

**Physical & Quantitative Biology, CHE/PHY 558**  
**Fall 2014**

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**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.

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- 8/25) Intro. Structural basis of biology. Time & space scales. [OK]  
8/27) Probabilities. Counting states as a basis of entropy (MDF 1, 2) [OK].  
8/29) Entropy and Energy as driving forces (MDF 3) [OK].
- 9/01) **NO CLASS**, Labor Day.  
9/03) Partial derivatives (MDF4).  
9/05) Max Ent & The Boltzmann Distribution Law (MDF 5).
- 9/08) Energies and enthalpies. Thermodynamic states (MDF 6).  
9/10) Free energies, chemical potentials (MDF 8, 9) [\* , a].  
9/12) Microscopic modeling and the Boltzmann law (MDF 10) [\* , a].
- 9/15) Equilibrium constants. Binding affinities (MDF 13).  
9/17) Liquids & phase equilibria (MDF 14).  
9/19) Solvation. Free energies of transfer (MDF 16).
- 9/22) Diffusion. Fick's Law. Physical dynamics (MDF 17, 18).  
9/24) Chemical rate models. Mass-action kinetics (MDF 19) [f, OK].  
9/26) Transition states. Activation barriers (MDF 19) [f].
- 9/29) Coulomb interactions. How charges interact (MDF 20) [OK].  
10/01) Electrostatic potentials (MDF 21).  
10/03) Electrochemical equilibria (MDF 22) [OK].
- 10/06) Salts shield charges. The Poisson-Boltzmann model (MDF 23) [OK].  
10/08) Intermol forces: van der Waals, dipolar, hydrogen bonds (MDF 24).  
10/10) **MIDTERM EXAM** [\*].

- 10/13) Properties of water. Hydrophobic solvation (MDF 30, 31) [OK].  
 10/15) Polymers: random-flights, entropies & constraints (b, MDF 33, 34).  
 10/17) Polymer solutions: Flory-Huggins theory (MDF 32, 33) [b, OK].
- 10/20) Adsorption, binding polynomials (MDF 27) [OK].  
 10/22) Binding cooperativity (MDF 28).  
 10/24) Bio-machines (MDF 29).
- 10/27) Protein structures (PP1) [c, OK].  
 10/29) Protein function and mechanisms (PP2) [c, OK].  
 10/31) Protein stability (PP3).
- 11/03) Protein cooperativity: helix-coil transitions (PP4) [\* , a, OK].  
 11/05) Protein folding & aggregation (PP4) [\* , c, OK].  
 11/07) Protein folding kinetics. Markov models. Energy landscapes (PP5) [a].
- 11/10) Protein evolution and sequence space (PP6) [\* , g].  
 11/12) Bioinformatics, sequence comparisons (PP7) [\* , g, OK].  
 11/14) Drug discovery 1: Comp-aided design, dock, virtual screening [\* , d].
- 11/17) Drug discovery 2: Scoring, sampling, free-energy methods [\* , d].  
 11/19) MD, QM, docking and informatics in Biopharma [e].  
 11/21) Extra day, at the moment. (Review, for exam?)
- 11/24) **FINAL EXAM.**  
 11/26) **NO CLASS**, Thanksgiving break.  
 11/28) **NO CLASS**, Thanksgiving break.
- 12/1) Research Project Presentations.  
 12/3) Research Project Presentations.

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 MDF = Molecular Driving Forces, chapter numbers. PP = Protein Principles, draft textbook. \* means KD is away. "OK" means we have a videorecorded lecture available in case you want to use it.

### Lecturers

- (a) Darrin York, Taisung Lee @ Rutgers.
- (a) Jin Wang.
- (b) Helmut Strey.
- (c) Markus Seeliger.
- (d) Joe Allen & Rob Rizzo.
- (e) Wendy Cornell.
- (f) Gabor Balazsi.
- (g) Jason Wagoner