

## **BP205 Molecular Dynamics of the Cell**

10 weeks / 2 lectures per week

Room S261 Genentech Hall

April 1 – June 6, 2008

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Grading: 6 Homework Sets 60% Group Work OK  
Midterm 20% Individual / Time limit  
Final 20% Individual / Time limit  
Homework and Exams handed out one week before they are due

### **SYLLABUS**

April 1: **Class Overview / Relative Length and Time Scales in the Cell**

April 3: **Molecular Motions in the Cell A**

- Brownian Motion
- Random walks and 1-D diffusion
- Calculation of a probability distribution from a random walk
- Single molecule studies of repressor diffusion on DNA and Dynein on a microtubule

April 8: **Molecular Motions in the Cell B**

- Fick's Law and the diffusion equation
- Steady-state and time-dependent (Gaussian) solutions
- Coordinate Systems (Cartesian, Cylindrical, Spherical)
- Diffusion-limited binding in solution
- Binding to membrane receptors on the cell surface
- Protein diffusion in the cytosol of muscle cells
- FRAP studies of protein diffusion in bacteria
- Dependence of the diffusion constant on protein molecular weight
- Diffusion of DNA in the cell

April 10: **Molecular Motions in the Cell C**

- Flux as an external force
- Lateral diffusion in a membrane (Saffman-Delbruck)
- Single molecule measurement of lateral diffusion
- Diffusion-limited binding on a cell surface
- Brownian ratchets
- Protein translocation as a Brownian ratchet

April 15: **Metabolic Flux Analysis A**

- Mass balance and steady-state analysis
- Linear algebra

- Inferring unknown fluxes from measured fluxes
- Analysis of citric acid production in *Candida*

HOMEWORK 1 DUE

April 17: **Metabolic Flux Analysis B**

- Objective functions and linear programming
- Catabolic metabolism in lactic acid producing bacteria
- Phenotype phase plane analysis
- Evolution of glycerol utilization in *E. coli*

April 22: **Fluid Flow on the Scale of a Cell A**

- Scaling arguments and dimensionless numbers
- Life at low Reynold's Number
- Turbulent versus laminar (time-reversible) flow
- Why can't a bacterium swim like Flipper?

HOMEWORK 2 DUE

April 24: **Fluid Flow on the Scale of a Cell B**

- Diffusion-advection equation
- Peclet Number: convection versus advection
- Can a bacteria get more food by swimming?
- Can a cilia enhance food uptake by sweeping fluid against the cell surface?
- Evolution of the volvocine green algae flagellum
- Cilia and embryogenesis (Hensen's node and symmetry breaking)

April 29: **Reaction Kinetics A**

- Conversion of a reaction set into differential equations
- Elementary mass action kinetics
- De-dimensionalizing equations: protein dimerization example
- Timescales: protein degradation example
- Using timescales to simplify equations
- Michaelis-Menton kinetics revisited
- Single molecule enzyme kinetics (new)

HOMEWORK 3 DUE

May 1: **Reaction Kinetics B**

- Steady-state analysis
- Stability of the steady-state
- Timescale for the response from perturbation
- Autocatalysis example
- Stability of a set of multiple differential equations
- Jacobian, Trace, Determinant, Eigenvalues
- HIV progression example
- Bifurcations / Autocatalysis II example

- May 6      **Kinetics of Gene Regulation**
- Network dynamics
  - Shea-Ackers formulation
  - Binding polynomials and cooperativity
  - Negative autoregulation
  - Positive autoregulation
  - Biphasic response
- MIDTERM DUE
- May 8      **Reaction-Diffusion**
- New lecture
- May 13     **Dynamic Response in Cellular Networks (Hana)**
- Fundamentals
- May 15     **Negative Feedback (Hana)**
- Proportional, integral, and derivative control
  - Sensitivity analysis
  - Perfect adaptation in bacterial chemotaxis and Hog pathway (yeast)
- May 20     **Positive Feedback (Hana)**
- Ultrasensitivity and hysteresis
  - Reversible and irreversible cellular decisions
  - Phase plane analysis and regions of attraction of stable equilibria
- HOMEWORK 4 DUE
- May 22     **Performance Tradeoffs in Cellular Networks (Hana)**
- Nested feedback loops and regulatory architectures
  - Simple network motifs, transcriptional circuits, and signaling cascades
  - Heat shock response
- May 27     **Enzymatic Cycles (Chao)**
- Role in signaling and control networks
- HOMEWORK 5 DUE
- May 29     **Population Genetics (Chao)**
- June 3      **Boolean Networks (Chao)**
- June 5      **Robustness, Optimization, and Emergent Properties**
- HOMEWORK 6 DUE
- June 12     FINAL DUE