APh150: Physics of Biological Structure and Function

Winter 2003

When: To be determined
Who: You and me (Rob Phillips, x 3374, phillips@aero.caltech.edu, 221 Steele)
Where: 104 Watson
What: See below!
How: Lecture twice a week and weekly homework. No exams. Your grades will be based upon your homework grades (75 %) as well as on a term paper (25%). I will NOT accept late homeworks (late means anytime after class is over the day the homework is due) unless you have a mindblowingly good excuse. As for collaboration with others, you may discuss the homework with others, but your explanations and derivations must be your own and your logic should be carefully explained and the *significance* of your results should also be explained. If you hand us a sloppy homework the grader will likely be unable to penetrate your logic and you will lose points.

1 Course Overview and Philosophy

As noted in a recent article by Dennis Bray (Nature, **412**, 863 (2001)), "It seems inescapable that, at least at the level of molecules and cells, biology is moving from an era of data-collection to one of hypothesis-driven research. Progress in this new field will be driven by informed and increasingly quantitative theories..." This new quantitative era in the molecular and cellular description of biological systems has been ushered in in part by a new wave of experimental techniques that allow for the manipulation of the machinery of the cell in unprecedented ways. Indeed, it is now possible to access quantities such as the critical force to unzip DNA or the atomic-scale motions associated with the action of molecular motors. The aim of this course is to take stock of these developments from a quantitative perspective.

2 Course Outline

1. **Hierarchies in Biology**

   - *Spatial Scaless in Biology.* From molecules to tissues.
   - *Temporal Scales in Biology.* From femtoseconds to evolutionary time scales.

2. **The Great Polymer Languages: Macromolecular Structure.**

   - *Building Blocks of the Living World.* The Big Four.
   - *Deterministic structure: from atoms to continua.* Atomic-level descriptions of macromolecules. PDB files. Ramachandran plots. Continuum descriptions of polymer structure.
   - *Statistical Geometry.* Why it is necessary to introduce statistical measures of structure. Random walks and biopolymer size and shape.
   - *Biopolymers in cells and in vitro.*

3. **The Great Polymer Languages: Macromolecular Dynamics.**

   - *Dynamics of Systems in Equilibrium.* Brownian motion as a paradigm. Brownian motion and its role in biological systems.
   - *Deterministic Forces on Diffusing Particles.* Stokes drag.
   - *Random Forces on Diffusing Particles.* Langevin equation.
   - *Spherical Diffusion.* Chemoreception.
   - *Slithering and Jiggling of Polymers.* Rouse and Zimm. Gel electrophoresis.

4. **Macromolecules at Work: Part 1.**

- *Single Molecule Biomechanics.* Single molecule experiments - optical tweeezers, atomic-force microscopy, etc. The entropic spring. Large deformations of DNA and proteins.
- *Elastic Theory of Polymers.* Beam theory. Statistical mechanics revisited. Persistence length. Sequence dependent elasticity.

5. **Macromolecules Talk.**

   - *Equilibrium Constants and Mass Action.*
   - *Polymerization.* Cytoskeletal polymerization. DNA replication and transcription.
   - *Critical micelle concentration.*
   - *Viral Assembly.*
   - *Ligand/Receptor Interactions.* Myoglobin and hemoglobin. ATP. Gene expression.

6. **Macromolecules at Work: Part 2.**

   - *Molecular Motors in Biology.*
   - *Translocation Ratchet.*
   - *Translational Motors.* The curious case of kinesin.

7. **Macromolecular Organization and Orchestration.**

   - *DNA Organization.* Viral DNA packing. Bacterial chromosomes. Eucaryotic chromosomes.
   - *Phenomenology of membranes.* Molecular perspective. Lipid bilayers.
   - *Elasticity theory of membranes.* Differential geometric description of membranes. Energetics of membrane deformation.
   - *Equilibrium shapes of membranes.* The question of shape. Case study: red blood cells.
   - *Membrane Inclusions.* Membrane inclusions - membrane proteins.

8. **Cell Movements.**

   - *Cells in Solution.* Phenomenology of cellular motility. Random walk revisited: the directed random walk. Life at low Reynolds number. Mechanics of flagellae. Random walks and bacterial motion.
   - *Cells on Surfaces.*

3 Possible Term Paper Ideas

I begin by reminding you that the spirit of this course is to make sure that everytime we discuss biological phenomena that: a) we make simple estimates to get a feel for the numbers and b) that we build simple models that provide intuition about that particular phenomenon. Your term paper will be judged on the basis of the extent to which you are creative in establishing both estimates and models about your subject. Regurgitating other peoples models and estimates will NOT qualify as a successful term paper. To that end, the term paper will be put forth in two installments. On Wednesday, February 12 you must submit a one page summary of what your project will be about, what references will be pertinent to your undertaking and what you intend to estimate and model. Some possible term paper ideas are given below:

- *DNA packing in viruses.*
- *DNA packing in bacteria.*
- *DNA packing in eucaryotic cells.*
- *Gene regulation and genetic networks.*
- *Dynamics of molecular motors: kinesin.*
- *Polymer translocation in biology.*
- *Statistical mechanics of protein folding.*
- *The machinery of ATP synthesis.*

- *Self-assembly: viruses or cytoskeleton or something else.*
- *Cell adhesion.*
- *Cell signaling.*
- *Voltage gated ion channels.*
- *Mechanically activated ion channels.*
- *DNA packing in viruses.*
- *Flagellar motion and life at low Reynolds number.*

4 Bibliography

My logic in providing the following list of references is to give you a wide view of some of the important books (both pedagogically and as scholarly works) that have been written to describe this important field. In addition to the works listed here, you should count on a steady supply of readings from the current literature. Indeed, this course is going to be reading intensive since most of the audience will lack either the biological or physical background and will have to make up for such holes in part through extracurricular reading.

B. Alberts, D. Bray, A. Johnson, J. Lewis, M. Raff, K. Roberts and P. Walter, *Essential Cell Biology*, Garland Publishing, 1998. This book has become one of my prized possessions and is usually the first place I look each time I am trying to understand the current thinking on biological phenomena.

D. Boal, *Mechanics of the Cell*, Cambridge University Press, 2001. This book will serve as one of the two main texts for the quarter. Boal has assembled a very nice collection of insights into the ways in which mechanics can be applied to the living world.

J. Howard, *Mechanics of Motor Proteins and the Cytoskeleton*, Sinauer Associates, 2001. Howard's book is full of interesting insights and will serve as our second central source of reading.

Nelson, P., *Biological Physics: Energy, Information, Life.* Nelson's unfinished manuscript will provide readings on a range of topics during the course.

A. Y. Grosberg and A. R. Khokhlov, *Statistical Physics of Macromolecules*, AIP Press, 1994. I find this to be a fantastic book, full of interesting insights into the ways in which polymer physics can be used to explore problems of biological interest.

S. Vogel, *Life in Moving Fluids*, Princeton University Press, 1994. I love this book and although it is not centrally related to the present course, I couldn't resist recommending it.

J. Israelachvili, *Intermolecular and Surface Forces*, Academic Press, 1992. The subject of this book is much larger than is implied by the title. We will make reference to Israelachvili's discussion both when discussing forces in the material world and also in the context of self-assembly.

C. R. Calladine and H. R. Drew, *Understanding DNA*, Academic Press, 1999. This book provides a window on DNA which makes a good deal of contact with the perspective that will be brought to this important molecule in the course.

M. Doi, *Introduction to Polymer Physics*, Oxford University Press, 1996. this book is short and sweet and provides a readable introduction to many of the ideas from polymer physics that we will borrow in our attempt to understand the mechanics of biological macromolecules.

P.-G. de Gennes, *Scaling Concepts in Polymer Physics*, Cornell University Press, 1979. de Gennes classic epitomizes the appeal of "universal" insights, especially as practiced by a master.

A. Y. Grosberg and A. R. Khokhlov, *Giant Molecules*, Academic Press, 1997. A very nice introduction to the physics of macromolecules. Describes many of the arguments that will be made in our course.

U. Seifert, *Configurations of fluid membranes and vesicles*, Adv. Phys., **46**, 13 (1997). Seifert provides a detailed description of the elasticity of membranes as well as insights into the current understanding of equilibrium shapes.

H. C. Berg, *Random Walks in Biology*, Princeton University Press, 1993. A must read. Berg has all sorts of fun and interesting things to say.

S. A. Safran, *Statistical Thermodynamics of Surfaces, Interfaces and Membranes*, Perseus Publishing, 1994. A statistical physics treatment of membranes and interfaces.

M. Doi and S. F. Edwards, *The Theory of Polymer Dynamics*, Clarendon Press, 1986. Doi and Edwards have some important discussions of the motion of polymers in crowded environments.