An Alternative Model For Molecular Organization in Biological Membranes

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Numerous models have been proposed for the molecular organization of lipids and proteins within biological membranes. Each model has its own merits and is consistent with at least some of the evidence derived from one or more membrane species, but no general structure applicable to all membranes is yet available. In fact such a structure may not exist. It is possible, however, that there are specific associations between lipid and protein molecules which do contribute to the structure of most biological membranes.

Several reviews of membrane organization at the molecular level have recently been published. It is not within the scope of the present article to further weigh the evidence for various proposed structures. It is intended, rather, to suggest an alternative model for lipid-protein associations in membranes, which to the author’s knowledge has not been previously emphasized. The model is consistent with several lines of evidence which in past studies have been used to support a variety of apparently contradictory hypothetical structures. It also suggests several definitive experimental tests.

Since the model is specifically derived for lipid-protein complexes within membranes, it would be useful to briefly outline structural features of current models of this interaction.

Protein-Lipid-Protein Membrane Models

Protein-lipid-protein (PLP) models are represented by the familiar structures proposed by Davson and Danielli and Robertson in which a bimolecular layer of lipid is sandwiched between two layers of protein (Fig. 1). The hydrocarbon tails of the lipid are directed inward, and in modern variations a certain amount of the protein may extend into or through the interior lipid phase. The major forces by which lipid and protein associate in PLP structures would be electrostatic in nature, involving interaction between phospholipid head groups and charged protein groups.

Lipid-Protein-Lipid Membrane Models

A great deal of interest has recently been focused on measurements of optical parameters in membrane protein. Optical rotatory dispersion (ORD), circular dichroism (CD) and infrared spectra have provided evidence that the major portion of membrane protein is α helical. Certain anomalies in the spectra from various membranes were also found. For instance, ORD and CD spectra tended to be red shifted and were of remarkably low amplitude. These results led several groups to suggest that at least the α helical portion of membrane protein was in a nonpolar environment such as would
be provided by lipid hydrocarbon chains. Thus, in the lipid-protein-lipid (LPL) model it is envisaged that lipid is still present in two layers but that membrane protein is arranged as a hydrophobically bound core between the lipid layers (Fig. 2) with the lipid chains directed into or around the bound protein. The major forces between lipid and protein in LPL structures would be London–van der Waals dispersion forces and hydrophobic interactions. Major contributions of hydrophobic interactions to membrane stabilization have also been proposed by previous investigators on the basis of other lines of evidence.

Particulate Membrane Models

A third membrane model is the concept of particulate or sub-unit membranes. This concept does not place the lipid in layers but rather considers that membranes are composed of lipoprotein sub-units which may be dispersed and reconstituted into membranes by specific techniques. In a sense, the particulate model is a variation of the LPL concept, since much of the protein is considered to be in the interior of the membrane with hydrophobic interactions stabilizing the structure.

An Alternative Model For Lipid-Protein Associations

A major difficulty in the PLP concept arises when forces binding proteins to the lipid bilayers are considered. As noted previously, the obvious forces would be electrostatic in nature. However, many membrane proteins do not behave as though this were a simple charge interaction. A major portion of the protein is in fact strongly bound to the membrane and can be readily solubilized only by rather drastic measures such as use of detergents.

Strong lipid-protein interactions are provided by LPL membrane models in which protein is bound hydrophobically to the interior structure of the membrane, but it is difficult to imagine how the α helices of a large protein molecule might be distributed among the hydrocarbon chains of lipid