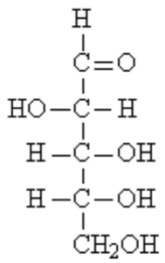
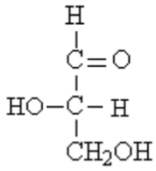
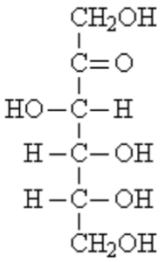
Lecture 3:
Exercise Carbohydrates and Proteins

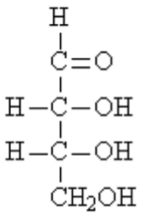
Question 1:

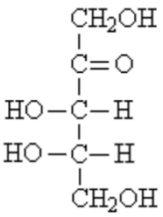
Below you will find linear structures of several monosaccharides. Classify them based on the (1) length of carbon chain, (2) functional group and (3) stereochemistry (handedness).





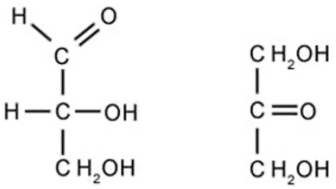






Question 2:

The smallest monosaccharides are trioses, glyceraldehyde and dihydroxyacetone shown below:



Glyceraldehyde

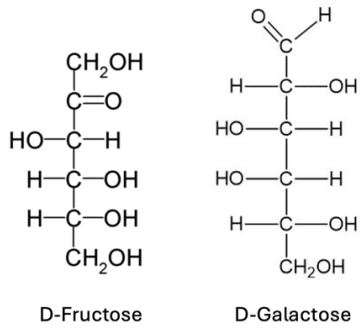
Dihydroxyacetone

a) Can you draw the stereoisomeric versions of each monosaccharide? Include the D- or L-annotation.

b) Can these monosaccharides assemble into cyclic forms in aqeuous solutions? Explain.

Question 3:

Below are the linear structures of D-fructose and D-galactose.



D-Fructose

D-Galactose

a) Draw the cyclic structures of each sugar in alpha (α) stereoisomeric form and indicate the location of anomeric carbon. How does the beta (β) form differ from the alpha?

b) Lactulose (galatose-β(1→4)-fructose) is a disaccharide used in the treatment of constipation and hepatic encephalopathy. It is assembled from **1 D-galactose** and **1 D-fructose** building block through **β-1,4 O-glycosidic linkage**. Draw the structure of this disaccharide based on the cyclic forms of each monosaccharide building block.

c) Melibiulose (galactose-α(1→6)-fructose) is another disaccharide assembled from the same buidling blocks using the **α(1→6) O-glycosidic bond**. Draw the structure of this disaccharide based on the cyclic forms of each monosaccharide building block.

Question 4:

Which of the following statements are TRUE, and which are FALSE?

a. Protein domains are units of secondary protein structure.

b. Glycine is less-restricted in terms of possible φ and ψ angles, which is why it is often found in loop structures in proteins.

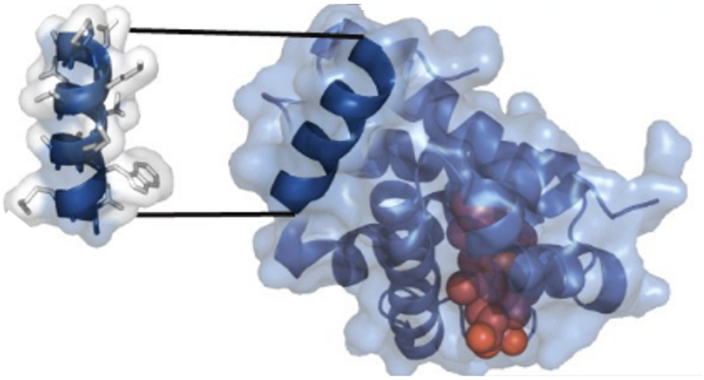
c. Glutamine (Gln) is more hydrophobic compared to Asparagine (Asn).

d. The net charge of hydrophobic amino acids (e.g., Ala) would not change if the pH was set to 1.

e. Proline residues favor forming *cis* peptide bonds while *trans* is found less frequently.

Question 5:

Why are isolated secondary structural elements typically not stable in isolation, even though all backbone hydrogen bonds are satisfied?

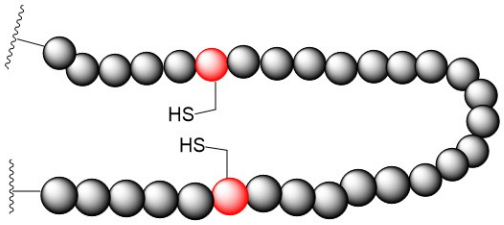


Question 6:

Draw the structure of a tripeptide: **Ala-His-Lys**. Identify and label the N-terminus, the C-terminus and the two peptide bonds. Indicate the backbone rotation angles (**ω**, **ϕ**, **ψ**) around both peptide bonds.
a) How much rotational movement is allowed for the **ω** angle? Why?
b) How much rotational movement is allowed for **ϕ**, **ψ** angles? What chemical diagram defines the most favorable **ϕ**, **ψ** angles for amino-acids?

Question 7:

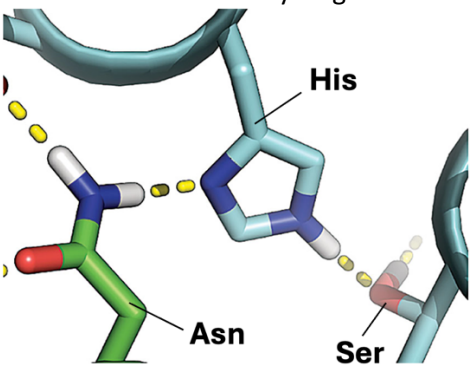
See below structure of a polypeptide chain with 2 cysteine residues that directly face each other.



a) Will this peptide assembly differ if the protein was located inside versus outside of a cell? How?
b) Can the assembly of this peptide be influenced by treatment with external chemicals possessing oxidizing or reducing properties? What would be the outcome in each case?
c) Cysteine is an amino-acid that can be used to covalently attach chemical groups, labels or even other proteins. Can you describe how this could work? What would be the necessary chemical group that the binding partner must have in order to attach?

Question 8:

Below you will find a structure of a small region inside a random protein, showing Histidine (His) interacting with surrounding residues (Asn and Ser), in a solution that is at neutral pH (=7.0). In the image, the carbons are depicted cyan/green, oxygens are red, nitrogens are blue, and hydrogens are white. Carbon-bound hydrogens and double bonds are intentionally not shown to improve visibility.



a) Can you identify which interaction is formed between His and Asn (dashed line)? What about His and Ser?

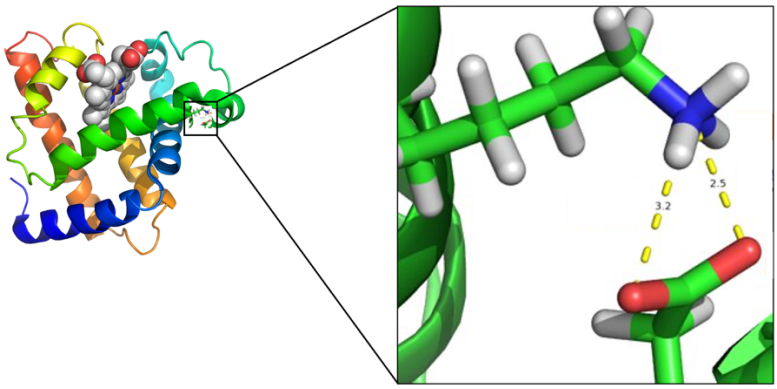
b) Can you describe what will happen with the Histidine residue if the pH of the solution was decreased to 4.0?

c) How will this affect the interaction network?

Question 9:

Mutations are changes in the order of nucleotides in DNA genes that translate into changes in amino-acid sequence of the corresponding gene-encoded proteins. If a mutation occurs at a single amino-acid position, it is called a point-mutation. Biochemists often intentionally introduce point-mutations in their proteins of interest to perturb underlying interaction networks and evaluate how the mutated amino-acid(s) impact protein structure or function.

Below you will find a close-up view of the interface of 2 protein domains highlighting two amino-acids that interact with each other at the interface of two domains. In the close-up panel, carbons are depicted in green, hydrogens in white, nitrogens in blue and oxygens in red.



a) Can you identify the two amino-acids based on the side chains groups?

b) Can you identify the type of interaction that is created by these two amino-acids? Calculate the energy associated with this interaction if the average distance between the functional groups is 3.0Å. Assume aqueous environment with the dielectric constant (D) of 80.

c) The biochemist working on this project hypothesized that this interacting pair is the key to keeping the two helical domains and the entire protein structure stabilized in the current state. The next step is to test that by mutating one of the two amino-acids in this pair to a different type of amino-acid that would completely disrupt this interaction. The biochemist will then measure if the mutation really impacted the 3D assembly of this domain. Given the type of interaction between these amino-acids, what mutations would you propose for testing? Propose a few alternatives if you can and discuss what mutations would have the strongest effect. What would be the effect of simultaneously mutating the two amino-acids to each other (swapping their respective locations)?