

This Week's Citation Classic

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Vandenheuvel F A. Study of biological structure at the molecular level with stereomodel projections. I. The lipids in the myelin sheath of nerve. *J. Amer. Oil Chem.Soc* 40:455-71, 1963. [Animal Research Institute, Canada Department of Agriculture, Ottawa, Ontario, Canada]

Data on myelin obtained from analytical, X-ray, and other studies have been integrated by using exact molecular parameters and force calculations. A plausible tri-dimension arrangement of molecules in the lipid bilayer of myelin was obtained. [The SC[®] indicates that this paper has been cited over 200 times since 1963.]

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"Late in 1961, I came across an article proposing an arrangement of lipid chains in membranes. The figure describing this arrangement was undoubtedly the most detailed thus far published on the subject. However, molecular parameters and spacings were inaccurate to the point that the lipid density estimated from this drawing was 3 times that expected! The thought occurred to me that while a more realistic model could undoubtedly be produced, such a model would be more interesting, and probably more useful, if it were based on data for a specific membrane system, such as myelin. Thus the above paper, soon to be followed by a study of the whole myelin membrane,¹ came into being.

"This work met with immediate acceptance in part, I believe, because the DNA model of Watson and Crick had convinced many scientists that accurate molecular models are important research tools in biology where structure and function are indissolubly linked. Indeed, this paper showed how properties of myelin could be predicted from a realistic

tri-dimensional model of this structure. As in the case of DNA, the basic data were of diverse disciplinary origin, and the methods used for their integration relied on exact molecular parameters and properties. No doubt the myelin paper gave a further boost, not only to the use of molecular models, but also to the multidisciplinary team approach to membrane research.

"The myelin paper displays several models of lipid molecules which later were used by others, either to represent lipid components of biological structures, in some cases other than membranes, or to back up various arguments and theories. Hence, these models have been reproduced in many papers, review articles, and books. Another feature of the myelin paper to which reference is often made is a detailed discussion of inter- and intramolecular forces as they specifically apply to membrane components. It is probable that the paper is still used as a reliable reference because none of several increasingly sophisticated X-ray investigations made over the last 15 years has seriously challenged its conclusions regarding the structure of myelin.

"It is evident that this paper involved considerable graphical work of a painstaking, very precise nature. Less obvious is the time and effort required by countless trial and error molecular force estimations made without the benefit of a computer. With the deadline imposed by the symposium at which the paper was to be delivered, the work had all the ingredients of a grueling task. Perhaps it was. All I can remember, however, is a feeling of elation, as, one by one, the pieces of the puzzle fell into place."

1. Vandenheuvel F A. Structural studies of biological membranes: the structure of myelin. *Ann. NY Acad. Sci.* 122:57-76, 1965.