**Robertson J D.** The ultrastructure of cell membranes and their derivatives. *Biochem. Soc. Symp.* **16**:3-43, 1959.
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**Electron microscopic (EM) observations on many biological membranes as seen in thin sections were reviewed and interpreted in molecular terms based on an analysis of nerve myelin. A general model of membrane molecular architecture was presented emphasizing the ubiquity of the lipid bilayer and chemical asymmetry. [The *SCI*® indicates that this paper has been cited over 455 times since 1961.]**

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"This paper reviewed a number of observations that I had made during the mid-1950s regarding the molecular architecture of biological membranes. That decade began with many doubts about the exact role of the lipid bilayer in the molecular architecture of biological membranes, but it ended with a note of certainty expressed in this paper. Earlier work had suggested a crucial role for lipid bilayers in membrane structure. There was, however, doubt about how many were present, the manner in which proteins were associated with the lipids, and indeed whether or not any particular model could be applied generally. There were also doubts about whether or not there might be mosaic patches of pure protein contiguous with lipid regions. The EM studies reviewed dispelled the doubts about membrane thickness and led to the certainty that biological membranes contained one, and only one, lipid bilayer and further that a useful general model of membrane molecular architecture could be proposed.

"About 1956 I applied two new developments in EM technique, permanganate fixation and epoxy embedding, and observed a triple-layered pattern in all cell membranes and membrane organelles studied. The membrane measured ~ 7.5 nm in thickness and appeared as a pair of dense strata each ~ 2 nm thick bordering a light central zone. The work provided the first direct evidence that nerve myelin consisted only of Schwann cell membranes to the resolution of the sections (~ 2 nm). Partly on the basis of these observations I stated that the basic pattern resulted from the presence of one lipid bilayer as the fundamental core structure. A general model was proposed consisting of a lipid bilayer with protein at or in its polar surfaces in the dense strata. The idea of asymmetry due to polysaccharides in the outer surface was also advanced. This paradigm, called the unit membrane model, was the first one to make explicit the principle that biological membranes in general have *one* lipid bilayer as their basic structure. It resembled the earlier Danielli-Davson one but differed significantly in that only one bilayer was stipulated along with chemical asymmetry.

"At the time, these ideas met with considerable resistance partly because permanganate was a poor general fixative, but it is good and selective for membranes and revealed them in the manner that is now regarded as standard. Somehow the idea arose that I claimed all cell membranes were molecularly identical, a complete misinterpretation. Perhaps in my enthusiastic pursuit of getting across the idea that there was a *common molecular architecture* in membranes which could be defined, I gave the impression I was saying that all membranes were molecularly identical. Perhaps the problem here was that I was thinking in terms of molecules while others were not.

"The hydrophobic core of the bilayer is now known to be sometimes traversed by hydrophobic polypeptide chains. The model has been modified to take this into account but the main point was the establishment of the ubiquity of the bilayer, which I believe is now generally accepted. I have recently published work in this field."[1,2]

1. **Robertson J D.** The anatomy of biological interfaces. (Andreoli T E, Hoffman J F & Fanestil D D, eds.) *Physiology of membrane disorders.* New York: Plenum, 1978. p. 1-26.
2. ----------. The nature and limitations of electron microscopic methods in biology. (Andreoli T E, Hoffman J F & Fanestil D D, eds.) *Physiology of membrane disorders.* New York: Plenum, 1978. p. 61-93.