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PROGRESS IN PROTEIN–LIPID INTERACTIONS

Progress in Protein–Lipid Interactions

A. Watts and J.J.H.H.M. De Pont
Editors

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VOLUME 1

An international review series designed to critically
evaluate actively developing areas of research in protein-lipid interactions

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Preface

'Protein-lipid Interactions' has been initiated with the aim of allowing authors to present not a comprehensive review but a highly critical assessment of specific aspects of research into protein-lipid interactions in membranes. Active specialists have been asked to *freely* reappraise past work in the light of our present understanding, give new, possibly unpublished data, and then identify those areas which they believe show greatest potential for our future understanding of membrane biology.

The series will be aimed at established workers wishing to gain a fresh insight into their own interest in the field of protein-lipid interactions, or new researchers wanting to learn about other active areas of the topic. The editors have made an attempt to maintain a balance between the physical and biochemical approaches to the study of protein-lipid interactions.

In this first volume, one view of the many available theories used to describe protein-lipid interactions has been presented by Jim Abney and Jack Owicki. Magnetic resonance methods, probably still the most controversial, yet direct, approach to describing the dynamic interactions between proteins and lipids, are described by Myer Bloom and Ian Smith for deuterium nuclear magnetic resonance and Derek Marsh for spin-label electron spin resonance. Ben de Kruijff and his colleagues describe the way in which phosphorus nuclear magnetic resonance can identify lipid polymorphism in membranes and also monitor the modulation of these effects by proteins.

Bob Clegg and Winchil Vaz have described fluorescent methods, backed by some theoretical treatment, used to determine the relative movements of lipids and proteins in membranes. David Schachter has given his view of the function of intestinal plasma membranes in relation to lipid fluidity. Roberto Bisson and Cesare Montecucco conclude the first volume with a survey of the use of photoreactive phospholipids to study lipid-protein interactions. Although most work so far has approached protein-lipid interactions from the lipid viewpoint, as reflected in the composition of this volume, some attempt has been made to balance function and structure which loosely implies biochemical and biophysical studies. We hope to reach a broad readership and promote interdisciplinary discourse on this fascinating topic.

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Watts/De Pont (Eds.)
Progress in Protein-Lipid Interactions

CHAPTER 1

Theories of protein-lipid and protein-protein interactions in membranes

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I. Introduction

About 15 years ago it became apparent to a number of biochemists and biophysicists that biological membranes and model membranes behave in many ways like two-dimensional fluids. It also became apparent that a substantial fraction of membrane-associated proteins are integrally embedded in the bilayer membrane, and that some completely traverse it. These realizations were synthesized into the fluid-mosaic model of biological membranes (Singer and Nicolson, 1972), a paradigm that holds sway today with some modifications. One such modification, for example, is to include the immobilizing effects of cytoskeletal interactions.

The intervening years have brought substantial increases in our knowledge about membranes, due in large part to the application of new or refined experimental methods. There have been concomitant efforts on the part of theorists to construct detailed molecular or thermodynamic models that integrate and interpret the experimental work. The largest number of theoretical papers have dealt with pure lipid bilayers, especially the lipid bilayer phase transition. These have been reviewed well elsewhere (e.g., Nagle, 1980), and we do not consider them here except as they relate to our main topics: theoretical models of protein-lipid and protein-protein interactions in membranes.

Abbrevations: DMPC, dimyristoylphosphatidylcholine; DMR, deuterium magnetic resonance; DPPC, dipalmitoylphosphatidylcholine; DSC, differential scanning calorimetry; EPR, electron paramagnetic resonance; SPT, scaled particle theory; T_c, temperature of lipid bilayer phase transition.

We have focused on the influences that intrinsic membrane proteins have on membrane lipids, the effects of the lipids on the proteins, and the phase behavior and lateral distribution of both components. Unfortunately, spatial constraints have required the omission of a number of major topics. We do not discuss the mechanisms of lateral diffusion or the relationship of the diffusion coefficient to molecular geometry and environment. Nor do we discuss the behavior of cholesterol in membranes, in spite of the fact that cholesterol is much like a very small intrinsic membrane protein and has been the subject of a large amount of research.

We have concentrated on the most detailed statistical-mechanical and thermodynamic treatments. Our goal has been to give a reasonably comprehensive picture of the insights that theory has provided into a number of important membrane phenomena. We have also tried, in the spirit of this series, to assess deficiencies in the theoretical treatments and to recommend areas where more theoretical work seems most needed.

Finally, it is worth stating our opinion of the rôle of theory in this field. Clearly, predictive power and agreement with prior experiments are important for any scientific theory. Nevertheless, biological membranes – and even model membranes – are so complicated that any tractable theory must become only a caricature of the real system. If the caricature leads to recognizable consequences, then we hope that its few remaining features are indeed the most important ones for explaining the observations. Given the rampant approximations, conclusions must be rather tentative. It is then useful to examine several differing treatments of a phenomenon, to see whether some consensus emerges.

II. Effects of proteins on membrane lipids

1. SUMMARY OF EXPERIMENTAL RESULTS

A substantial body of experiments, beginning with the electron paramagnetic resonance (EPR) results of Jost et al. (1973), has shown that intrinsic membrane proteins alter the properties of nearby phospholipids in the membrane. We will take the liberty of summarizing these findings below without detailed attribution, directing the interested reader to review articles for further information (Chapman et al., 1979; Jost and Griffith, 1980; Marsh and Watts, 1982; Seelig et al., 1982; Silvius, 1982; Marsh, 1983).

Magnetic-resonance experiments have shown remarkably similar results for different proteins. Typically, EPR experiments on spin-labeled lipids show distinguishable signals from bulk lipid and lipid associated with the protein as discussed in Chapter 4 of this Volume. The latter, usually called boundary lipid or annular lipid, shows little motional averaging on the EPR time scale (ca. 10–100 ns). In