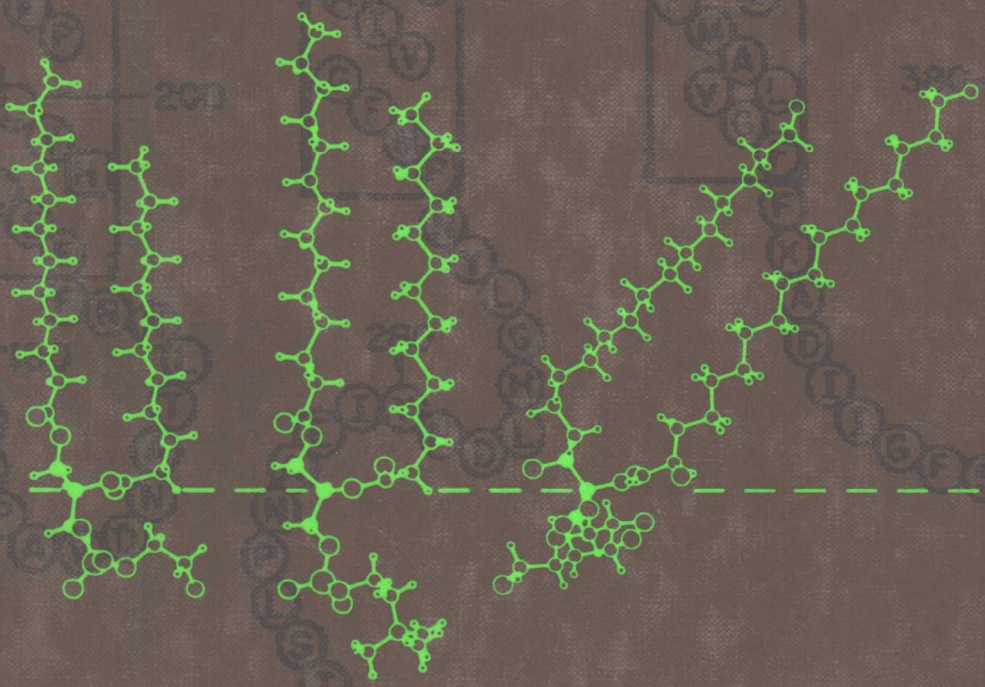
Robert B. Gennis

Biomembranes

Molecular Structure and Function



Springer-Verlag

Robert B. Gennis

Biomembranes

Molecular Structure and Function

With 142 Figures in 236 Parts

Springer-Verlag
New York Berlin Heidleberg London Paris
Tokyo Hong Kong Barcelona Budapest

Robert B. Gennis
School of Chemical Sciences
University of Illinois at Urbana-Champaign
Urbana, IL 61801, USA

Series Editor:
Charles R. Cantor
Department of Human Genetics and Development
College of Physicians and Surgeons
Columbia University
New York, NY 10032, USA

Library of Congress Cataloging-in-Publication Data
Gennis, Robert B.
Biomembranes: molecular structure and function/ Robert B. Gennis.
p. cm.—(Springer advanced texts in chemistry)
Bibliography: p.
Includes index.
ISBN 0-387-96760-5 (alk. paper)
1. Membranes (Biology) I. Title. II. Series.
QH601.G435 1989
574.87'5—dc19 88-26558

Printed on acid-free paper

Typeset by Precision Graphics, Champaign, Illinois.
Printed and bound by R.R. Donnelley & Sons, Harrisonburg, Virginia.
Printed in the United States of America.

9 8 7 6 5 4 3

ISBN 0-387-96760-5 Springer-Verlag New York Berlin Heidleberg
ISBN 3-540-96760-5 Springer-Verlag Berlin Heidelberg New York

Series Preface

New textbooks at all levels of chemistry appear with great regularity. Some fields like basic biochemistry, organic reaction mechanisms, and chemical thermodynamics are well represented by many excellent texts, and new or revised editions are published sufficiently often to keep up with progress in research. However, some areas of chemistry, especially many of those taught at the graduate level, suffer from a real lack of up-to-date textbooks. The most serious needs occur in fields that are rapidly changing. Textbooks in these subjects usually have to be written by scientists actually involved in the research which is advancing the field. It is not often easy to persuade such individuals to set time aside to help spread the knowledge they have accumulated. Our goal, in this series, is to pinpoint areas of chemistry where recent progress has outpaced what is covered in any available textbooks, and then seek out and persuade experts in these fields to produce relatively concise but instructive introductions to their fields. These should serve the needs of one semester or one quarter graduate courses in chemistry and biochemistry. In some cases, the availability of texts in active research areas should help stimulate the creation of new courses.

New York, New York — CHARLES R. CANTOR

Preface

The study of membranes has become a meeting ground for a number of diverse scientific disciplines ranging from biophysics to molecular biology. Students can enter the realm of membrane research from almost any direction, as physicists or genetic engineers or almost anything in between. To write a textbook that will be useful to such a wide audience is a challenge. There are, however, a body of knowledge and a set of guiding principles which should be comprehended by anyone who wants to appreciate the current state of research in biomembranes. I have focused on these fundamentals. My perspective is that of a biochemist and I have organized the text primarily around molecular structure and structure-function correlations. The book should be useful for graduate-level courses or for self-guided reading in the broad area of membrane structure and function, or it could be used to provide background information required for courses on special topics such as transport, receptors, signal transduction, or membrane biogenesis. The citations in the text cover through the end of 1987.

I have tried to create a text that I would have liked to have as a student first entering the field as well as one that I will find useful as an active research scientist. With these goals in mind, I have tried to bring some perspective to an awesome body of work by showing how research studies in diverse areas are related to each other and to a common conceptual framework. I have included ample documentation to make it easy for the reader to go directly to the research literature to probe more deeply into areas that can only be briefly discussed in a text of this sort. There may already be more detail given in the text to suit some readers, but I feel the density of information provided is suitable for an advanced textbook. It is always an easy matter to skip over sections in which one is not interested.

I would like to thank a number of individuals who have been helpful and encouraging during the long, seemingly endless, process of writing this book.

Many friends and colleagues were kind to read portions of the manuscript and offer encouragement and advice as well as point out errors. I would like to thank the following: Richard Anderson, Vyto Bankaitis, Lewis Cantley, Charles Cantor, Tony Crofts, John Cronan, Pieter Cullis, Tom Ebrey, Don Engelman, Gerry Feigenson, Sidney Fleischer, George Fortes, Michael Glaser, Neil Green, Lynne Guildensoph, Ari Helenius, Rick Horwitz, Wayne Hubbel, Ken Jacobson, Ron Kaback, Jim Kaput, Steve Kaufman, David Kranz, Vishnawath Lingappa, Mark McNamee, Chris Miller, Eric Oldfield, Elliot Ross, Ted Steck, and John Whitmarsh. Special thanks go to J. Keith Wright, who has been particularly helpful in efforts to improve the manuscript, to Ann Dueweke, who was a great help in collecting the copyright permissions and in putting the list of references in order, and to Karen Shannon at Precision Graphics (Champaign, Illinois) for all the figures. Thanks are also due to all those who were helpful in proofreading the final manuscript: Kathe Andrews, Rose Beci, Visala Chepuri, Tom Dueweke, Hong Fang, John Hill, Tamma Kaysser, Kiyoshi Kita, Laura Lemieux, Gail Newton, Kris Oden, Petr Pejsa, Jim Shapleigh, Steve Van Doren, Cecile Vibat, Melissa White, and Chris Yun.

Finally, my deep gratitude goes to the excellent secretarial service provided within the physical chemistry office at the University of Illinois by Evelyn Carlier, Jan Williams, Karen McTague, and Betty Brillhart.

Urbana, Illinois ROBERT B. GENNIS

Contents

Chapter 1
Introduction: The Structure and Composition of Biomembranes

1.1 The Importance and Diversity of Membranes

Membranes play a central role in both the structure and function of all cells, prokaryotic and eukaryotic, plant and animal. Membranes basically define compartments, each membrane associated with an inside and an outside. If this were all they did, membranes would be considerably less interesting than they are. But, membranes not only define compartments, they also determine the nature of all communication between the inside and outside. This may take the form of actual passage of ions or molecules between the two compartments (in and out) or may be in the form of information, transmitted through conformational changes induced in membrane components. In addition, attached to membranes are many cellular enzymes. Some of these enzymes catalyze transmembrane reactions, involving reactants on both sides of the membrane or molecular transport. Others are involved in sequential reactions involving a series of enzymes which are concentrated in the plane of the membrane, thus facilitating efficient interactions. Still other enzymes have membrane-bound substrates and/or are involved in the maintenance or biosynthesis of the membrane. Most of the fundamental biochemical functions in cells involve membranes at some point, including such diverse processes as prokaryotic DNA replication (e.g., refs. 807, 777, 803), protein biosynthesis, protein secretion, bioenergetics, and hormonal responses.

Electron micrographs of mammalian cells reveal the wealth of membranous organelles which comprise a large part of the intracellular volume. It is now clear that the structural principles for all these membranes are basically the same. Furthermore, these structural similarities apply also to plant cell membranes and bacterial membranes. These common features, recognized by Robertson in the late 1950s (1231), allow us to apply lessons learned in one membrane system, such as the erythrocyte membrane, to other systems, tempered with a reasonable

degree of caution. This caution is necessary because, paradoxically, one of the most salient points to be made about membranes is their remarkable diversity. This diversity is due primarily to the different functions of the proteins present in each membrane and to the way in which these proteins interact with each other as well as with cytoplasmic components. These interactions result in distinct morphologies, such as in the microvilli of the intestinal epithelium or the tubular endoplasmic reticulum, and may result in lateral inhomogeneities within a given membrane (see Section 4.5). The main point is that there is a common ground for studying membranes in general, but that an appreciation for the subject lies in large measure in the comprehension of the molecular and biological basis for the diversity in membrane structure and function.

Progress in the study of membranes has come from exploiting the advantages for studying the membranes from a variety of organisms. Bacteria have relatively simple envelopes containing one or two membranes, which can be manipulated genetically or by altering the growth conditions. Enveloped viruses enter animal cells by membrane fusion (Section 9.52) and exit by budding (Section 4.53). The maturation of viral proteins provides an excellent experimental system for studying membrane protein biosynthesis (Section 10.2).

Eukaryotic cells have numerous membranous organelles, and each membrane is unique in composition, structural detail, and function. In order to understand the motivation behind many of the studies described in later chapters it is important to have some background in the biological functions of these various membrane systems. Figure 1.1 shows a schematic indicating the various membranes as they appear in a generic animal and plant cell. Note that the appearance of the organelles will be different in other cell types, and, in addition, some cells, such as the rod cell of the retina or the skeletal muscle cell, have highly specialized membranes which have unique functions.

(1) *Plasma membrane*: The plasma membrane defines the boundaries of the cell and is the point of contact between the cell and its environment. As such, the plasma membrane contains specialized components involved in intercellular contacts and communication, hormonal response, and transport of both small and large molecules into and out of the cell. However, the plasma membrane is itself divided into specialized regions in those cells which are simultaneously in contact with different environments. Figure 1.2 shows the location of the *apical* and *basolateral* plasma membrane domains for a hepatocyte and for a polarized epithelial cell. The apical membrane is that which is in contact with the "external" environment, such as the bile canaliculus in the case of the liver cell or the gastrointestinal lumen for an epithelial cell in the gut. The apical membrane can contain specialized structures such as the *microvilli*, which can be organized to form the *brush border membranes* in some absorptive cells. Microvilli greatly increase the effective surface area of the membrane and facilitate efficient transport. The basolateral membrane is that which is in contact with other cells (lateral or contiguous membrane) or blood sinusoids (sinusoidal membrane). In the hepatocyte, the lateral and sinusoidal membranes are morphologically and biochemically separable (402).

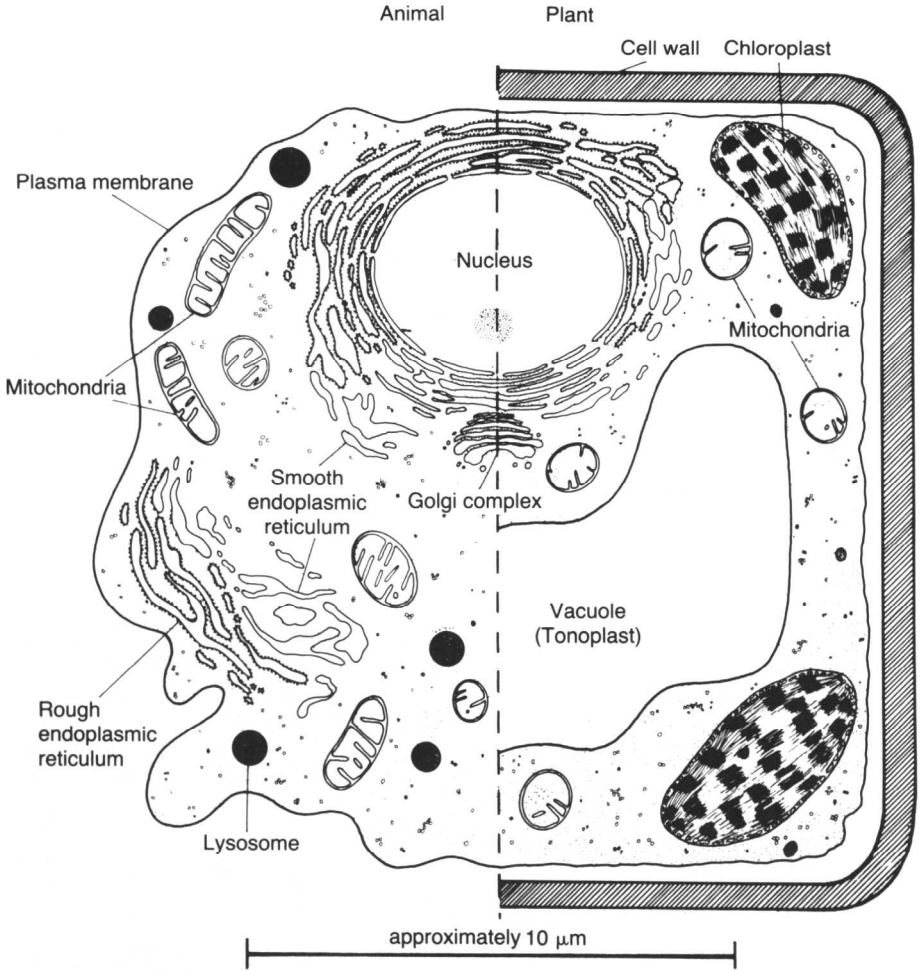


Figure 1.1. Schematic showing organelles of eukaryotic animal and plant cells as revealed by electron microscopy. Adapted from ref. 425a.

The basolateral membrane in the hepatocyte contains several specialized structures for cell–cell adhesion and intercellular transport.

Tight junctions seal the contacts between cells to prevent mixing the contents of the bile and blood vessels.

Gap junctions contain a regular array of pores that allow small molecules to pass through the plasma membranes of two adjacent cells. Electron microscopic and biochemical studies have revealed some molecular detail of these pores, showing each to contain a hexagonal array of protein subunits (see Section 8.21).

Desmosomes also function as adhesion sites between cells and are involved in

contacts between the plasma membrane and cytoskeletal elements (see Section 4.3).

The apical, lateral, and sinusoidal portions of the plasma membranes are morphologically distinct and have unique compositions and functions. If the cells are disrupted gently, these specialized regions of the plasma membrane can be physically separated and purified (402). It is not understood on a molecular level how these specialized domains of the plasma membrane are maintained in the cell, but, clearly, there cannot be free diffusion of all membrane components between them (see Section 4.51).

(2) *Nuclear membrane*: The nuclear envelope which is present in interphase cells appears in electron micrographs as a double membrane, with a narrow space in between called the perinuclear space (459). The nuclear envelope appears to be formed from portions of the endoplasmic reticulum (see below) and these two systems may, in fact, be physically continuous. The most prominent morphologi-

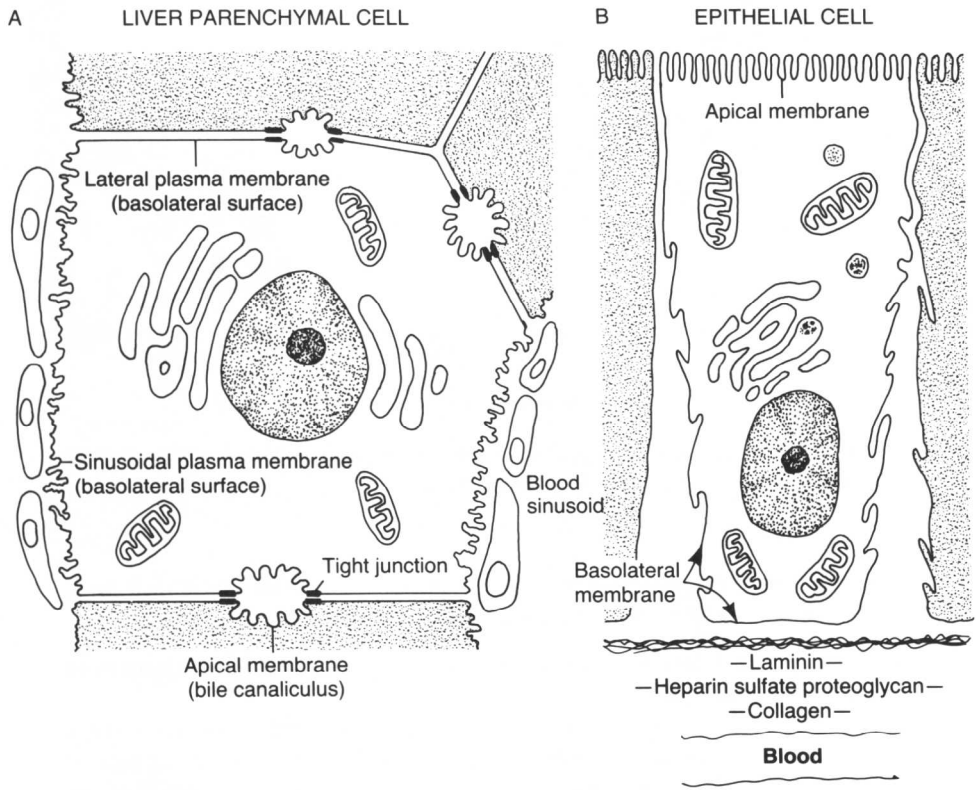


Figure 1.2. Schematic showing the plasma membrane domains of (A) a hepatocyte, and (B) a polarized epithelial cell.