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Biological physics in four lectures and three applications

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Abstract

An introduction to Biological Physics is provided by three applications of Statistical Mechanics to current problems of biological interest. They are the possibility of lateral phase separation in the plasma membrane, the design of a vesicle sensitive to its environment which could be used for drug delivery, and the process of fusion of biological membranes.

Keywords: Biological physics; Phase separation; Rafts; Drug delivery; Membrane fusion

1. Introduction

Once more. Say you are in the country; in some high land of lakes. Take almost any path you please, and ten to one it carries you down in a dale, and leaves you there by a pool in the stream. There is magic in it. Let the most absent-minded of men be plunged in his deepest reveries- stand that man on his legs, set his feet a-going, and he will infallibly lead you to water, if water there be in all that region. Should you ever be athirst in the great American desert, try this experiment, if your caravan happen to be supplied with a metaphysical professor. Yes, as every one knows, meditation and water are wedded for ever.

Ch. 1, Moby Dick

Biological Physics has become an enormously diverse, and fruitful, area of study. It has provided the field of Physics with a host of difficult and intriguing problems, from the motion of individual motor proteins to the organization of entire cells, while Physics has provided, in its turn, a clarifying, quantitative, and predictive approach to these problems which has often been lacking. There is no way that I could possibly traverse the provinces of this discipline. Instead I shall try to give a flavor of this discipline from work that I have carried out in the last several years.

It is clear to any physicist who has interacted with a biologist that the world view of these two communities is quite different. I would summarize it as follows; Given a collection of objects, a physicist would ask what is common to them; a biologist would ask what distinguishes them. Each point of view has its strengths and its weaknesses. In particular, the physicist, in his desire to cut away what he believes to be unnecessary complications, has to ask himself whether he is not eliminating the very essence of the problem. This question is, of course, at the heart of a theoretical physicist's favorite pastime; model building. Again, I hope that the tension between simplicity and complexity emerges from these lectures.

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To the students who might read these notes, I will add the personal observation that working in Biological Physics provides the opportunity to interact with others in many other disciplines, some of whom think like you, and some who do not. The interactions are often maddening and frustrating, but they are equally likely to be stimulating and rewarding. I have found the ratio of the latter to the former to be large enough, and the whole enterprise brings me a great deal of pleasure.

1.1. First lecture: Introduction to the self-organization of amphiphiles

In the first lecture, I shall introduce some of the molecules with which I shall be dealing, namely, various lipids. After a brief description, I shall turn to their most interesting feature, their ability to assemble themselves into various structures. The most interesting structure, biologically, is the lipid bilayer. I will then set a seemingly simple task; to calculate the areal density of lipids in such a bilayer. This will illustrate some of the difficulties inherent in a description of these systems.

1.1.1. Lipids

Lipids consist of a hydrophilic head group and, usually, two hydrophobic hydrocarbon tails. The two are connected to a backbone, often the simple three-carbon molecule glycerol, $HOCH_2CH(OH)CH_2OH$. These, then, are called glycerolipids. So let us start with the head group. We remove one OH group from one of the carbons at the end of the chain of three in glycerol (we'll call this position 3) and one H from phosphate, H_2PO_4 and put them together, then remove the remaining H from the phosphate and an OH from some alcohol ROH to make the headgroup RPO_4 which is attached at position 3 on the backbone. (see Fig. 1.) One of the oxygens is ionized and thus is negatively charged. What molecule R is distinguishes the headgroup. Two of the most common are ethanolamine, $CH_2CH_2N^+H_3$, and choline, $CH_2CH_2N^+(CH_3)_3$ which give these lipids their names of phosphatidylethanolamine and phosphatidylcholine. I note two things. First, the head groups, with the negatively charged oxygen and the positively charged nitrogen, have a dipole which interacts with the dipoles of water. Second, the choline is significantly bigger than the ethanolamine as one has replaced each of the H attached to the nitrogen by the much larger methyl group, CH_3. The effects of this difference in architecture will appear often.

Now to the tails. We make them from fatty acids of the form $CH_3(CH_2)_xCOOH$ and attach them to the glycerol backbone at positions 1 and 2 by removing the OHs from the glycerol and the H from the acid. The chains are distinguished by their number of carbons, and whether they are saturated, as in the formula for the fatty acid I gave above, or whether they are unsaturated, that is, have any double bonds. Usually, but not

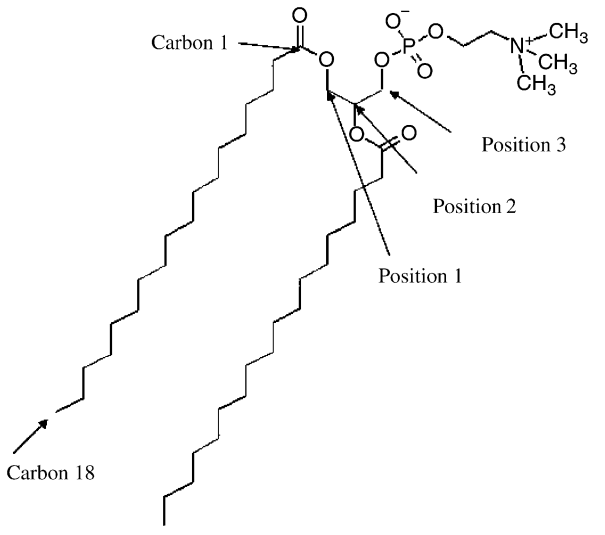

Fig. 1. A schematic of the lipid DSPC, which has two saturated tails of 18 carbons each attached to the glycerol backbone at positions 1 and 2. The phosphatidylcholine headgroup is attached at position 3.