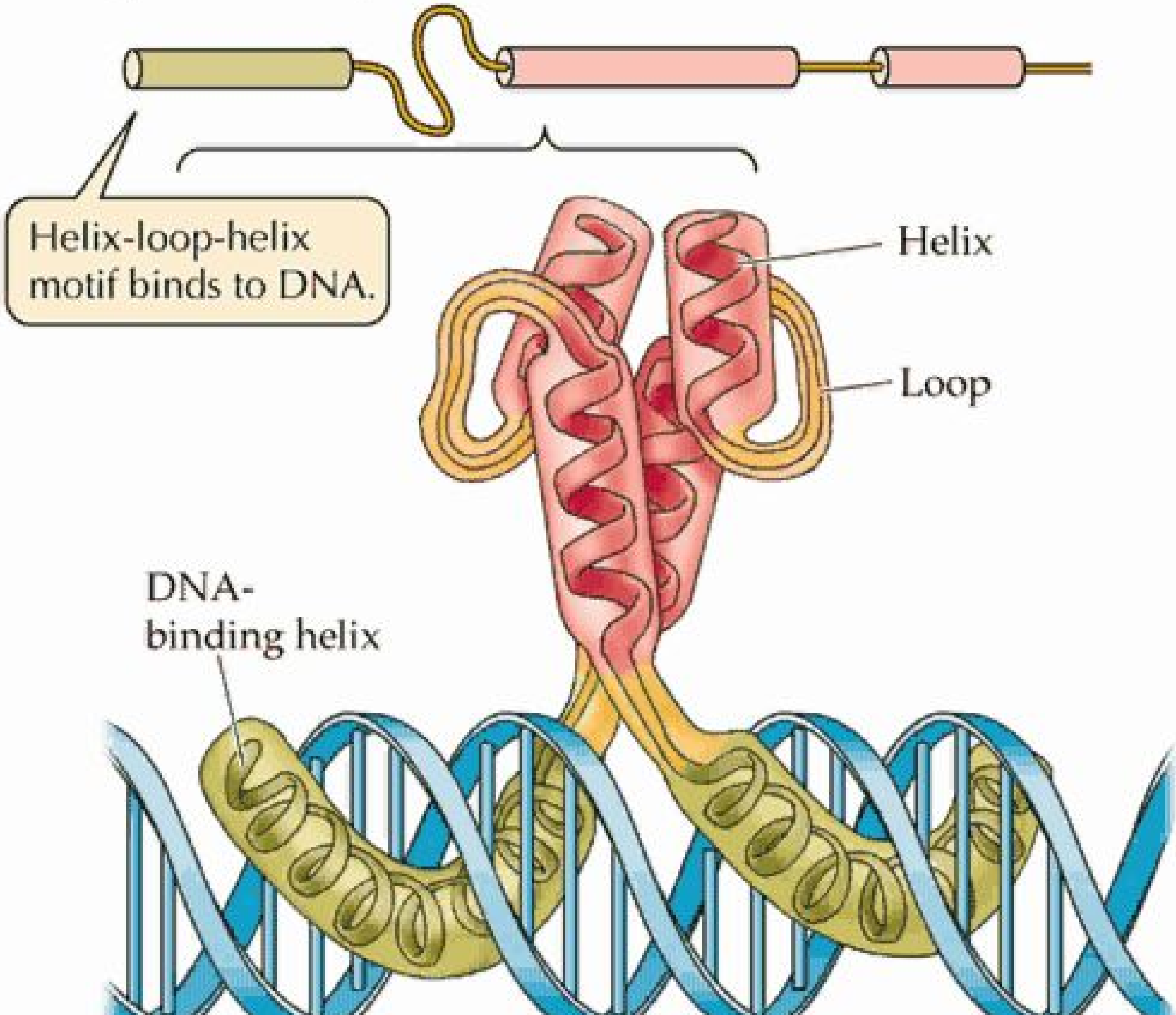
(*b*) **Zinc fingers**

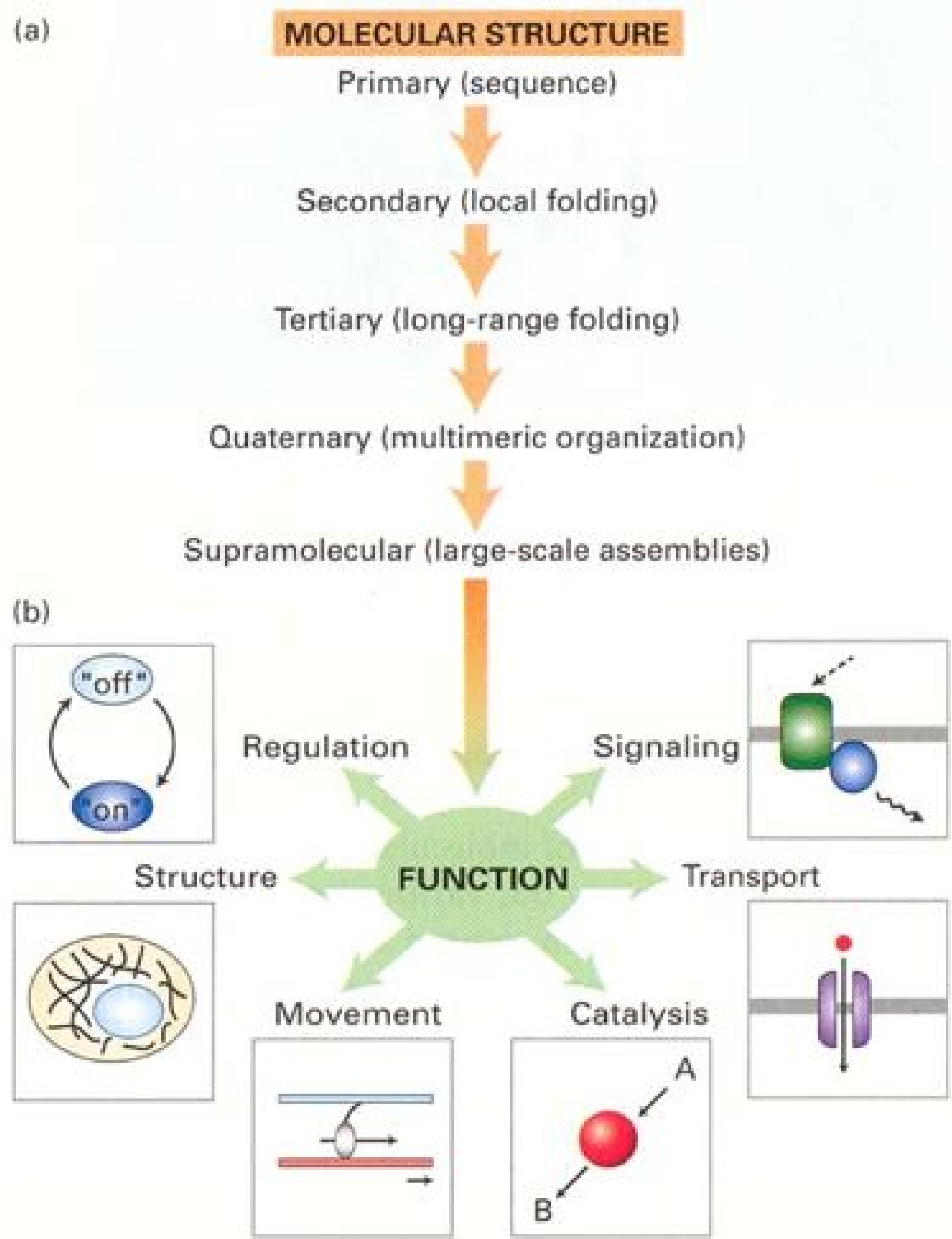


(*c*) **Leucine zipper**



(*d*) **Helix-loop-helix**

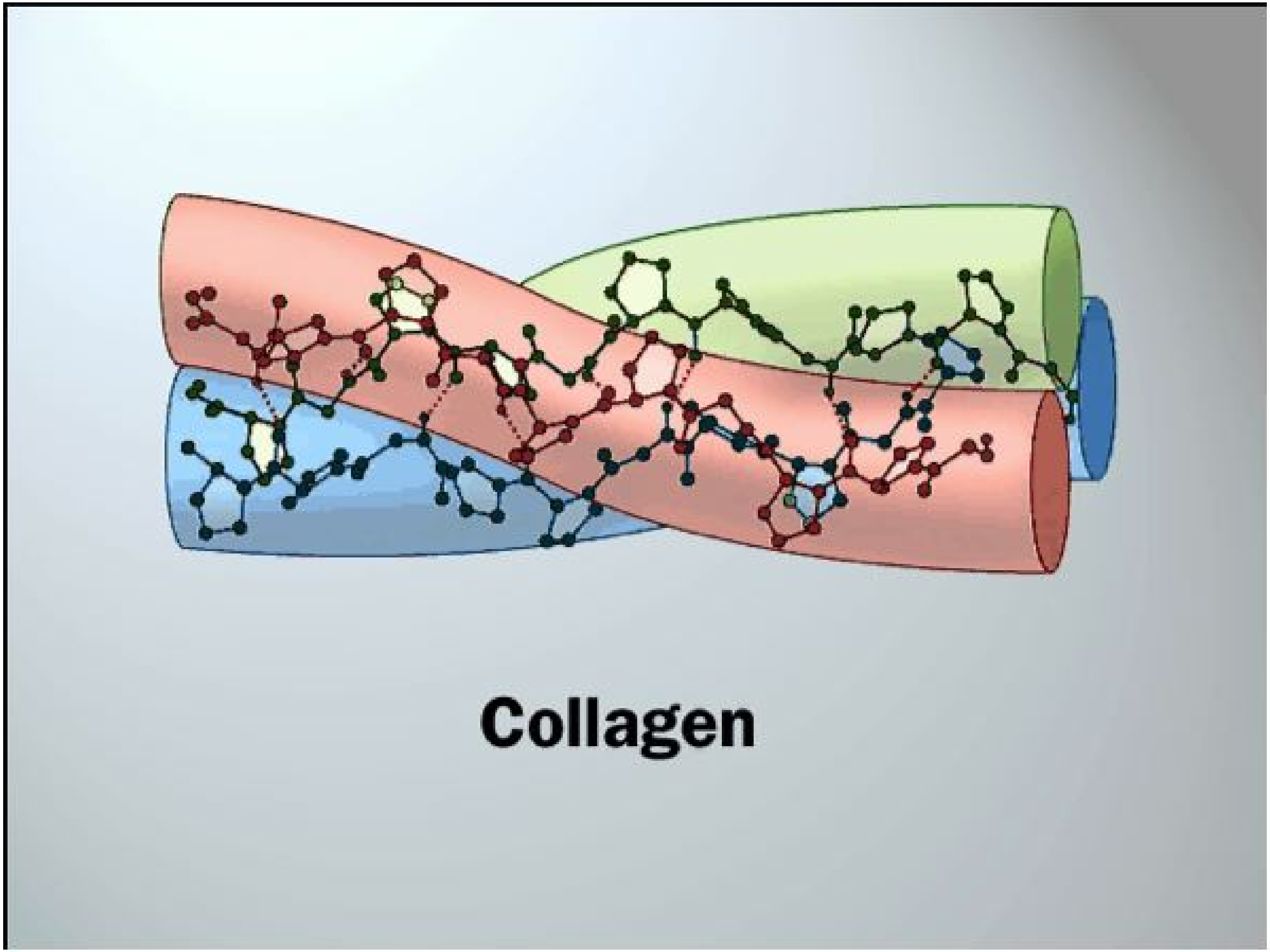



(a)
MOLECULAR STRUCTURE
Primary (sequence)
Secondary (local folding)
Tertiary (long-range folding)
Quaternary (multimeric organization)
Supramolecular (large-scale assemblies)
(b)
"off"
"on"
Regulation
Signaling
Structure
FUNCTION
Transport
Movement
Catalysis
A
B

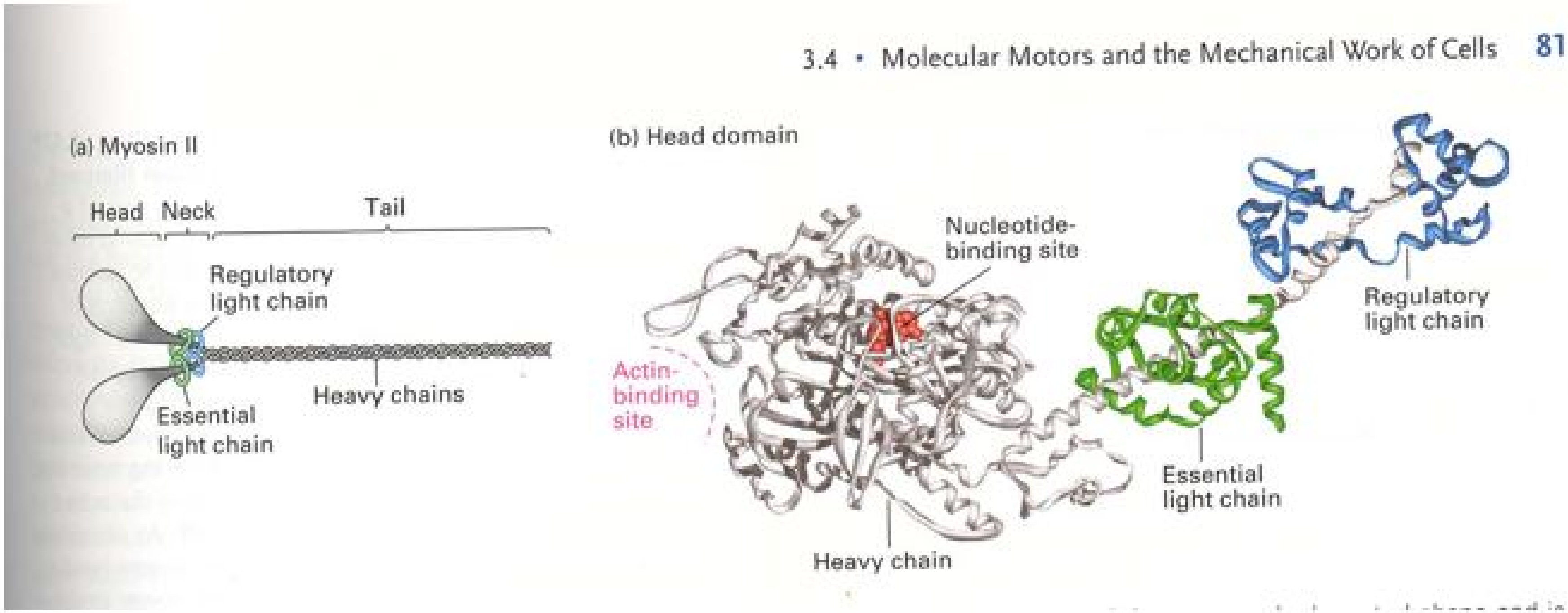
Some classes of proteins

- Structural
- Contractile
- Transport
- Storage
- Growth factors
- Hormones
- Enzymes
- Antibodies

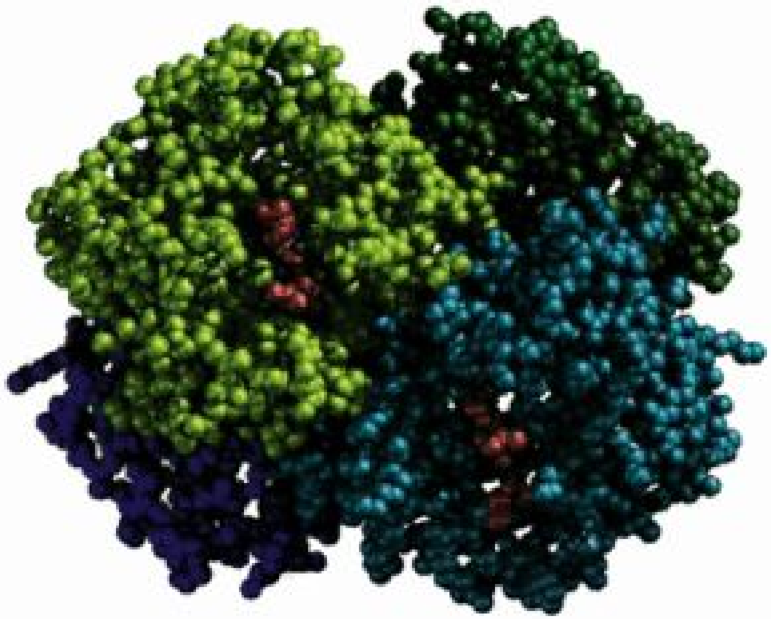
EXAMPLE OF STRUCTURAL PROTEIN

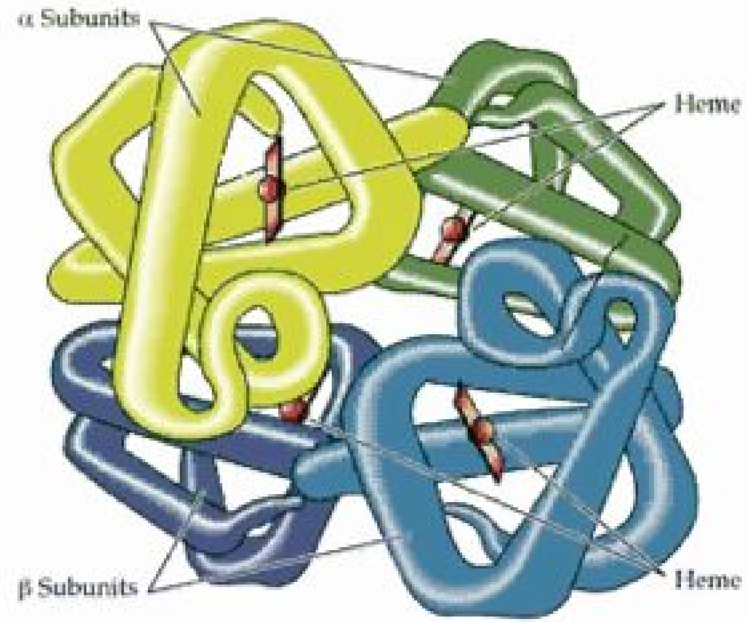


EXAMPLE OF CONTRACTILE PROTEIN AKA MOLECULAR MOTOR

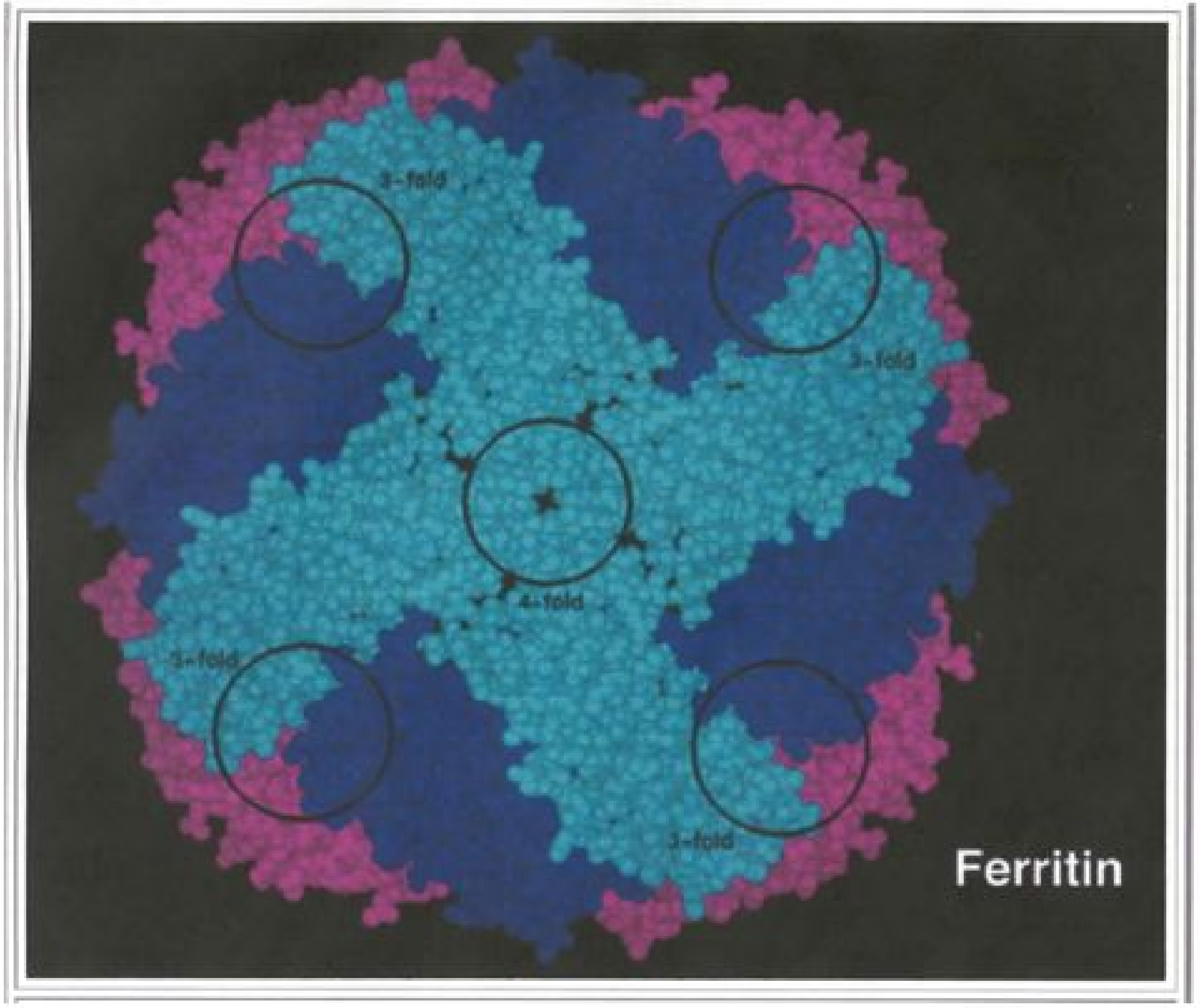


EXAMPLE OF TRANSPORT PROTEIN



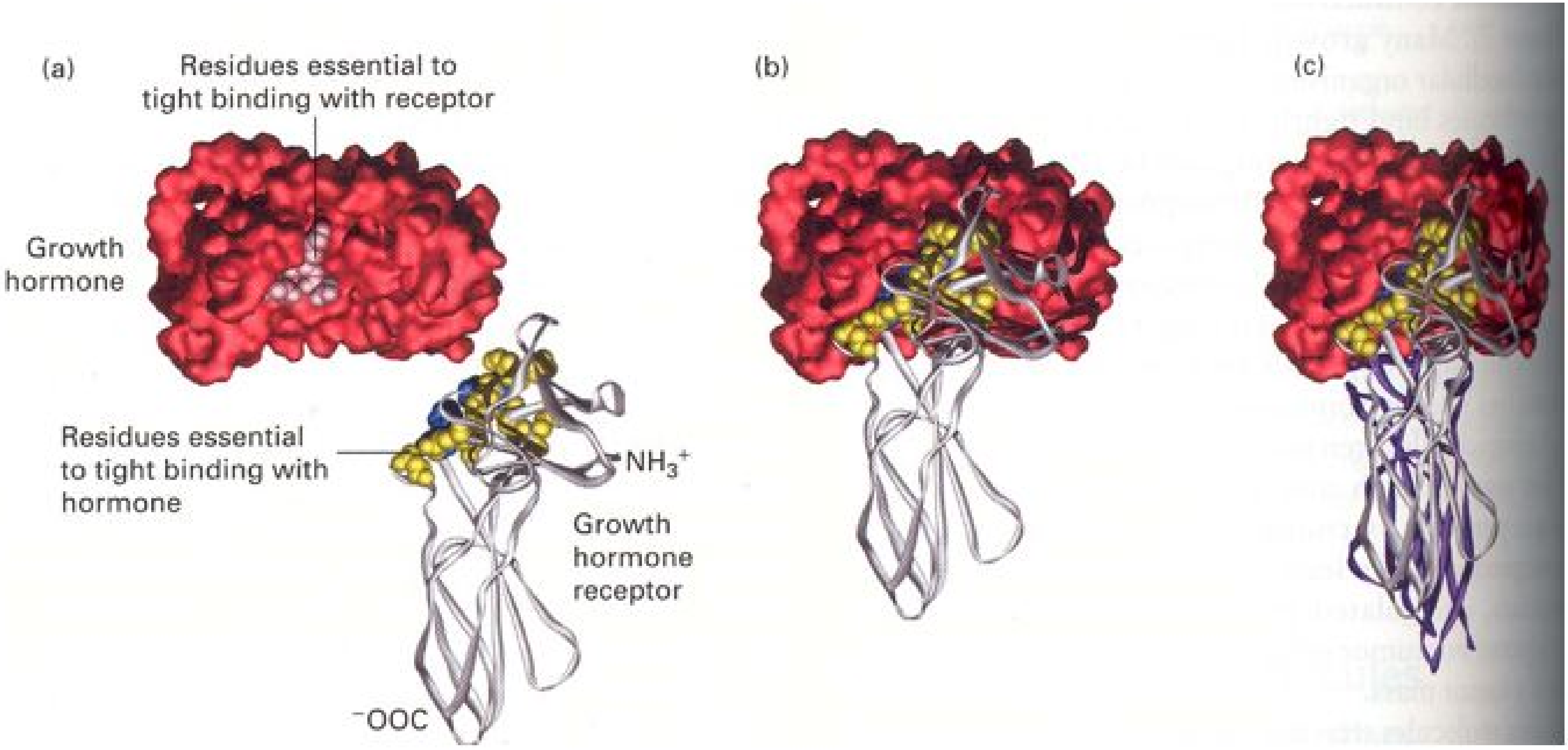


EXAMPLE OF A STORAGE PROTEIN

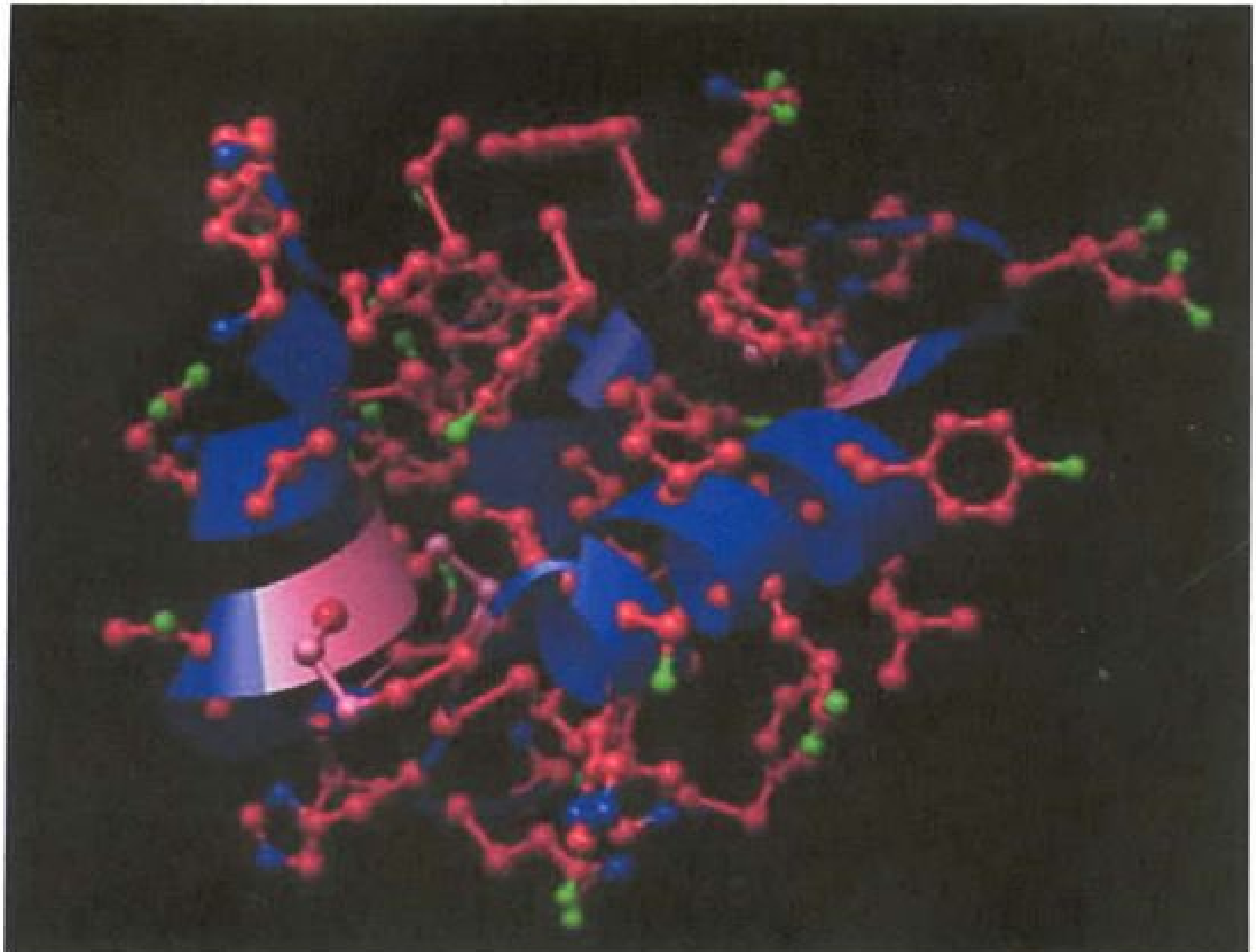


http://www.chemistry.wustl.edu/~edudev/LabTutorials/Ferritin/FerritinTutorial.html

EXAMPLE OF A GROWTH FACTOR

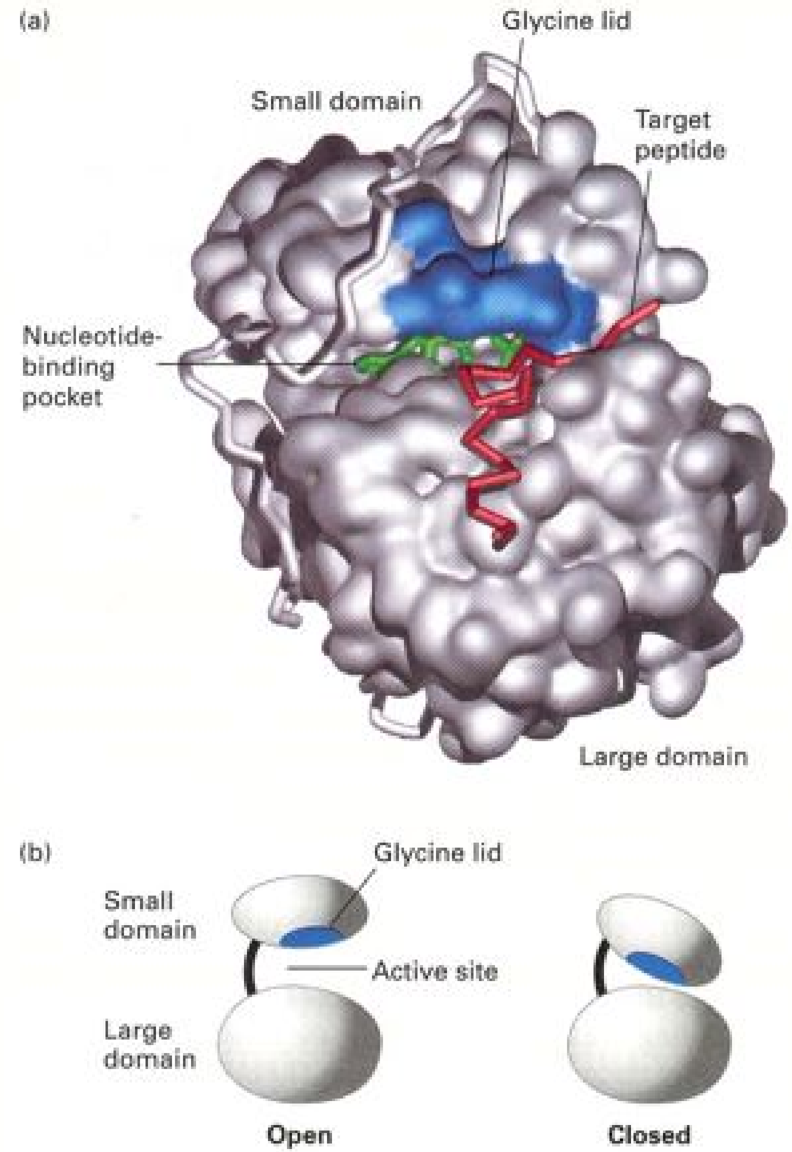


EXAMPLE OF A HORMONE



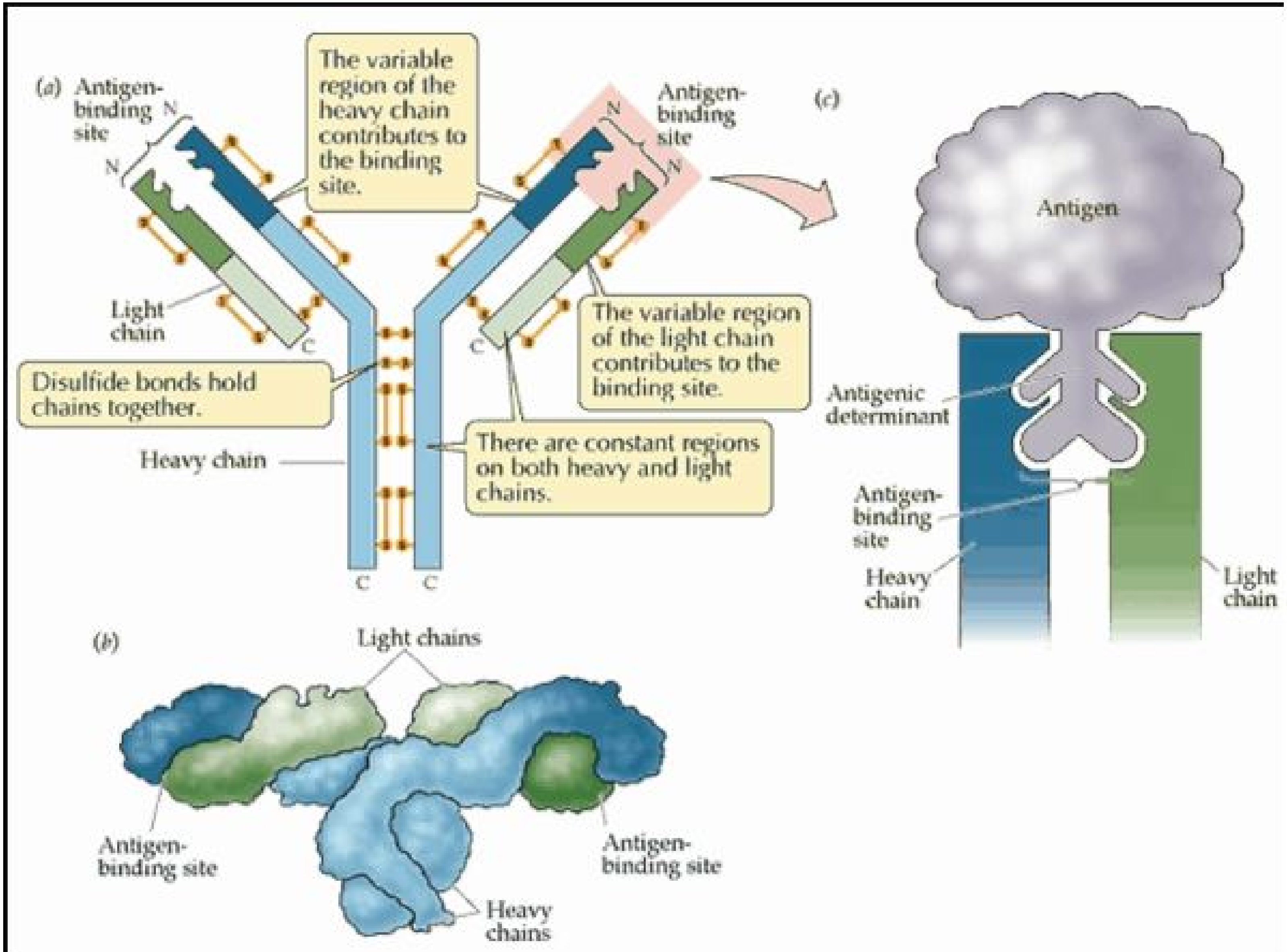
http://upload.wikimedia.org/wikipedia/id/thumb/d/d9/Insulin.jpg/300px-Insulin.jpg

EXAMPLE OF AN ENZYME



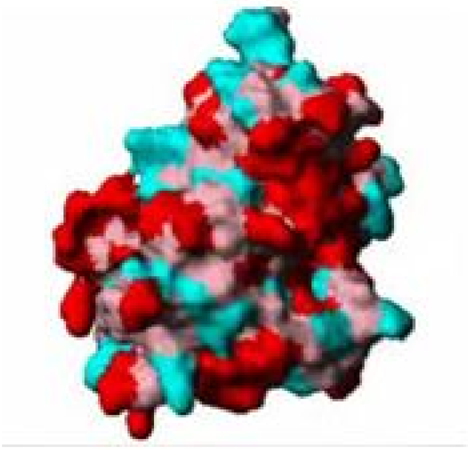
▲ FIGURE 3-17 Protein kinase A and conformational change induced by substrate binding. (a) Model of the

EXAMPLE OF AN ANTIBODY

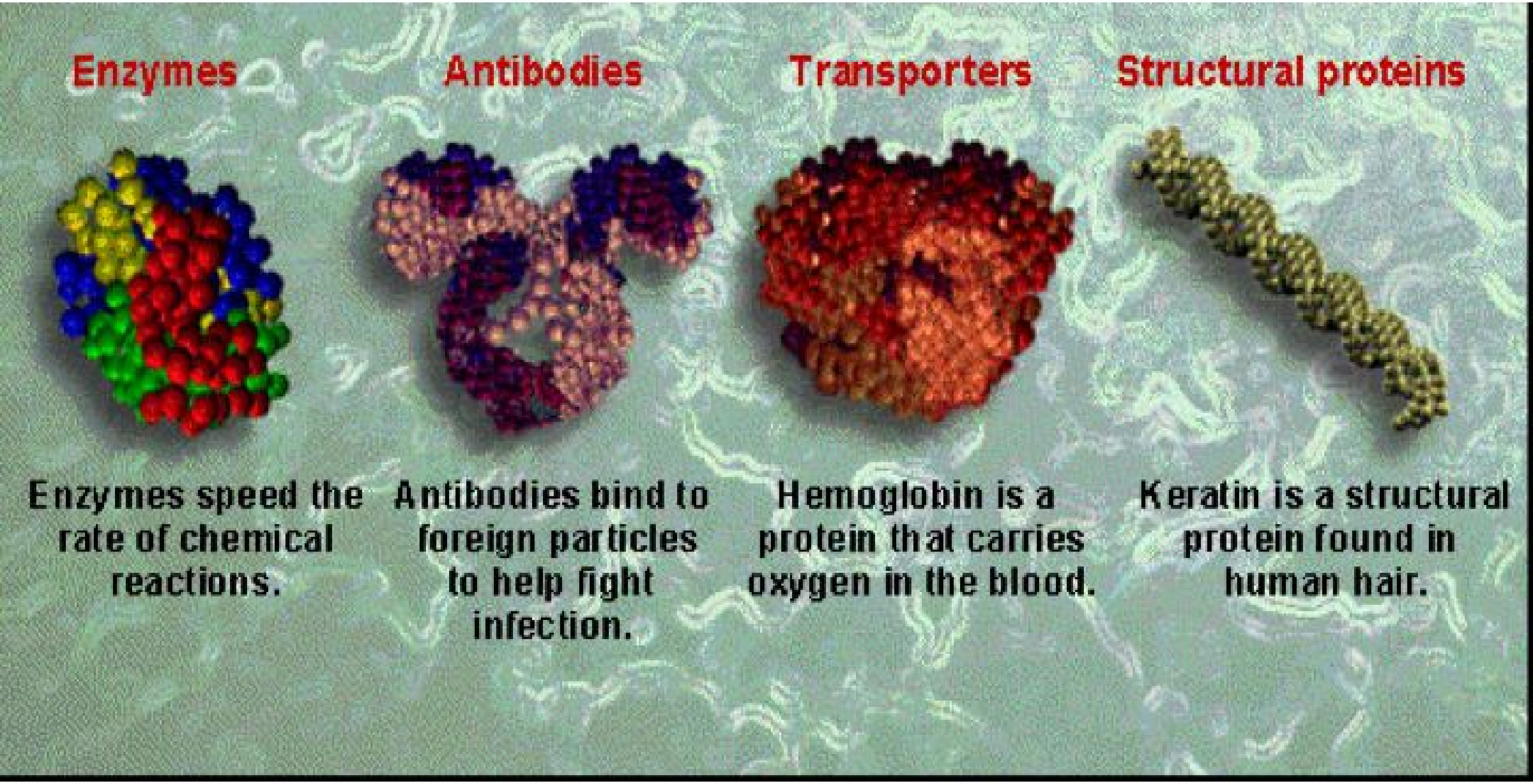


Proteins come in many shapes

- The shape of the protein gives it its function
- Some transport molecules around the body
- Others fit into receptors to turn processes on or off
- There are thousands of different proteins and each has its own specific function



Proteins have many functions

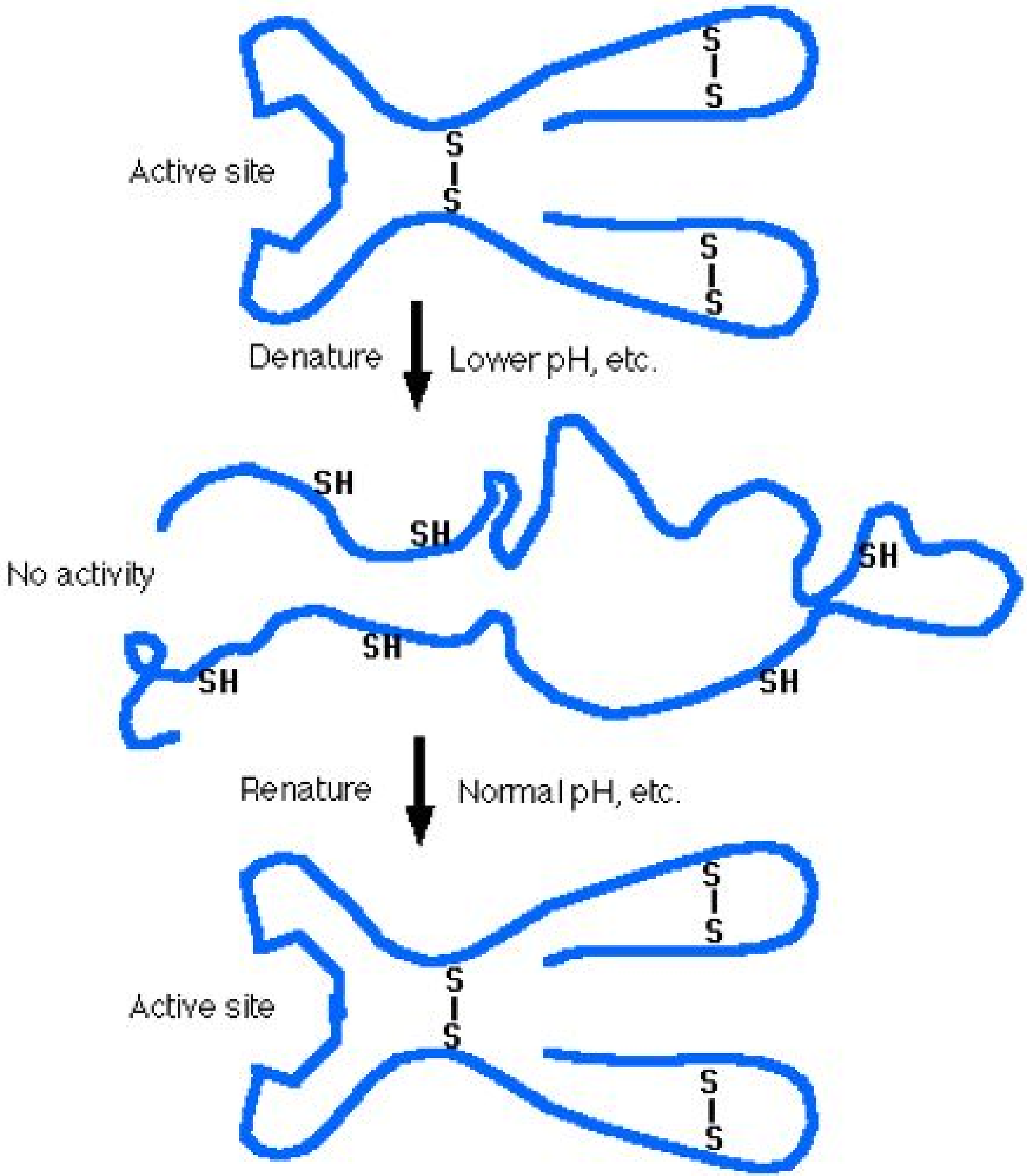


Protein domains

- The tertiary structure of many proteins is built from several **domains**
- Often each domain has a separate function to perform for the protein, such as:
  - binding a small ligand (e.g., a peptide in the molecule shown here)
  - spanning the plasma membrane (transmembrane proteins)
  - containing the catalytic site (enzymes)
  - DNA-binding (transcription factors)
  - providing a surface to bind specifically to another protein
- In some (but not all) cases, each domain in a protein is encoded by a separate exon in the gene encoding that protein

Protein Denaturation

- The function of a protein is absolutely dependent on its three-dimensional structure
- The following are agents can disrupt this structure thus **denaturing** the protein:
  - changes in pH (alters electrostatic interactions between charged amino acids)
  - changes in salt concentration (does the same)
  - changes in temperature (higher temperatures reduce the strength of hydrogen bonds)
  - presence of reducing agents (break S-S bonds between cysteins)
- None of these agents breaks peptide bonds, so the primary structure of a protein remains intact when it is denatured



Active site
S
S
S
S
S
S
Denature
Lower pH, etc.
SH
SH
No activity
SH
SH
SH
SH
Renature
Normal pH, etc.
Active site
S
S
S
S
S
S

Summary

- The function of a protein is determined by its shape
- The shape of a protein is determined by its primary structure (sequence of amino acids)
- The sequence of amino acids in a protein is determined by the sequence of nucleotides in the gene (DNA) encoding it