Lipid Composition, Permeability and Structure of Biological Membranes

By L. L. M. VAN DEENEN (*Department of Biochemistry, University of Utrecht, Utrecht, The Netherlands*)

Detailed structural analyses of membranes in combination with chemical syntheses of individual molecular species of phospholipids stimulated investigations on the barrier properties of membrane model systems. The permeability of liposomes has been demonstrated to depend on: (a) the nature and charge of the polar head groups of phospholipids; (b) the chain length, and number, position and geometry of unsaturation of the fatty acid constituents of phospholipids; (c) the phospholipid/sterol ratio, and chemical structure and configuration of the sterol. Induction of variations in the lipid composition of bacterial and animal cells demonstrated that these lipid parameters contribute to the permeability behaviour of natural membranes in a way similar to that observed in artificial lipid membranes. Cells appear to be equipped with enzymes that control the chemical make-up of membrane lipids to maintain the physical properties between certain limits and to compensate for environmental factors.

The lipid composition of membranes may not only govern simple diffusion processes but also determine the rate of carrier-mediated transport. Experiments on liposomes showed that valinomycin is highly active in promoting K^+ leakage from liposomes of phosphatidylglycerol, but its action is immobilized nearly completely in liposomes of lysylphosphatidylglycerol, a positively charged phospholipid of bacterial origin. In agreement with these observations it was found that the rate of valinomycin-facilitated transport across the membrane of *Staphylococcus aureus* was related to the ratio of phosphatidylglycerol to lysylphosphatidylglycerol. The action of valinomycin is dependent on the nature of the fatty acid constituents of phospholipids and on the phospholipid/sterol ratio. A qualitative extrapolation of these results to natural interfaces appears to be warranted, leading to the proposal that the efficiency of a carrier is related to the lipid composition of its membrane locus.

Phospholipase A_2 (from porcine pancreas and of known primary structure) and pure phospholipase C (from *Bacillus cereus*) have been used as models for lipid-protein interactions and as tools for membrane topography. Comparison of the action of these enzymes on defined lipids and on isolated and native membranes revealed significant differences among the molecular architectures of the various structures. Whereas both enzymes hydrolysed the phosphoglycerides in erythrocyte 'ghosts', pure phospholipase A_2 and phospholipase C could not attack these constituents of intact erythrocyte membranes.

Recombination of proteins and lipids from erythrocyte membranes demonstrated that both electrostatic and hydrophobic associations (in this sequence) are involved in the formation of structures that show electron-microscopic images similar to those of the erythrocyte membrane.

The results of the various approaches are interpreted in terms of a non-uniform molecular alignment of lipids and proteins within one membrane, although a significant but varying contribution of lipid bilayers explains adequately a number of barrier properties of several biomembranes.

Inositol Lipid Metabolism and the Cell Membrane

By J. N. HAWTHORNE (*Department of Chemistry, University of Calgary, Calgary, Alberta, Canada*)

Phosphatidylinositol is widely distributed in the animal and plant kingdoms, and is a constituent of most subcellular membranes. The phosphorylated derivatives diphosphoinositide and triphosphoinositide have a more limited distribution, and are associated particularly with a number of plasma-membrane structures. Their monoesterified phosphate groups have a considerable affinity for bivalent cations, particularly Ca^{2+} (Hendrickson & Fullington, 1965; Hawthorne & Kai, 1970).

The strongly bound Ca^{2+} of the erythrocyte membrane is attached to diphosphoinositide and triphosphoinositide. The Ca^{2+} content of the membrane depends on the concentration of these lipids, which are formed from phosphatidylinositol by phosphorylation with ATP. It is possible that the permeability of the membrane is affected by the polyphosphoinositide content, and therefore the Ca^{2+} content. Charalampous (1971) has shown that inositol-deficient mammalian cells in tissue culture are unable to concentrate K^+ to the same extent as normal cells, and this could be a related phenomenon.

The polyphosphoinositides of brain are chiefly found in myelin, another plasma-membrane structure, though they are metabolically inactive in this location. A small and very active pool may be associated with the neuronal plasma membrane and axolemma. Diphosphoinositide synthesis is most active in the outer membrane of nerve-ending particles (Harwood & Hawthorne, 1969), and the incorporation of phosphate into triphosphoinositide is much more rapid in nerve trunks than in sympathetic ganglia (Yagihara *et al.*, 1969). This active metabolism may be associated with permeability changes accompanying the action potential and again dependent on Ca^{2+} binding (Hawthorne & Kai, 1970).