LECTURE 8: INTRODUCTION TO INTRA- AND INTERMOLECULAR FORCES

Outline :

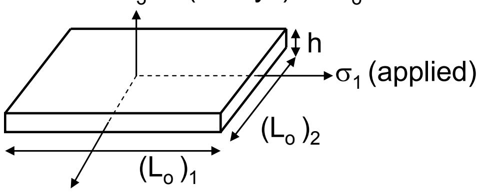
Objectives: To explore the qualitative origins of intra- and intermolecular forces

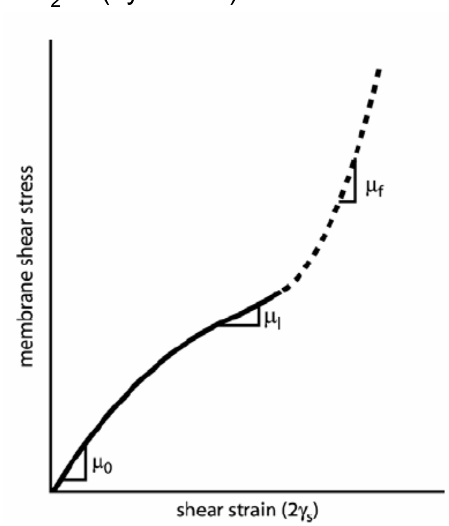
Readings: Course Reader documents 16-19

Multimedia : Protein folding demo on Bonding and protein structure (California Lutheran University)

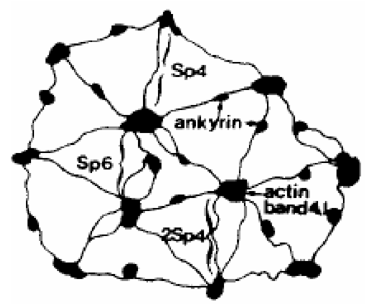
SINGLE CELL MECHANICS

-single cell AFM imaging
-motivation (musculoskeletal tissue, circulatory system, brain)
-experimental methods 1) localized area of the cell is deformed AFM, magnetic bead, 2) mechanical loading of an entire cell micropipette aspiration, optical trap, 3) simultaneous mechanical loading of a population of cells (shear flow, cell force monitor)
-cell modeling *(Dao, et al 2003 J. Mech. Phys. Solids.)*
• The composite is modeled as an isotropic, elastic, continuum, incompressible (constant volume), constant surface area
Constitutive Law : stress vs. strain relationship that describes a particular material





Single macromolecule Gaussian linear elastic Hookean spring F=kr → summing over a network of random coil molecules



"Triangulated Network"

[1] Mohandas, et al. Mechanical properties of the red cell membrane in relation to molecular structures and genetic defects. *Annu. Rec. Biophys. Struct.* **1994**. 23:787-818

$$\underbrace{U}_{\text{Strain energy of a 3D rubber elastic network}} = \underbrace{\frac{G_o}{2}\left(\lambda_1^2+\lambda_2^3+\lambda_3^2-3\right)}_{\text{Neo-Hookean Rubber Elasticitry}} + \underbrace{C_3\left(\lambda_1^2+\lambda_2^3+\lambda_3^2-3\right)^3}_{\text{nonGaussian Nonlinear Strain Hardening Term}}$$

$$\left.\begin{array}{l} \lambda = \text{extension or stretch ratio, } \lambda_1 = \dfrac{(L_f)_1}{(L_o)_1}, \lambda_2 = \dfrac{(L_f)_2}{(L_o)_2}, \lambda_3 = \dfrac{(L_f)_3}{(L_o)_3} \\ G_o = \text{shear modulus} \\ \text{uniaxial normal stress, } \sigma_n(N/m^2) = \dfrac{\partial U}{\partial \lambda_1} \end{array}\right\rangle \text{by definition}$$

$$\text{constant volume constraint} = \lambda_1\lambda_2\lambda_3 \rangle \text{ from definition of extension ratio \& geometry}$$

CLASSIFICATION OF INTRA- AND INTERMOLECULAR FORCES

(within individual molecules) (between individual molecules)

-Definitions : **Interaction** (more general), **force** (push or pull), **bond** (the attraction between atoms in a molecule or crystalline structure)→ all intra- and intermolecular forces are electrostatic in origin → key to life on earth (e.g. water, cell membranes, protein folding, etc.)

-strength measured relative to the thermal energy (room temperature) : **$k_BT = 4.1 \bullet 10^{-21}$ J** : "ruler"

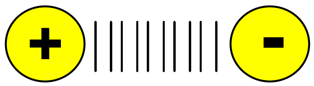
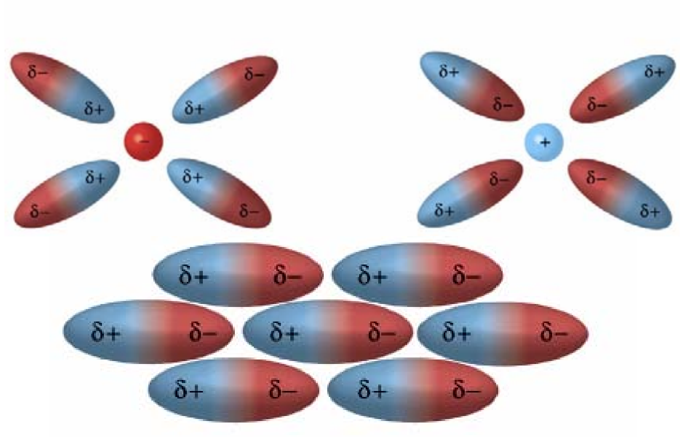
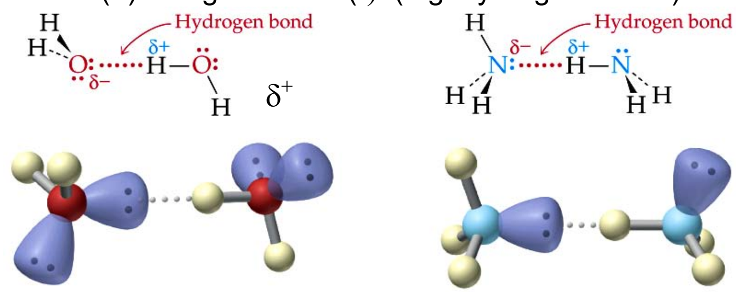
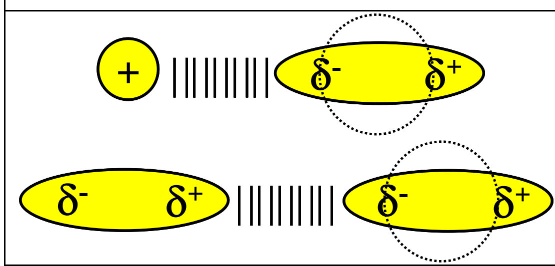
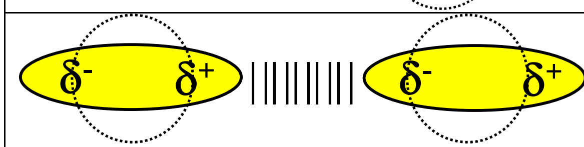
noncovalent (II. and III.)

I. Primary or Chemical	II. Secondary or Physical	III. "Special"
● individually strong > k_BT ● outer orbital e- shared that the discrete nature of the atom is lost ● quantum mechanical in origin ● covalent → possess specificity, directionality, stoichiometry ● metallic → delocalized electrons **covalent, metallic, ionic (in air)**	● individually weak ≤ k_BT ● no e- sharing; between two or more atoms so discrete nature of atoms preserved ● more subtle attraction in origin between (+) and (-) charges typically lack specificity, directionality, stoichiometry **ionic (in water), polar, polarization, dispersion**	● broad range of strength ● controversial ● not a "true" bond **hydrophobic, hydrophilic, polymer effects (e.g. excluded volume, entropic elasticity), electrostatic double layer)**

- Biological systems and bottom-up self-assembly is based on the balance and interplay of intra- and intermolecular forces.

-Noncovalent interactions allow for dynamic systems, i.e. breaking reversible reforming bonds doesn't require much energy)/individually weak, forces are cumulative → stable in parallel.

SPECIFIC TYPES OF INTRA- AND INTERMOLECULAR FORCES

	**Ionic** -Coulombic attraction between oppositely charged species -individually strong, however greatly weakened in the presence of water (e.g. center of proteins→strong, DNA-proteins)
	**Polar Interactions** polar = asymmetric distribution of charge ● attractive force between an ion and a permanent dipole or two permanent dipoles where the (+) charge attracts (-) (e.g. hydrogen bonds)  (-all 3 atoms in water can H-bond, up to 4 per molecule, important in biology because it is able to form weak interactions with so many different chemical species)
	**Polarization Interactions** ● an ion or dipole in the vicinity of a nonpolar atom or molecule causes an instantaneous polarization and electrostatic attraction
 larger the e- cloud easier to distort (> polarizability)	**London Dispersion** ● nonpolar-nonpolar and induced dipole - induced dipole ● charge fluctuation, the (+) nucleus of a nonpolar atom attracts the (-) charged electron cloud of another nonpolar atom → an instantaneous induced, short lived fluctuating dipole, -takes place in all atoms / molecules,

HYDROPHOBIC ("WATER FEARING") INTERACTIONS

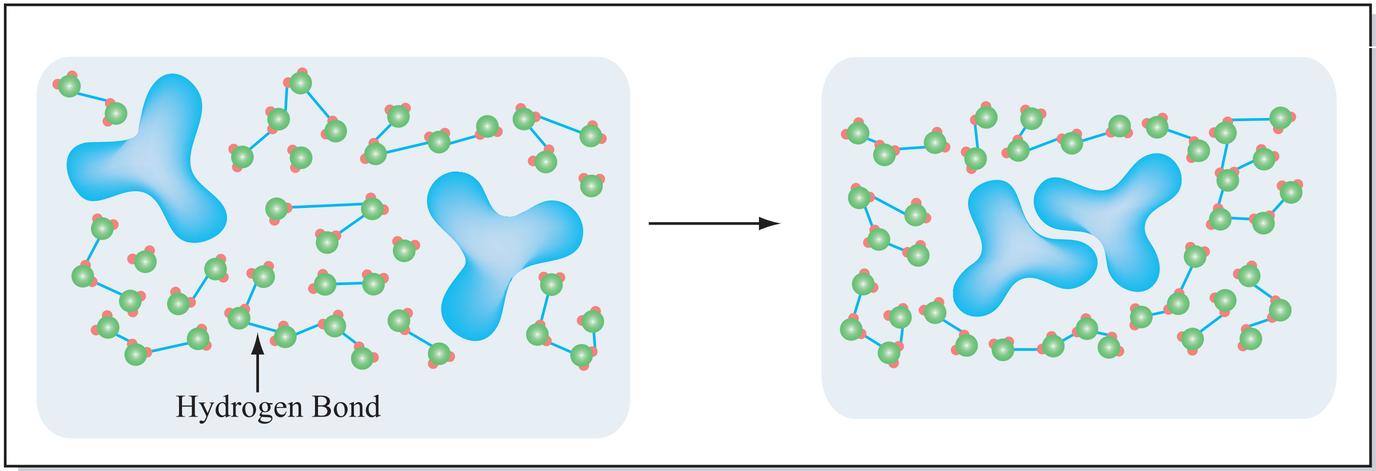


Figure by MIT OCW.

● attraction and association between nonpolar molecules in aqueous solution caused by their inability to form H-bonds with water so as to minimize disruption of H-bonds in water (non-directional, entropy driven since water has a more ordered structure around nonpolar molecules)

●e.g. alkanes, hydrocarbons, fluorocarbons, inert atoms

●can be long range

●Conversely **hydrophilic** interactions result in repulsion in order to maximize their interaction with water, **amphiphile**- having both hydrophilic and hydrophobic chemical constituents, **solvophobic** (fearing other solvents)

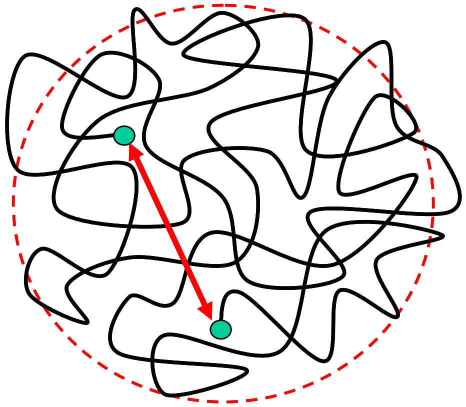
●→ important for fouling/biocompatibility of implanted devices, protein folding

http://en.wikipedia.org/wiki/Image:Dew_2.jpg

Courtesy of Michael Apel.

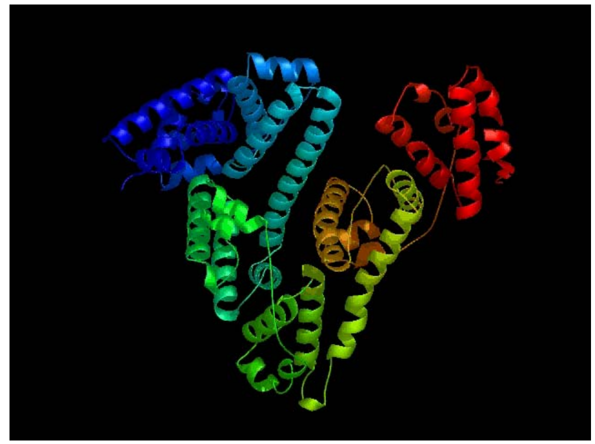
NONCOVALENT INTERACTIONS IN FOLDED PROTEINS

Random coil



→ balance between entopic elasticity and noncovalent attractive forces

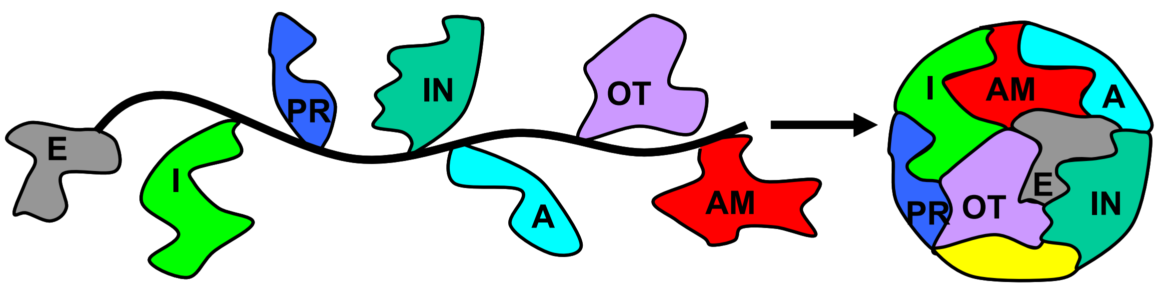
Human Serum Albumin



Adapted from Grosberg and Khokhlov, Giant Molecules

Hierachical levels :

1) **Chemical** : peptide bonds)
2) **Primary** : sequence of amino acids
3) **Secondary** : local chain configuration (α-helix, β-sheet), loops
4) **Tertiary** : additional chain folding over longer distances
5) **Quaternary** : globular domains
6) **Modular** : linear array of covalently attached domains in series



"denatured" biologically inactive "native" state biologically active

→**DEMO** : Noncovalent interactions in proteins, chymotrypsin (digestive proteolytic enzyme, catalyzes chemical reactions to break down proteins into amino acids)

SELF-ASSEMBLING PEPTIDE AMPHIPHILES FOR REGENERATIVE MEDICINE

Hartgerink, et al. Science, **2001** "*Self-assembly and mineralization of peptide-amphiphile nanofibers*"

1) alkyl tail = hydrophobic promotes self-organization
2) cysteines used for polymerization of sulfides
3) flexible linker to give some molecular mobility
4) phosphorylated serine interacts with calcium ions and promotes mineralization
5) cell adhesion ligand RGD

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