Structure of Biological Membranes

Edited by

Sixten Abrahamsson and Irmin Pascher
University of Göteborg
Göteborg, Sweden

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Structure of Biological Membranes

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IN MEMORIAM

Dr. Hermann Träuble died on July 3, 1976 shortly after the Symposium. This is a great loss to his colleagues and to Science.

Preface

Since 1965 the Nobel Foundation sponsors, through grants from the Bank of Sweden Tercentenary Fund, Symposia on subjects which are considered to be of central scientific importance and for which new results of a special interest have been reached. The aim of these Symposia is to bring together, by personal invitation, a limited number of leading scientists from various countries to discuss the current research situation within the field and to define the most urgent problems to be solved.

One of the most important fields in modern biomedical research concerns the structure and function of biological membranes. Research on this subject is very active and important scientific contributions appear at an increasing rate. It was therefore considered highly appropriate to devote Nobel Symposium 34 to the structure of membranes in order to get an expert summary of what is now known in the field.

The Symposium was held at Hotel Billingehus in Skövde (about 150 km from Göteborg), Sweden, from June 7 to 11, 1976. In addition to the grant from the Nobel Foundation financial support was received from the Nobel Institute of Chemistry of the Royal Academy of Sciences and from the Science Fund of Wilhelm and Martina Lundgren.

The Symposium was attended by some 50 scientists. The papers in this Volume had been distributed in advance to all participants. Therefore only summary presentations needed be given at the Symposium and the main emphasis was put on discussions.

The Organizing Committee for the Symposium was composed of S. Abrahamsson (chairman), K. Larsson, I. Pascher (secretary) and H. Virgin with an Advisory

Bord consisting of A. Engström, L. Ernster and G. Lundgren.

A special effort for rapid publication has been made by the contributors and publisher which is greatly appreciated.

S. Abrahamsson

I. Pascher

Contents

Lecturer

MOLECULAR ARRANGEMENT AND CONFORMATION OF LIPIDS OF RELEVANCE TO MEMBRANE STRUCTURE

Sixten Abrahamsson, Birgitta Dahlén, Håkan Löfgren, Irmin Pascher & Staffan Sundell

Dept. of Structural Chemistry, Faculty of Medicine, University of Göteborg, P. O. B., S-400 33 Göteborg 33, Sweden

INTRODUCTION

Intact membranes as well as membrane components have been studied extensively by various physical and chemical methods. Important data have accummulated but more specific structural information on the atomic level is still necessary in order to obtain a detailed understanding of lipid-lipid and lipid-protein interactions and of variations in structure and composition of lipids observed in different types of membranes. Only then will it be possible to explain the function of the different constituents and their significance for various membrane properties.

X-ray diffraction methods provide detailed structural information but require access to single crystals of pure and homogenious compounds. Studies of intact biological systems such as the membranes on the other hand will only give the overall molecular arrangement. The solid state is, of course, static in comparison with biological systems but it is known from many fields that structural features in crystals often reflect conditions in less ordered systems.

The lipid bilayer in the membranes varies in fluidity. In the gel state the molecules have such a close proximity that local order resembling that in the solid state most likely exists. As furthermore a conformational change in the hydrocarbon chain of one lipid molecule directly affects neighbouring chains in a cooperative way the arrangement of hydrocarbon chains in pure complex lipids should be of relevance to the bilayer structure.

Even if the conformation of a molecule is dependent on its environment, intramolecular forces give rise to preferred conformations. These manifest themselves by existing in different molecular surroundings and may also be apparent from energy calculations.

In the structure of glycerylphosphorylcholine (Abrahamsson & Pascher, 1966), for example, the two independent molecules of the asymmetric unit both show a characteristic gauche conformation about the $\overset{+}{N}$-C-C-O bond. This has been found to exist in a number of other related compounds as surveyed by Sundaralingam (1972) and also recently in an actual phospholipid, 1,2-dilauroyl-(DL)-phosphatidylethanolamine (Hitchcock, Mason, Thomas & Shipley, 1974).

At this Department we are systematically studying by X-ray diffraction techniques lipids varying from fairly simple ones to complex membrane constituents. Special interest has been devoted to molecular packing behaviour such as the arrangement of hydrocarbon chains and in connection herewith the stacking of cholesterol skeleta and their accommodation into a lipid matrix. Furthermore major research efforts have concerned the correlation between structure and function of sphingolipids.

ARRANGEMENT OF HYDROCARBON CHAINS

In lipids a number of modes of lateral packing of hydrocarbon chains with parallel axes are possible. As seen along the axes, the chains can either have their planes parallel or at approximately right angles to each other. The packing is usually described in terms of a subcell with the c_s axis ($\sim$ 2.55 Å) along the chain direction and the other two axes representing repeat distances between chains. Symbols O, M and T denote orthorhombic, monoclinic and triclinic symmetry and $\perp$ and $\parallel$ mutual chain plane orientation. Sometimes a prime is used to differentiate subcells with otherwise similar symbols.

Some characteristics of T$\parallel$, O$\perp$, O′$\perp$ and O$\parallel$ were described by Abrahamsson, Ställberg-Stenhagen & Stenhagen (1963). Later other packings were discovered: M$\parallel$ (Abrahamsson & Westerdahl, 1963) and O′$\parallel$ (Abrahamsson & Ryderstedt-Nahringbauer, 1962) (Fig. 1). Segerman (1965) discussed the chain packings in terms of rows of identical chains and introduced a different nomenclature. This has not been used here as it does not account for new more complex chain arrangements.

In actual structures there are considerable random deviations from these idealized subcells. The O$\perp$ packing, however, shows principally important systematic variations. On heating, the short

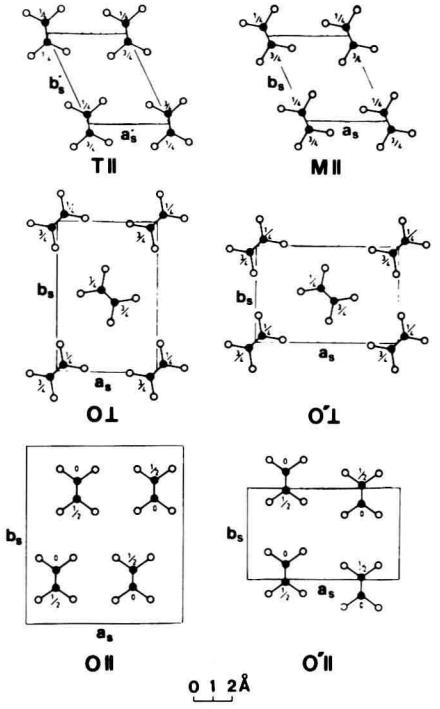

Fig. 1
Hydrocarbon chain packing subcells. Numbers at the carbon atoms represent fractional coordinates along the c_s axis.

subcell axis, a_s, remains constant ($\sim$ 5 Å) or decreases slightly, whereas there is a marked expansion of the normally 7.40 Å b_s axis. Similarly, substituents can be accommodated into the O⊥ matrix by the chain axes separating in the same direction. In 12-D-hydroxyoctadecanoic acid methyl ester (Lundén, 1976) hydroxyl groups and their hydrogen bond system are given enough space without local chain distorsion by expanding the b_s dimensions to 7.87 Å (Fig. 2). This gives a cross section area per chain of 19.5 $Å^2$ as compared to 18.5 $Å^2$ in pure hydrocarbons. Though a quite different situation exists in sodium dodecyl sulphate (Sundell, 1976 a) in that the packing of the bulky polar groups leaves the chains with too much space, the chain matrix adapts in an analogous way by keeping one subcell axis nearly constant (5.1 Å) whereas the other expands to 8.2 Å giving a chain area of 20.9 $Å^2$. It should be noted that even though the chains in the latter case are considerably separated and consequently disordered with large thermal motion, a normal all anti-planar conformation is maintained in the chains (Fig. 3).

Near their melting point many lipids exist in the so called α-form giving powder diffraction patterns implying a hexagonal symmetry of the carbon chains. The subcell dimensions corresponding to O⊥ are then 4.9 and 8.6 Å with a cross section of 21.1 $Å^2$. This is generally considered to be the chain arrange-

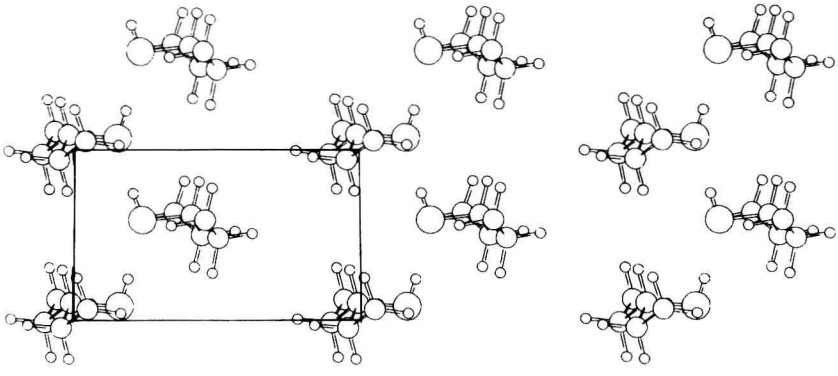

Fig. 2 The chain packing with accommodated hydroxyl groups in 12-D-hydroxyoctadecanoic acid methyl ester.

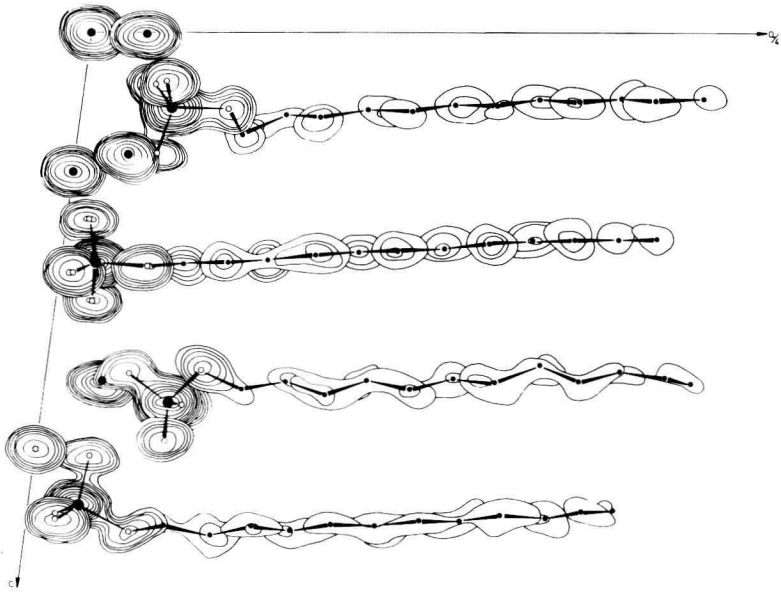

Fig. 3 Electron density map of sodium dodecyl sulphate showing the four molecules in the asymmetric unit.

ment in membrane lipid bilayers in the gel state. Even with this separation of the chain axes the hexagonal symmetry cannot be due to rotation of the chains about their axes (behaving as cylinders) but is rather caused by disorder. As already pointed out by Andrew (1950) in connection with an NMR-study, a completely synchronous motion of hexagonally arranged carbon chains with twofold symmetry is impossible in a defined lattice. In fact, even moderate oscillations about the chain axes will lead to displacement of molecules within the lipid layer. In the super liquid state in monolayers (Harkins, 1944) in which a vigorous lateral movement in the tightly packed liquid layer is observed, the chains most likely do rotate completely.

Recently we have found two new types of chain packing in a cholesteryl ester (Abrahamsson & Dahlén, 1976 a, b) and a cerebroside (Pascher & Sundell, 1976) which appear to be of principal significance for the condensed state of the lipid matrix of membranes. In cholesteryl-17-bromoheptadecanoate the steroid skeleta determine the general packing and the chains cannot adopt positions suitable for any earlier known lateral arrangement. The chain axes are roughly hexagonally ordered as in the expanded O $\perp$ case but the chains are closer packed with cross section area of only 19.3 Å^2. Both these conditions can be achieved simultanously only by a hybrid type of lateral stacking. The packing can formally be derived by a twinning operation on O $\perp$ and can be described as being built up of pleated sheets in which all chains have parallel planes. Adjacent sheets have opposite tilt of the chain planes (Fig. 4). We

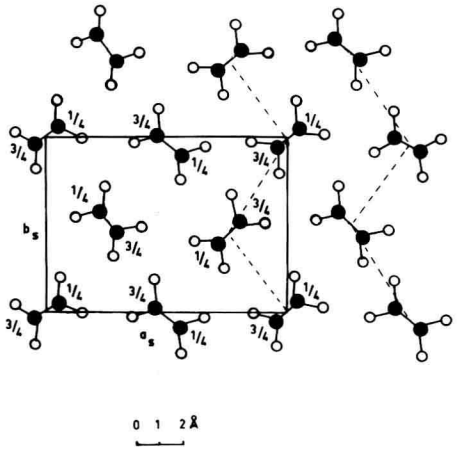

Fig. 4 Idealized subcell of cholesteryl-17-bromoheptadecanoate. Dotted lines indicate pleated sheets of chains with parallel planes.