Lecture #2

Probes/Targets Building Blocks

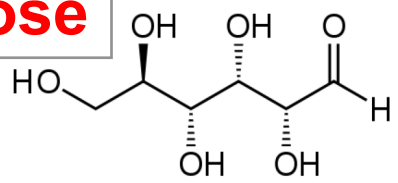
Lecture Outline

(Book Bio/CMOS: Chapter' paragraphs §3.3-3.8)

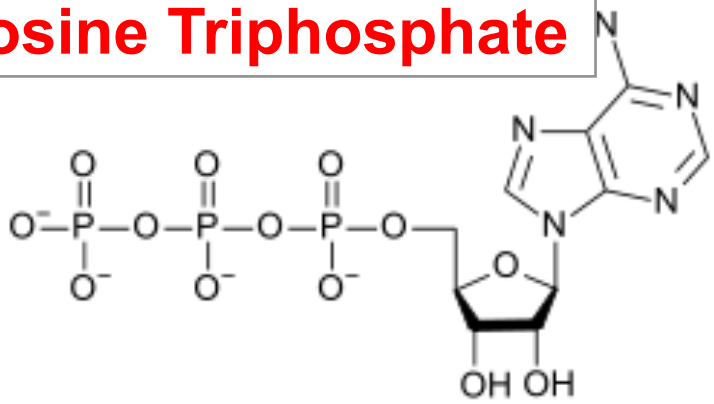
- Metabolites
- Linkers
- Peptides
- Poly-peptides
- Proteins
- DNA

Human metabolites

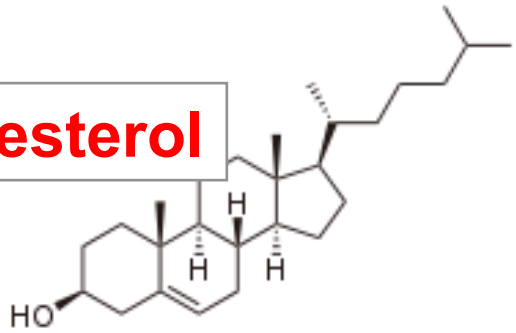
D-glucose

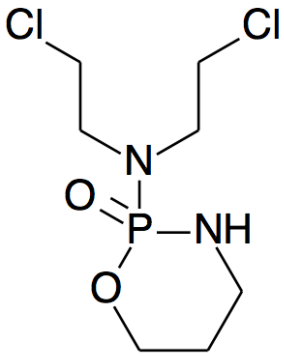


Adenosine Triphosphate

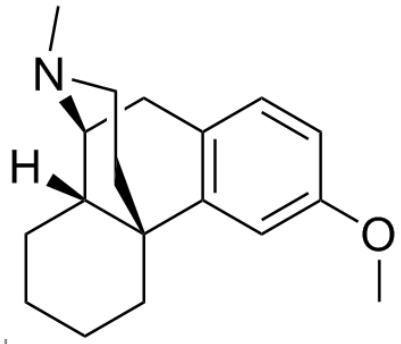


Cholesterol

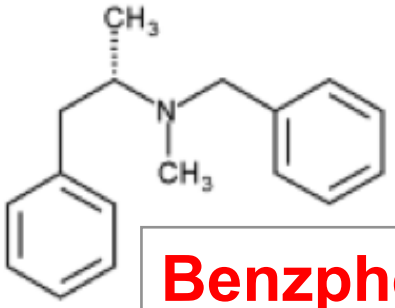




Dextromethorphan

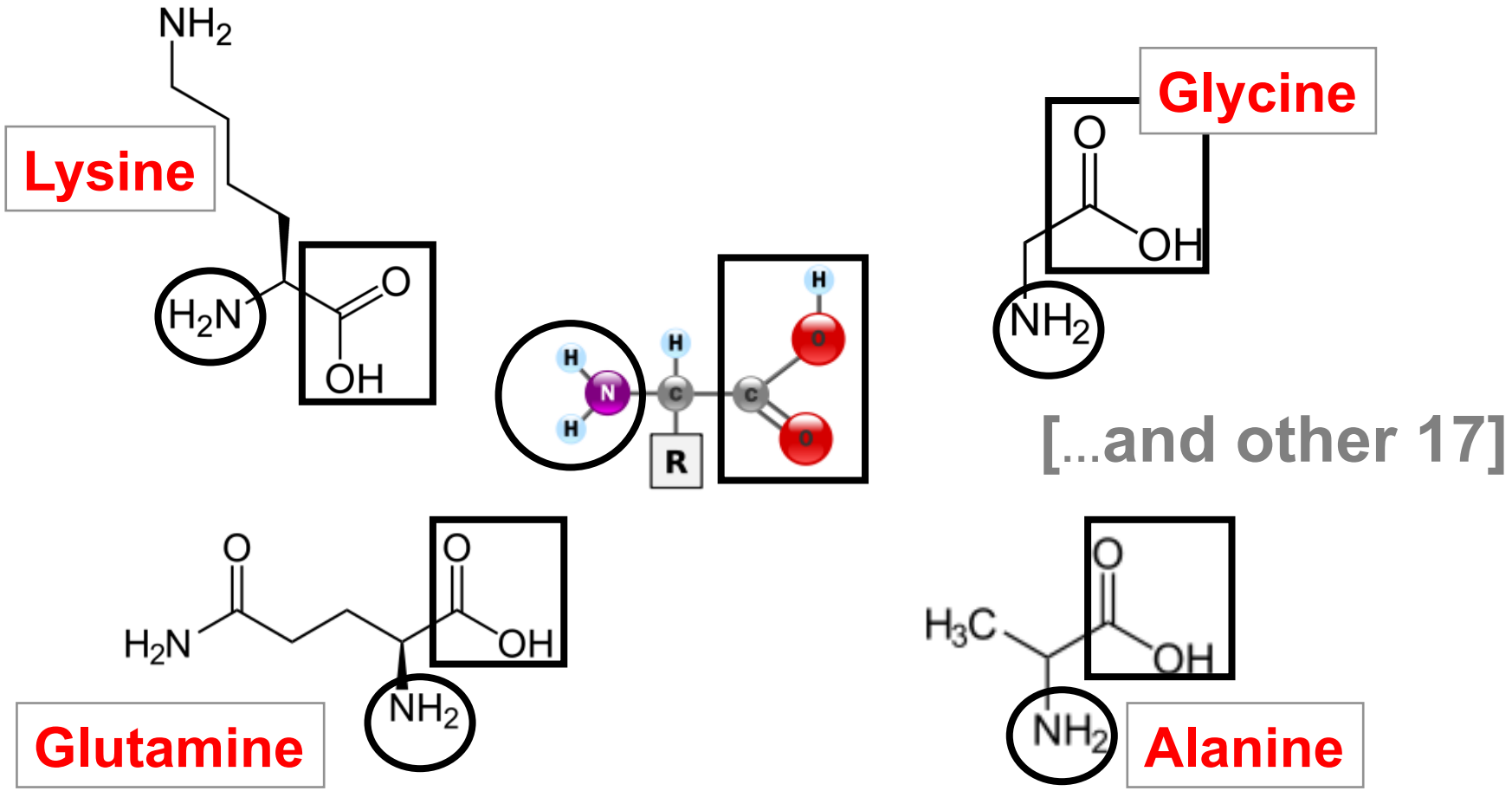


Cyclophosphamide



Benzphetamine

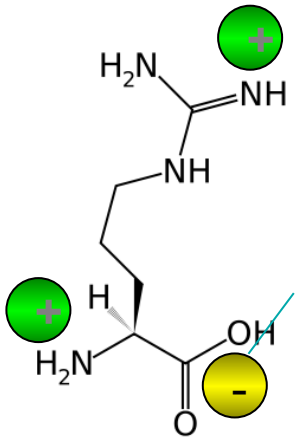
Amino Acids



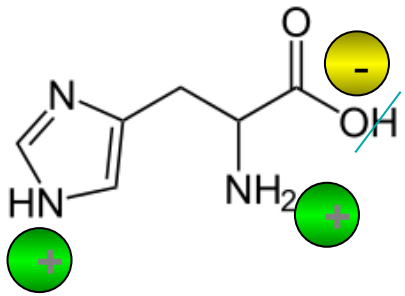
Amino acids are molecules containing an amine group (NH2), a carboxylic acid group (COOH) and a side chain that varies between different amino acids

Charged AA

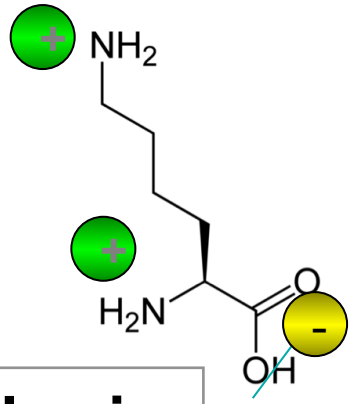
Positively Charged



Arginine

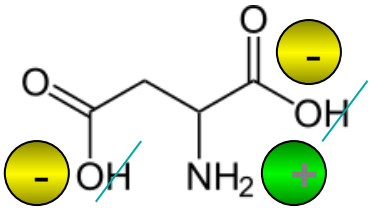


Histidine

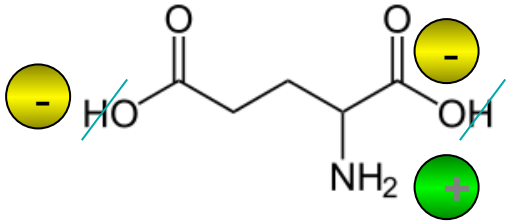


Lysine

Neg. Charged

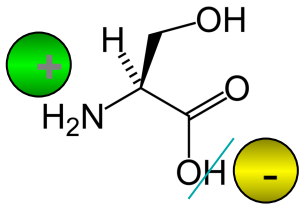


Aspartic Acid

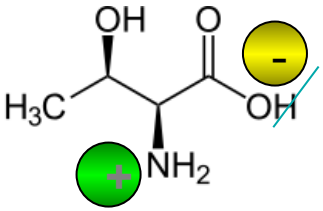


Glutamic Acid

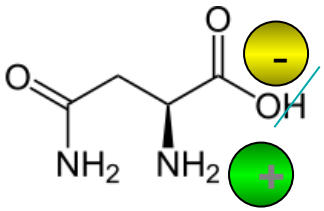
Polar Uncharged



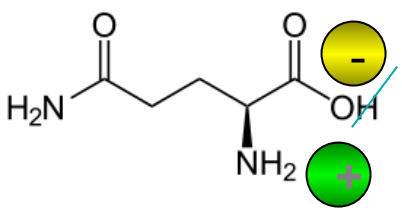
Serine



Threonine



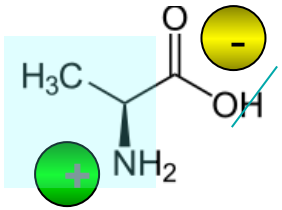
Aspargine



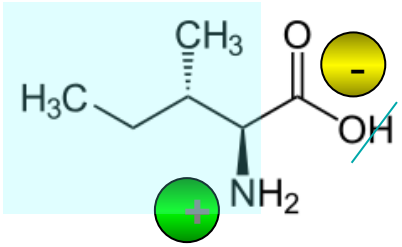
Glutamine

Hydrophobic AA

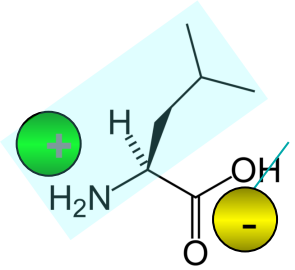
Hydrophobic Side Chains



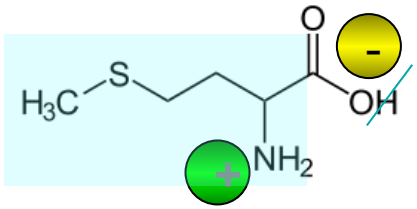
Alanine



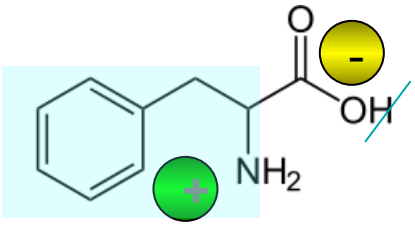
Isoleucine



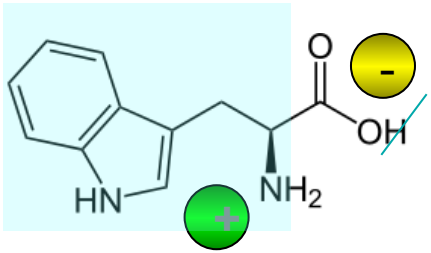
Leucine



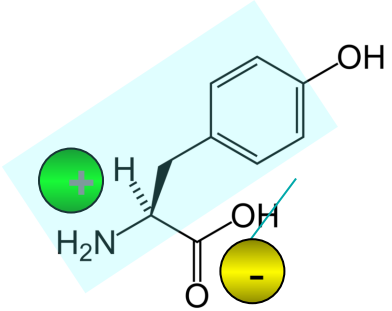
Methionine



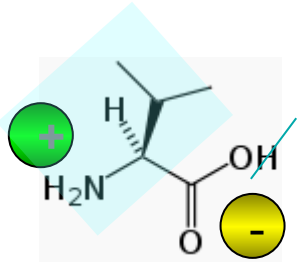
Phenylalanine



Tryptophan



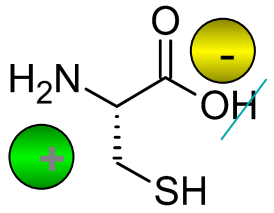
Tyrosine



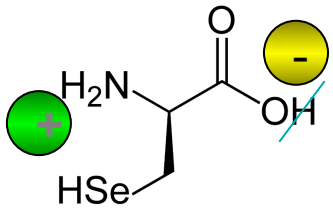
Valine

Neutral AA

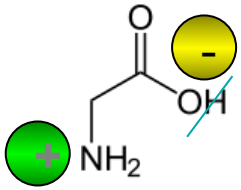
Special Cases



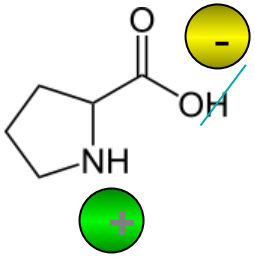
Cysteine



Selenocysteine

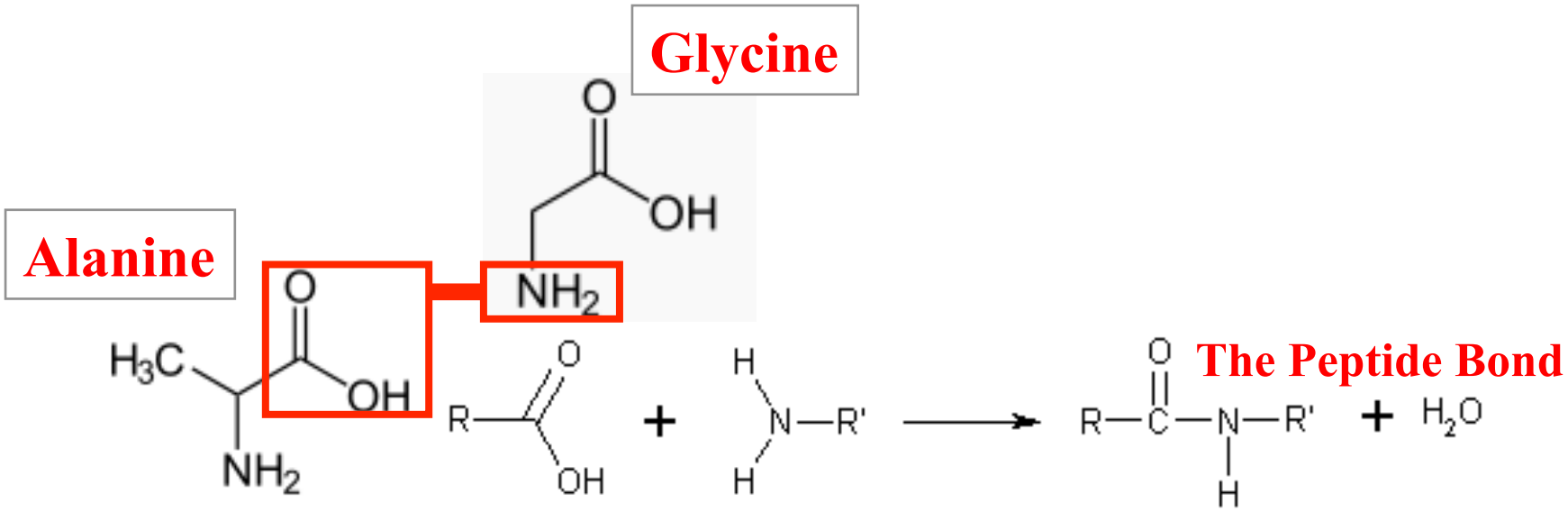


Glycine



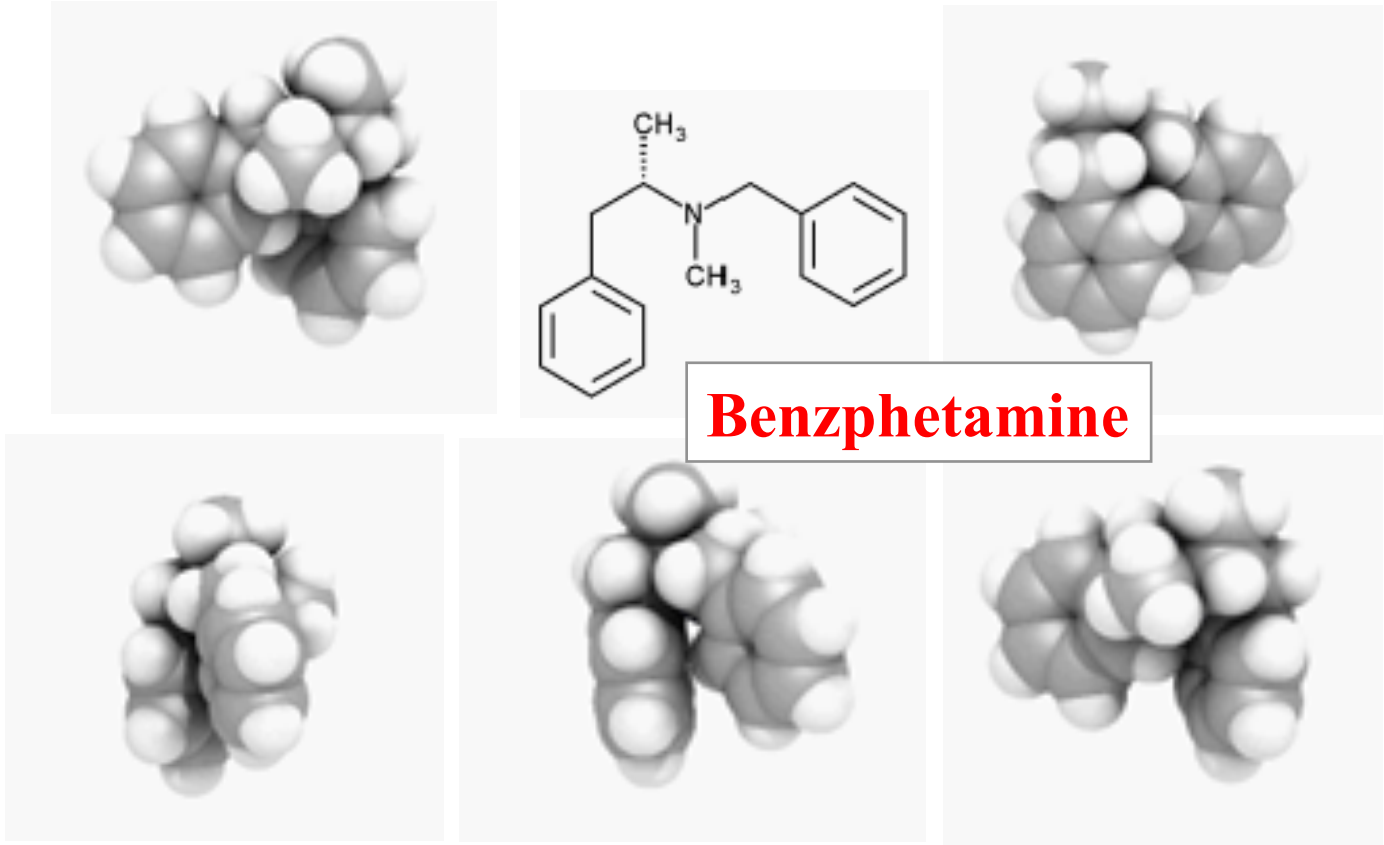
Proline

The Peptides



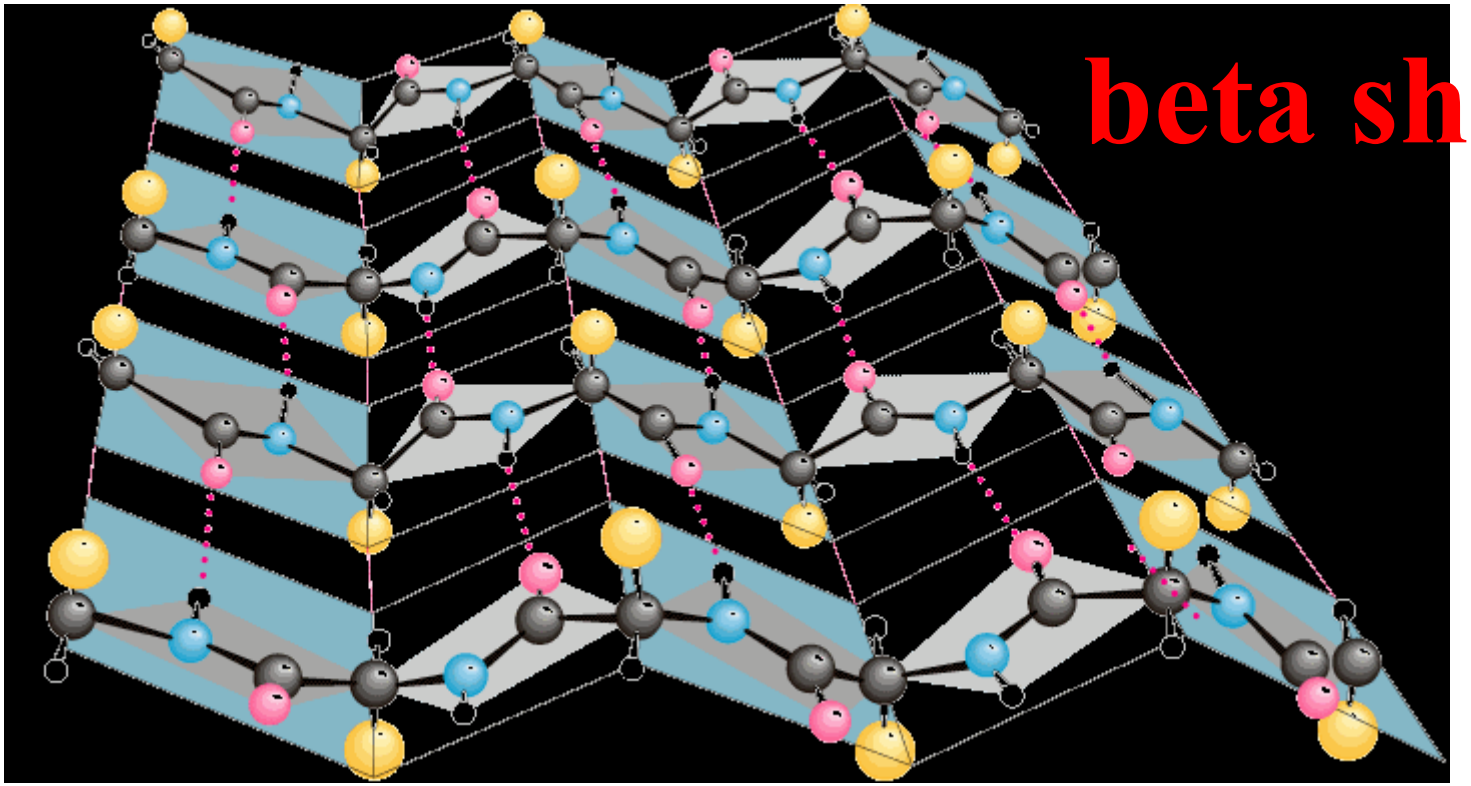
Peptides are short polymers formed by linking amino acids in a defined order

The importance of 3D Conformation



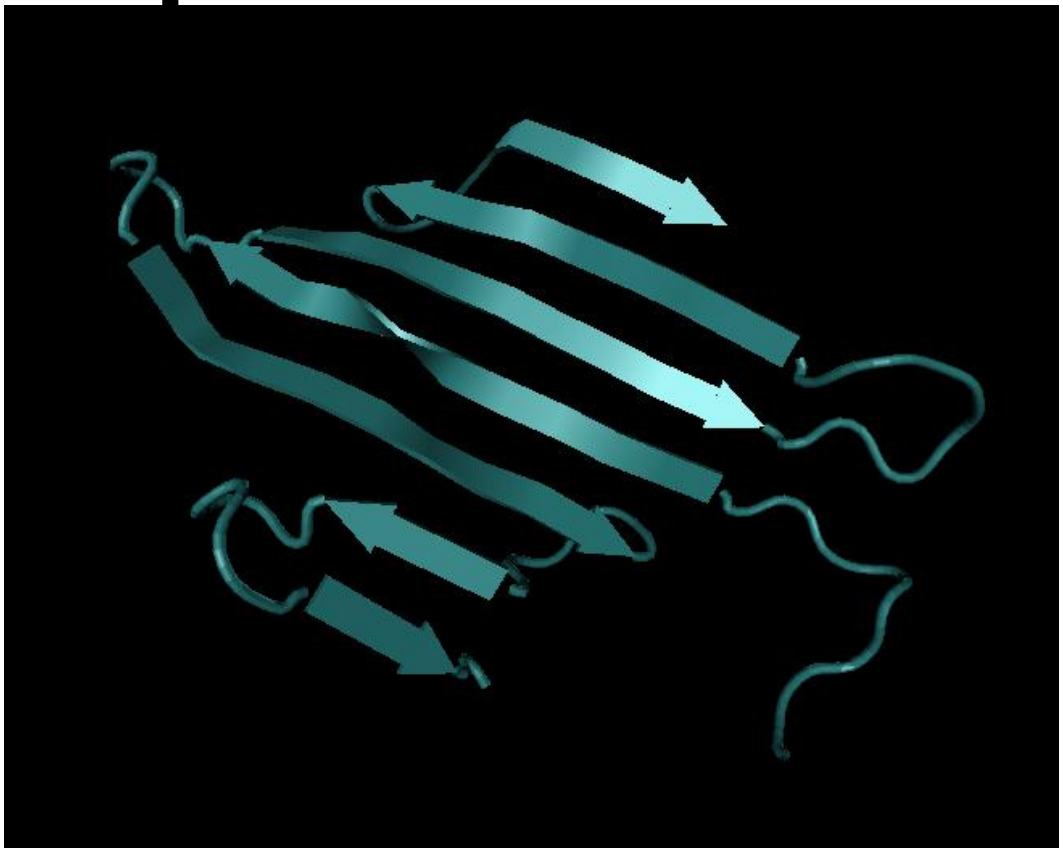
The 3D shape of a molecule may be so important for its biological function

Poly-Peptides 3D structure



Peptides are short polymers that assume particular 3D structure: e.g. the beta-sheet

Poly-Peptides 3D structure



The Beta-sheets are usually visualized as a string with a terminal arrow

Poly-Peptides 3D structure

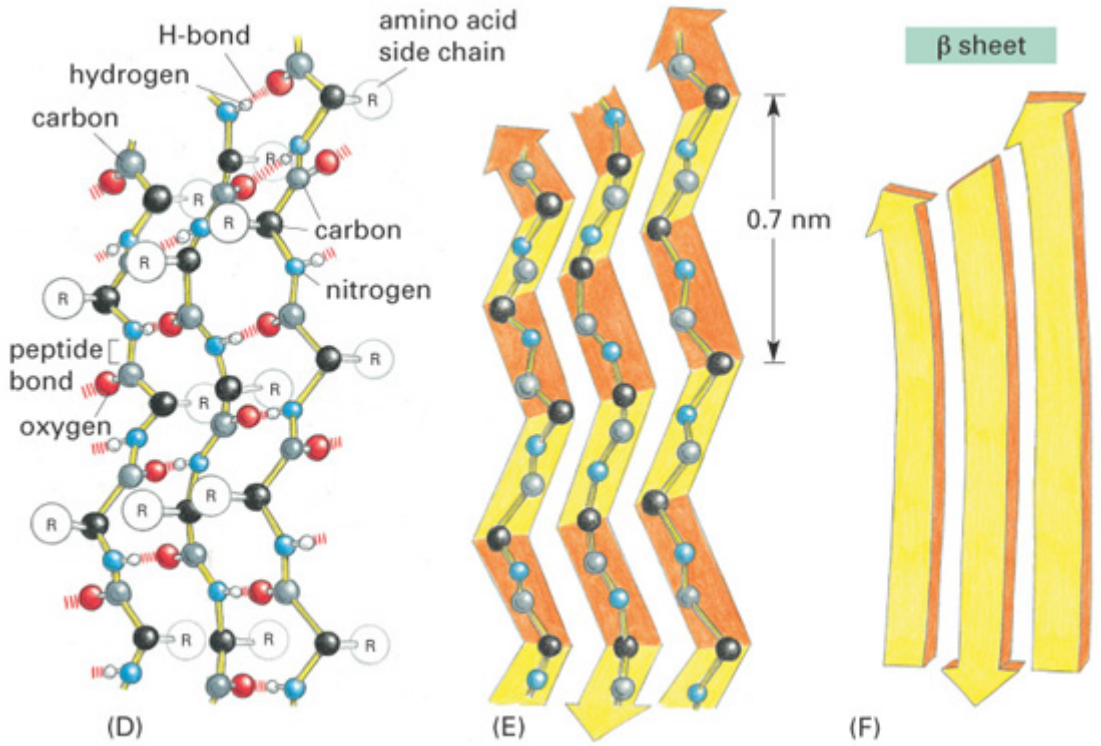
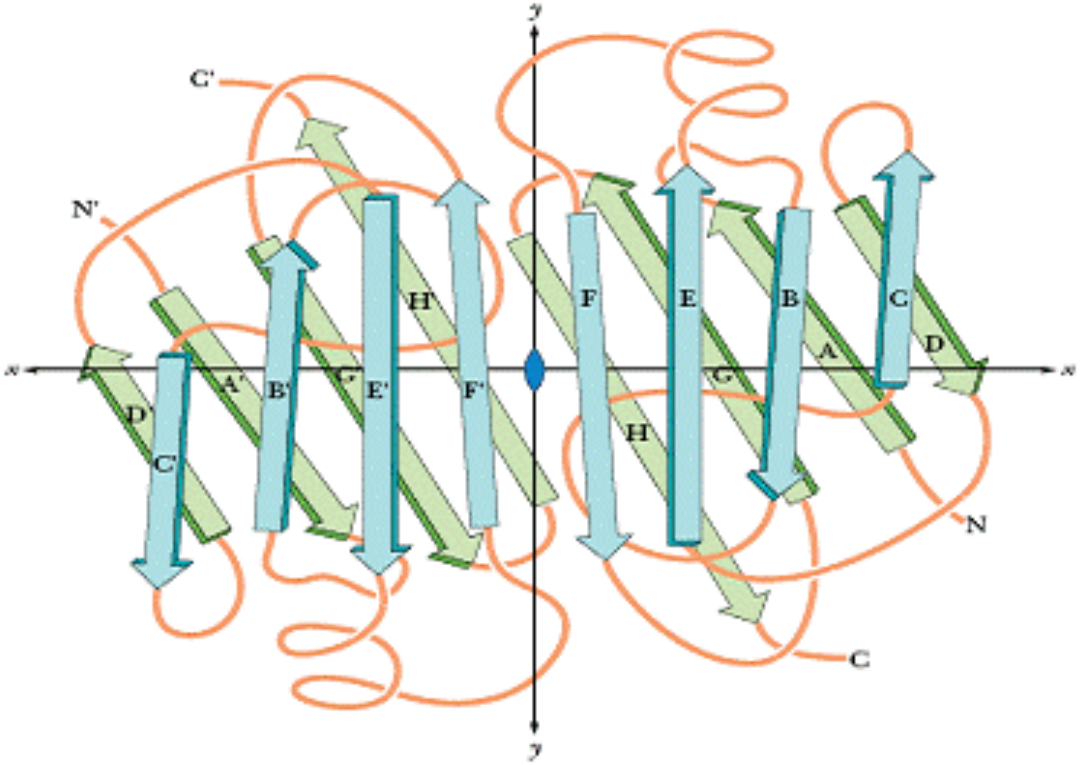


Figure 4-10 part 2 of 2 Essential Cell Biology, 2/e. (© 2004 Garland Science)

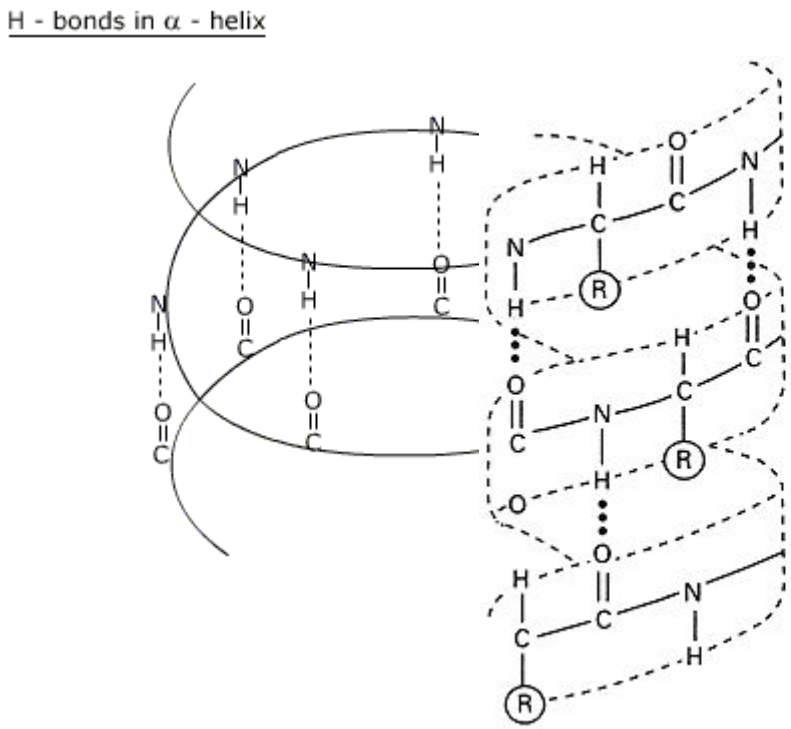
The arrows of the beta-sheets are pointing to the carboxylic groups

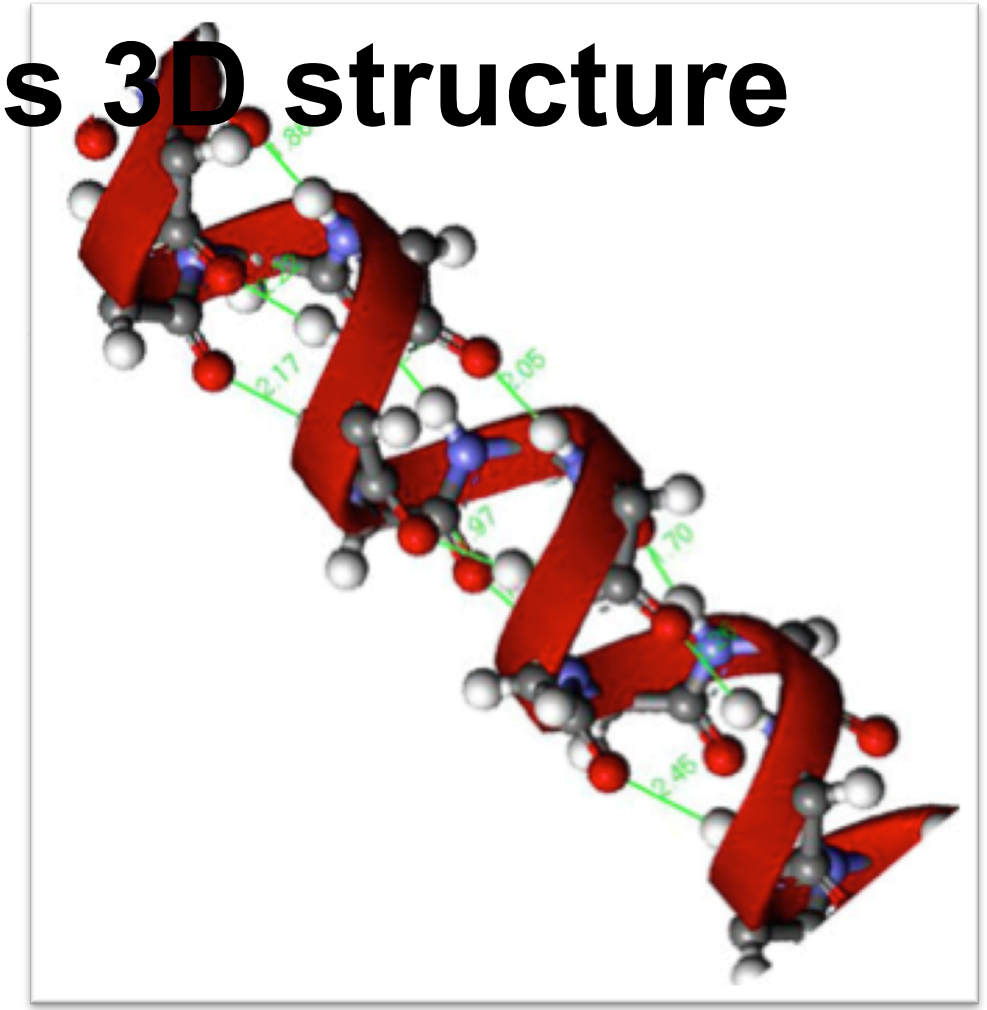
Poly-Peptides 3D structure



Different beta-sheet chains may be organized in more complex 3D super-structures

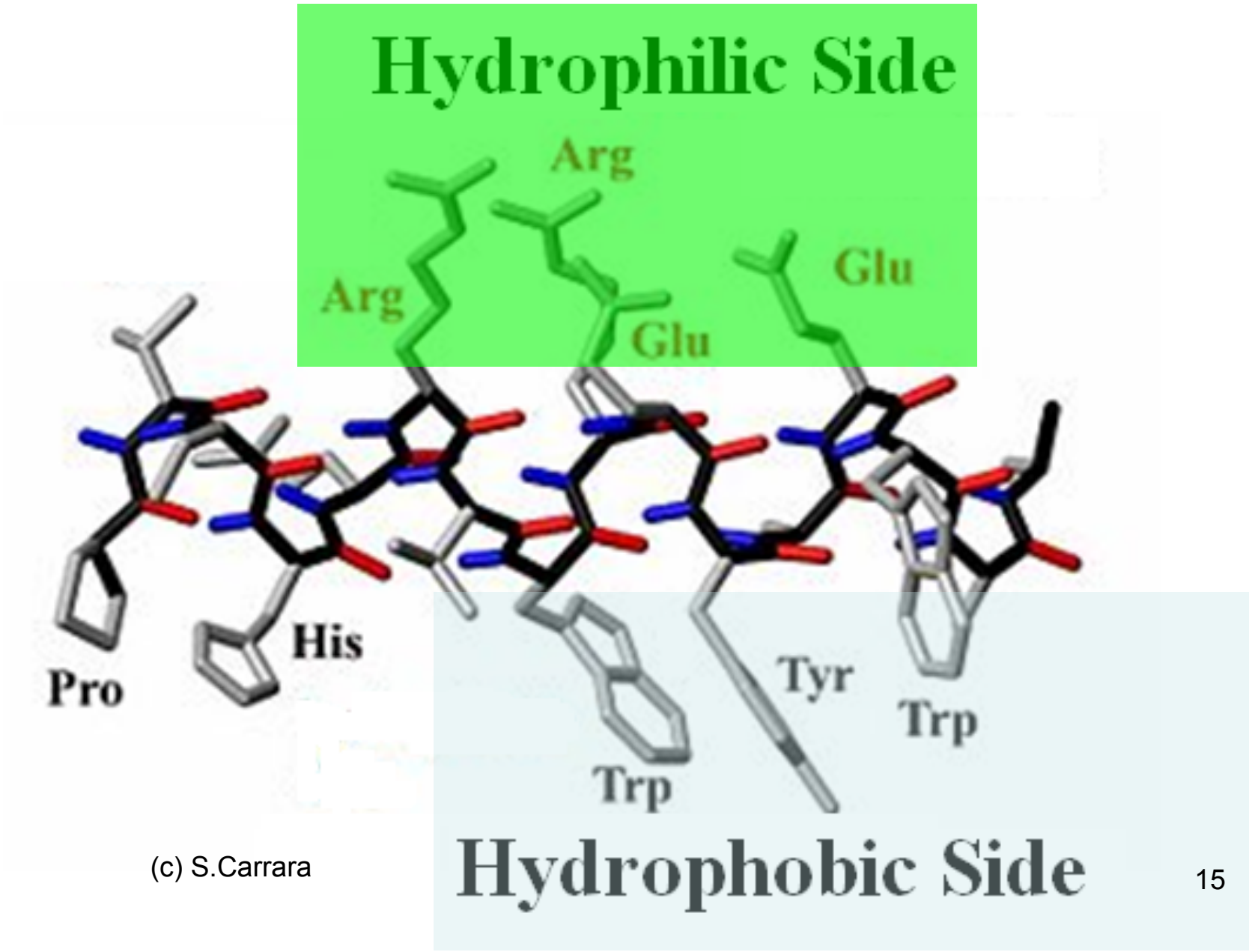
Poly-Peptides 3D structure



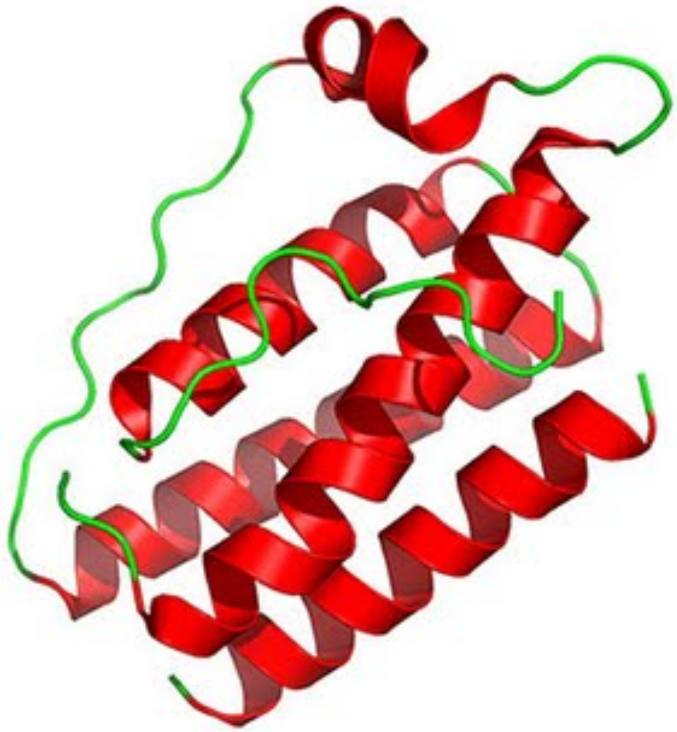


The week hydrogen bonds may create helix structures in poly-peptides

Hydrophobicity of the α-helix

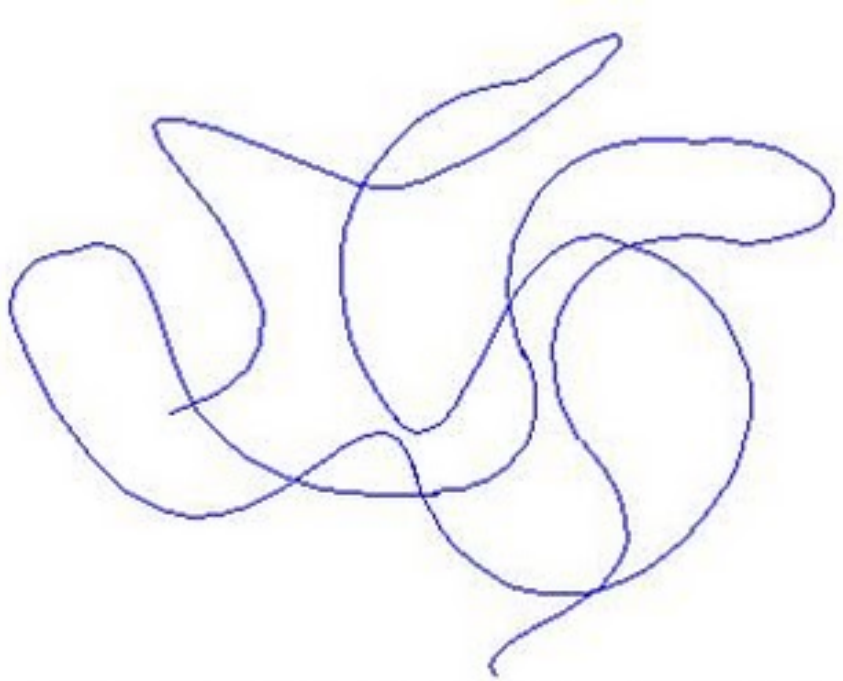


Poly-Peptides 3D structure

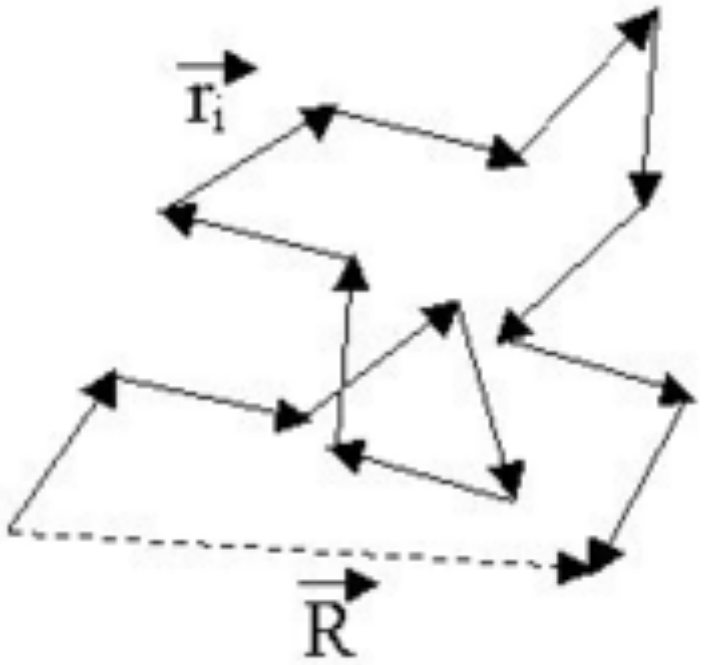


Different alpha-helix chains may be organized in more complex 3D super-structures

Poly-Peptides 3D structure

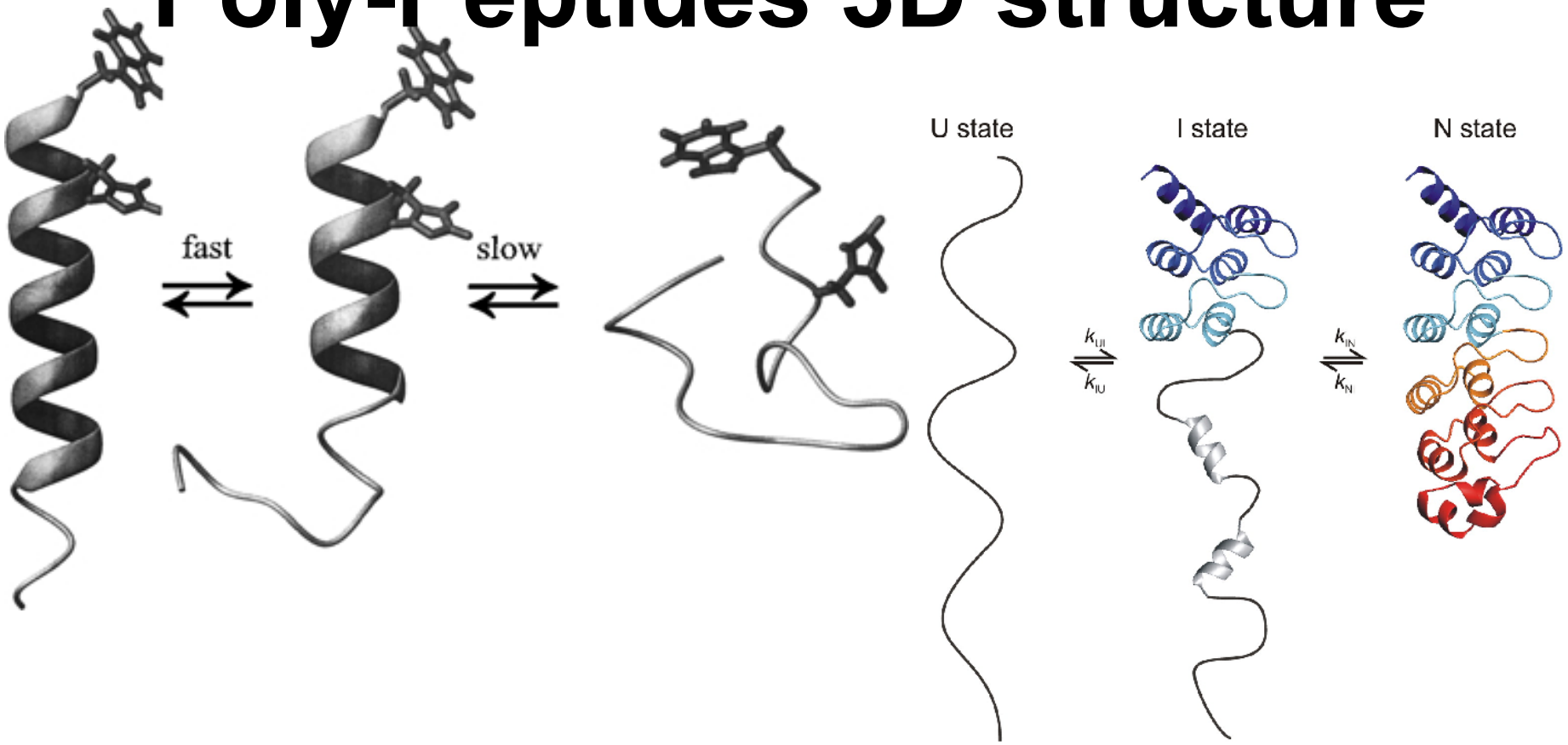


A polymer molecule tangled in a random coil.



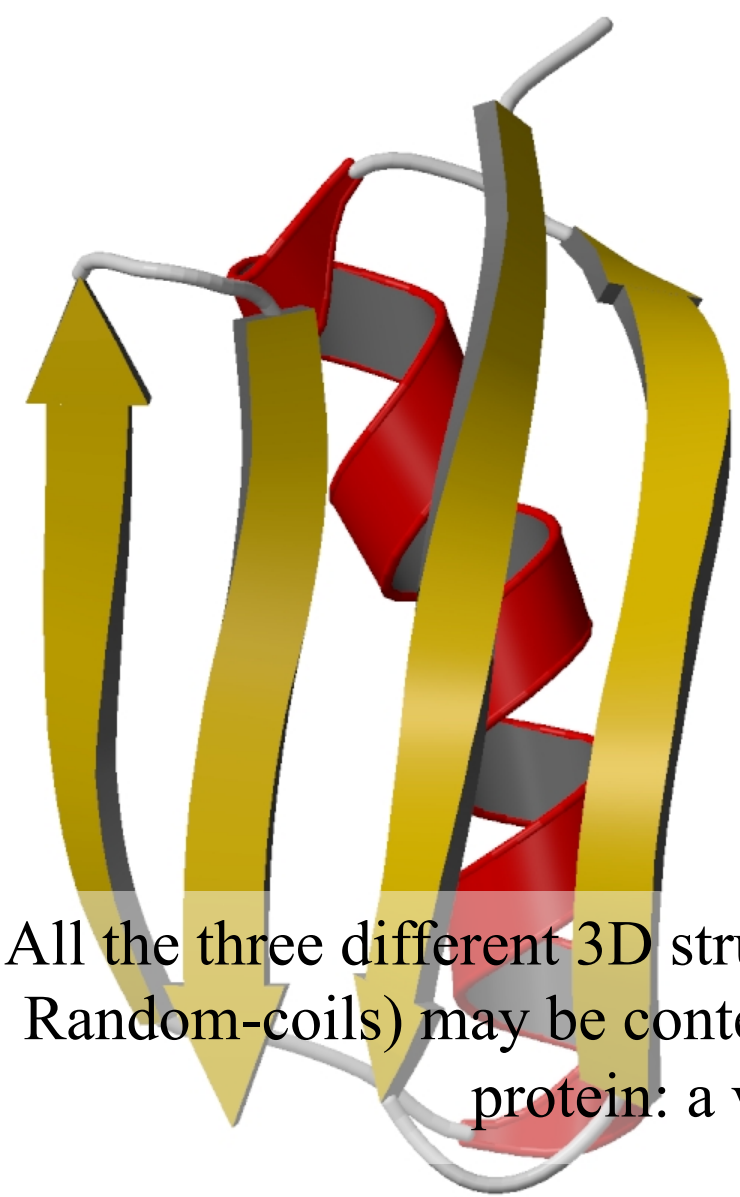
Peptides are short polymers that assume particular 3D structure: e.g. random-coil

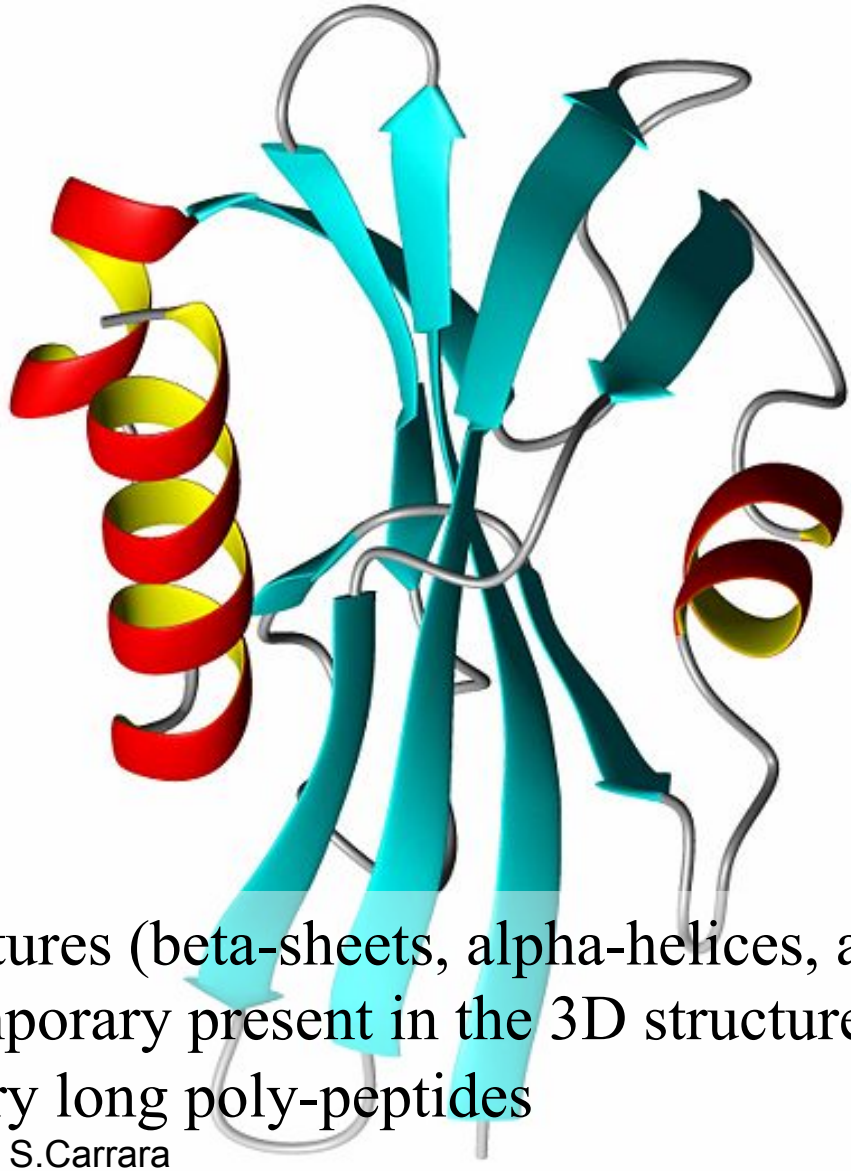
Poly-Peptides 3D structure



Poly-Peptides may be organized in different 3D structures by molecular states-transition

Poly-Peptides 3D structure



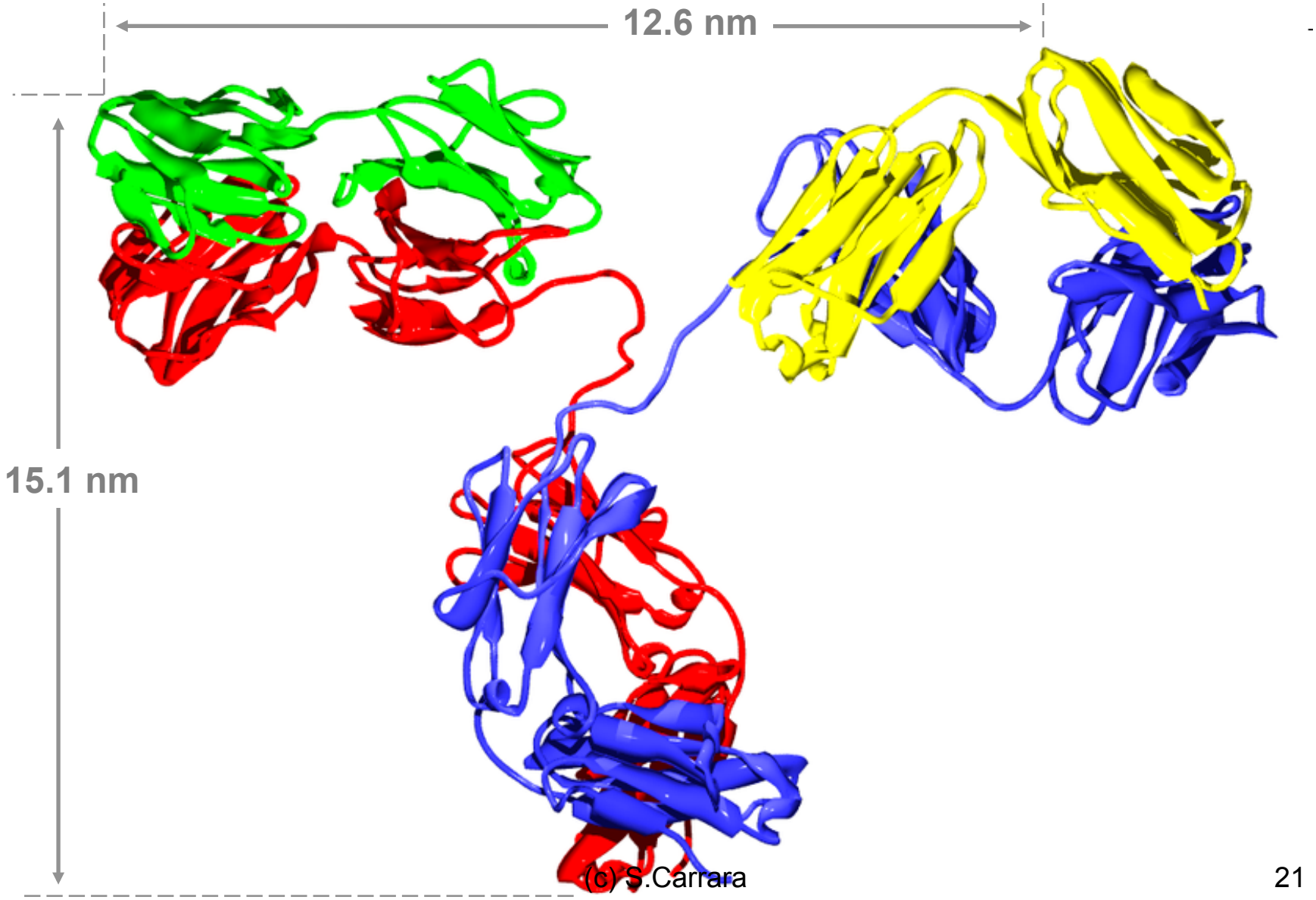


All the three different 3D structures (beta-sheets, alpha-helices, and Random-coils) may be contemporary present in the 3D structure of a protein: a very long poly-peptides

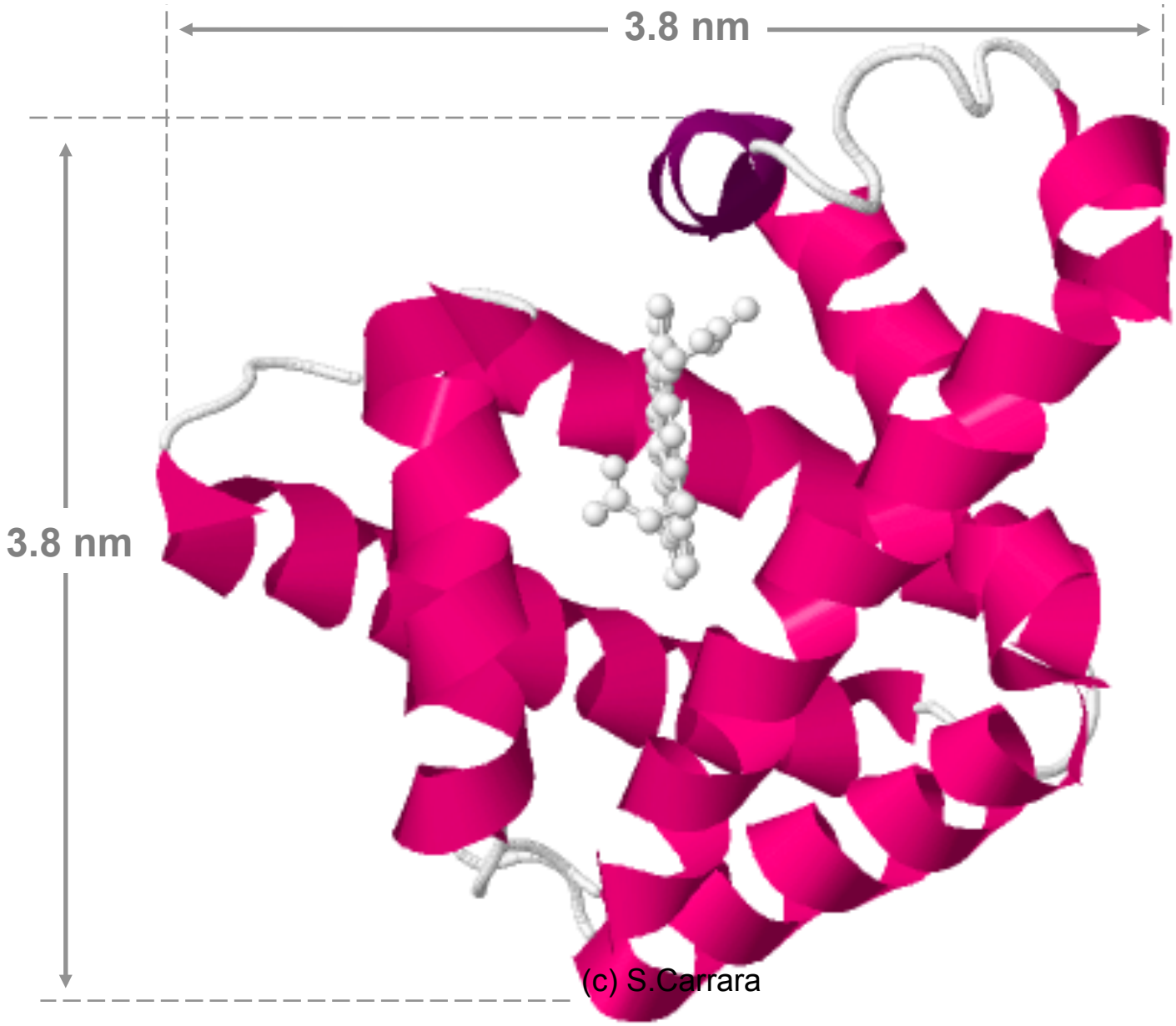
Proteins

More complex bio-molecules are called **Proteins**, which are **polypeptides**, organic compounds made of amino acids arranged in a linear long chain and folded into a 3D usually complex form organized in beta-sheets, alpha-helices, and random-coils conformations

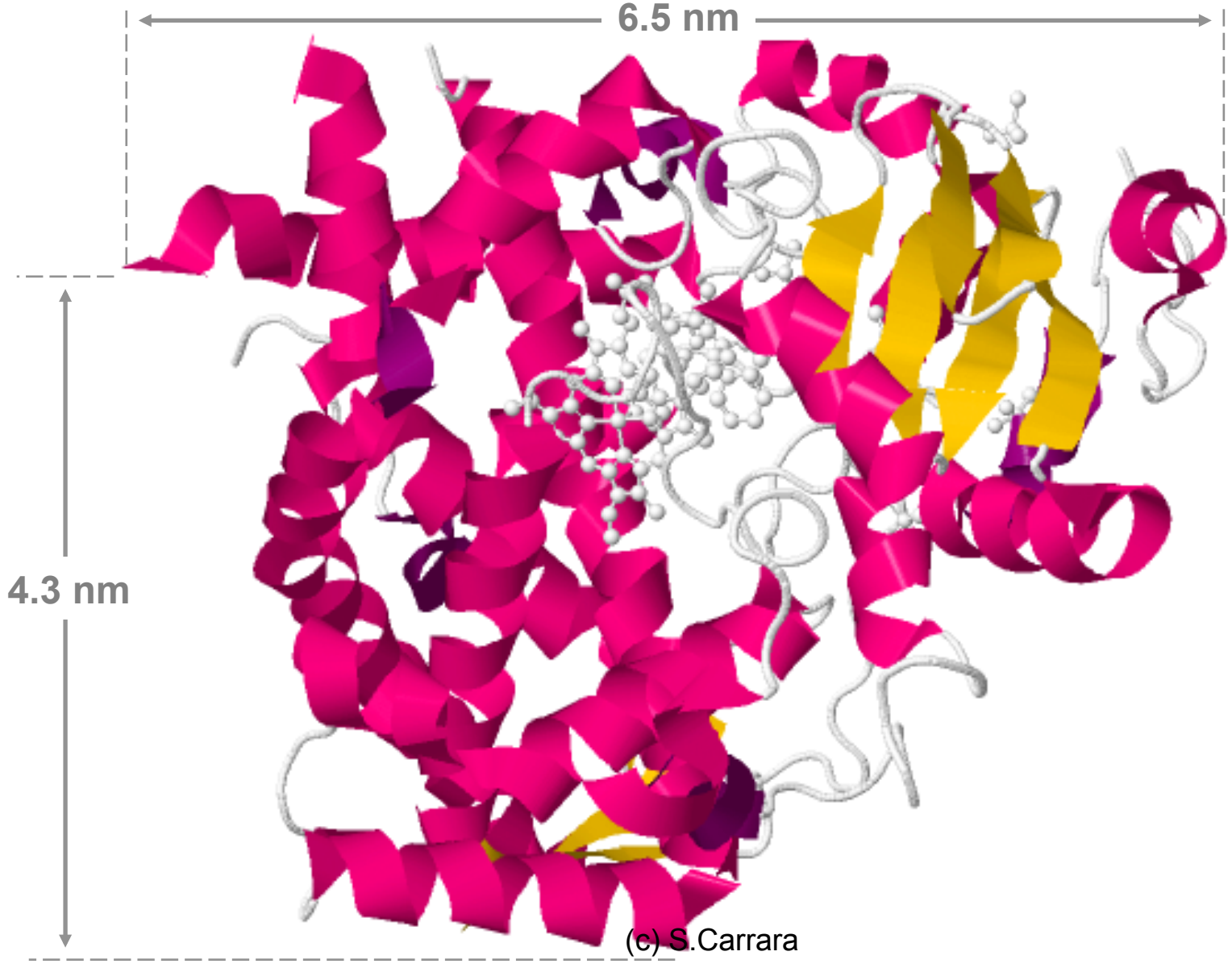
Antibody



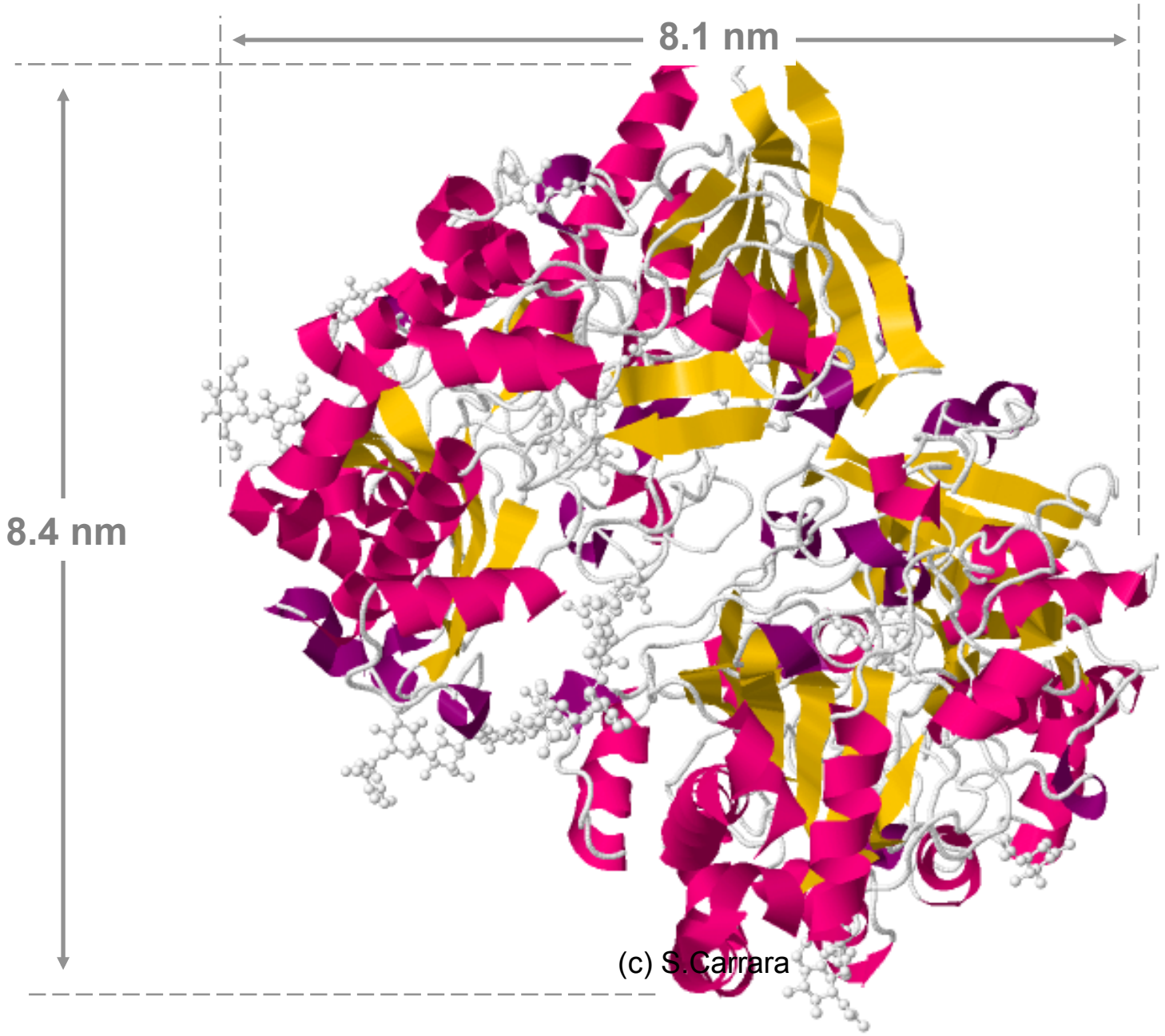
Myoglobin

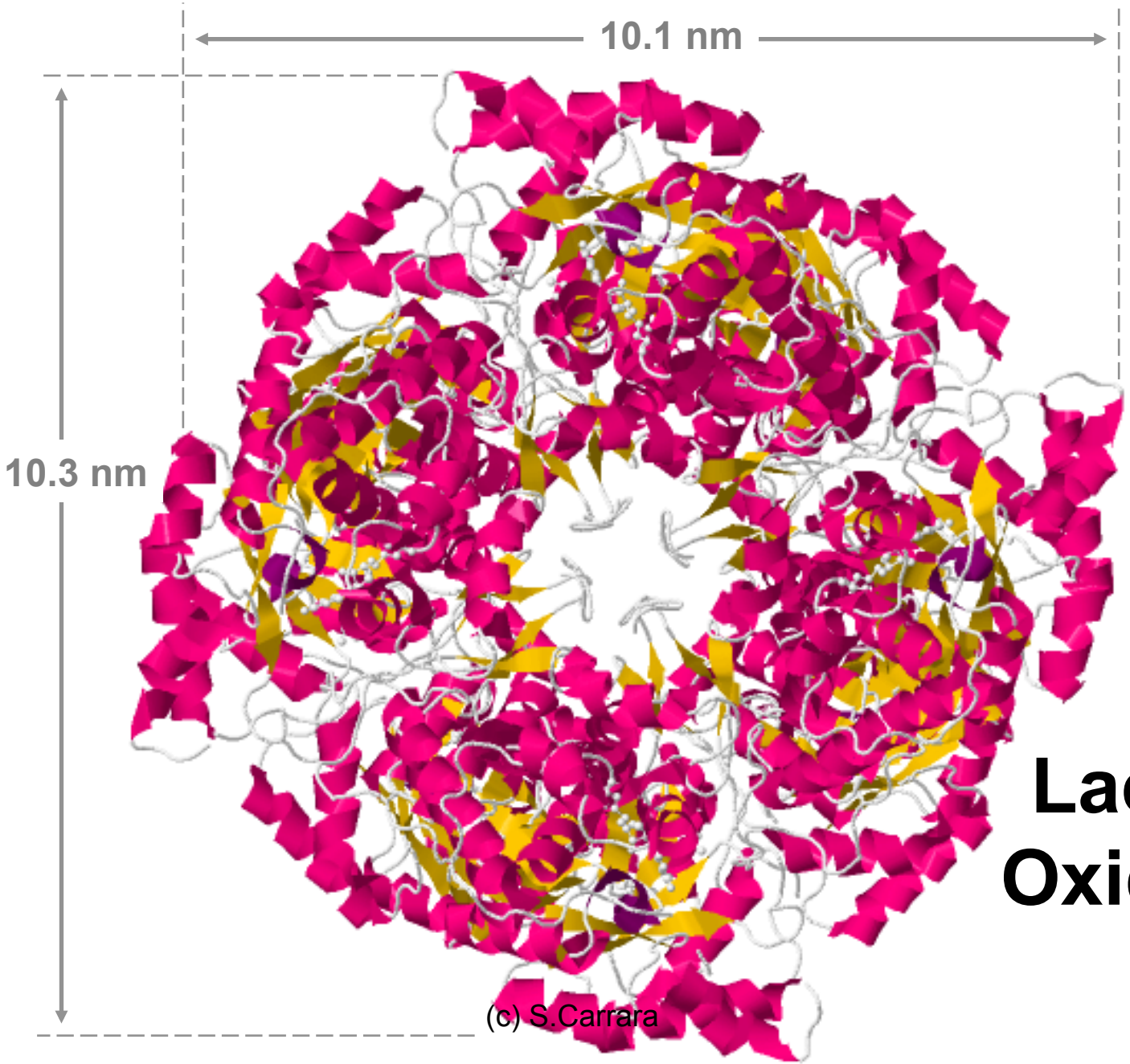


Cytochromes P450



Glucose Oxidase





Lactate Oxidase

Structure-TO-Function in Proteins

Enzymes	catalytic activity A ------> B
Transport Proteins	bind & carry ligand molecules (hemoglobins)
Storage Proteins	ovalbumin (egg), ferretin (iron), casein (milk)
Contractile Proteins	can contract, change shape (actin & myosins) and make up elements of cytoskeleton & muscles
Structural Proteins	provide support... collagen fibers of tendons (wounds), elastin of ligaments, keratin of hair & feathers, fibroin of silk & spider webs
Defensive Proteins	provide protection: antibodies (IgG), fibrinogen, thrombin, and snake venoms (digestive enzymes)
Regulatory Proteins	regulate metabolic processes: includes hormones, transcription factors & enhancers

Different 3D structures lead to different protein functions

Outline on DNA

(Book Bio/CMOS: Chapter' paragraphs §3.9 and §4.1-3)

- Nuclear bases
- DNA
- RNA
- DNA hybridization
- DNA/RNA role in biological cells

DNA

Another fundamental molecules in Biochemistry is the DNA

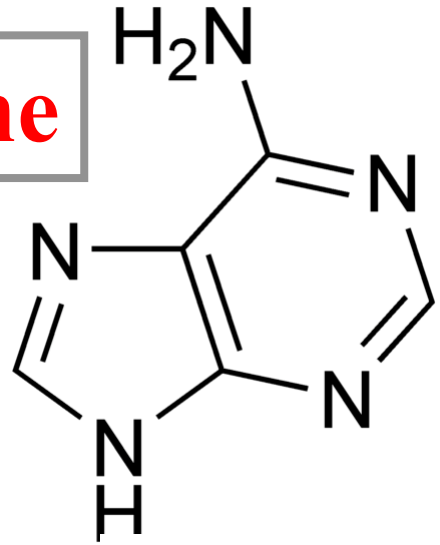
DNA

Definition

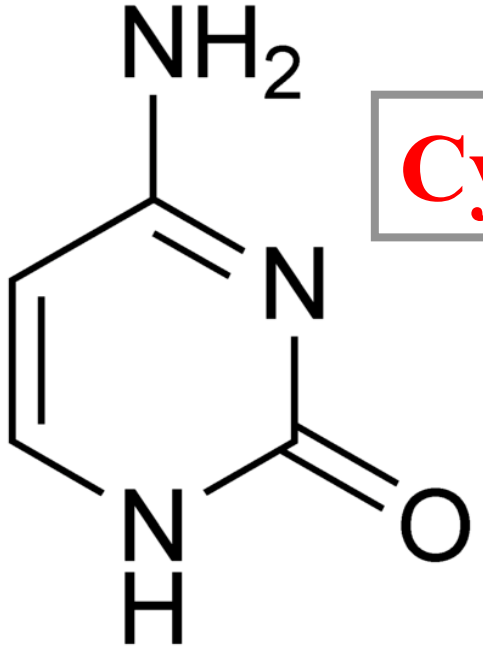
is a **nucleic acid** that contains the genetic instructions used in the development and functioning of all known living organisms and some viruses.

DNA Bases

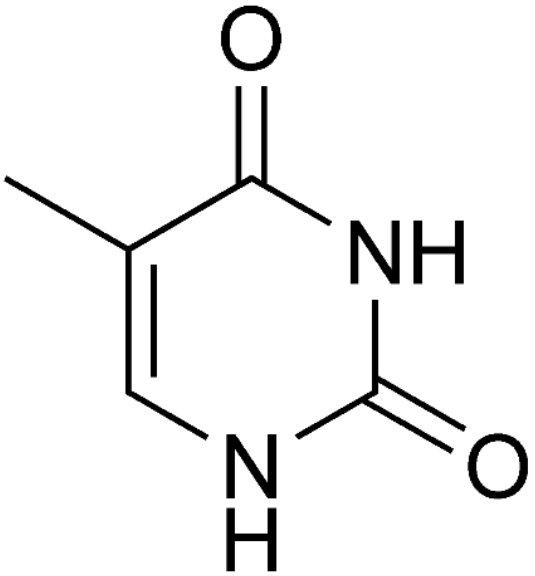
Adenine



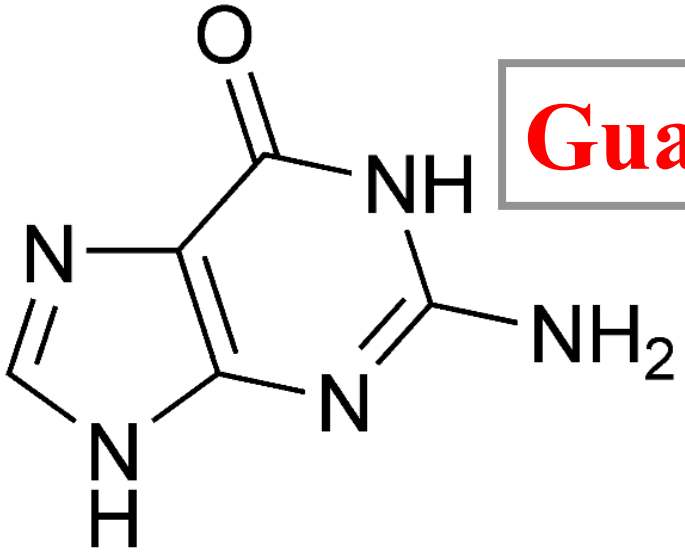
Cytosine



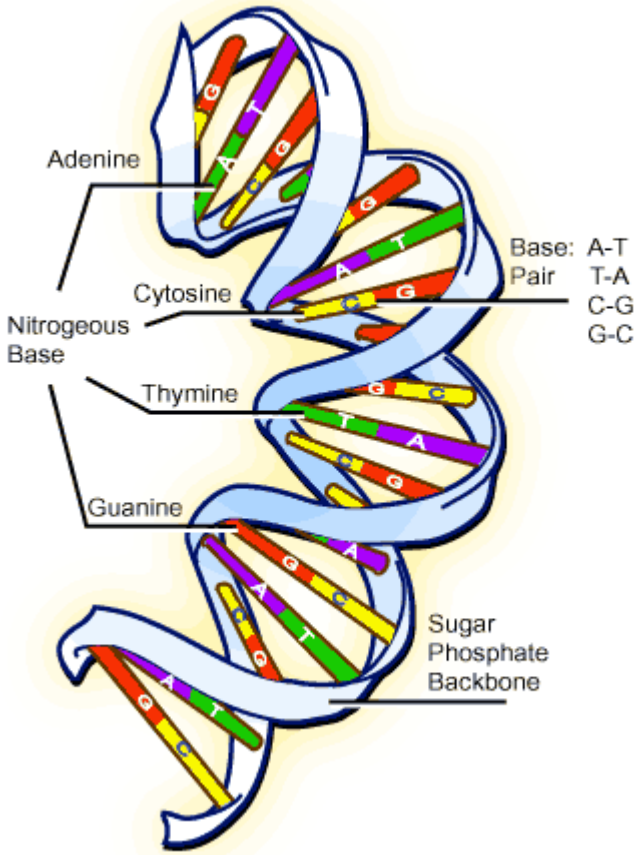
Thymine



Guanine

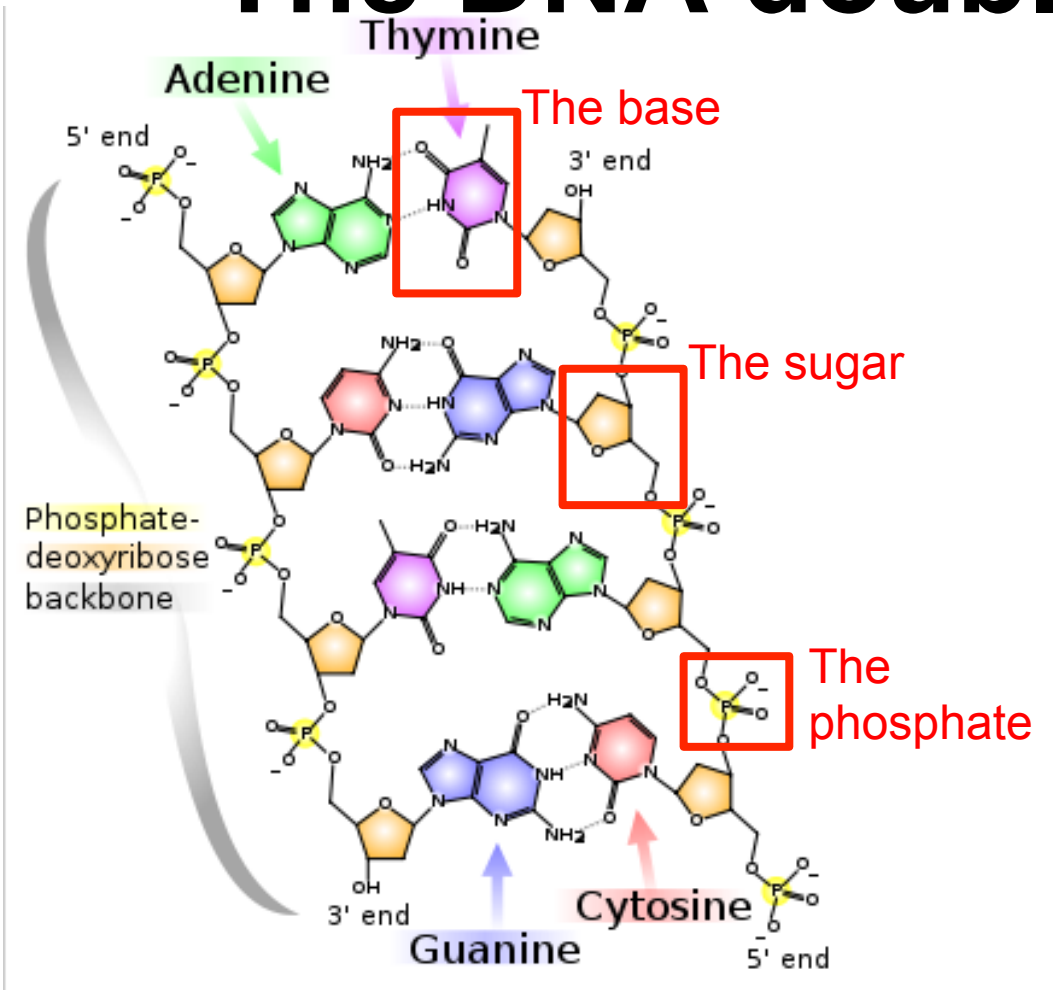


DNA



DNA is constitutes by a Sugar Phosphate backbone and by four Nitrogenous Bases

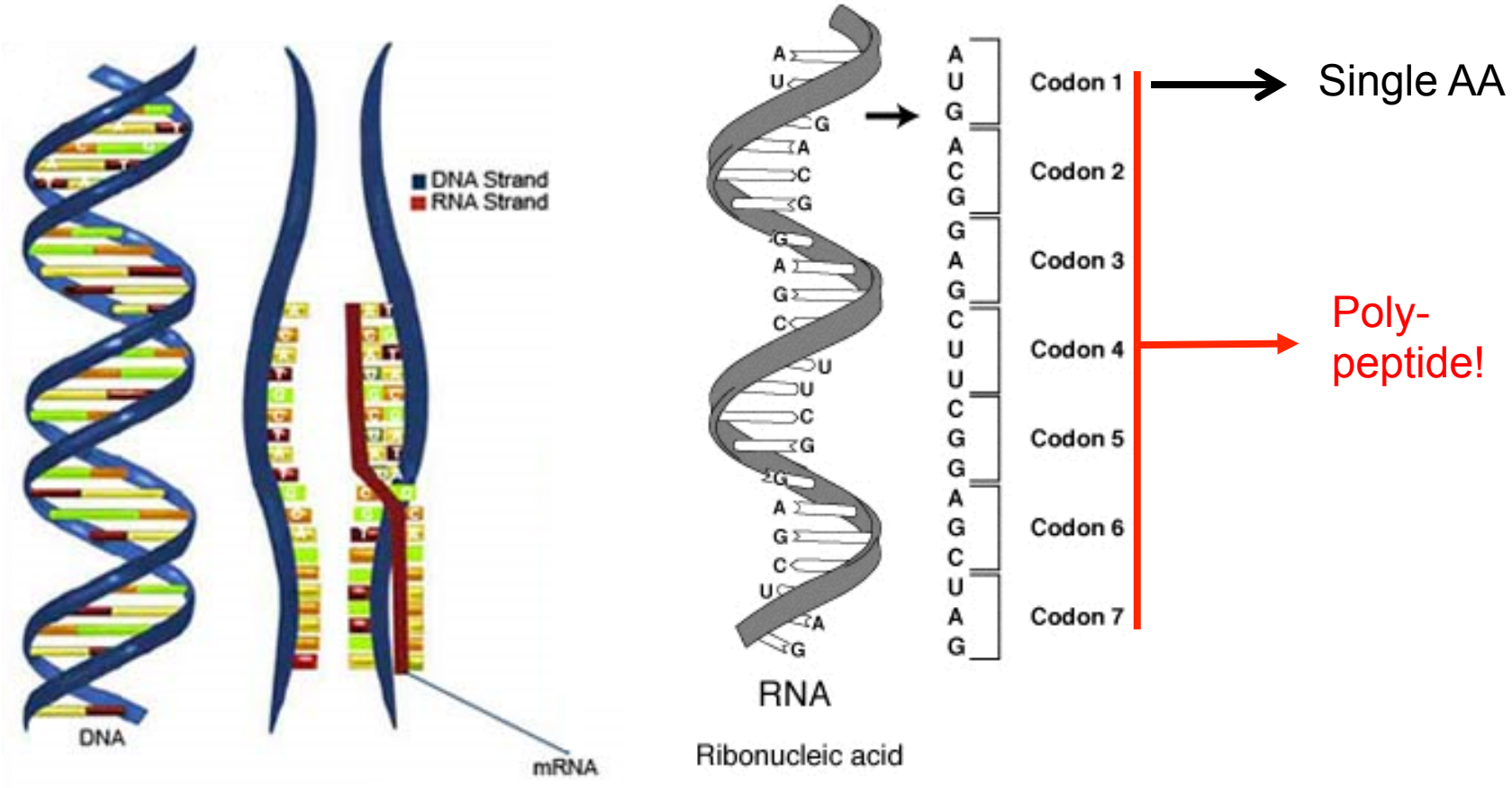
The DNA double helix



The two DNA strands are also called « polynucleotides » since they are composed of simpler units called nucleotides. The nucleotide is composed of a nitrogen-containing base as well as a monosaccharide sugar, called deoxyribose, and a phosphate group.

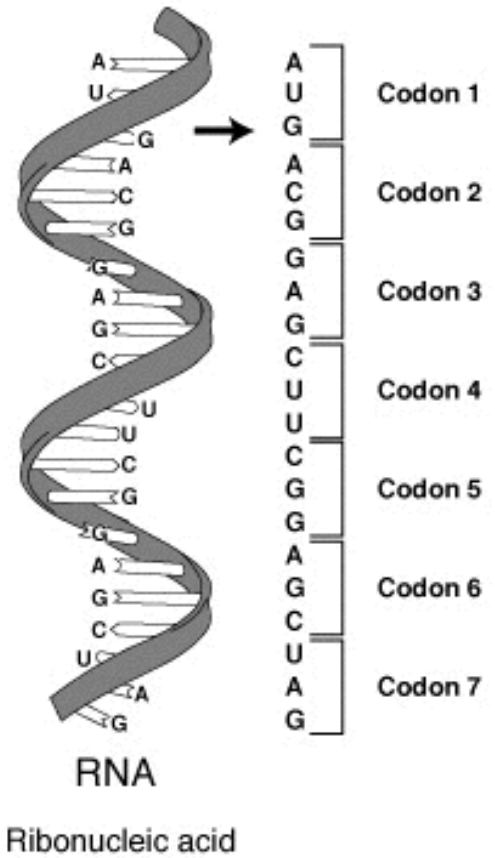
The base pairing forms very long double strength DNA chains

RNA decodes the genes



The RNA is another similar molecule useful to decode the genetic code

DNA/RNA differences



RNA and DNA are both nucleic acids. They differ in four main ways:

- **RNA is mainly a single-stranded molecule (DNA is double-stranded)**
- **RNA usually has a much shorter chain of nucleotides**
- **RNA less stable than DNA because it is more prone to hydrolysis because it contains *ribose* while DNA contains *deoxyribose***
- **RNA has as fourth base the Uracil, an unmethylated form of thymine (while DNA has thymine)**

Molecules in water

We typically find organic or biological molecules in water-based human tissues (blood, serum, urine, saliva, etc…)

Two important components of any solution:

1. The organic/biological molecule is then called **solute** because it is dissolved in water
2. The water is then called **solvent** because it is the other substance where the solute is dissolved

Solutions

More in general (Definition):

"A solution is a **homogeneous mixture** composed of two or more substances"

Two important components:

1. The **solute** is the dissolved substance
2. The **solvent** is the other substance where the solute is dissolved

Different computations for the same concentration

- **Percent Composition in weight (%)**
- **Percent Composition in volume (%)**
- **Molar Concentration (M) (Molarity)**

Composition in Molar Concentration

Definition:

the number of moles ?
contained in each liter of
solution (solvent + solute)

The Mole of a pure substance

Definition:

the amount of substance the correspond to a number of molecules (or atoms) equal to the Avogadro Number = $6.022\ 10^{23}$

The Mole of a pure substance

Operational definition:

the amount of substance that contains an equal number of elementary entities as there are atoms in 12 gr of the isotope carbon-12

The Molecular weight

Definition:

the amount in grams of substance that contains a number of molecules equal to the Avogadro Number

Composition in Molarity

4.59 mg of Glucose Oxidase in 0.5 µl of blood serum

$$GOD(mw) = 153{,}000$$

$$\frac{4.59mg}{153{,}000} = 3 \cdot 10^{-8} \, \#\, of\ mole$$

$$Molarity = \frac{\#\, mole}{0.5\mu l} = \frac{3 \cdot 10^{-8}}{5 \cdot 10^{-7}} = 60\, mM$$

Buffer Solutions

Because the 3D conformation is key for biological functions, then a proper liquid-water environments is always required to support the right molecules' conformation.

When artificially built, such special environments assuring functionality to life systems are called **buffer solutions**.

A more general definition of a buffer includes a water solution with salts and other organic molecules too, in order to provide the right electrostatic interactions between the molecules and the solute

In summary, water solutions of

- Bio-markers may be simple (glucose, …) or complex (myoglobin, ..) molecules
- A simple molecule is a short chain of single atoms
- Amino-Acids are simple molecules with amino and carboxylic groups
- A peptide is obtained by joining two amino-acids
- A poly-peptide is a chain of peptides
- A protein is a complex molecules obtained with a very long poly-peptides
- DNA/RNA are extremely long chains of Nucleic Acids