

Physics 650: Minicourse in Biological Physics

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Spring 1997

Recent years have seen great progress in understanding the structure and function of cell-biological subsystems using the ideas and techniques of physics. Some of these advances have come from progress in experimental method (confocal and fluorescence microscopy, optical tweezers...), while others come from the development of new tools in statistical mechanics. At the same time the study of biological systems holds the promise of creating new artificial materials with remarkable properties (microtubules, self-assembled monolayers, monodisperse polymers...).

Perhaps surprisingly, biomembranes and biopolymers also turn out to have a great beauty and depth when regarded as *purely physical* systems. We will mainly focus on this third point of view, but will keep the others in mind as well.

There will be about seven 90-minute lectures. There will be one short project. The list of topics is still evolving, but here is a general summary with some background references. Most likely I will cover a few classic calculations drawn from the literature cited below, together with their experimental confirmation.

Prerequisites:

A general background in statistical mechanics will be assumed.

Tentative Outline:

1. *Basic facts about cells*: What is life? The main problems as Schrödinger saw them. Crick's Central Dogma. Types of cells. Survey of experimental techniques.
 - B. Alberts, D. Bray, J. Lewis, M. Raff, K. Roberts, and J. Watson, *Molecular biology of the cell* (Garland, 1989), chap. 1–4; 10–13.
2. *Forces in the microscopic world*: Coulomb forces; solvation; van der Waals forces; screening; the diffuse electric double layer; hydrogen bonds; the hydrophobic effect.
 - J. Israelachvili, *Intermolecular and surface forces*.
 - Samuel A. Safran, *Statistical thermodynamics of surfaces, interfaces, and membranes* (Addison-Wesley 1994).
3. *Survey of major small and large molecules*: Dissociation and pH; fatty acids; amino acids; nucleotides; DNA, RNA, proteins; phospholipids; micelles and bilayers. Transmembrane proteins; other protein complexes; chromatin.
 - Alberts, above.
4. *Physics of the micron world*: Elasticity theory; diffusion; fluctuation/dissipation; fluid mechanics. The Most Important Idea of Physics.
 - L. Landau and E. Lifshitz, *Theory of elasticity* 3rd ed. (Pergamon, 1986), §§1–5; 11–20.

- H. Berg, *Random walks in biology* (2nd edition).
 - E. Purcell, *Life at low Reynolds number* Am. J. Phys. **45** (1977) 3.
5. *DNA basics; elasticity; entropic tension:*
 - C. Calladine and H. Drew, *Understanding DNA* (Academic, 1992).
 - R.H. Austin et al, “Stretch genes,” *Physics Today* Feb. 1997, pp. 32–38.
 - Marko and Siggia, “Stretching DNA” (below).
 6. *DNA topology; the Link formula; supercoiling:*
 - Strick, et al (below); Fain, Ostlund, Rudnick (below).
 7. *Elastic theory of lipid bilayer membranes:*
 - L. Peliti, in David and Ginsparg, below.
 8. *Fluctuation effects in bilayer membranes: differences from polymers; persistence length; wandering; entropic tension; steric repulsion; flicker of red blood cells.*
 - Evans and Rawicz (below); Helfrich and Servuss (below); Safinya (below).
 - Brochard and Lennon (below).

Possible Paper Topics

This list will grow. I’ll supply you with starter references and you’ll find more yourself. Talk to me if you have another topic in mind.

- . Mechanical properties of stiff-polymer gels like actin (MacKintosh/Käs).
- . DNA supercoiling (Rudnick et al).
- . DNA-membrane complexes (Lasic et al.; other papers below; Dan).
- . Budding and sorting in the Golgi apparatus (Oster; Rothman).
- . Microtubule self-assembly and targeting (Leibler).
- . Ordering and pattern formation in amphiphile monolayers (Lubensky/MacKintosh).
- . Role of cholesterol in modulating physical properties of bilayers (Bloom; Gennis).
- . Mechanical properties of the membrane/spectrin-network complex (Discher).
- . Lipid tubules (Selinger/Schnur).
- . Membrane-mediated interactions between proteins; self-assembly (Dan/Safran; Goulian/Pincus).
- . Kinesin, dynein, other motors (Block; Oster; Prost/Ajdari; Leibler).
- . Conformal Diffusion of vesicles of complex topology (Seifert; Michalet/Bensimon).
- . Flicker of red blood cells (Brochard/Lennon; Engelhardt et al; Milner/Safran).
- . Information-theoretic aspects of DNA; “junk” DNA (Mantegna et al).
- . Protein-folding model based in hydrophilic/phobic data (Li/Wingren; Dill).
- . DNA condensation: When like charges attract (Oosawa; Bloomfield/Rouzina; Bruinsma/Gelbart).
- . Diffuse double layer, DLVO theory (Safran, Israelachvili).
- . Counterion condensation about charged rods (leBret/Zimm).
- . Membrane adhesion (Evans, Seifert, Sackmann).

Further General Reference

- P. Chaikin and T.C. Lubensky, *Principles of condensed matter physics* (Cambridge).

- F. David and P. Ginsparg, eds. *Fluctuating geometries in statistical mechanics and field theory* (Les Houches 1994).
- Gennis, *Biomembranes*
- D.S. Goodsell, *The machinery of life* (Springer-Verlag, 1993).
- D. Nelson *et al.*, eds, *Statistical mechanics of membranes and surfaces*, (World Scientific, 1989).
- T. Powers, Ph.D. dissertation, Penn (1995).
- W. Saenger, *Principles of nucleic acid structure* (Springer, 1984).
- Samuel A. Safran, *Statistical thermodynamics of surfaces, interfaces, and membranes* (Addison-Wesley 1994).
- A. Vologodskii, *Topology and physics of circular DNA* (CRC Press, 1992).

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- C. Bean, “The physics of porous membranes,” in *Membranes — macroscopic systems and models* ed. G. Eisenman (Marcel Dekker, 1972).
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- K. Berndl et al, “Shape transformations of giant vesicles,” *Europhys Lett* **13**, 659 (1990).
- S.M. Block, in *Noninvasive techniques in cell biology*, 375-402, (Wiley-Liss, New York 1990); K. Svoboda and S. M. Block, *Annu. Rev. Biophys. Biomol. Struct.*, **23**, 247, (1994); A. Simon, Ph.D Thesis, Univ. of Chicago, (June, 1992). [Laser Tweezer Techniques.]
- M. Bloom, “The evolution of membranes,” in R. Lipowsky and E. Sackmann, eds., *Structure and dynamics of membranes* (Elsevier, 1995) [role of cholesterol, etc]; M. Bloom, E. Evans, and O. Mouritsen, *Quart. Rev. Biophys.* **24** (1991) 293 [mattress model].
- F. Brochard and J. Lennon, “Frequency spectrum in the flicker phenomenon in erythrocytes,” *J. Phys. France* **36** (1975) 1035.
- P. Cluzel, A. Lebrun, C. Heller, R. Lavery, J.-L. Viovy, D. Chatenay, and F. Caron, “DNA: an extensible molecule,” *Science* **271** (1996) 792–794.
- N. Cozzarelli and J. Wang, *DNA topology and its biological effects* (CSHL Press 1990).
- F. David, in *Statistical mechanics of membranes and surfaces*, D. Nelson *et al.*, eds, (World Scientific, 1989); F. David, in *Two dimensional quantum gravity and random surfaces*, ed. D.J. Gross, T. Piran and S. Weinberg (World Scientific, 1992).
- H.-G. Döbereiner et al, “Spinodal fluctuations of budding vesicles,” *PRL* **75**, 3360 (1995); H.-G. Döbereiner and U. Seifert, “Giant vesicles at the prolate-oblate transition,” *Europhys. Lett.* **36** (1996) 325.

- H.-G. Döbereiner et al, "Mapping vesicle shapes into the phase diagram," preprint.
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- E. Evans, "Entropy-driven tension in vesicle membranes and unbinding of adherent vesicles," *Langmuir* **7** (1991) 1900.
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- B. Fain, J. Rudnick, and S. Östlund, "Conformations of linear DNA," preprint (1996).
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- M. Frank-Kamenetskii, *Unravelling DNA*.
- D. Fygenson, Ph.D. thesis, Princeton University, 1996. [Micropipette techniques.]
- Alexander Yu. Grosberg, Alexei R. Khokhlov, *Statistical physics of macromolecules*.
- Happel and Brenner, *Low-Reynolds number hydrodynamics*.
- S. Hecht, "Energy, quanta, and vision," *J. Gen. Physiol.* **25** (1942) 819.
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- W. Helfrich, "Elastic properties of lipid bilayers," *Z. Naturforsch.* **28C** (1973) 693.
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