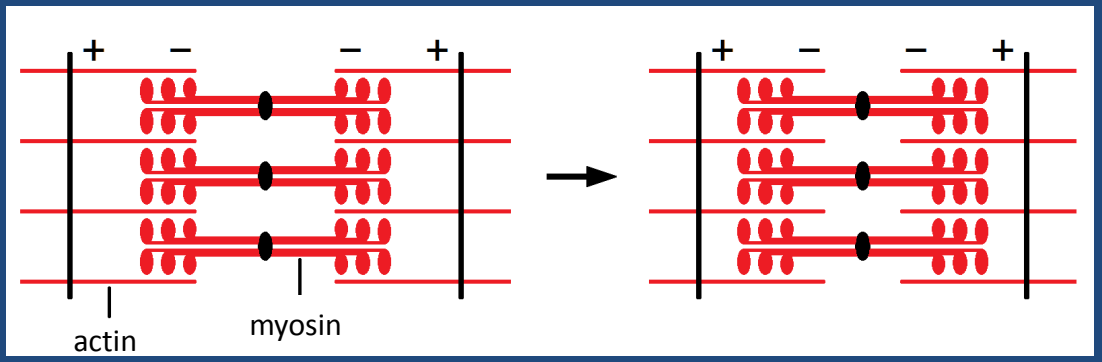
Proteins: composition, structure, properties and functions. Primary, secondary, tertiary and quaternary structure of protein molecules

Department of Biology, Medical Faculty, Medical University of Sofia

Protein functions

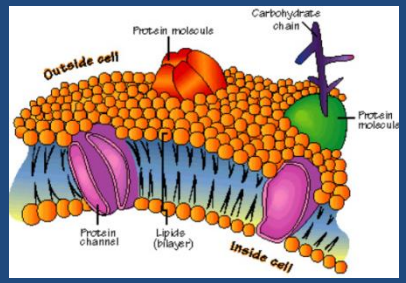
Support (structural proteins, e.g. actin)

Motility (motor proteins, e.g. myosin)

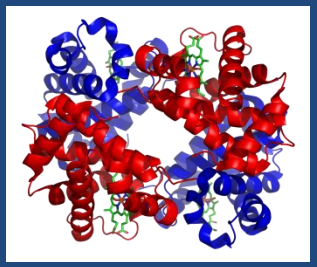


Catalysis (enzymes)

Transport (membrane transporters, hemoglobin)

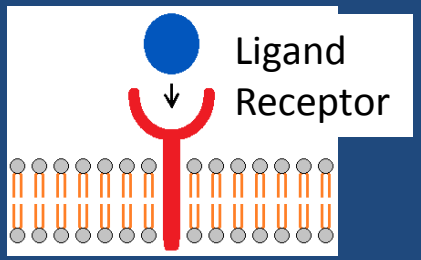


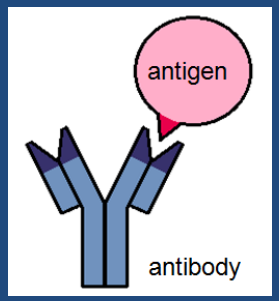
140264jd/flickr.com



R. Wheeler/Wikimedia

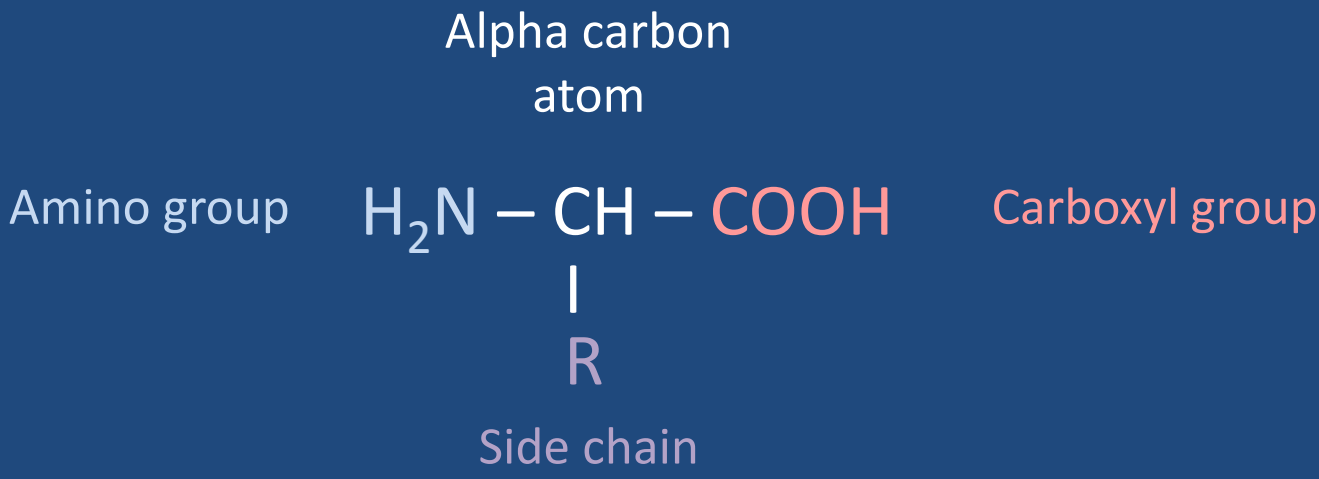
Specific recognition and binding (receptors, antibodies etc.)





Protein composition

Proteins are polymers of alpha amino acids:

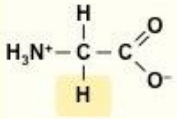


$H_3N^+ - CH - COO^-$

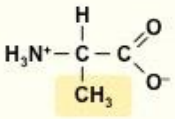
R

Amino acids dissociate in water

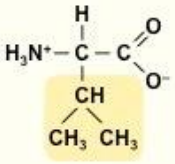
NON-POLAR



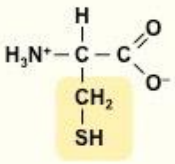
Glycine
(Gly / G)



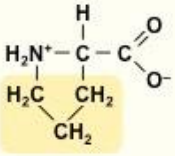
Alanine
(Ala / A)



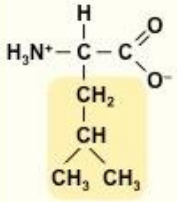
Valine
(Val / V)



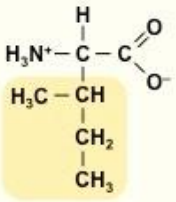
Cysteine
(Cys / C)



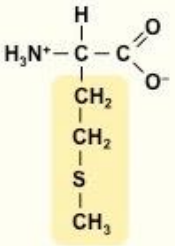
Proline
(Pro / P)



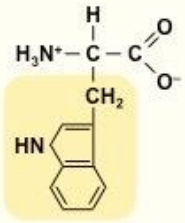
Leucine
(Leu / L)



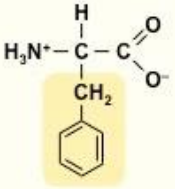
Isoleucine
(Ile / I)



Methionine
(Met / M)

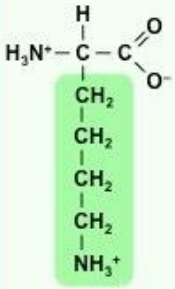


Tryptophan
(Trp / W)

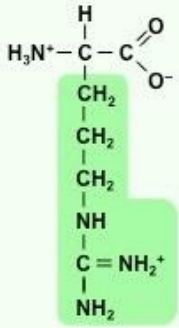


Phenylalanine
(Phe / F)

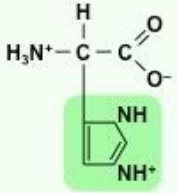
+ CHARGE



Lysine
(Lys / K)

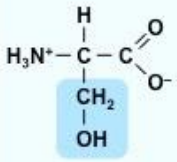


Arginine
(Arg / R)

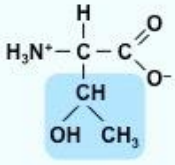


Histidine
(His / H)

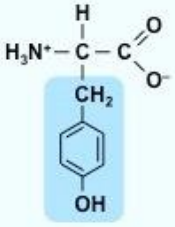
POLAR



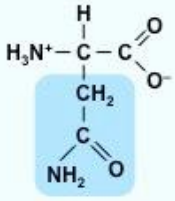
Serine
(Ser / S)



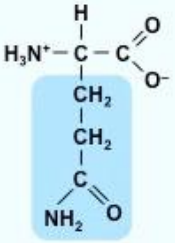
Threonine
(Thr / T)



Tyrosine
(Tyr / Y)

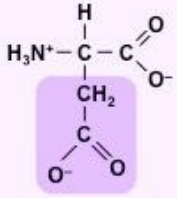


Asparagine
(Asn / N)

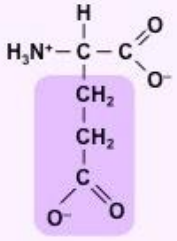


Glutamine
(Gln / Q)

– CHARGE

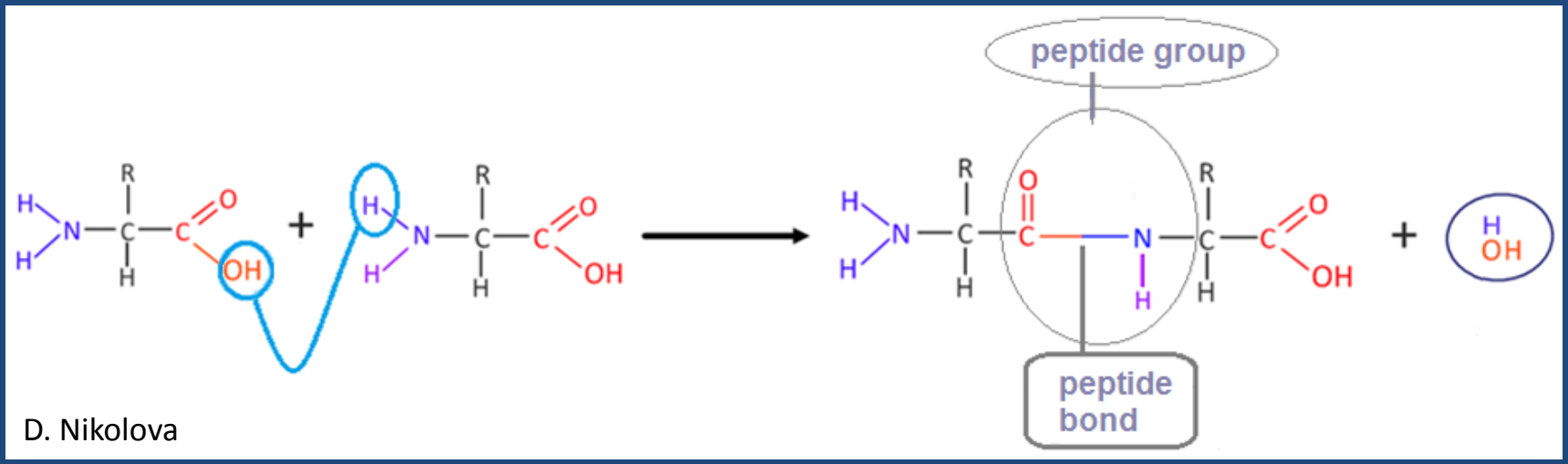


Aspartic Acid
(Asp / D)

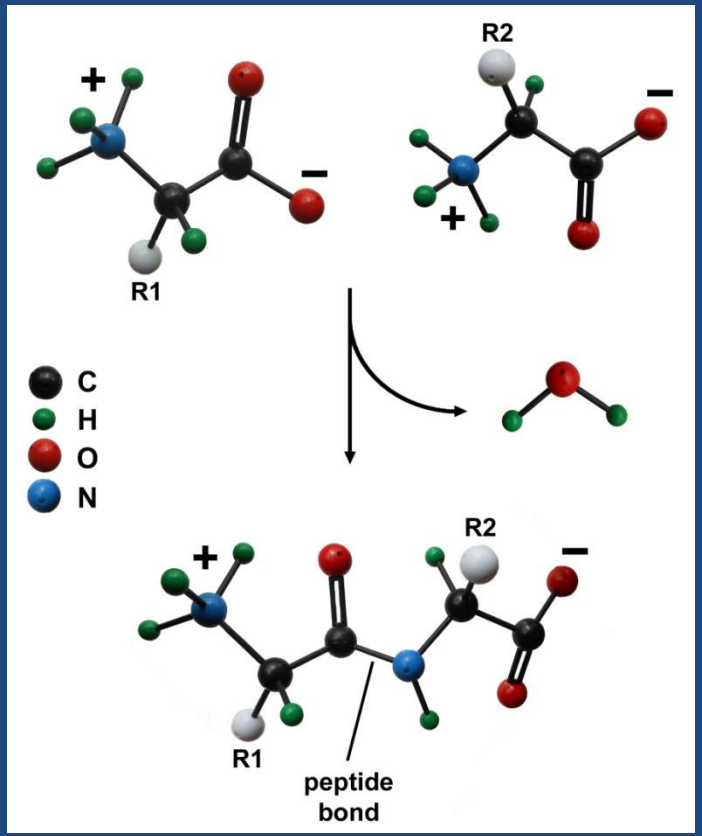


Glutamic Acid
(Glu / E)

https://socratic.org/questions/which-part-of-an-amino-acid-s-structure-makes-it-unique-from-other-amino-acids



Two amino acids bind together to form a dipeptide



Polypeptide chains

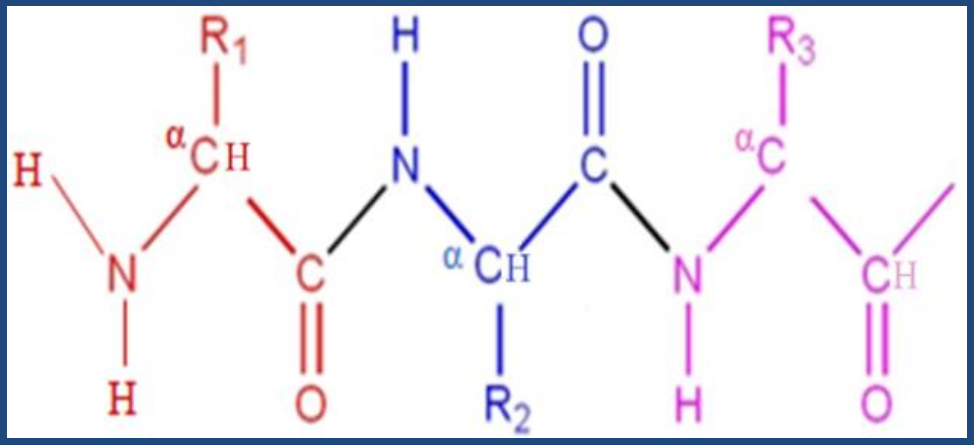
Numerous amino acids bind together to form a polypeptide chain:

N terminus C terminus

$$H_2N – CH(R1) – CO – NH – CH(R2) – CO – \ldots – NH – CH(Rn) – COOH$$

peptide bond

We see that the polypeptide chain has a monotonous “backbone”: $(\text{-NH-CH-CO})_n$, from which side chains are protruding.



D. Nikolova

Protein structure

There are 4 levels of organization of protein molecules

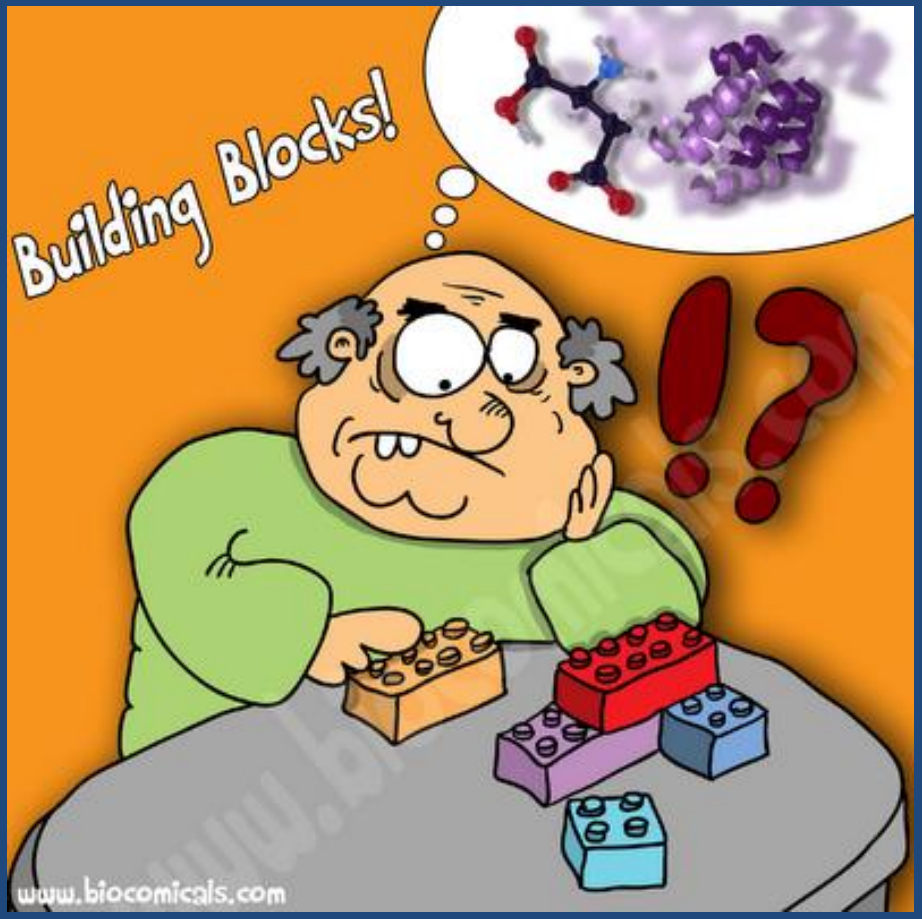
Primary structure = the sequence of the polypeptide chain

This includes:

- Number of amino acids (from <60 to >1500)
- Composition of amino acids (more basic, more acidic, more polar neutral, more hydrophobic…)
- Order of amino acids (how they are arranged in the polypeptide chain)

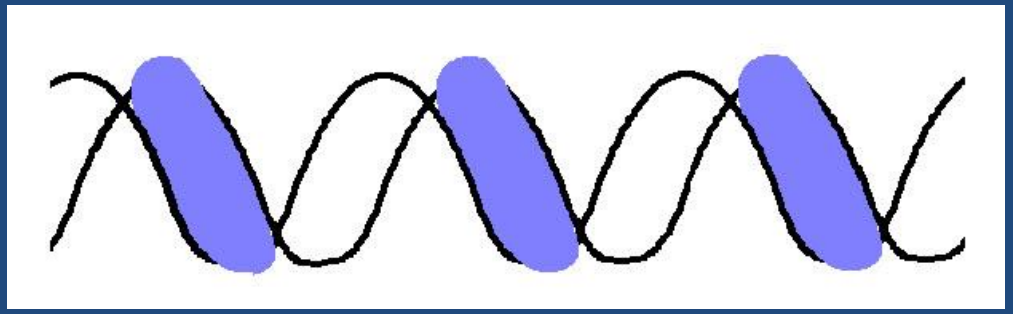
The primary structure is determined by the respective gene. It is based on peptide bonds between adjacent amino acids.

Primary structure ultimately determines all other levels of structure, plus the function of the protein.



Cartoon from www.biocomicals.com

Example 1: protamine
(major protein of sperm nucleus, packs DNA)



Small to fit in the DNA groove: 58 amino acids

H_2N-Glu-Arg-Thr-His-Gly-Gln-Ser-His-Tyr-Arg-Arg-Arg-His-Cys-Ser-Arg-Arg-Arg-Leu-His-Arg-Ile-His-Arg-Arg-Gln-His-Arg-Ser-Cys-Arg-Arg-Arg-Lys-Arg-Arg-Ser-Cys-Arg-His-Arg-Arg-Arg-His-Arg-Arg-Gly-Cys-Arg-Thr-Arg-Lys-Arg-Thr-Cys-Arg-Arg-His-COOH

Rich at basic amino acids to bind acidic DNA:

38 basic amino acids (blue) vs. only 1 acidic (red)

Example 2: sickle-cell anemia

Shutterstock

methionine - valine - histidine - leucine - threonine - proline - glutamate...

methionine - valine - histidine - leucine - threonine - proline - valine...

Just a single nucleotide mutation results in glutamic acid being substituted by valine in one of the hemoglobin polypeptide chains. Consequently, hemoglobin has an altered spatial structure, which causes a change in the shape of erythrocytes. Distortion of the red blood cell shape from a smooth, doughnut-like shape to ragged and full of spikes, making it fragile and susceptible to breaking within capillaries.

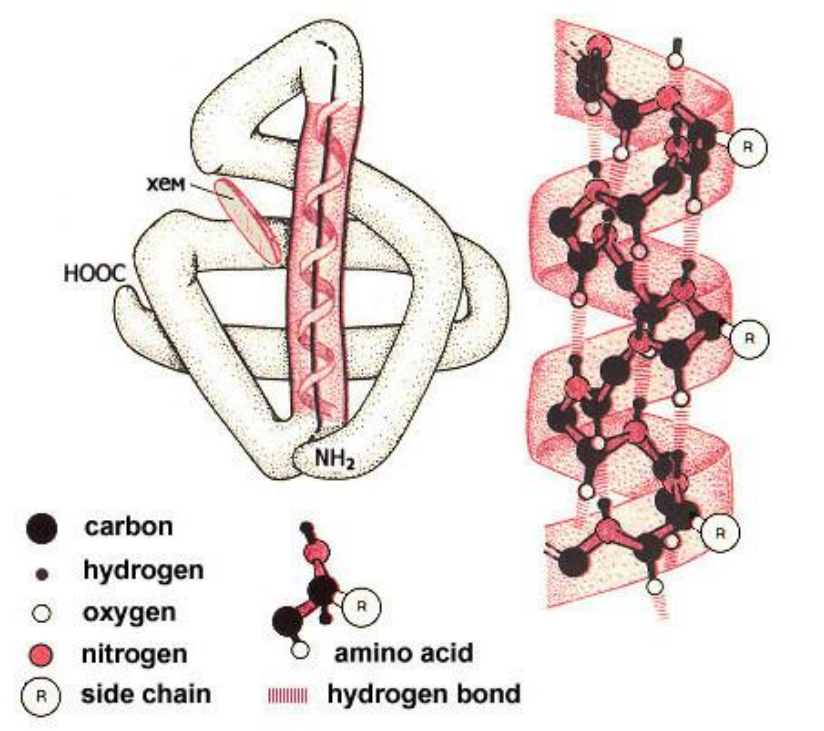
The next 3 levels form the spatial structure of proteins

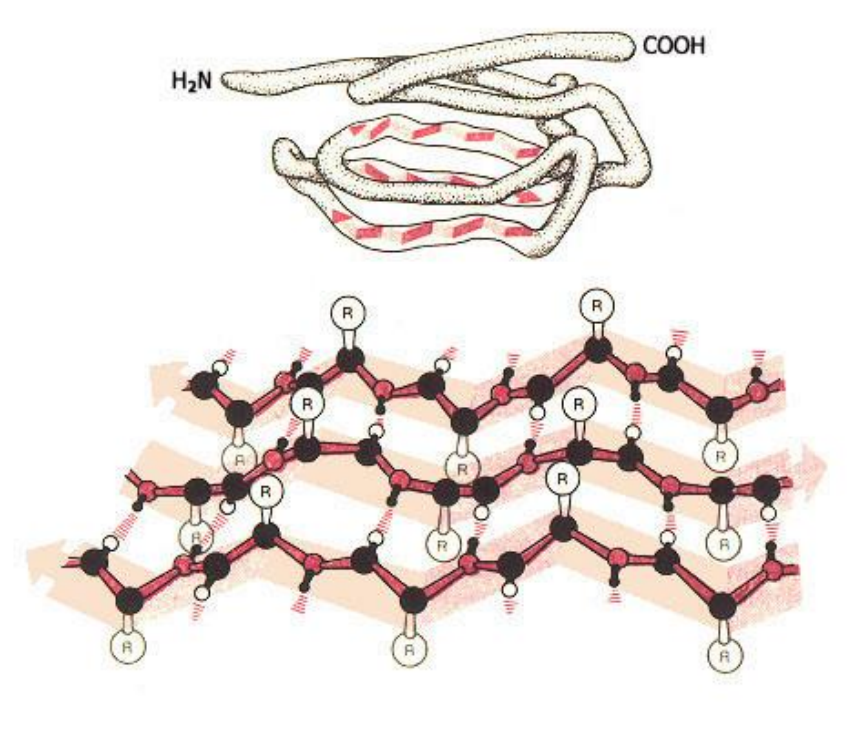
Secondary structure

The secondary structure is regular folding based on numerous hydrogen bonds between non-adjacent peptide groups of the $(\text{-NH-CH-CO})_n$ backbone.

$$> N - H :::: O = C <$$

There are two basic types of secondary structure:
alpha helix (e.g. in myoglobin) beta sheet (e.g. in immunoglobulin)



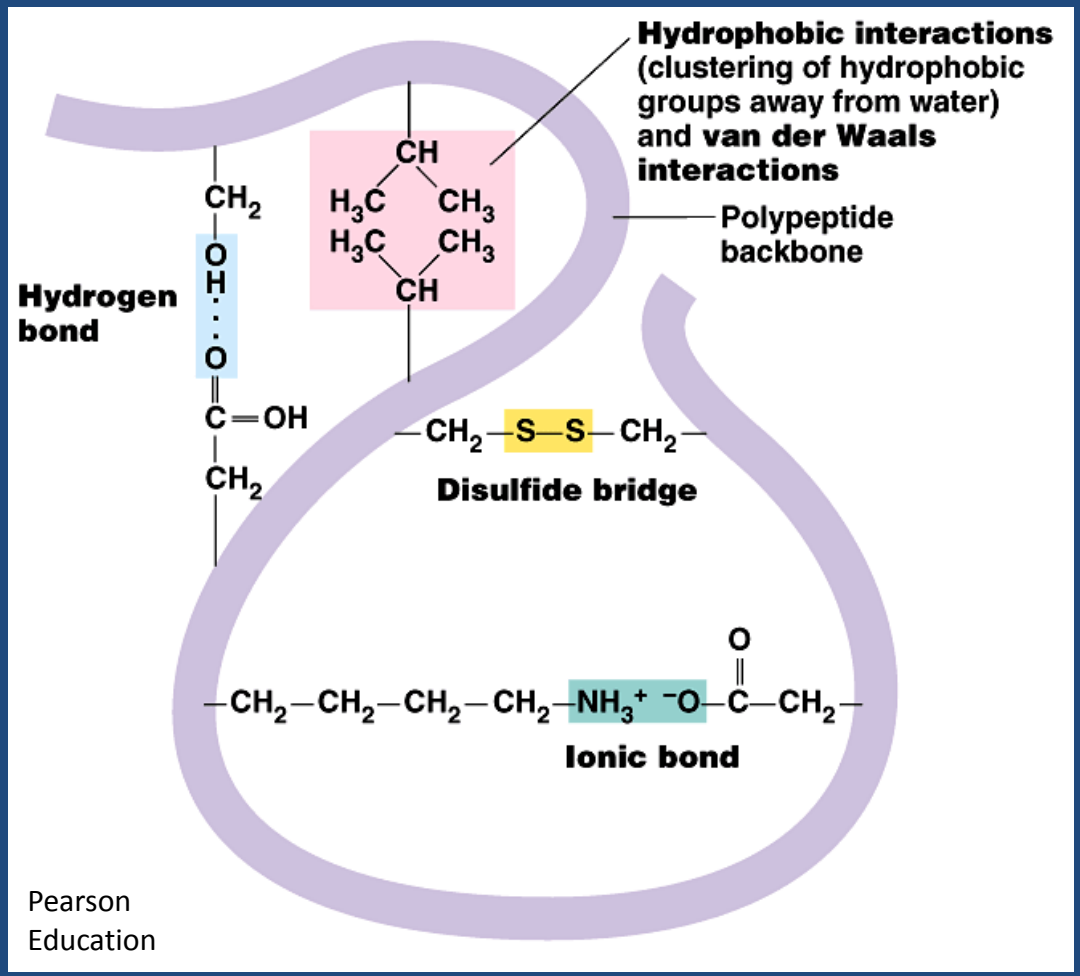


Drawings from *Molecular Biology of the Cell*

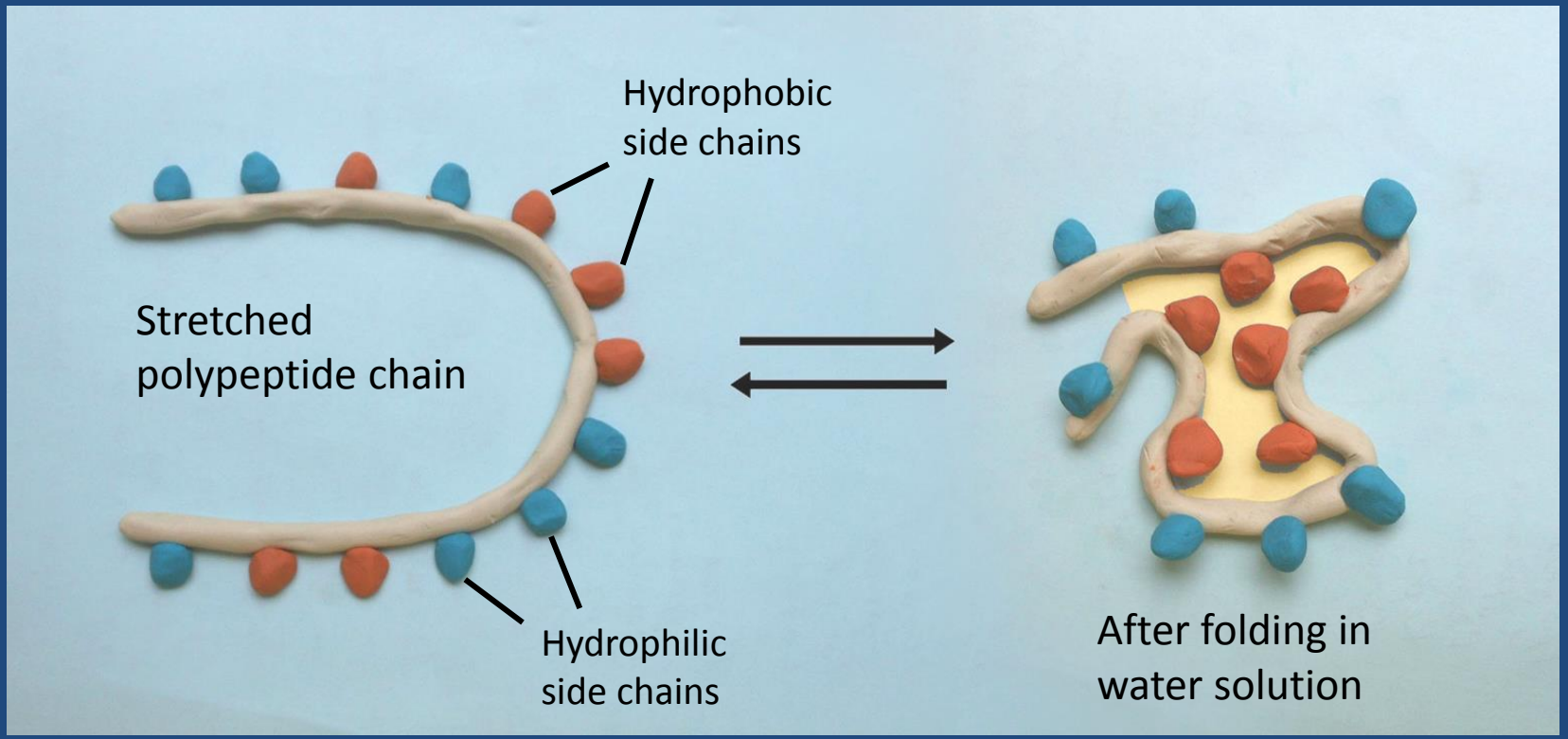
Tertiary structure

The tertiary structure is the final 3D folding of the polypeptide chain as a result of irregular but non-random bending of parts not included in secondary structure. It is based on interactions between side chains of distant amino acids.

$$-CH_2-SH + HS-CH_2- \rightarrow -CH_2-S-S-CH_2-$$



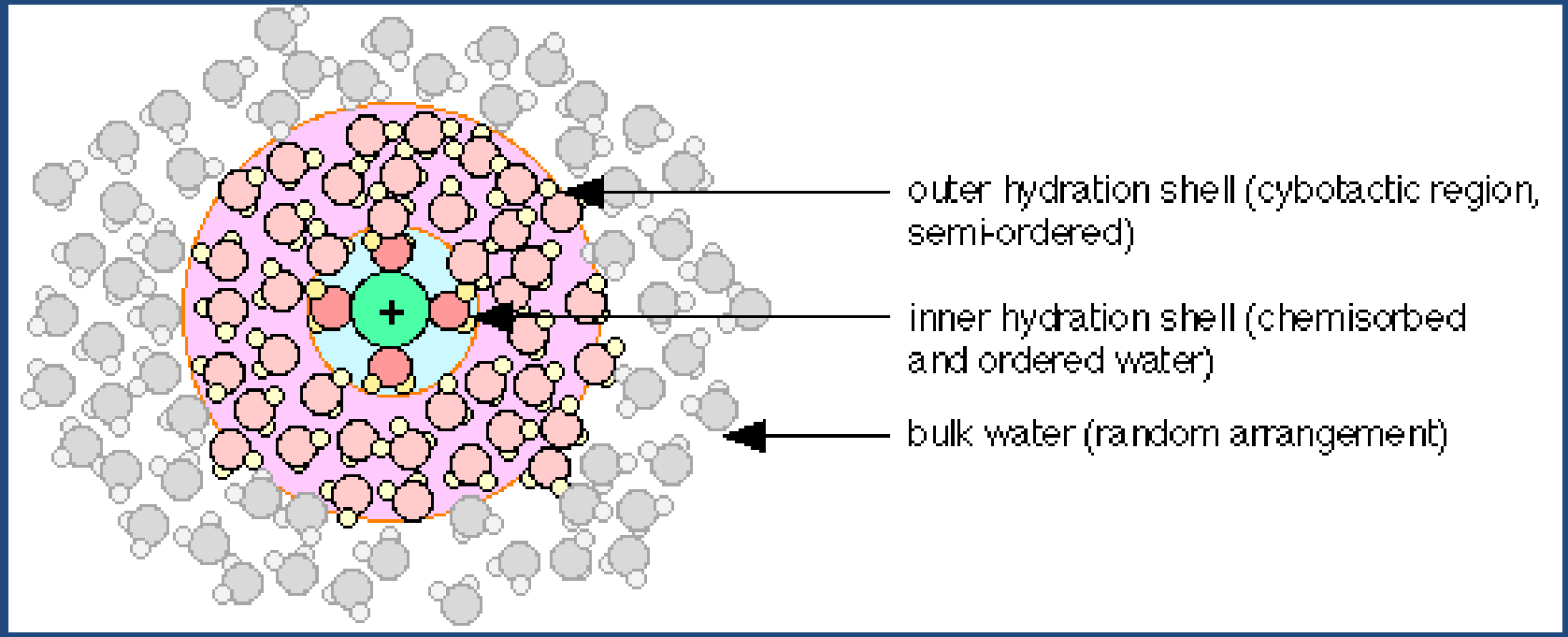
Hydrophobic interactions



(Based on an idea from Alberts et al. *Molecular Biology of the Cell*.)

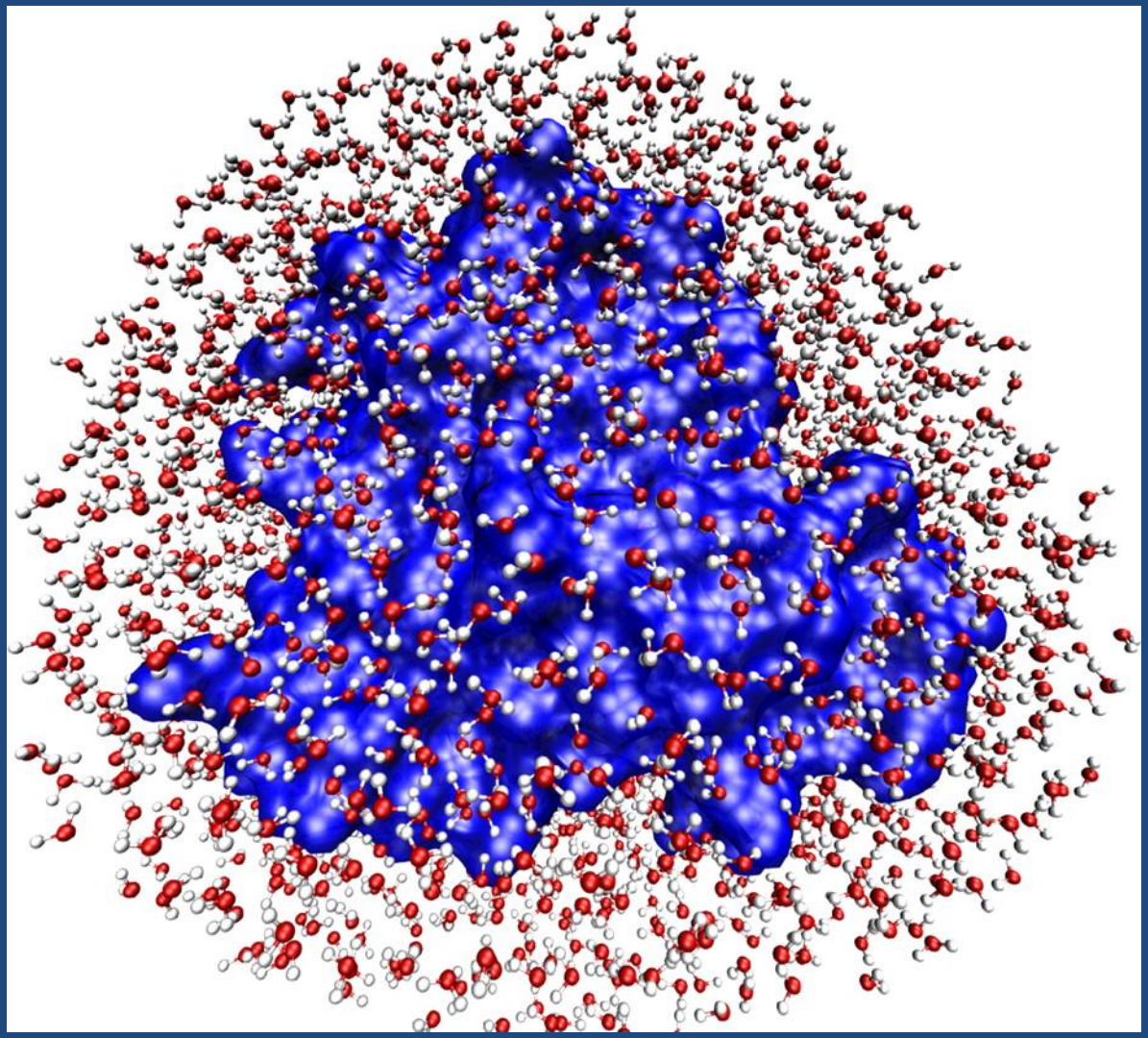
The hydrophobic effect is the tendency of nonpolar substances to aggregate in an aqueous solution and exclude water molecules. The word hydrophobic literally means "water-fearing", and it describes the segregation of water and nonpolar substances, which maximizes hydrogen bonding between molecules of water and minimizes the area of contact between water and nonpolar molecules.

Hydration shell



Ion with hydration shell (scheme by Stephen Lower, www.chem1.com)

https://www.pnas.org/content/106/13/5129



The hydration shell of myoglobin. Diagram of myoglobin (blue surface) with water molecules. The waters form a shell ≈5 Å thick around the protein.

Quaternary structure

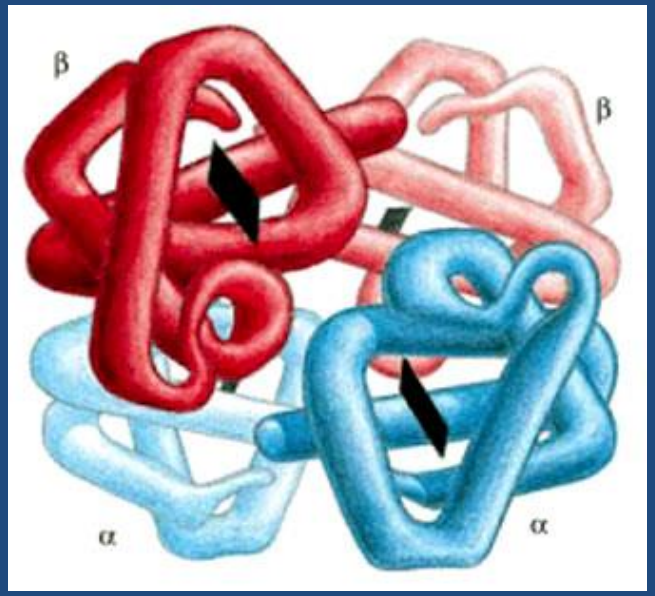
Proteins assembled from two or more polypeptide chains (called subunits) have quaternary structure.

It is supported by the same type of bonds as in tertiary structure.

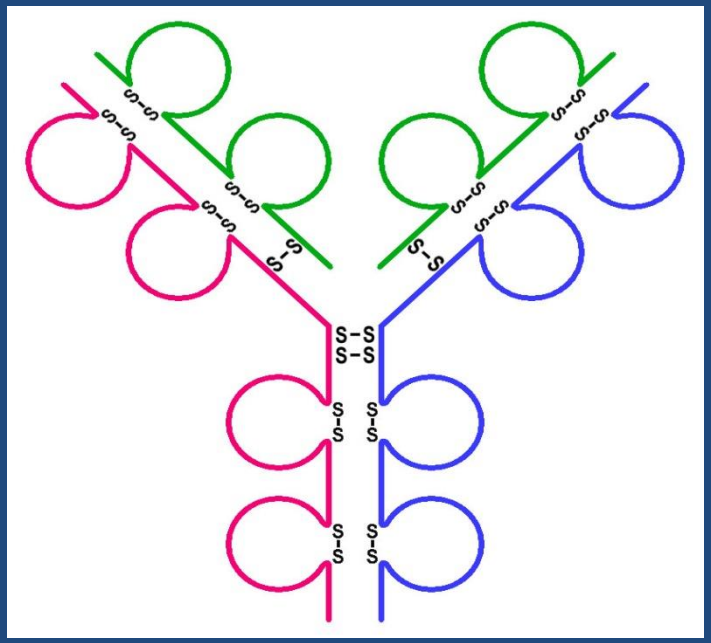
Myoglobin has only tertiary structure…

(Images from *Molecular Biology of the Cell*)

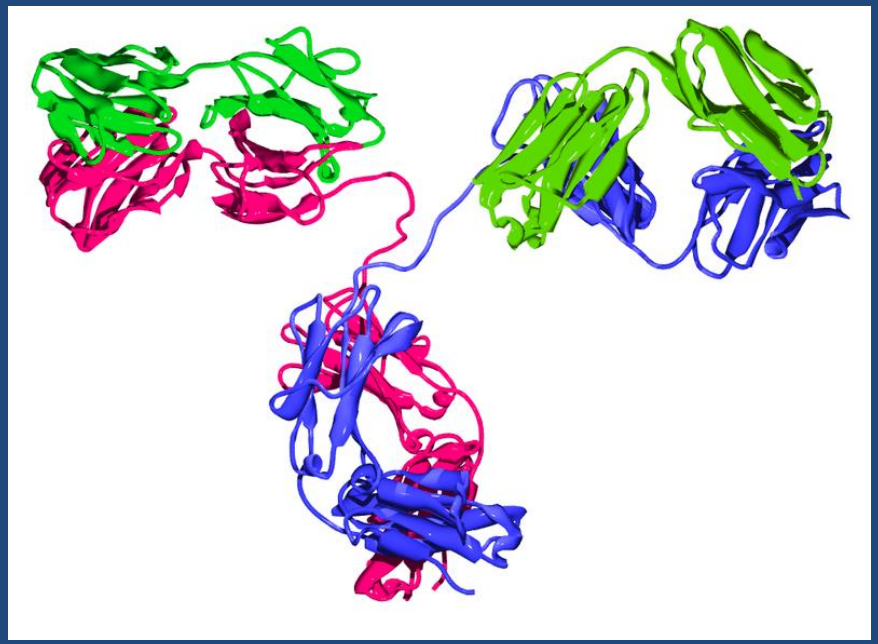
…but the related protein hemoglobin is formed by 4 subunits (2 alpha and 2 beta chains), bound non-covalently.



Spatial structure of immunoglobulins (antibodies)



Schematic drawing of IgG

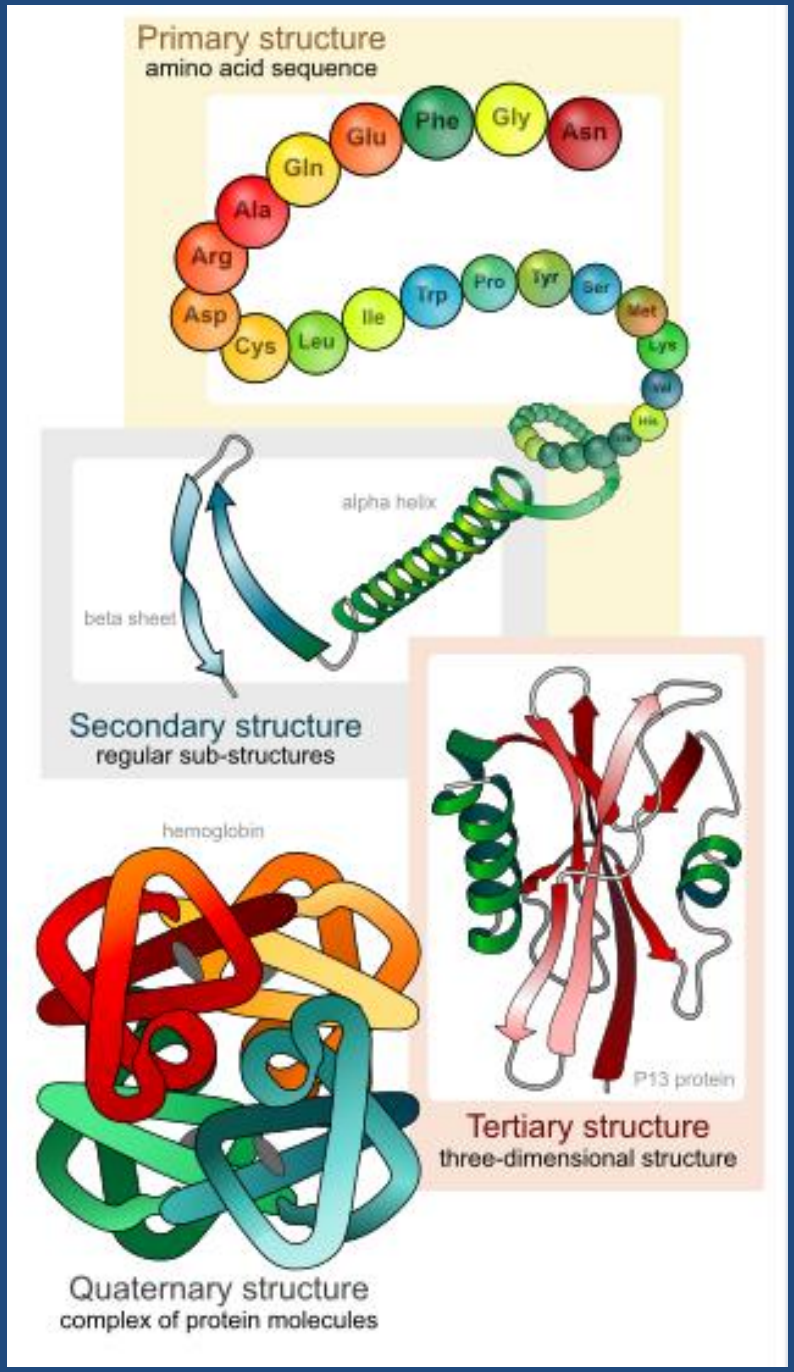


Molecular model of IgG

(by Tim Vickers, adapted)

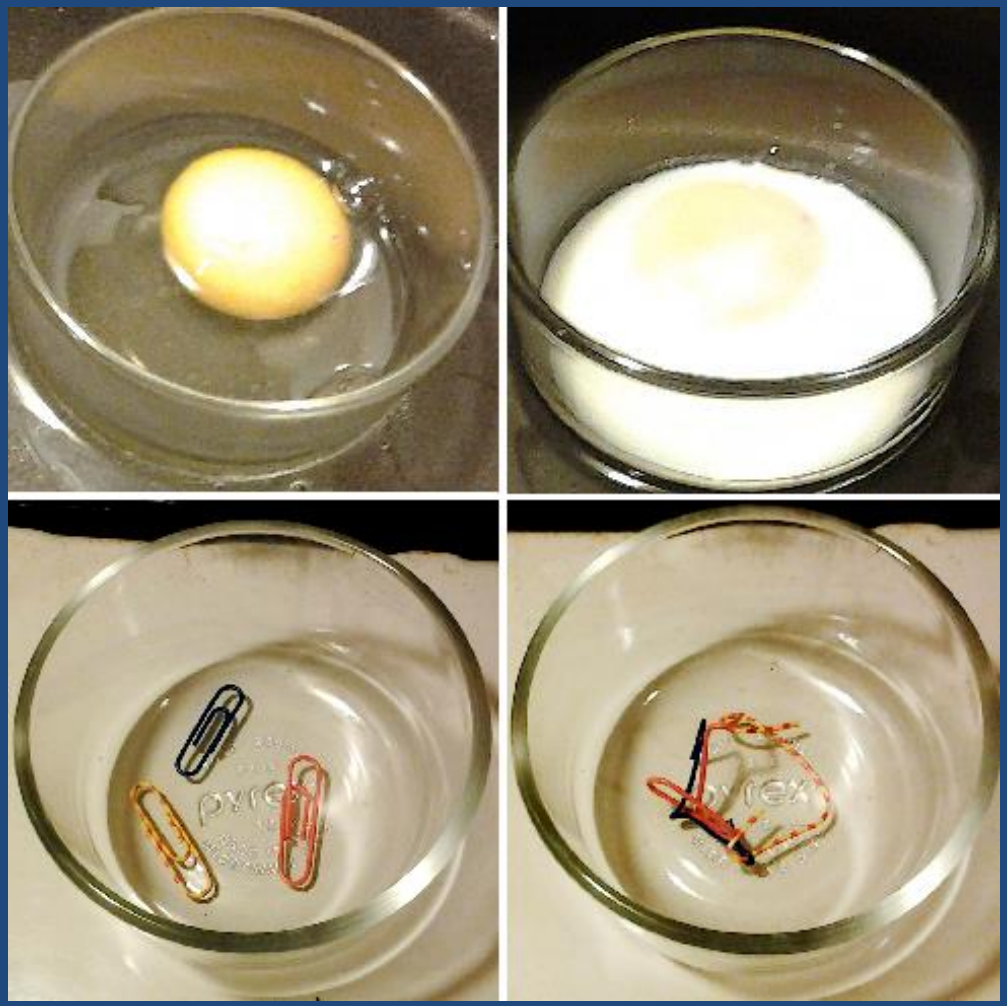
One IgG molecule consists of 4 polypeptide chains

The four structures again



Mariana Ruiz / Wikimedia

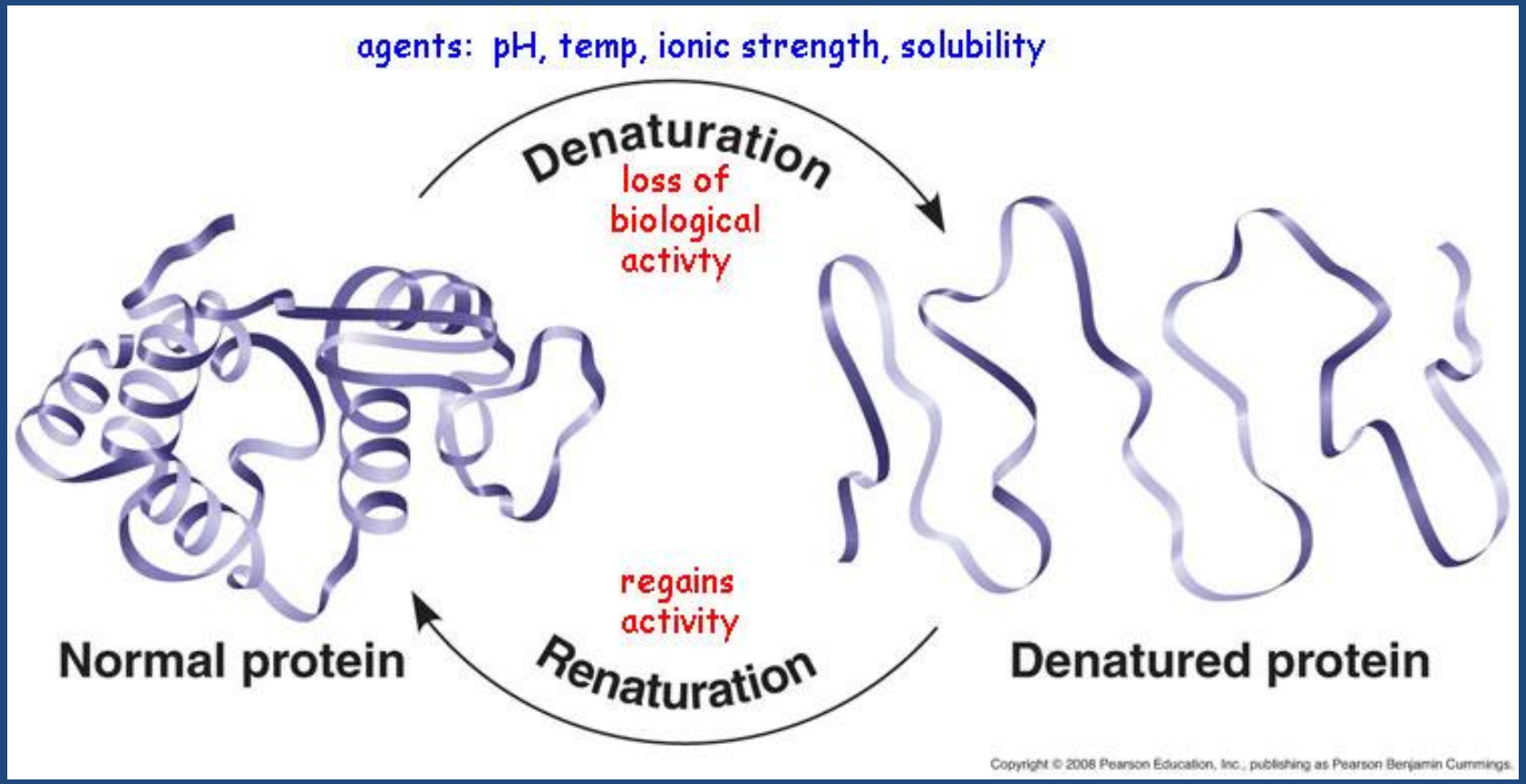
Native state of proteins and its loss (denaturation)



Rmadla / Wikimedia

The denaturation of the proteins of egg white by heat – as when boiling an egg – is an example of irreversible denaturation. The denatured protein has the same primary structure as the original, or native, protein.
Paperclips provide a visual analogy to help with the conceptualization of the denaturation process.

The opposite process (renaturation) is possible, but don’t rely on it



Pearson Education