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Book Reviews

Liposomes: From Physics to Applications by D. D. Lasic

Elsevier, Amsterdam, 1993. 580 pages. $256 cloth

Reviewed by Alec D. Bangham, The Cottages, Cambridge, England

The behavior of solvent extracted biological (membrane) lipids when placed in water has fascinated microscopists for generations. The more sophisticated their microscopes, the more intriguing the structures to be seen. Thus, with polarizing filters and first-order red compensators the field is filled with lurid colored tubes, spheres and, occasionally helices. An inquisitive viewer will poke them and marvel at their mobility and robustness. Their characteristic birefringent properties prompted investigation by x rays by those who had such equipment and who, in turn, confirmed the existence of very precise inter- and pan-molecular structure. It was, however, the realization some 30 years ago that all of these structures spontaneously arrange themselves into systems of *closed membranes later to become known as liposomes* that transformed their chemical, physical, physicochemical, biochemical, and biological significance. Biologists needed their cells and sub-cellular vesicles to be compartmentalized by a single bilayer of phospholipids but were quite unable to isolate such structures without destroying them. As it turned out, liposomes could be made simply by shaking appropriate (dry) phospholipid mixtures in excess water. Solutes present in the water became sequestered, artificial cells were made in seconds, and problems related to the *passive* properties of cell membranes could be studied. Biophysicists wanted to know how solutes crossed membranes and how membranes fused. Biochemists wanted to know whether they could reconstitute enzyme activity lost as a result of some separation procedure. Pharmaceutical chemists wanted to know whether these man-made bags could be used to deliver toxic drugs to specific sites. In less than 30 years, some 15,000 papers have been published. Chronologically, these divergent interests became recorded, first as maverick papers in subject-specific journals, then as major elements in reviews of specific fields such as membrane structure and function to be followed by multi-authored books encompassing the proceedings of an international conference or the whims associated with personal retirement.

And then suddenly, the appearance of this single-author book revealing a comprehensive and impressive understanding of the scientific, biological, and commercial aspects of the liposome. Lasic is clearly a physicist who has become enamored of biological problems in contrast to so many (perhaps too many) liposomologists who were biologists indulging in physics. His intuitive approach to the whole subject is summarized in his Preface where he states, "I strongly believe that all the complex characteristics and behaviour of liposomes can be understood by general and simple laws and that the fate (biological presumably) of liposomes in any environment depends upon their mechanical and surface properties." And later, "Most of the peculiar behaviour of liposomes as exhibited in many various observations and applications can be understood, explained and unified in a general model using elementary laws of mechanics, colloid and surface chemistry, and biology." Arrogant claims yet not entirely unjustified for the diligent reader of this book.

The book, all of 600 pages are printed and illustrated to a high standard as might be expected from Elsevier Science Publishers BV. Lasic divides his text into four major Parts, each subdivided into Chapters which, confusingly, are sequentially numbered (24) through the four Parts. Confusingly, also, the References to the Chapters are only to found at the end of a Part, some distance ahead. On the other hand, the unsolicited 15 pages of Appendices are to be applauded; somehow one feels secure when an author defines the nuts and bolts of his business.

Part I deals with the chemistry of lipids and, in particular, those uniquely disposed to form liposomes. It deals with the structure of amphiphile aggregates (phase diagrams) and the practical and pragmatic preparation of liposomes. Chapter 4 is a long overdue presentation of the mechanisms of liposome formation from a thermodynamic and topological point of view examining, for example, how solutes become entrapped, and what strains and stresses might develop in bilayers composed of molecules of different size and shape? A very interesting 45 pages. Part II covers the applications of liposomes in basic sciences. A point has been lost here in omitting to emphasize the seminal feature of liposomes, namely, their ability to compartmentalize. Had the smectic mesophases of membrane phospholipids *not* formed closed and very selectively impermeable structures, it is doubtful whether this book would have been written. This reviewer is disappointed that none of the dozen or so papers from his and other laboratories dealing with the physical effects of temperature, pressure, and presence of membrane-soluble solutes (anesthetics) on permeability, are referred to. "To a field whose most powerful model for seven decades has been a jar of olive oil, the liposome's arrival was a liberating force," claimed one leading pharmacologist. Degrees of disorder must surely be a relevant "basic" property for any model of a cell membrane having to respond to all three parameters every millisecond of its existence?

Part III deals with the fashionable and remunerative aspects of liposomes, their exploitation for drug delivery. Again, were it not for the fact that liposomes spontaneously formed perm-selective membrane systems, the whole subject would collapse. Indeed, their application might well have collapsed had it not been realized that at least two kinds of liposome were needed as delivery agents, one whose surface was immediately recognized as being "foreign" and the other being "invisible." The former, together with its load of drug, would end up assisting the extraordinarily efficient macrophage system, while the latter would circulate around the body like an erythrocyte for many days giving a particular, well vascularized lesion a chance to be dosed. It is a pity that the "invisible" ones are referred to as being "stable"; stability has already been (correctly) assigned to some of their chemical and physical attributes contributing, in turn to their shelf life, see Appendix 5.

Part IV deals with "other applications of liposomes," and Lasic prefaces it by warning readers "to be critical of the data presented, particularly if not supported by scientific experiments." This reviewer thinks this somewhat too cynical an introduction to a Chapter entitled "Cosmetic applications of liposomes." Drugs and cosmetics appeal, ultimately, to their users, and a good bedside manner hurts no-one.

It is a remarkable volume, authoritative, informative, and comprehensive, if not just a little convoluted and expansive in its English.

Biophysique Moléculaire: Structures en Mouvement by Michel Daune

InterEditions, Paris, 1993. 583 pages. 232 French francs

Reviewed by Philippe F. Devaux, Institut de Biologie Physico-Chimique, Paris, France

There are several master text books in Biochemistry, Genetics, or Cell Biology. Yet, no one up to now had dared to write a text book entitled "Molecular Biophysics." This reflects a fundamental difficulty associated with the ambiguous limits of the latter discipline. Michel Daune, professor at the University of Strasbourg, who has a long experience of teaching in the area of molecular biophysics has attempted to fill the gap in his recently published book: "Biophysique Moléculaire. Structures en mouvement." According to Michel Daune, molecular biophysics should explain quantitatively all biological phenomenon at a molecular level from the laws of physics. This definition, I think, underestimates the historical aspects of life that should be taken into account. What I mean is that a physicist of genius, in his office, cannot deduce the way living systems are today on earth, from the laws of physics only. There are many different ways life could exist that are compatible with the laws of physics. Evolution is responsible for the organization of cells for the purpose of reproduction and survival. But the same arbitrariness prevails as in the building of a car. Thus, a book on molecular biophysics that pretends to explain the phenomenon underlining living organisms has first to describe how life is actually organized at a molecular level, that is, to include the content of a text book on biochemistry, genetics, and possibly also cell biology! What sense is there to describe, for example, the interaction of ions with RNA or the folding of proteins if the reader ignores what these macromolecules do? Thus, a certain frustration can result from the reading of such a book. By contrast, a book on molecular biology gives the impression of a world of semi-logic, where molecules interact to achieve a program. In fact, most people think they understand molecular biology because they know which molecule interacts with which. The important issue seems to be the identification of the molecules: their ultimate ID is provided by their sequence! That is precisely where molecular biophysics starts. The molecular biophysicist is supposed to explain how such molecules interact. For that purpose, he must know theoretical physical chemistry as well as the principles of sophisticated physical techniques. Indeed, molecular biophysics is closely associated with the idea of instrumentation. The abstract book of the 1994 American Biophysical Society meeting in New-Orleans states that a "prominent paradigm of biophysical research involves the elucidation of the structural basis of biological function, using physical methods." This clearly indicates that the emphasis on methods is a characteristic of biophysics. Unfortunately, in most cases these methods cannot be explained in simple terms.

My long introductory remarks are meant to explain that it is in practice impossible to write a completely satisfactory book on molecular biophysics. Either it is incomplete, with arbitrary choices of topics, or it remains at a low level and does not give any insights into the techniques nor on the function of the molecules described. Michel Daune has deliberately decided to minimize the developments concerning the techniques. He has chosen to provide undergraduate students in biophysics with a book containing the indispensable knowledge of physical-chemistry associated with the several domains investigated by molecular biophysicists. Through this introductory book, he gives them the keys that will allow them to start thinking in terms of physical chemistry about the problems of molecular biology. Knowledge of this level of culture is indispensable for communication between biophysicists who, at some stage of their career, will have to switch from soluble proteins to membrane proteins, from proteins to DNA or from lipids to proteins. The chapters of this book are useful introductions to the various areas and, at the same time, it shows that the same problems are encountered in different fields. For example, the influence of intermolecular forces, the role of ions, the problem of time scale, etc. But this book may not satisfy completely the reader who looks for a specialized area of biophysics and find "his question" only partially touched upon.