Notes 10/10

Wednesday, October 10, 2007
10:00 AM

Proteins: Hemoglobin Part I

Oct. 10, 2007

Office Hours

- My O.H.'s are not a bonus hour of lecture
  - Have specific questions BEFORE arriving
  - If you aren't participating then you must leave
  - 440 students: 1 Dr. Villa
- There are 6 TAs and each has 2 h of OH per week. Take advantage of it.
- Tutors at Covell Commons and AAP
- Form study groups now before it's too late
- Virtual office hours on VOH
- No more office hours for Dr. Villa on Tuesday

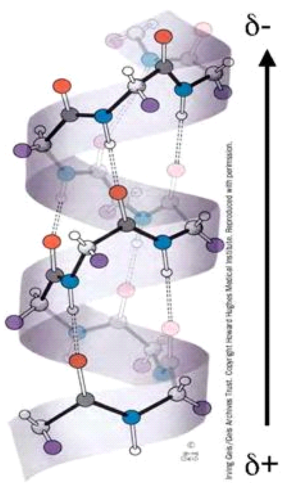
See your Tas about:

- L-handed vs R-handed
- The example pI calculation chart for Arg

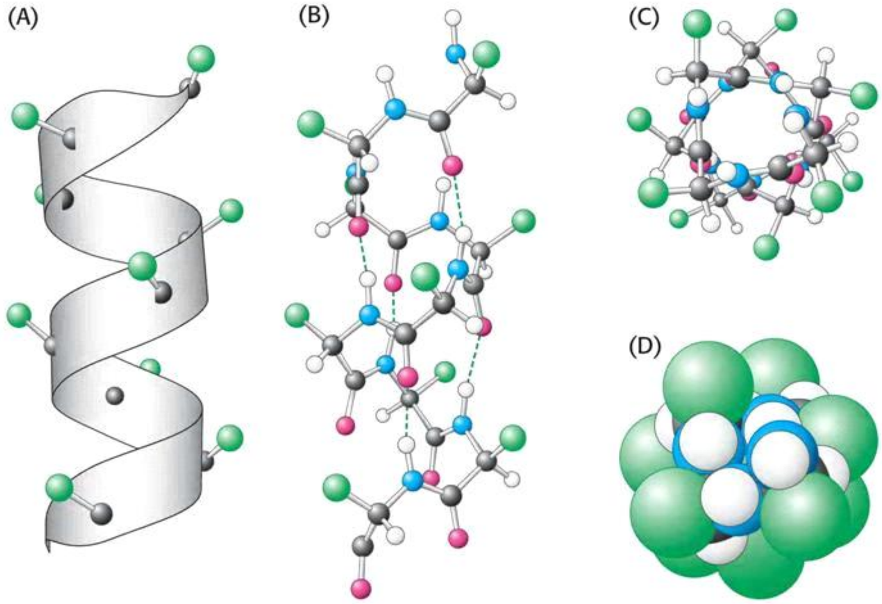
- Oct. 4th slide with Tuftsin--Omit

Review of alpha-helix

- Intrachain H-bonds are formed between peptide bond elements 4 residues apart
- residue #1 H-bonds with residue #5,
- residue #2 H-bonds with residue #6,
- residue #3 H-bonds with residue #7, etc.
- If the residue number is “n”, it will H-bond with residue “n+4”

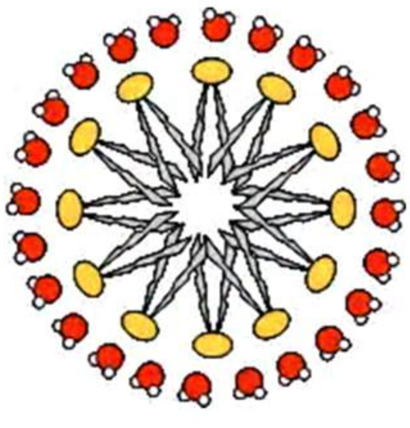


The α-helix



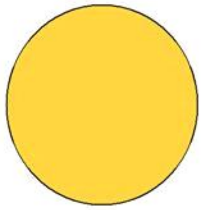
Micelles

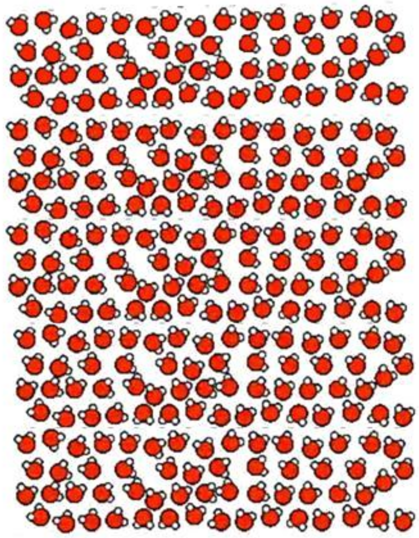
- Water is inherently disordered



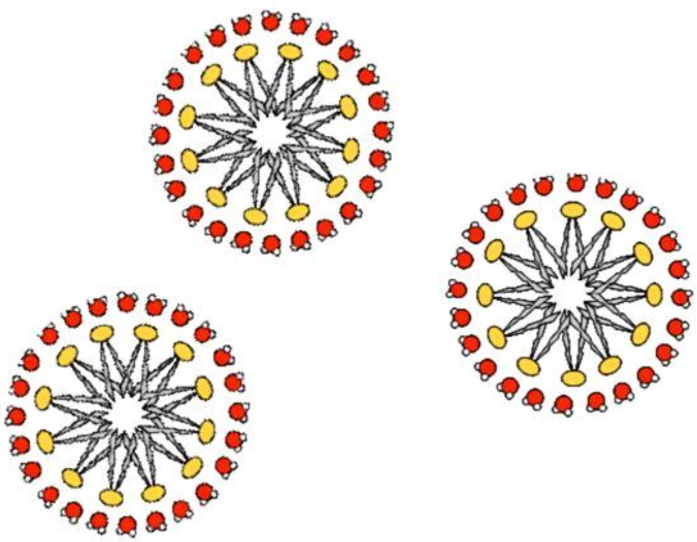
Water is inherently disordered

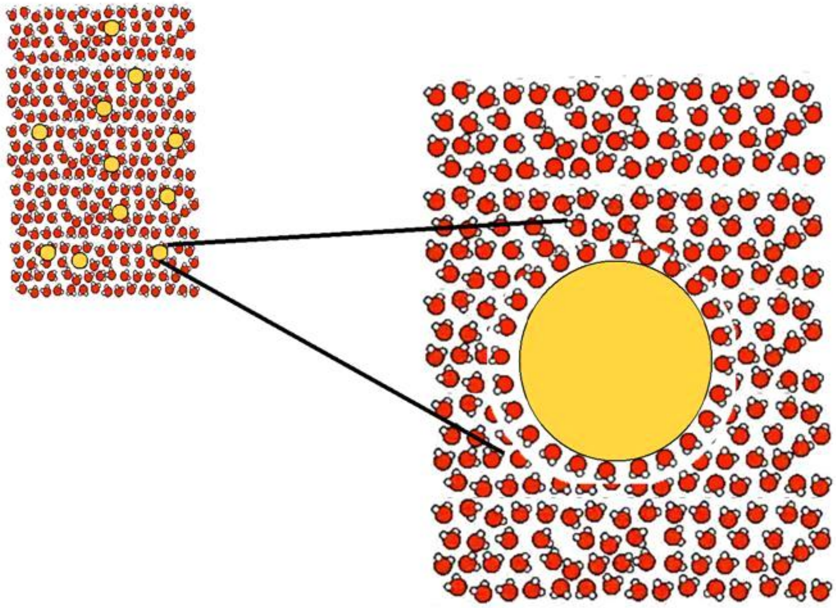
- What happens when a lipid droplet is added to water and agitated?



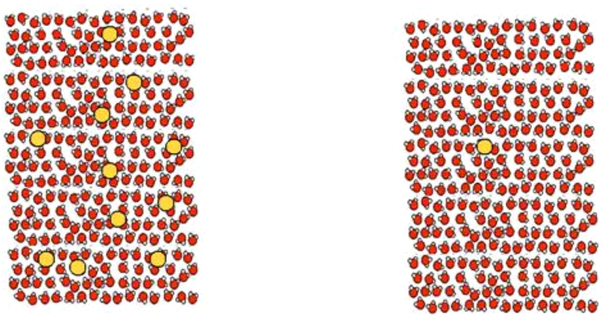


Micelles Form

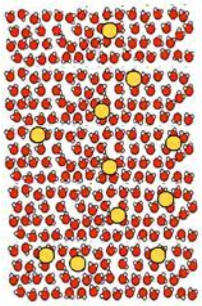


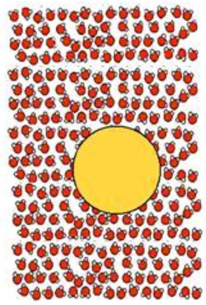


Which one has more ordered water?



Now which one has more ordered water?



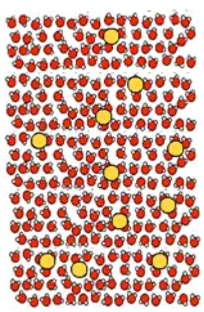


lower entropy
more ordered

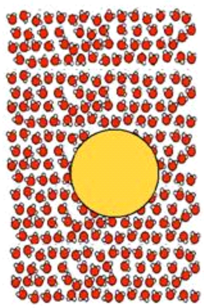
higher entropy

Hydrophobic Effect

- when lipids are present, water molecules have to arrange themselves in a more ordered way
- The less order there is in an arrangement, the more likely the arrangement is to happen
- clumping together of lipid molecules reduces the amount of water that has to be ordered

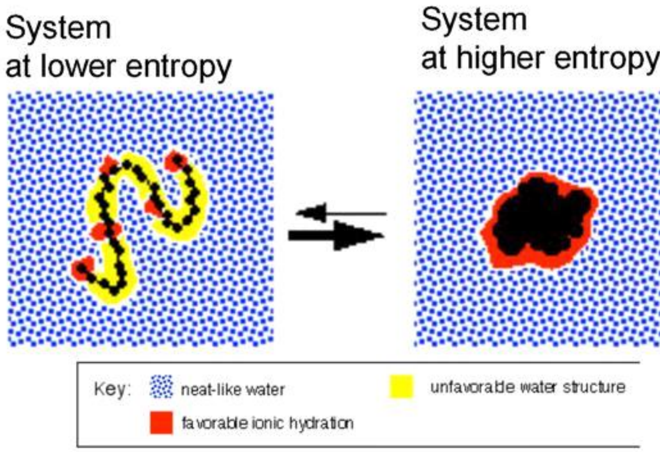


System at lower entropy

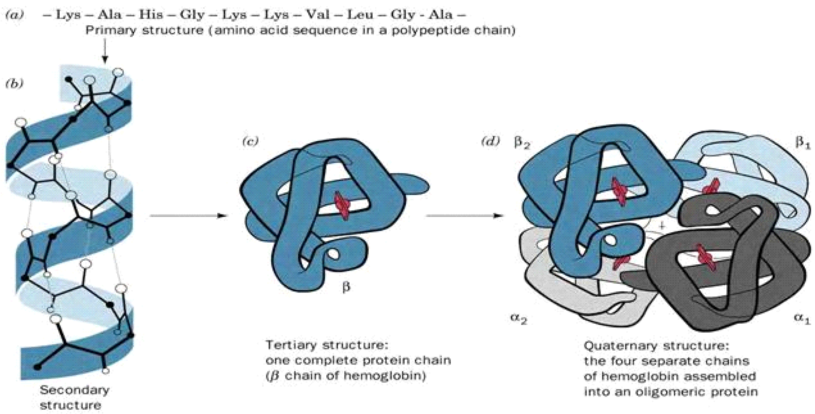


System at higher entropy

Hydrophobic effect helps drive protein folding



The structural hierarchy in proteins



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Proteins in Action

- Now that we've focused on protein structure, let's focus on how structure dictates a protein's function

Oxygen

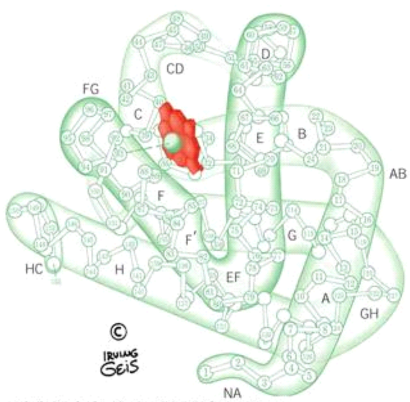
- Aerobic metabolism relies on the presence of oxygen
- Aerobic processes yield more E than corresponding anaerobic process
- However, oxygen is not very soluble in water (only about 10^{-4} M in blood plasma)
- Very, very small organisms can absorb oxygen via simple passive diffusion
- We are big and about 70% water
- How do we and other animals get oxygen to cells?

Oxygen-binding proteins

- Two important oxygen-binding proteins evolved in animals
- Hemoglobin (Hb) and myoglobin (Mb)
- Hb and Mb are related and have been well studied
- Mb and Hb are compact globular proteins
- Hb allows whole blood to carry up to 0.01 M O_2

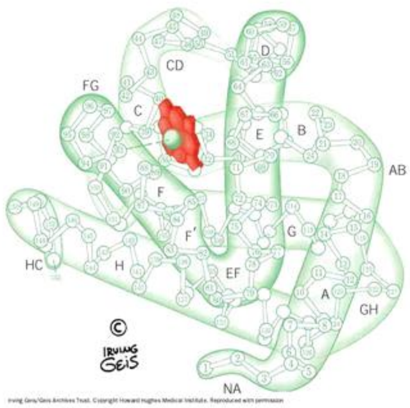
Myoglobin

- Mb is composed of a single chain
- Major function is to transport oxygen in muscle (skeletal, cardiac)
- Gives muscles their red color
- Diving sea mammals are rich in Mb compared to terrestrial mammals



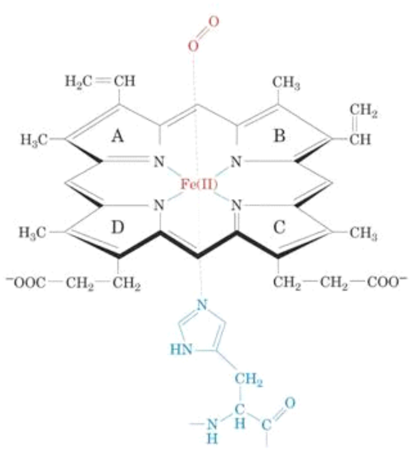
Myoglobin

- Single polypeptide chain of Mb forms a "cradle"
- Heme prosthetic group sits in cradle
- O_2 binding depends on heme's oxidation state
- What is heme?



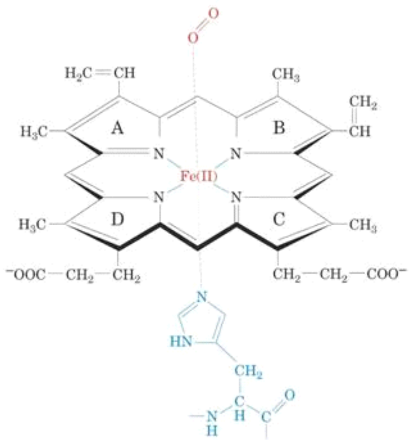
The heme group

- Porphyrin ring system
- A, B, C, D = pyrrole rings
- Complexes an iron ion
- Iron ions (ferrous or ferric) prefer six ligands
- 4 ligands in one plane (nitrogens of the pyrroles)
- 1 ligand above (O_2) and below (His side chain) plane



The heme group

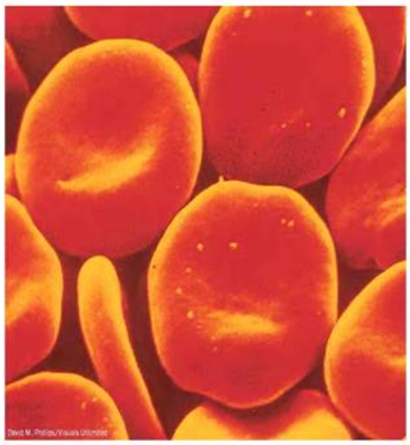
- Small molecules can replace O_2
- CO, NO, H_2S
  - bind with greater affinity
  - toxic



erythrocyte = red blood cell

What about Hb?

- Hemoglobin (Hb) makes up 33% of the weight of an erythrocyte
- Scanning electron microscope of human erythrocytes



Hemoglobin

- Red blood pigment
- Major function is to transport oxygen throughout body
- Hb is a compact tetramer
- Hb is a model for protein quaternary structure and allosteric function
- $\alpha_2\beta_2$ tetramer
  - Two α chains, two β chains