Topics for student seminars in 33-767, SS 2019

1. Meselson-Stahl experiment to characterize DNA replication

When DNA is replicated, the two strands are opened and each one is complemented with the now missing nucleotides. Brilliant reasoning and experiments showed that this is the case – long before one had the means to really look that closely at the situation.

M. Meselson and F.W. Stahl, Proc. Natl. Acad. Sci. USA 44 (1958), 671; F.L. Holmes, Trends Biochem. Sci. 23 (1998), 117

2. Hershey-Chase experiment to identify the chemical identity of genetic material

DNA is the carrier of genetic information. The first ones to prove this were Alfred Hershey and Martha Chase, in 1952, and they used radioactive labeling and a kitchen blender to do so.

A.D. Hershey and M. Chase, J. Gen. Physiol 36 (1952), 39

3. Effects of dimensionality on diffusion

The efficiency of a diffusion process to deliver ligands to a target depends on dimensionality. There is a cross-over between 2D or 3D diffusion being more efficient as a function of system size. How does this argument impact transport on the cellular level?

G. Adam and M. Delbrück, in Structural Chemistry and Molecular Biology, Rich and Davidson, eds., Freeman, San Francisco (1968), 198

4. Physics of chemoreception

How many receptors does a cell need on its surface to efficiently sense the presence of a substance? Does most of the cell surface need to be covered? What if the cell needs receptors for 1000 different substances? Does this imply that each one can only be sensed very poorly (for lack of space for so many receptors)?

H.C. Berg and E.M. Purcell, Biophys. J. 20 (1977), 193

5. Bilayer mechanics assessed with the pipette aspiration technique

The aspiration of vesicles using micropipettes is a powerful experimental technique to quantify bilayer material constants. How is this done experimentally and theoretically? The following two papers present a classical description of the technique and a surprising more modern application.

R. Kwok and E. Evans, Biophys. J. 35 (1981), 637; E. Evans and W. Rawicz, Phys. Rev. Lett. 64 (1990), 2094

6. Helfrich repulsion between fluctuating membranes

Pushing fluctuating membranes together impedes their fluctuations and is thus an entropically unfavorable event. This leads to an amazingly strong repulsion between the membranes.

W. Helfrich and R.M. Servuss, Nuovo Cimento D 3 (1984), 137

7. Bilayer-protein hydrophobic thickness mismatch: The mattress model

How do bilayers adapt to membrane proteins with a mismatch in hydrophobic thickness? How do interactions between the mismatched proteins arise from the elastic bilayer deformations? Describe experimental evidence for this effect.

O.G. Mouritsen and M. Bloom, Biophys. J. 46 (1984), 141; T. J. McIntosh and S. Simon, Annu. Rev. Biophys. Biomol. Struct. 35 (2006), 177

8. Membrane channel characterization with the patch clamp technique

Patch clamp is an experimental approach to characterize the kinetics of ion transfer mediated across membranes by ion channels. How does the technique work, what does one learn, and what are the issues? The following paper was written by the heroes of the field:

B. Sakmann and E. Neher, Annu. Rev. Physiol. 46 (1984), 455

9. Anomalous diffusion in cell biology

Diffusive motion in biology often does not follow the usual paradigm of "distance traveled is proportional to square root of time". How are the resulting anomalies detected and what do they imply for our understanding of membranes?

M.J. Saxton and K. Jacobson, Annu Rev. Biophys. Biomol. Struct. 26 (1997), 373

10. Molecular crowding and depletion forces

Excluded-volume effects are responsible, or take part in, many biological phenomena: Specificity in ligand-receptor binding, osmosis, the behavior of macromolecules under confinement. A elucidating example of the depletion force that arises from "molecular crowding" in a cleverly chosen model system is described in

A.D. Dinsmore, D.T. Wong, P. Nelson, and A.G. Yodh, Phys. Rev. Lett. 80 (1998), 409

11. Single-molecule unfolding experiments

Individual RNA, DNA or protein molecules can be stretched using the AFM, optical or magnetic tweezers. The resulting force-distance curves offer unique insight into the structure and energetics of these molecules, which can be teased out using well-understood theoretical tools. Examples of beautiful experiments include

J. Liphardt, B. Onoa, S.B. Smith, I. Tinoco Jr., and C. Bustamante, Science 292 (2001), 733

12. Mechanosensitive channels in bilayers

Mechanosensitive channel proteins function as security valves that protect cells from rupture by sudden changes in, for example, the osmotic environment. How are such channels characterized in vitro and how do their functional properties depend on bilayer structure?

E. Perozo, A. Kloda, D.M. Cortes, and B. Martinac, Nat. Struct. Biol. 9 (2002), 696

13. The gramicidin channel

The antibiotic, gramicidin has been studied for a long time as a model system for a diffusion-dependent ion channel in membranes. What is the transport mechanism and why does the gramicidin pore show selectivity for different ions?

O.S. Andersen, R.E. Koeppe and B. Roux, IEEE Trans. Nanosci. 4 (2005), 10

14. Osmotic pressure in viral capsids

DNA in a bacteriophage capsid is confined to a space with dimensions much below the persistence length, and therefore under considerable pressure. How large is this pressure? How can it be measured? What implications does it have on DNA injection into host cells?

D.E. Smith et al., Nature 413 (2001), 748; A. Evilevitch et al., Proc. Natl. Acad. Sci. USA 100 (2003), 9292

15. Protein insertion into membranes

What are the physical aspects of protein insertion into bilayer membranes in the cell? How does Nature solve the problem of inserting a linear, water-soluble object (i.e., a freshly synthesized polypeptide) into the hydrophobic interior of a mebrane?

S.H. White, J. Gen. Physiol. 129 (2007), 363; G. von Heijne, Nat. Rev. Mol. Cell Biol. 7 (2006), 909

16. DNA-protein interactions in gene regulation

How does protein binding to DNA control gene expression? – The thermodynamics and kinetics of conformational rearrangements and the role of diffusion in reduced dimensions are described in

P.H. von Hippel, Annu. Rev. Biophys. Biomol. Struct. 36 (2007), 79

17. Molecular DNA origami

The geometric and hydrogen bonding properties of DNA may be utilized for the design of nanoscale objects of almost arbitrary shape. These result from the self-organization of DNA sequences that encode the formation of unusual structural motifs such as branching building blocks. This exciting new technology, while currently in the playing stage, may soon form the backbone of a molecular-scale nanotechnology.

P.W.K. Rothemund, Nature 440 (2006), 297; N.C. Seeman, Mol. Biotechnol. 37 (2007), 246

18. Molecule-by-molecule polymer analysis with membrane-reconstituted nanopores

Toxin channels that spontaneously insert into membranes to kill target cells can be reconstituted in bilayers where they form single nanometer-sized pores that connect two otherwise separated compartments. This is demonstrated by measuring driven ion currents between those compartments. The passage of larger polymers, such as DNA or PEG, is then detected by the blockage of the current of small ions. This has broad application potential from polymer analysis and multi-analyte detection to all-electric DNA sequencing.

J.J. Kasianowicz et al., Proc. Natl. Acad. Sci. USA 93 (1996), 13770; J.W.F. Robertson et al., Proc. Natl. Acad. Sci. USA 104 (2007), 8207; H. Bayley and P.S. Cremer, Nature 413 (2001), 226

19. Super-resolution optical microscopy – the physics and the prospects

The sensitive detection of single chromophores attached to biomolecules of interest has made it feasible to image biological structures within cells at a resolution that undercuts Abbe's diffraction limit. A contemprary review of the underlying science and engineering is given in

M.A. Thomson, M. D. Lew and W.E. Moerner, Annu. Rev. Biophys. 41 (2012), 321

20. Magnetic tweezers to study mechanical properties and coiling of DNA

Elastic properties of nucleic acid polymers can be studied through attached microbeads suspended in magnetic fields. Such magnetic "tweezers" have yielded a wealth of information on the elastic properties of (coiled) DNA and have provided critical insights into the dynamic activity of DNA-processing enzymes, as reviewed in

I. De Vlaminck and C. Dekker, Annu. Rev. Biophys. 41 (2012), 453