# METHODS IN MOLECULAR BIOLOGY™

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# Liposomes

## Methods and Protocols
## Volume 2: Biological Membrane Models

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# Preface

Efforts to describe and model the molecular structure of biological membranes go back to the beginning of the last century. In 1917, Langmuir described membranes as a layer of lipids one molecule thick [1]. Eight years later, Gorter and Grendel concluded from their studies that "the phospholipid molecules that formed the cell membrane were arranged in two layers to form a lipid bilayer" [2]. Danielli and Robertson proposed, in 1935, a model in which the bilayer of lipids is sequestered between two monolayers of unfolded proteins [3], and the currently still accepted fluid mosaic model was proposed by Singer and Nicolson in 1972 [4].

Among those landmarks of biomembrane history, a serendipitous observation made by Alex Bangham during the early 1960s deserves undoubtedly a special place. His finding that exposure of dry phospholipids to an excess of water gives rise to lamellar structures [5] has opened versatile experimental access to studying the biophysics and biochemistry of biological phospholipid membranes.

Although during the following 4 decades biological membrane models have grown in complexity and functionality [6], liposomes are, besides supported bilayers, membrane nanodiscs, and hybrid membranes, still an indisputably important tool for membrane biophysicists and biochemists. In vol. II of this book, the reader will find detailed methods for the use of liposomes in studying a variety of biochemical and biophysical membrane phenomena concomitant with chapters describing a great palette of state-of-the-art analytical technologies.

Moreover, besides providing membrane biophysicists and biochemists with an immeasurably valuable experimental tool, Alex Bangham's discovery has triggered the launch of an entirely new subdiscipline in pharmaceutical science and technology. His observation that the lamellar structures formed by phospholipids exposed to aqueous buffers are able to sequester small molecules has lead to the development of the colloidal drug delivery concept. Following initial studies of enzyme encapsulation in liposomes as an approach towards the treatment of storage diseases [7, 8], a few years later in two New England Journal of Medicine landmark papers, Gregory Gregoriadis outlined the huge carrier potential of liposomes in biology and medicine [9, 10]. The following 2 decades saw immense efforts in academia and in soon-to-be-founded start-up companies to turn Gregoriadis' vision into clinical reality. These 20 years of intense work in liposome laboratories around the world finally culminated with the FDA (USA) approval of the first injectable liposomal drug, Doxil, in February of 1995. Today, liposomes present the prototype of all nanoscale drug delivery vectors currently under development. Lessons learned in the history of over 40 years of Liposome Technology should be heeded by new investigators in the emerging field of pharmaceutical and biomedical nanotechnology. Volume I of this book is dedicated to state-of-the-art aspects of developing liposome-based pharmaceutical nanocarriers.

All chapters were written by leading experts in their particular fields, and I am extremely grateful to them for having spent parts of their valuable time to contribute to this book. It is my hope that together we have succeeded in providing an essential source of practical

know-how for every investigator, young and seasoned ones alike, whose research area involves in one way or another phospholipids, glycolipids, and cholesterol.

Last but not least, I would like to thank John Walker, the series editor of "Methods in Molecular Biology," for having invited me to assemble this book and above all for his unlimited guidance and help throughout the whole process.

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