BP205 Molecular Dynamics of the Cell
10 weeks / 2 lectures per week
Room S204 Genentech Hall
January 6 – March 12, 2009
Tuesday 8:30 – 10:00
Thursday 10:30 – 12:00

TAs: Monica Tremont (Biophysics) monica.tremont@ucsf.edu
MATLAB
David Burkhardt (Biophysics) david.h.burkhardt@gmail.com
Programming

Grading:
4 Homework Sets 40% Group Work OK
Midterm 20% Individual
- 4 hour continuous time limit
- 1 week to complete
- no collaboration
- open everything except web
- no computer necessary

Homework and midterm handed out one week before they are due
- hand out on Tuesday / due next Tuesday

Final Report 40%
- 4 page / form of a journal letter

SYLLABUS

January 6: **Class Overview**
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

January 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

January 13: **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

HOMEWORK #1 handed out (Monica)

January 15: **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?

January 20: **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 embriogenesis (Hensen's node and symmetry breaking)

HOMEWORK #1 DUE

HOMEWORK #2 handed out (Monica)

January 22: **Single Molecule Kinetics**

- Michaelis-Menton kinetics for a single enzyme
- Kinetic rates and probabilities
- Opening and closing single ion channels

January 27: **Reaction Kinetics**

- Elementary mass action kinetics
- De-dimensionalizing equations: protein dimerization example
- Timescales: protein degradation example
- Using timescales to simplify equations
- Michaelis-Menton kinetics revisited

HOMEWORK #2 DUE

HOMEWORK #3 handed out (David) – include 1 MATLAB problem

January 29: **Stability and Simple Bifurcations**

- Steady-state analysis
- Stability of the steady-state
- Timescale for the response from perturbation
- Autocatalysis example
- Bifurcations / Autocatalysis II example

Monica runs MATLAB tutorial on Friday, January 29

February 3: **Kinetics of Gene Regulation**

- Network dynamics
- Shea-Ackers formulation
- Binding polynomials and cooperativity
- Positive and Negative autoregulation
- Biphasic response

HOMEWORK #3 DUE

Homework #4 handed out (David) – include 1 AUTO problem

February 5: **Numerical Methods**

- Euler's Method

	• Improved Euler's Method • Runge-Kutta Method – adaptive step size • Stiff Equations • Numerical methods for bifurcation analysis (AUTO) **David runs AUTO tutorial on Friday, Feb 6**
February 10	**Bifurcations of 2-Dimensional Systems** • Jacobian, eigenvalues, • *In vivo* HIV dynamics • Spread of disease epidemics • Cell-cell communication • Negative autoregulation Homework #4 DUE MITERM HANDED OUT
February 12	**Multistability** • Null clines and cooperativity • The appearance of multiple steady-states • Competition models • Positive feedback and bistability
February 17	**Oscillations A** MITERM DUE
February 19	**Oscillations B**
February 24	**Reaction-Diffusion** Project Topic (Title, equations, 1 paragraph summary) DUE
February 26	**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
March 3	**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 Project Background and Prior Work (1 pages) DUE
March 5	**Guest Lecture**
March 10	Project Help / Support
March 12	Project Help / Support
March 13	Final Report DUE by **5pm** email PDF to cavoigt@picasso.ucsf.edu

Format of Final Report (4 pages of text + figures)
Like a short "letter" format for an actual
If your paper has multiple concepts, pick one
Need to simplify to (at least) a 2-D system if your paper does not
Some papers may have concepts to references to models and not an actual model
The model does not (in fact, should not) have to be the one in the paper

Abstract (<500 words)

- Statement of conclusions

Background and Prior Work 1 single-spaced page

- Describe your system and perform a literature search and summarize
- Roughly 10 references

The Model ½ page

- Write differential equations
- Describe assumptions and any simplifications (timescales, etc)
- Describe where the parameters are from (or basis of approximations or ranges that make physical sense)
- What is different between your model and other models?

Results and Discussion 2 pages

- If you need to reduce the number of equations, make a timescale argument
- De-dimensionalize equations (if the paper you are assigned already has dedimensionalized equations, show the derivation of how they were obtained)
- Analytically solve for the steady-states and determine the range of possible behaviors
- Use MATLAB to identify parameter regions that produce each of the possible behaviors – make graphs showing how the parameters affect the time trajectories
- Use AUTO or other bifurcation analysis tool to perform a bifurcation analysis for one parameter that changes the behavior of the system
- Propose a "Reynolds' Number" or dimensionless parameter that dictates the behavior of your system

Figure 1 Draw a diagram of your system that includes the key interactions in your model, mark on the diagram your parameters

Table 1 Parameter symbol, name of parameter, value, and reference

Figure 2 Temporal behavior of your system – demonstrate different parameter regimes

Figure 3 Bistability analysis

References