Bond orientation properties in lipid molecules of membranes: molecular dynamics simulations

A.L. Rabinovich[1], A.P. Lyubartsev[2]
[1]Institute of Biology, Karelian Research Centre, Russian Academy of Sciences, 11 Pushkinskaya str., Petrozavodsk 185910, Russian Federation
[2]Division of Physical Chemistry, Department of Material and Environmental Chemistry, Stockholm University, Svänte Arrhenius väg. 16C, S 106 91, Stockholm, Sweden

Rapid development of computer power during the last decade has made molecular simulations of lipid membranes feasible for many research groups, which, together with the growing general interest in investigations of these very important biological systems has lead to tremendous increase of the number of research on the computational modeling of lipid membranes [A.P. Lyubartsev, A.L. Rabinovich, *Soft Matter*. 2011. V.7. No.1. P.25-39; A.L. Rabinovich, A.P. Lyubartsev, *Polymer Science. Ser.C.* 2013. V.55. No.1. P.162-180]. Natural membranes (biomembranes) are very complex heterogeneous systems consisting of many different molecules which are involved in a variety of cellular processes. The most commonly occurring chains of lipid molecules have 12 to 24 carbons and may contain 1 - 6 carbon - carbon double bonds of the *cis*-configuration in different positions. The polyunsaturated chains are of great importance in structure and functioning of natural membranes At the same time, full understanding of the effects of lipid unsaturation on various physical properties of membranes at the molecular level, affecting their functioning, is not yet achieved. Molecular dynamics and Monte Carlo computer simulations of various lipid membrane systems allow elucidating the detailed relations between the chemical structure and physical properties of various lipid molecules and membrane inclusions, to explain individual peculiarities of natural objects, to make forecasts concerning their behavior, etc. An understanding of the molecular basis of various physical properties of lipids allows one to narrow down the list of hypotheses under consideration about the possible functions of various components (such as acyl chains) in lipid membranes, e.g., the maintenance of proper bilayer fluidity and permeability, of the activity of membrane-bound enzymes, etc.

Series of molecular dynamics simulations of 16 hydrated liquid crystalline phase phosphatidylcholine bilayers were carried out in order to investigate systematically the role of double bonds in physical properties of lipid membranes. The simulation boxes were filled by 64 lipid molecules per monolayer and 30 water molecules per lipid. The two hydrocarbon tails, the glycerol section and the head group of the lipid molecules were treated in accordance with their known chemical structure. All hydrogen atoms were explicitly included in the computations. Phosphatidylcholine molecules contained 1 – 6 *cis* double bonds in unsaturated chain *sn*-2 (with 18, 20 or 22 carbons) and saturated *sn*-1-chains (with 16 or 18 carbons). The 16 unsaturated pure bilayer systems were coupled to an external temperature bath of 303 K and a pressure bath of 1 atm. After 20 ns relaxation trajectories the MD production runs of 80 ns were executed for all bilayer systems.

Different equilibrium structural and dynamic properties of the bilayers were defined, such as profiles of C-C and C-H bond order parameters of lipid molecules with respect to the bilayer normal, the orientational fluctuations of these bond vectors (probability density distributions of C-C and C-H bond orientations), the root mean square values of the positional fluctuations of all lipid atoms relative to the average atomic coordinates, etc. It was shown that the study of anisotropy degree of probability density distributions of bond orientations allows distinguishing extended regions with different types of angular fluctuations of bonds in a membrane formed by lipid molecules with unsaturated chains. The computed properties were compared with available experimental data and discussed in relation to their possible role in the biological functioning of membranes.

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