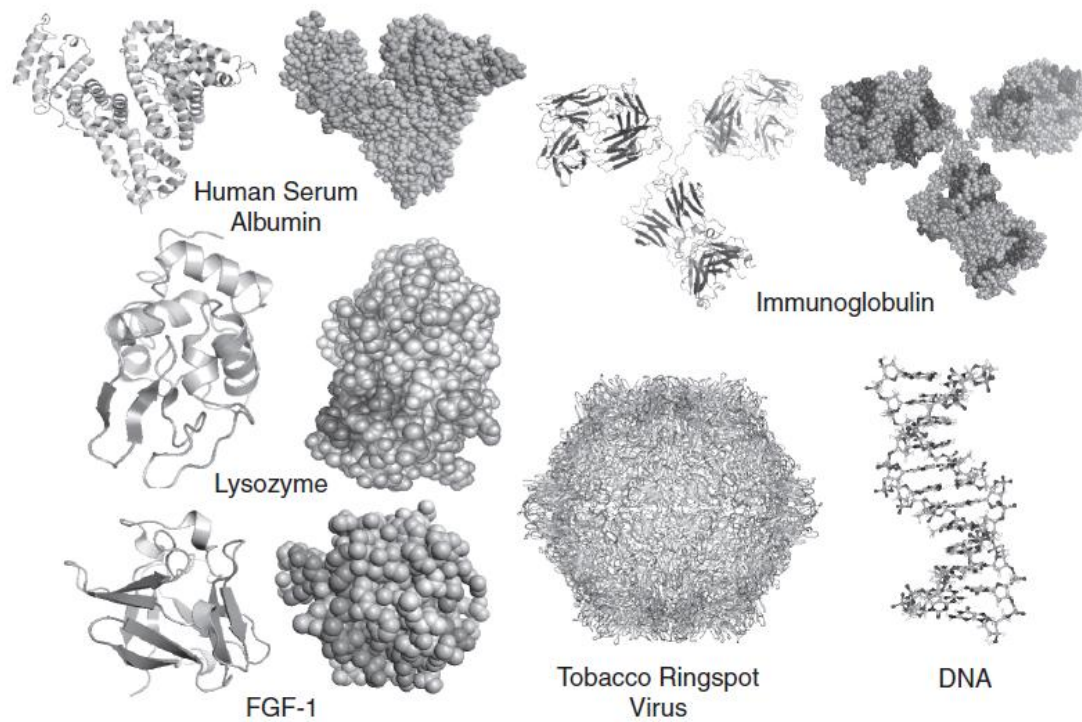


# Introduction; Amino Acids, Peptides and Proteins

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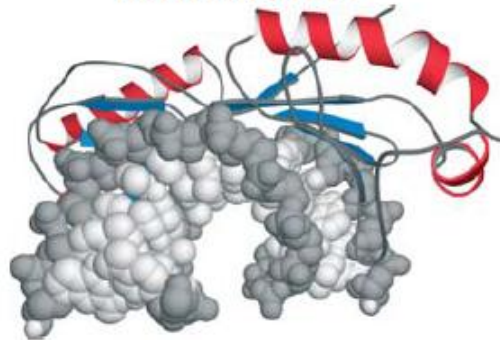


Proteins are the most abundant and functionally diverse molecules in living systems. Virtually every life process depends on this class of molecules. For example, **enzymes** and polypeptide **hormones** direct and regulate metabolism in the body, whereas **contractile proteins in muscle** permit movement. In bone, the protein **collagen** forms a framework for the deposition of calcium phosphate crystals, acting like the steel cables in reinforced concrete. In the bloodstream, proteins, such as **hemoglobin** and **plasma albumin**, shuttle molecules essential to life, whereas **immunoglobulins** fight infectious bacteria and viruses. In short, proteins display an incredible diversity of functions, yet all share the common structural feature of being linear polymers of amino acids.

## Binding

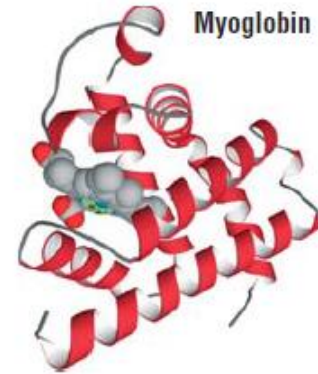
Specific recognition of other molecules is central to protein function. The molecule that is bound (the ligand) can be as small as the oxygen molecule that coordinates to the heme group of myoglobin, or as large as the specific DNA sequence (called the TATA box) that is bound—and distorted—by the TATA binding protein. Specific binding is governed by shape complementarity and polar interactions such as hydrogen bonding.

TATA binding protein



The TATA binding protein binds a specific DNA sequence and serves as the platform for a complex that initiates transcription of genetic information. (PDB 1tgh)

Myoglobin

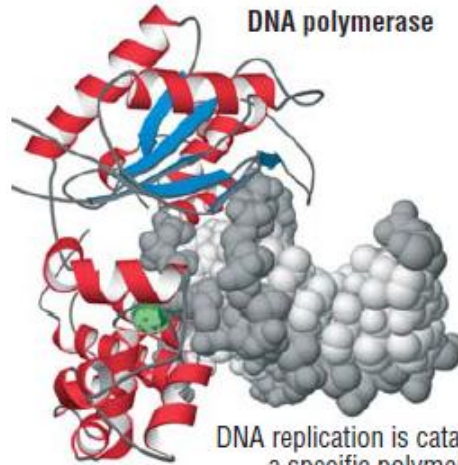


Myoglobin binds a molecule of oxygen reversibly to the iron atom in its heme group (shown in grey with the iron in green). It stores oxygen for use in muscle tissues. (PDB 1a6k)

## Catalysis

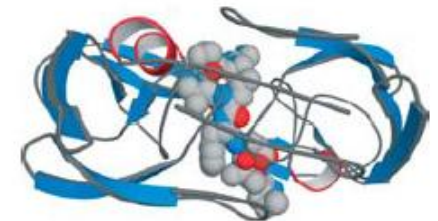
Essentially every chemical reaction in the living cell is catalyzed, and most of the catalysts are protein enzymes. The catalytic efficiency of enzymes is remarkable: reactions can be accelerated by as much as 17 orders of magnitude over simple buffer catalysis. Many structural features contribute to the catalytic power of enzymes: holding reacting groups together in an orientation favorable for reaction (proximity); binding the transition state of the reaction more tightly than ground state complexes (transition state stabilization); acid-base catalysis, and so on.

DNA polymerase



DNA replication is catalyzed by a specific polymerase that copies the genetic material and edits the product for errors in the copy. (PDB 1pbx)

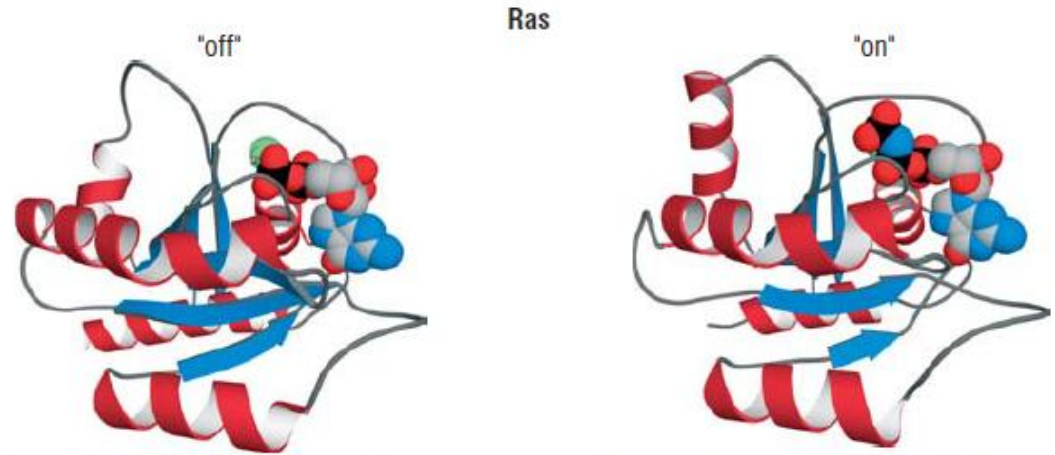
HIV protease



Replication of the AIDS virus HIV depends on the action of a protein-cleaving enzyme called HIV protease. This enzyme is the target for protease-inhibitor drugs (shown in grey). (PDB 1a8k)

## Switching

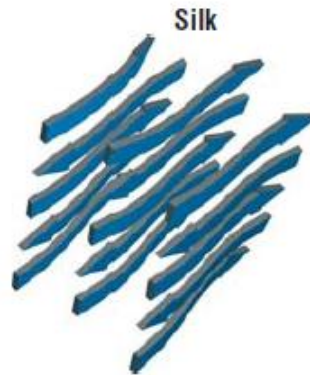
Proteins are flexible molecules and their conformation can change in response to changes in pH or ligand binding. Such changes can be used as molecular switches to control cellular processes. One example, which is critically important for the molecular basis of many cancers, is the conformational change that occurs in the small GTPase Ras when GTP is hydrolyzed to GDP. The GTP-bound conformation is an "on" state that signals cell growth; the GDP-bound structure is the "off" signal.



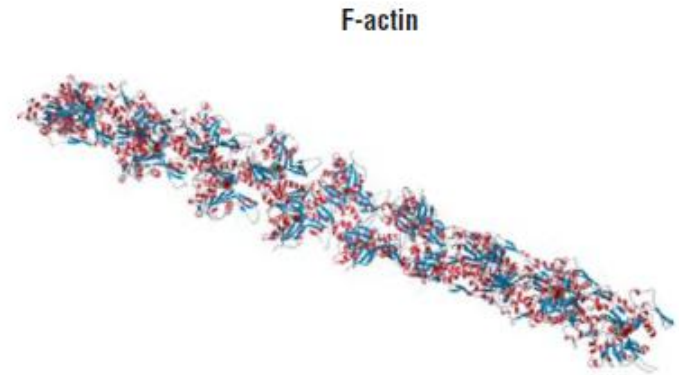
The GDP-bound ("off"; PDB 1pll) state of Ras differs significantly from the GTP-bound ("on"; PDB 121p) state. This difference causes the two states to be recognized by different proteins in signal transduction pathways.

## Structural Proteins

Protein molecules serve as some of the major structural elements of living systems. This function depends on specific association of protein subunits with themselves as well as with other proteins, carbohydrates, and so on, enabling even complex systems like actin fibrils to assemble spontaneously. Structural proteins are also important sources of biomaterials, such as silk, collagen, and keratin.



Silk derives its strength and flexibility from its structure: it is a giant stack of antiparallel beta sheets. Its strength comes from the covalent and hydrogen bonds within each sheet; the flexibility from the van der Waals interactions that hold the sheets together. (PDB 1slk)

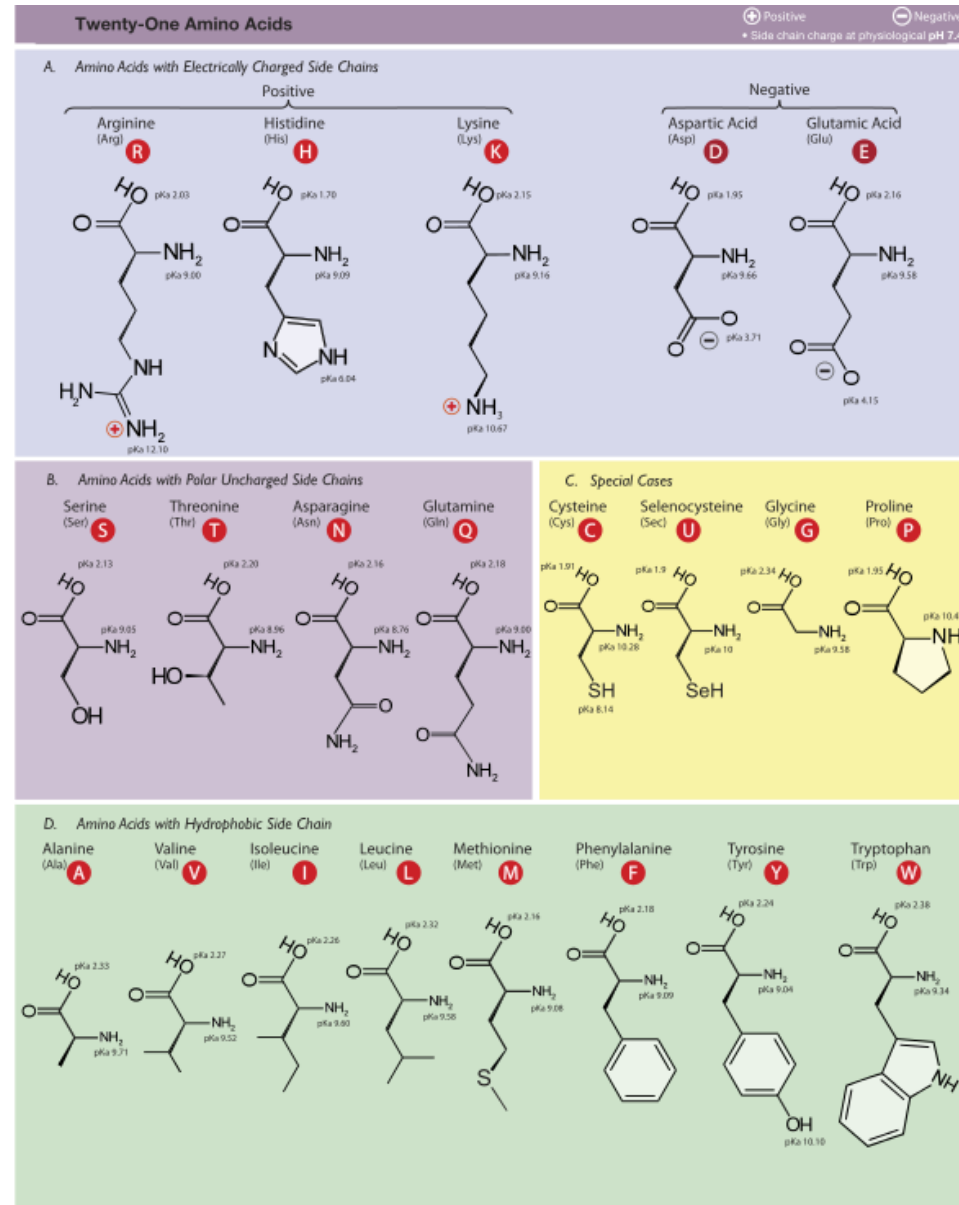
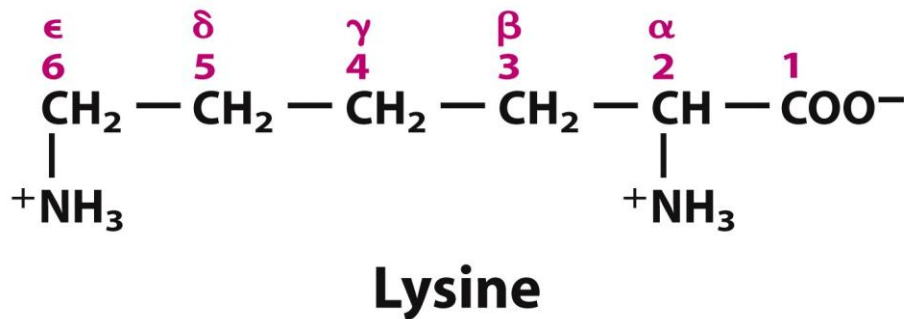


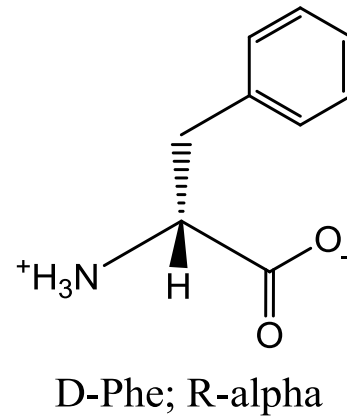
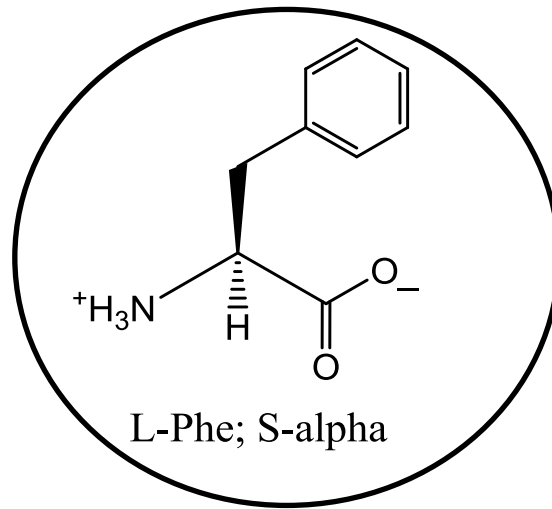
Actin fibers are important for muscle contraction and for the cytoskeleton. They are helical assemblies of actin and actin-associated proteins. (Courtesy of Ken Holmes)



# Amino Acids: the 20 Building Blocks

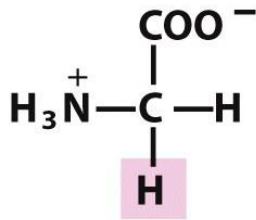
- The  $\alpha$ -carbon has always four substituents.
- All (except proline) have an acidic carboxyl group, a basic amino group, and an alpha hydrogen connected to the  $\alpha$ -carbon
- Each amino acid has a unique fourth substituent R (Side chain).
- In glycine, the fourth substituent is also Hydrogen.



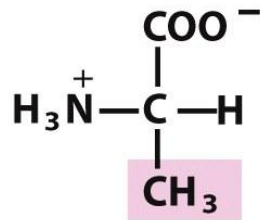


- Natural amino acids take L- Configuration.
- Amino acids are designated with one and three letter codes.
- Category of amino acids based on side chains
  - Hydrophobic
    - Aliphatic : Ala, Leu, Ile, Val, Pro, Gly
    - Aromatic : Trp, Phe, Tyr
  - Polar
    - Non-charged: Ser, Thr, Asn and Gln
    - Charged Amino Acids
      - Basic: Lys, Arg, and His
      - Acidic: Asp and Glu

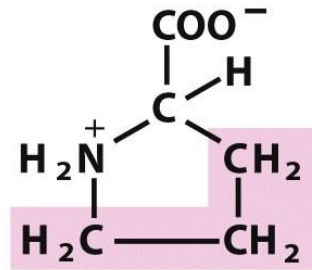
## Nonpolar, aliphatic R groups



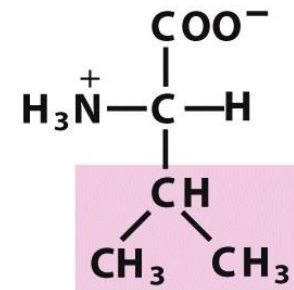
**Glycine**



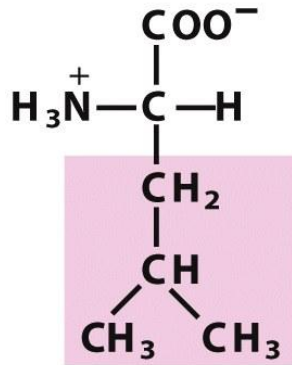
**Alanine**



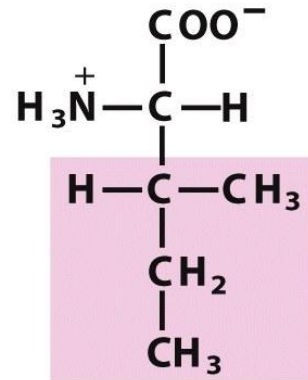
**Proline**



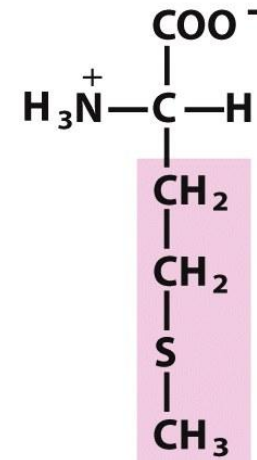
**Valine**



**Leucine**



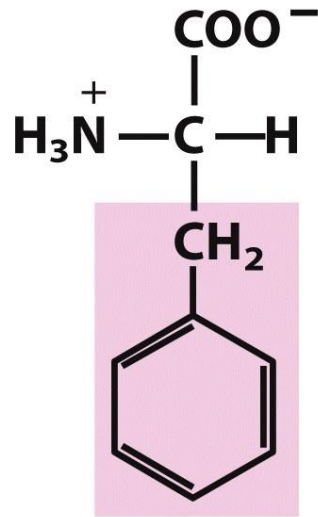
**Isoleucine**



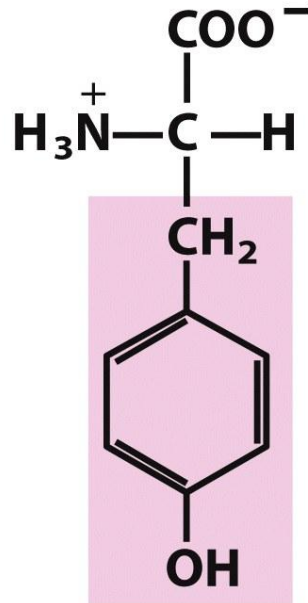
**Methionine**

These amino acid side chains are hydrophobic

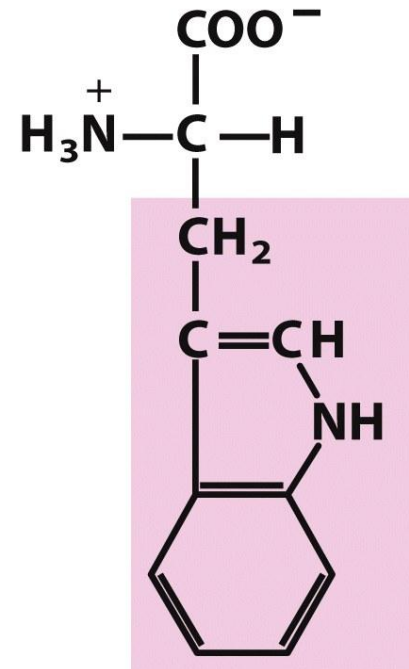
# Aromatic R groups



**Phenylalanine**



**Tyrosine**



**Tryptophan**

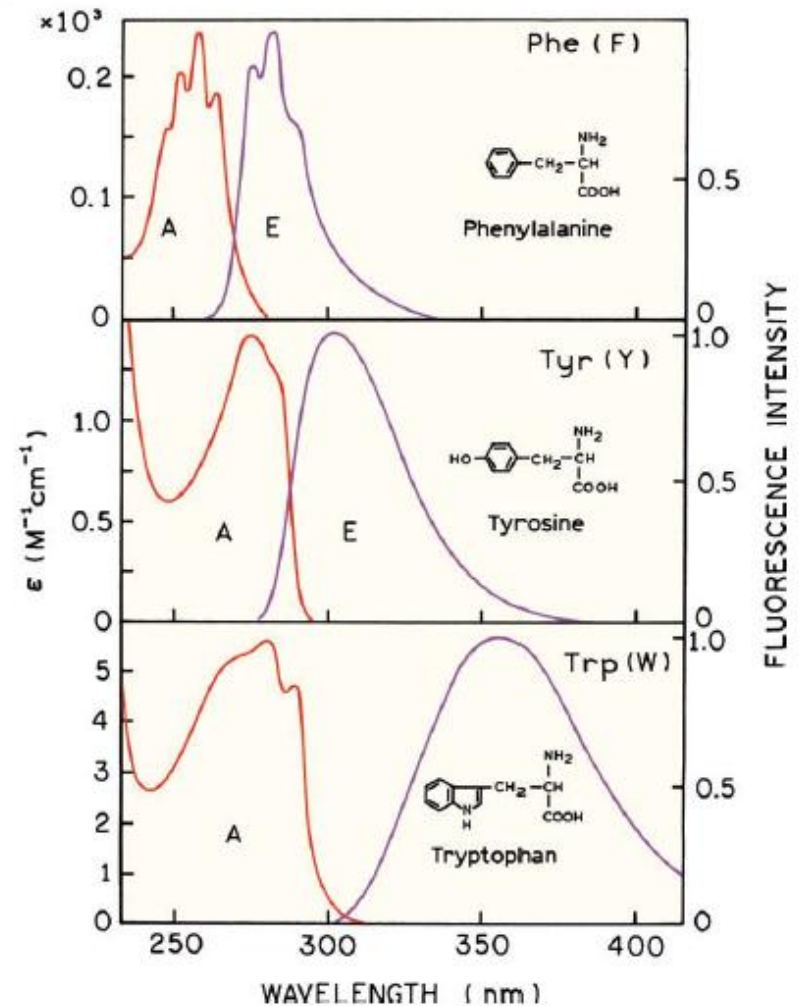
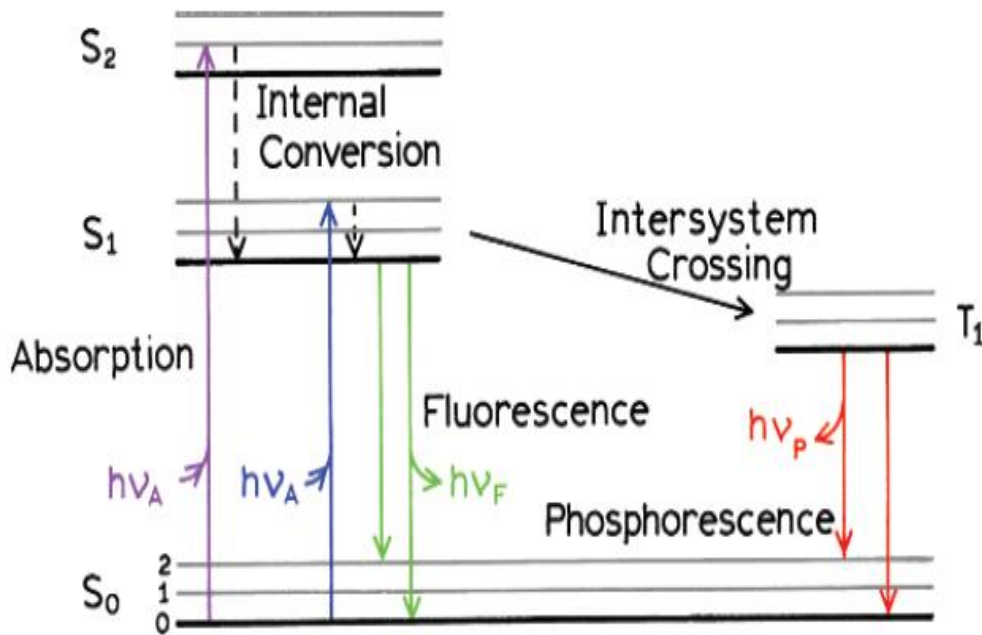
These amino acid side chains Absorb and emit light at  
different wavelength



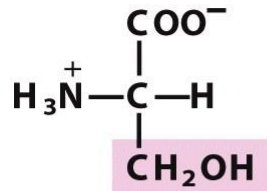


Alexander Jablonski (1898-1980)

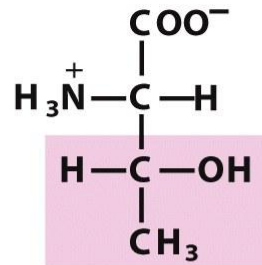
Absorption (A) and emission (E) spectra of the aromatic amino acids in pH 7.0



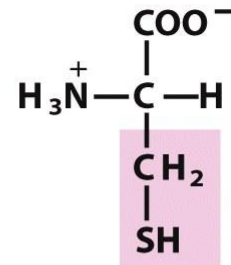
## Polar, uncharged R groups



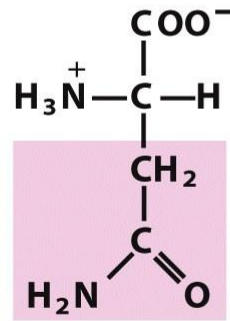
**Serine**



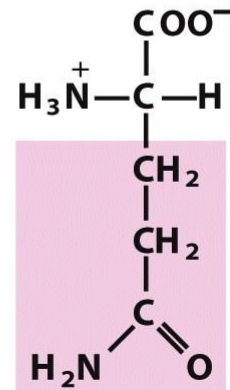
**Threonine**



**Cysteine**



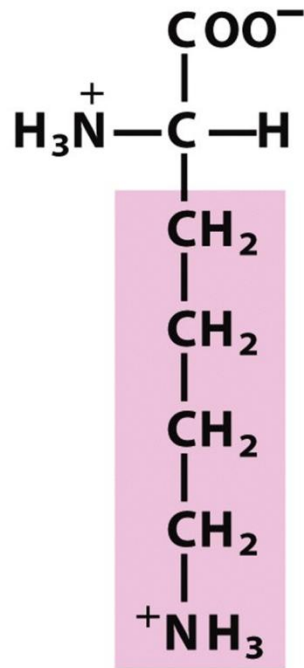
**Asparagine**



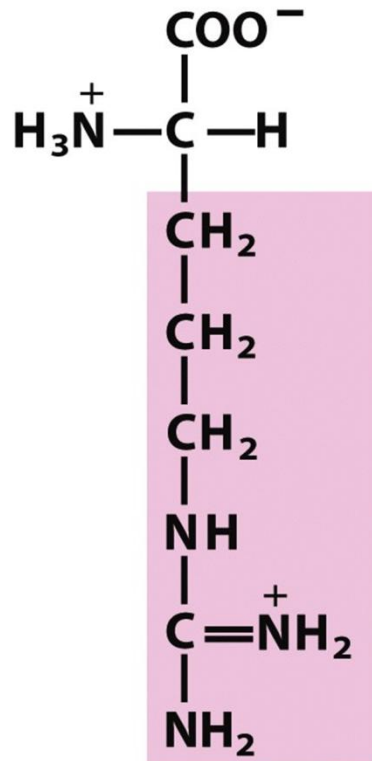
**Glutamine**

- These amino acids side chains can form hydrogen bonding.
- Cysteine can form disulfide bonds.

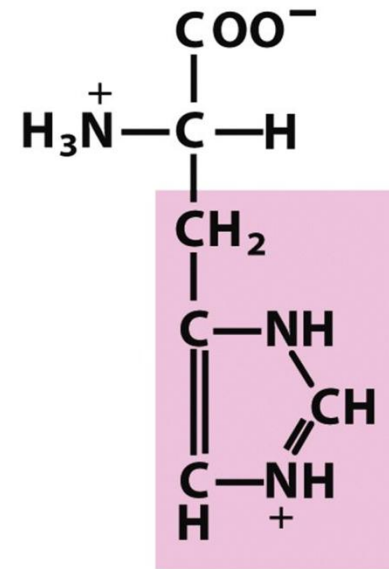
# Positively charged R groups



**Lysine**

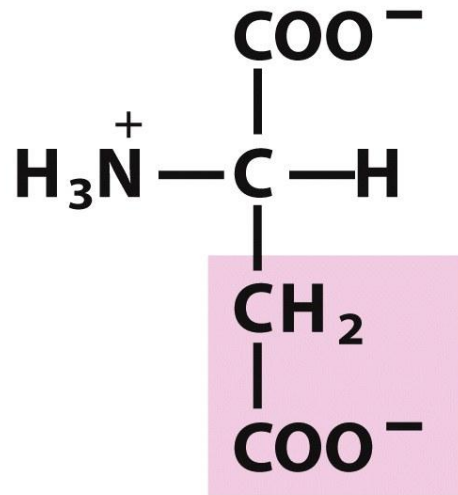


**Arginine**

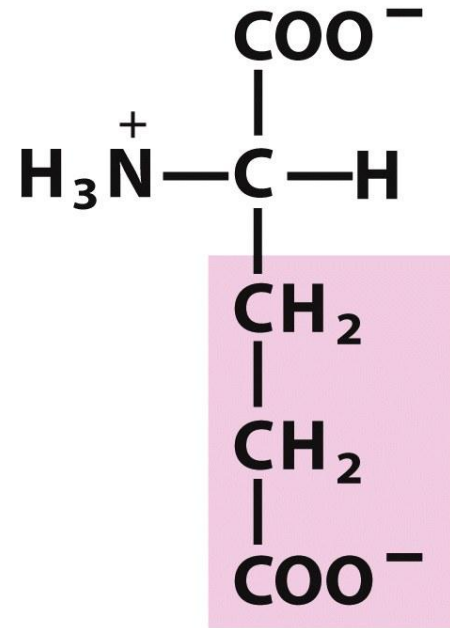


**Histidine**

# Negatively charged R groups

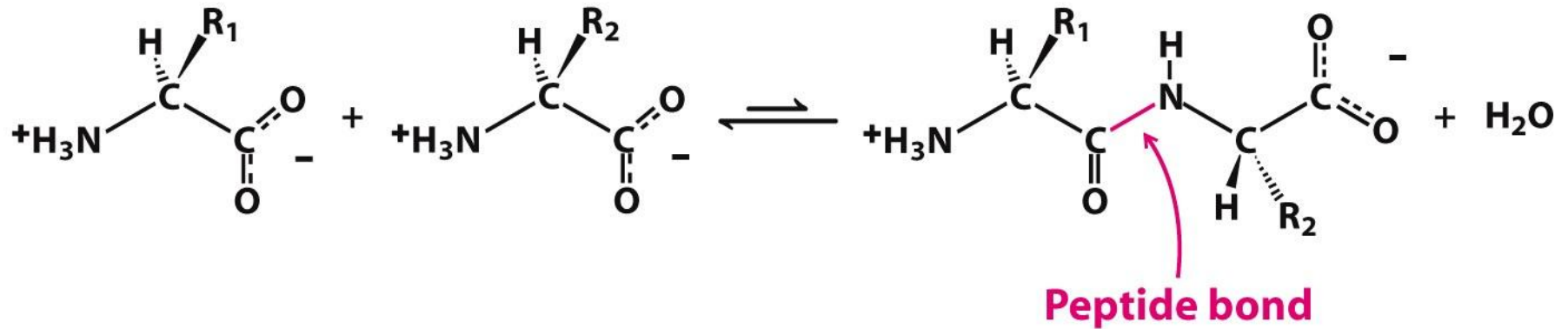


**Aspartate**

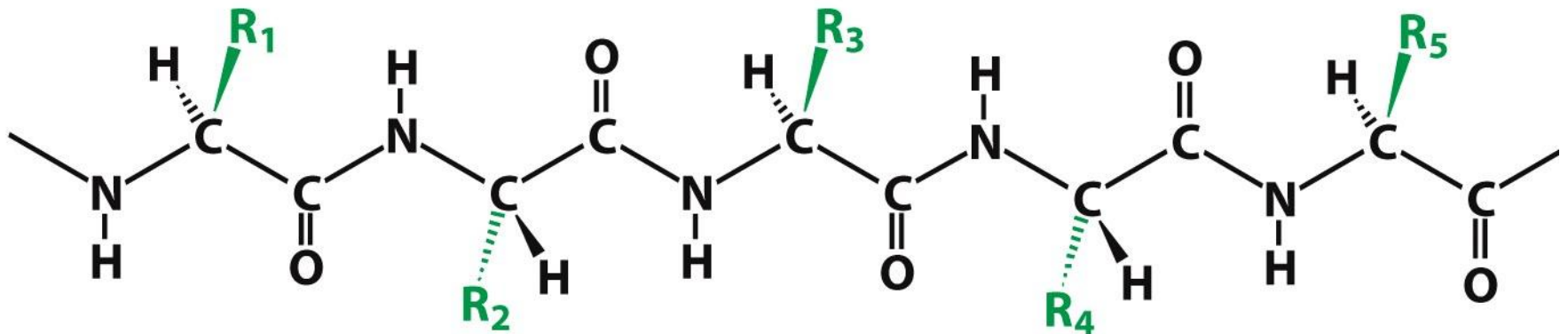


**Glutamate**

Amino Acids are linked in proteins by Peptide Bond through condensation reaction

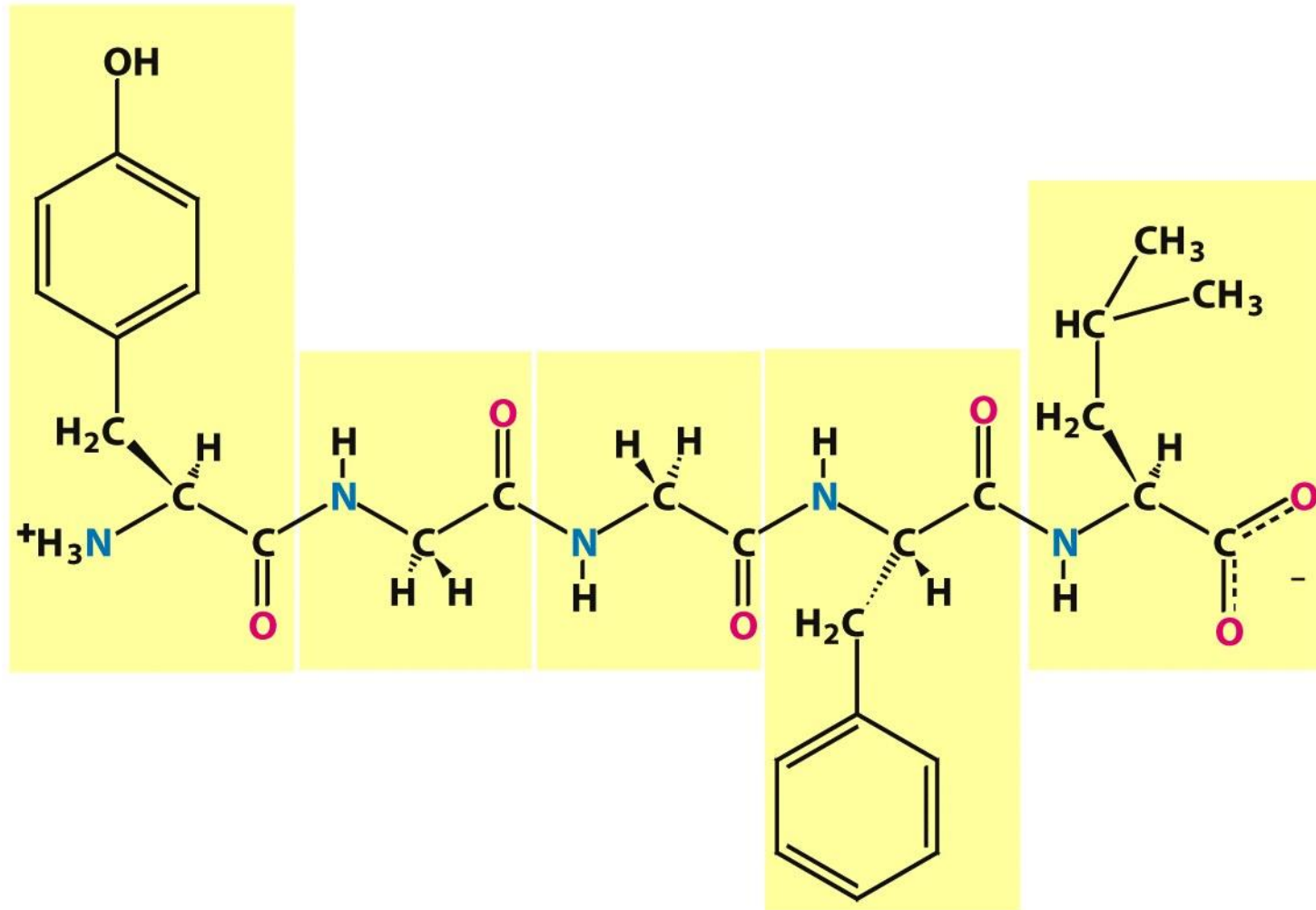


The polypeptide backbone is a repetition of the basic unit common to all amino acids. Amino Acid side chains define the structural/functional aspect of proteins.





Sequences of Amino Acids in proteins are usually written with either the three letter or one letter abbreviations



**Tyr**

**Gly**

**Gly**

**Phe**

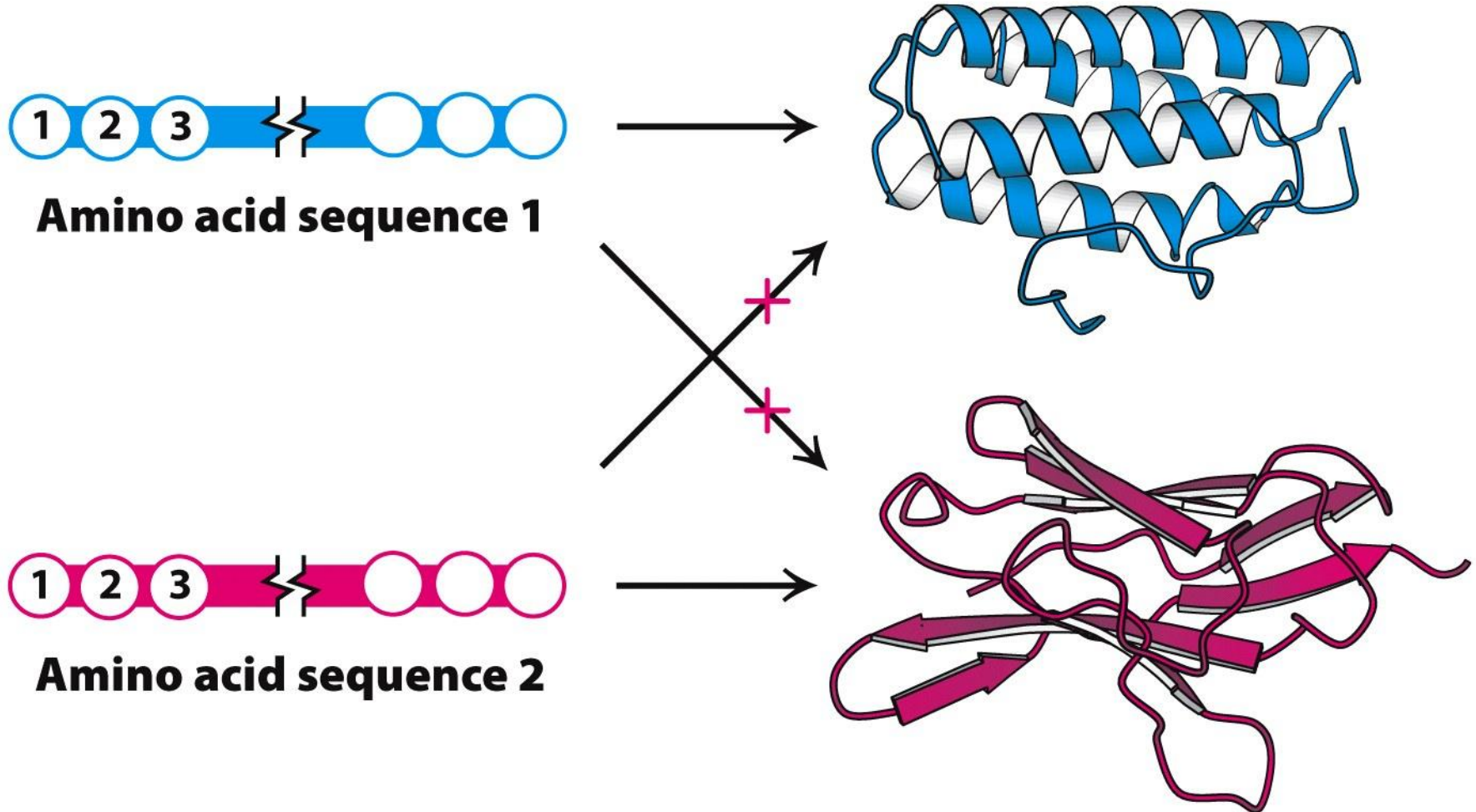
**Leu**

**Amino-terminal residue**



**Carboxyl-terminal residue**

# Amino Acid sequence defines the protein conformation



But to do so, different forces are needed to get to the final  
Most stable conformation  
“Next class”