

Evolution of Membranes from a Physics Perspective

MYER BLOOM

Abstract

Several examples are given of biological systems whose physical properties have been optimized via evolutionary processes. It is proposed that the systematic use of an "optimization of physics" hypothesis could lead to the discovery of new and unusual physical properties of biological systems. A speculative example involving membranes is presented.

Myer Bloom
CIAR Program on the Science of Soft Surfaces and Interfaces
Department of Physics and Astronomy
University of British Columbia
Vancouver, B.C., Canada V6T 1Z1
e-mail: bloom@physics.ubc.ca

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Introduction

When physical properties of biological materials are carefully studied, it is invariably found that they have been optimized, often in subtle ways. This is presumably a manifestation of evolutionary processes. I will give some well established examples of this "naive Darwinism" in regard to the optimization of *fundamental physical processes* and the *physical properties of biological materials*. Explicit and systematic use of the Optimization of Physics Hypothesis (OPH) might ultimately be helpful in finding unconventional questions leading, with insight, to new discoveries in biology

and/or physics. Of course many of these types of questions might be considered to be extremely speculative, stimulating but unlikely to be productive, and I give an example of one currently being discussed (Penrose, 1995). I will discuss various, reasonably well established, aspects of membrane fluidity in terms of the OPH including the role of cholesterol in eukaryotic cells (Bloom et al., 1991; Bloom and Mouritsen, 1995). Finally, I close with some speculations on where "really new Physics" associated with the properties of membranes might be found.

Examples of Optimization of Physics in Biological Systems

Examples from the physical properties of bacteria

Some of the most striking illustrations of the validity of the OPH are drawn from the myriad of phenomena occurring on the cellular length scale governing the function of individual prokaryotic cells. I expand a little on one of these below, *chemotaxis*, in order to illustrate the complexity involved in simultaneously optimizing several physical processes. *Magnetotaxis* is an instructive example of a different type. As described in detail elsewhere (Blakemore and Frenkel, 1981; Bloom and Mouritsen, 1995), *magnetotaxis* illustrates the optimum utilization of the material properties of a magnetic solid, *Magnetite* (Fe_3O_4), in a manner that exploits subtle aspects of magnetism.

Examples from neuroscience

Another class of phenomena, which I do not review because of lack of space, involves how the human brain collects and makes use of information associated with the sensors of our physical surroundings such as touch and other mechanical interactions (the somatic system), hearing (the ear), vision (the eye) and our manner of keeping track of motions and position of the head and body (the vestibular system) (Augustine et al., 1997).

A speculative example involving putative quantum mechanical aspects of consciousness

A stimulating example of a more speculative use of the OPH that has aroused much discussion and controversy in some circles is that some aspects of quantum mechanics and gravitational theory that are poorly understood at the present time may underlie the physical principles governing *consciousness* and how the brain works. Penrose (1995) suggests that quantum mechanical coherence on a macroscopic length scale, originating from the properties of microtubules, may underlie brain

function. Although the theoretical basis for his proposal is weak, it should be possible to subject it to an experimental test as discussed briefly at the end of this paper.

Chemotaxis: an example from the physical properties of bacteria illustrating the simultaneous optimization of several fundamental physical processes

Although not necessarily essential for survival, the capability of swimming up or down chemical gradients can provide bacteria with a significant biological advantage in obtaining food or escaping from poisons. The "apparatus" required to achieve such an advantage includes three distinct processes (Purcell, 1977; Berg and Purcell, 1977; Berg, 1988):

(i) a mechanism for swimming as fast as possible under conditions of extremely low Reynolds number (i.e. high viscous drag); this includes development of remarkable rotary motors that drive flagella of ingenious design leading to a swimming speed $v_s \approx 30\mu\text{m/s} \approx 30$ body lengths/s.

(ii) an efficient detector of the local density of specific types of molecules; Nature has discovered that 50% efficiency in detection of molecules striking the bacterial surface under diffusively governed conditions requires that only 0.1% of the surface need be covered by detectors.

(iii) a strategy for swimming up or down chemical gradients; optimum conditions for "directed random walk" up and down chemical gradients are obtained by swimming in a straight line for a time $\tau_s > D/(v_s)^2 \approx 1$ s, sufficiently long to "out-swim" the diffusion of the food molecules, which is characterized by a diffusion constant D . At the end of each swimming period, the molecular motor is reversed which, because of the peculiar structure of the flagella, leads to a type of cellular gyration that randomizes the cellular orientation before the next swimming period. The time τ_s is influenced by the measured counting rate for the detected

food molecules during a given swimming period as compared with the previous period. An increase (decrease) in the counting rate leads to a longer (shorter) period of uninterrupted swimming. This

"directed random walk" may be shown to be an extremely efficient way of swimming up or down chemical gradients.

Fluid Membranes and the OPH

Biological membranes are fluid under physiological conditions

Although I have never seen this point discussed in detail, the evolutionary driving force behind the ubiquity of membrane fluidity must surely be the important role played by integral membrane proteins in mediating the flow of matter and energy between the inside and outside of cells and organelles, and that conformational freedom is a requirement for protein function. Nature's strategy of building materials using an assembly of "bags" bounded by a fluid has resulted in many natural materials having ultra-soft mechanical properties (Bloom et al., 1991), the "engineering" of which poses problems of a different type than normally encountered by physical scientists and engineers.

Mixtures of lipids mediate the physical properties of membranes

An important control parameter for membrane fluidity is the degree of unsaturation of the fatty acyl chains comprising the lipid molecules that define the membranes; unsaturated bonds favour membrane fluidity at a given temperature and much has been written about that sort of thing in the spirit of the OPH. In a similar vein, there has been much discussion of the potential influence on physical properties of the myriad of lipid molecules found in biological membranes. My own point of view is that most of the different lipid mixtures found

in membranes are not there by accident, but have evolved in response to a need to optimize physical and chemical processes.

Cholesterol produces stronger and more impermeable plasma membranes in Eukaryotes

As an example, consider the high concentrations of cholesterol, or equivalent sterols, found in the plasma membranes of almost all eukaryotic cells, but not in prokaryotes. We believe the reason for this to be that cholesterol acts as an alloying agent with phospholipids to produce strong and relatively impermeable lipid bilayers, which is an important feature of plasma membranes of eukaryotic cells (Bloom et al., 1991; Bloom and Mouritsen, 1995).

Hydrophobic matching of lipids and proteins in membranes

Another manifestation of the validity of the OPH is the nature of the interactions between integral membrane proteins and phospholipid molecules, both of which are amphiphilic. The observed matching of the hydrophobic regions of the proteins and the lipid bilayer (in the fluid but not the gel phase!) leads to a strain-free membrane (Mouritsen and Bloom, 1993) which is desirable for efficient membrane function.

Poly-unsaturated Lipids in the Central Nervous System

As stated by Dratz and Holte (1992), see also (Brown, 1994), "retinal rod membranes have a very interesting fatty acid composition, containing 40-50% docosahexaenoic acid (22:6 ω -3), DHA. However, an understanding of the role of DHA in this and any other membrane is still in its infancy." This statement is still true even though DHA is known from nutritional studies (Crawford and Marsh, 1989) to be of crucial importance in the development of human brain function. This seems to me an example of a situation in which the OPH might lead to some new questions concerning the physics underlying cell biology. I hope that the following brief discussion of DHA from the perspective of the OPH will stimulate some such fruitful questions.

A mechanical role for DHA in the visual process

This question has implicitly been addressed by Dratz and Holte (1992) and Brown and his co-workers (Brown, 1994), who have arrived at similar conclusions in considering the possible role of DHA in stabilizing the MII (metarhodopsin II) conformation of rhodopsin in the biochemically-well-characterized cascade of molecular forms that follow the absorption of a photon in rod outer segment disk membranes. MII plays a crucial catalytic role in transducing the influence of the photon so as to close Na⁺ channels in the plasma membrane and ultimately generate an electrical signal to the brain. In particular, Michael Brown has studied carefully the influence of a variety of phospholipids of different head groups, acyl chain lengths and degrees of poly-unsaturation on the stability of MII in relation to MI (metarhodopsin I). He concludes that an important influence of DHA on the visual process is to promote mechanical conditions for MII stability in conjunction with other lipids that generate negative spontaneous curvature, i.e. H_{II} - formers. Personally, I find Brown's proposals to be plausible and sensible, i.e. it does appear that an important role of

DHA is to help stabilize the metastable MII form of rhodopsin long enough to catalyse important steps in the visual process via its coupling to the G-protein *transducin*. I suppose that one can argue that the role of DHA in the gray matter of the brain, where it is also present in large concentrations, could be to activate G-proteins there, but am not convinced that this is the whole story. There are so many disadvantages to this bizarre, difficult-to-make, easily-oxidized molecule that I believe there to be another role for DHA in the visual and central nervous systems that cannot be readily duplicated by other lipids.

Conjecture of an electrical role for DHA in vision and in the brain

In the spirit of the OPH, our group at the University of British Columbia (Miroslava Cuperlovic, Frank Linseisen, James Lloyd-Smith, and myself) has looked for loose ends in the characterization of the physics associated with the photoreception process in which DHA might be playing a crucial and as yet undiscovered role. We are in the process of examining theoretical aspects of the electrical polarizability of poly-unsaturated fatty acyl chains and, with the help of Professor Walter Hardy, we are developing a technique and instrumentation for examining the electrical response under physiological conditions of DHA-containing lipids over a frequency range from radio- (≈ 10 MHz) to microwave- (≈ 10 GHz) frequencies. Our conjecture is that DHA might be playing an as yet undiscovered signaling role in the visual and central nervous systems of mammalian systems. It must be admitted that the basis of our conjecture is somewhat tenuous; it is that, following the beautifully characterized enzymatic effects of MII (Brown, 1994), there seems to be a gap in the explicit theoretical description of the transfer, to the *rod inner segment*, of the electrical signal associated with the closing of Na⁺ channels in the plasma membrane of the *rod outer segment*. We speculate that DHA may give rise to unusual elec-

trical properties which speed up and improve the efficiency of signaling over the length of the photoreceptor cell. In making this conjecture, we have been stimulated by the enthusiasm and insights of Professor Michael Crawford, conveyed via both personal communications and his book (Crawford and Marsh, 1989). Based on the striking nutritional requirements for the essential fatty acids in the developing fetus, Professor Crawford has drawn attention to the potential role of DHA in the electrical activity required for brain function.

Finally, the instrumentation under development (see above) will allow us to check some possible experimental manifestations of the proposal by Penrose (1995) that important aspects of brain function and consciousness may require macroscopic quantum coherence to be associated with materials that comprise the brain. Though physicists and biologists have reacted to Penrose's proposal with understandable skepticism, his proposal does have the virtue of being capable of experimental verification.

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