Physical & Quantitative Biology, CHE/PHY 558
Spring 2013

Course goals: The central idea of this course is the free energy, the quantitative way we understand driving forces, i.e., the equilibria and rates in chemistry, physics and biology. We describe the underpinning components, the entropy and energy. We explore the microscopic interactions -- including hydrogen bonding, van der Waals, electrostatics and hydrophobic forces -- that explain physical and chemical mechanisms in biology and are the workhorse tools in computational drug discovery. We show how these basic ideas are applied: binding affinities are the basis for drug discovery; coupled binding is the basis for how biological machines convert energy and transduce signals; and polymer free energies are the basis for the folding of protein and RNA molecules.

1/28) Intro. Structural basis of biology. Time & space scales.
1/30) Probabilities. Counting states as a basis of entropy (MDF 1, 2).
2/1) Entropy and Energy as driving forces (MDF 3).

2/4) Partial derivatives (MDF4) (a).
2/6) Max Ent and the Boltzmann distribution law (MDF 5) (a).
2/8) Energies and enthalpies. Thermodynamic states (MDF 6).

2/11) Free energies, chemical potentials (MDF 8, 9).
2/13) Microscopic modeling and the Boltzmann law (MDF 10).
2/15) Equilibrium constants. Binding affinities (MDF 13).

2/18) Liquids & phase equilibria (MDF 14).
2/20) Solvation. Free energies of transfer (MDF 16).
2/22) Diffusion. Fick's Law. Physical dynamics (MDF 17, 18).

2/25) Chemical rate models. Mass-action kinetics (MDF 19).
2/27) Transition states. Activation barriers (MDF 19).
3/1) Coulombic interactions. How charges interact (MDF 20).

3/4) Electrostatic potentials (MDF 21) (a).
3/6) Electrochemical equilibria (MDF 22).
3/8) How salts shield charges. The Poisson-Boltzmann model (MDF 23).

3/11) Intermolecular forces: van der Waals, dipolar, hydrogen bonds (MDF 24).
3/13) Properties of water. Hydrophobic solvation (MDF 30, 31)
3/15) Adsorption, binding polynomials (MDF 27).

3/18 – 3/22) **Spring Break. No class.**

3/25) Binding cooperativity (MDF 28).
3/27) Bio-machines (MDF 29).
3/29) Polymers: Random flights & Flory-Huggins theory (MDF 32, 33) (b).

4/1) Polymer entropies, constraints and folding (MDF 33, 34) (d).
4/3) Protein structures (PP1) (c).
4/5) Protein function and mechanisms (PP2) (c).

4/8) Protein stability (PP3).
4/10) Protein cooperativity: helix-coil transitions (PP4).
4/12) Protein folding & aggregation (PP4).

4/15) Protein folding kinetics. Markov models. Energy landscapes (PP5) (a).
4/17) Protein evolution and sequence space (PP6).
4/19) Bioinformatics, sequence comparisons (PP7) (d).

4/22) Drug discovery 1: Lead identification: screening, informatics, DOCK (e) .
4/24) Drug discovery 2: computing binding affinities (e).
4/26) Role of physical & computational modeling in biopharma (c or f).

4/29 –) Student project presentations.

(a) Jin Wang (3)?
(b) Helmut Strey (2) – OK for 3/29 and 4/3, not 4/1.
(c) Markus Seeliger (2-4)?
(d) ??
(e) Rob Rizzo group (2).
(f) Wendy Cornell (1)?