Structure of the Plasma Membrane

An Electron-Microscope Study

By WALTER STOECKENIUS, M.D.

Electron micrographs of the cell membrane is compatible with the assumption that it consists of a bimolecular leaflet of lipid coated on both sides with protein.

Thin sections of fixed and embedded tissue from plants and animals show, in the electron microscope, a thin dense layer on the surface of the protoplasm which in all probability corresponds to the plasma membrane postulated by the physiologists. In many instances it can be seen to be a triple-layered structure, consisting of two outer dense layers and a central lighter layer, each approximately 25 Å wide (fig. 1). It has been termed the unit membrane. The resolution obtainable in such micrographs is of the same magnitude as the size of smaller organic molecules, but for an interpretation of the observed contrast distribution in terms of the molecular arrangement in the membrane, additional information is needed.

The preceding papers of this symposium have shown that the main constituents of the plasma membrane are polar lipids and protein and that the lipids are probably present in the form of a bimolecular leaflet. Such leaflets form spontaneously when lipid extracts from tissues are brought into contact with water. They can be prepared for electron microscopy by the same techniques as those used for whole tissues, e.g., fixation with OsO₄, dehydration in acetone, embedding in methacrylate, and sectioning. X-ray diffraction diagrams, taken after every step of this procedure, show that the basic lamellar structure of the lipid is preserved by this technique. In such preparations one bimolecular leaflet appears in the electron micrographs as a triple-layered structure similar to but not identical with the image of the plasma membrane. It consists of two outer dense bands approximately 8 Å wide and a central light layer of approximately 25 Å (fig. 2). This appearance can be shown to be due to an accumulation of osmium around the hydro-

Figure 1

Electron micrograph of a section through a rabbit erythrocyte. Fixed with OsO₄. Contrast was increased by “staining” the section with lead hydroxide. The triple-layered structure of the membrane is clearly visible. In this case the two outer dense lines are narrower than those found in the unit membranes of most other cell types. (1620/60; × 280,000.)

Figure 2

Electron micrograph of a highly swollen phospholipid preparation after OsO₄-fixation and sectioning. The bimolecular leaflets are separated by large spaces originally containing water. (910/59; × 280,000.)
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Figure 3
Scheme of the molecular structure and osmium distribution of the bimolecular leaflets shown in figure 2. The empty circles represent the hydrophilic groups of the phospholipid molecules, the black dots the osmium deposited in the structure.

Figure 4
Electron micrograph of bimolecular leaflets of phospholipid coated on both surfaces with protein. Fixed with OsO₄. The contrast has been enhanced by staining the section with lead hydroxide. The triple-layered structure is only visible where the plane of the lipid leaflets is oriented approximately normal to the plane of the section. (× 280,000.)

Figure 5
Scheme of the molecular arrangement in the structure shown in figure 4. The protein molecules are represented by the zigzag lines.
philic groups of the lipid molecules on the surface of the leaflet (fig. 3).

The main difference in appearance between the bimolecular leaflet of lipid and the cell membrane is the lesser density and width of the outer layers in the case of the lipid leaflet. If an appropriate protein, e.g., globin, is added to the solution in which the lipid leaflets form, this protein is adsorbed onto the surface of the lipid layers and increases the density and the width of the outer dark bands seen in the electron micrographs to 25 Å or more depending on the amount of protein present (figs. 4 and 5). Therefore, in such preparations, structures are found which are known to consist of one bimolecular layer of lipid with a layer of protein on both surfaces and which are identical in appearance to the image of the plasma membrane obtained by the same techniques. It follows that the structure of the plasma membrane as observed in high resolution electron micrographs is consistent with the molecular arrangement rendered in the Davson-Danielli model.

The observations and considerations that led Davson and Danielli to propose this model are largely independent of the morphological findings presented here. Moreover, Finean,5 using still another approach, arrives at the same conclusion. The evidence that the Davson-Danielli model correctly represents the molecular architecture of the plasma mem-

brane is therefore very strong. But this model only describes the general features of the membrane. Considerable refinement will be necessary before active transport and other phenomena can be linked to the molecular organization. There is some indication from recent electron-microscopical work that the material constituting the inner surface of the membrane is different from that on the outer surface and that specific enzymes may be bound to one surface. Although much more information is needed, it seems evident that the electron microscope is a promising tool in membrane research.

References