

A thermodynamic analysis of the effects of myelin basic protein (MBP) on DPPS and DPPG monolayers



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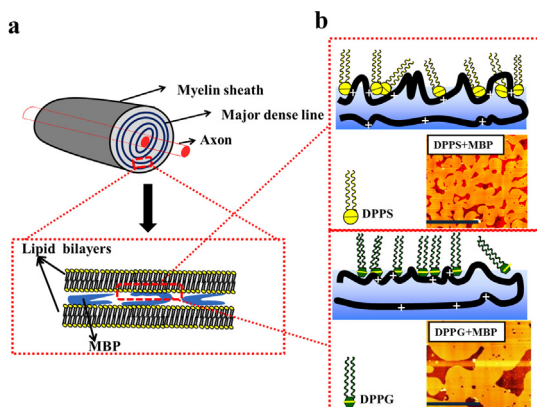
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HIGHLIGHTS

- The interactions between MBP and DPPS, DPPG at the air/water interface were studied by thermodynamic method and AFM.
- The quantitative analysis of the interaction of molecules.
- MBP could penetrate into both DPPS and DPPG monolayers depending on the concentration of proteins.
- These dates are meaningful to understand the myelination process.

GRAPHICAL ABSTRACT

Model of the (a) myelin sheath, (b) MBP/DPPS and MBP/DPPG



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ABSTRACT

Myelin basic protein (MBP) relate to multiple sclerosis, experimental cerebral spinal cord inflammation and other diseases of the central nervous system. It has important biological significance for the study the diseases which related to the interaction between myelin basic proteins (MBP) and DPPS, DPPG. In this paper, we studied the interaction between molecules at the air/water interface by thermodynamic method and atomic force microscopy (AFM). Experiments show that the average molecular area increases when the protein is incorporated into lipid monolayer. By means of analyzing surface pressure–mean molecular area (π -A) curves, a linear mass conservation plot (i.e. protein amount vs. a matching amount of lipids) was obtained. In addition, the protein partition coefficient and the mixing ration between protein and lipid were calculated. When the surface pressure of the monolayer was 10 mN/m, one MBP molecule could be combined with (58 ± 4) DPPS and (37 ± 6) DPPG molecules. The interaction between MBP and DPPG (or DPPS) to determine the nervous system of the disease has a good biophysical significance and medical value.

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1. Introduction

The interactions of proteins with lipid structures are necessary and important in various fields. A large number of biological

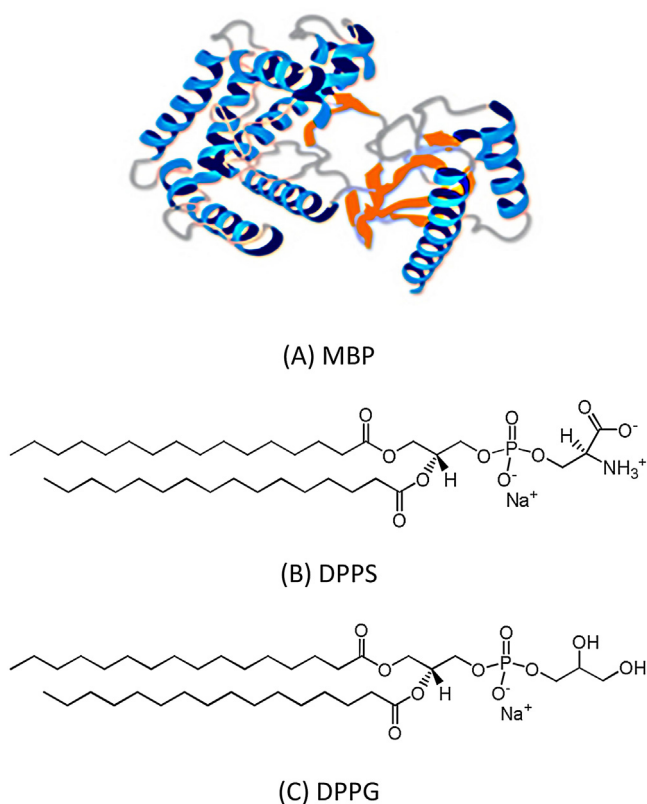
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Scheme 1. The chemical structure of DPPS and DPPG.

reactions take place at interfaces where the main constituents are proteins and lipids. The interaction between Langmuir phospholipid monolayers and proteins has studied using a number of methods. A. Jyoti et al. [1], by using Brewster angle microscopy (BAM) as a supporting technique, showed that the influence of the rate of compression is examined for a dipalmitoylphosphatidylcholine (DPPC) monolayer at the air/water interface. J. B. Li et al. [2], X. Wang et al. [3] and X. L. Wang et al. [4] studied the Phase behavior and structural changes of the dynamic adsorption and penetration of proteins into the monolayers of biologically important surfactants by BAM, film balance, pendent drop and grazing incidence X-ray diffraction (GIXD) techniques. In addition, Q. He et al. [5], from BAM, fluorescence microscopy (FM) images displayed the domain formation and changes during compressing complex films. Through comparison we found that the above mentioned in the literature is a qualitative study of interaction between proteins and lipids by BAM, FM, film balance, GIXD and pendent drop analysis, but the detailed mechanism of the interaction between protein and lipids is still unclear. Thence, our article makes a conclusion through the massive data, using the method of qualitative and quantitative analysis that the effect of proteins on the phospholipid membrane. Langmuir-Blodgett monolayer techniques create a kind of applicable biomimetic membrane system. In our model system, MBP has a high positive charge, which is likely to be crucial to its interaction with the negatively charged inner leaflet of the myelin membrane.

The myelin sheath of the central nervous system (CNS) is a lipid-rich, multilamellar membrane discontinuously wrapped around the nerve axon. Myelin basic protein (MBP) is the main protein component which makes up 30% of the protein content; the myelin membrane is composed by lipids of 70% [6–8]. The Scheme 1(A) shows the structure of MBP. Moreover, extracted from CNS in myelin membranes mature period, the 18.5 kDa MBP is identified as the major protein. In the neutral pH environment, MBP with a net positive charge of 19 and its isoelectric point is roughly 10 [9,10].

A large number of experimental studies on the MBP extracted have shown that [11–15] MBP not only inserts into myelin membrane through hydrophobic interactions with the lipid hydrocarbon tails, but also interacts electrostatically with the polar heads of anionic lipid due to relatively high positive charge residues. When there is the interaction between MBP and negatively charged lipid, the major dense line by the integration of oligodendrocyte cytoplasmic membrane could be formed and stabilized [16–18].

Firstly, from the medical point of view, MBP has an importance significant in many neurological diseases, such as multiple sclerosis (MS), experimental cerebral spinal cord inflammation (EAE). MBP is an intrinsically unstructured (disordered) protein in solution and in the lipid-free state, its structure is not fully unfold, but also retains some elements of β -sheet and α -helix. Lipids combining to the MBP induced folding of the protein. Study indicated that the interaction between MBP charge components and charged lipids, changing in MS and EAE tissues [19]. It is believed to be a more specific biochemical indicator which could reflect the existence of substantial damage and demyelization with CNS [19,20]. Secondly, from the biophysical aspect, some other studies have shown that the specific combination of MBP with different lipid components can alter the conformation of myelin membrane model [21]. The interaction between negatively charged lipids and protein is an interesting model system to study the basic physical properties. Recent research suggests that small changes in the lipid composition leads to changes in lipid domains, and the change of the structure and size of these domains will affect protein adsorption [22]. However, the focus of our work is on the systematic study of MBP interact with two kinds of electronegative lipid physical process and the mechanism of adsorption by using LB and AFM, which is very different from previous works, and this is also the major contribution of our work.

Myelin integrity is the foundation of the fast salutatory conduction of the nerve impulse along the axon. Therefore, the interaction of myelin basic protein with lipids is of the utmost importance to understand the essence of the interactions that maintain the structural integrity of myelin sheath [23,24]. Especially, attention has been paid to the interaction of MBP with membrane lipids. Minor changes in lipid composition in Myelin membrane will alter myelin membrane domain structure, size and the adsorption characteristics of the intermembrane. Overall, the research of the interaction between MBP and DPPS, DPPG has great biological significance and medical value for judging diseases of the nervous system. How is effect of the negative charge of DPPS and DPPG?

To answer the question, surface studies of the MBP and lipids at the air/subphase interface have been performed. To study the detailed interaction mechanism, investigation has been conducted on the process of MBP combined with lipids (DPPS, DPPG) monolayers, as representative of the negatively charged lipids. As shown in Scheme 1(B and C), DPPS and DPPG have been used in the study because they have identical hydrophobic side chains and differ only in their molecular head-group composition.

Nowadays, the interaction between lipids and MBP has been examined by a considerable amount of data in the literature [25,26]. For example, Fourier transform infrared spectroscopy, circular dichroism, and X-ray diffraction have established a temporal evolution of the structure of subphase penetrating the lipid phase together with the protein [27–29]. X-ray reflectivity experiments have concluded that the structural regularity of DPPG monolayers at the air water/interface has been destroyed [30]. In recent years, there is investigation about surface pressure measurement and fluorescent imaging of a monolayer composed of a myelin lipid mixture [31]. Besides, investigation has been conducted on the surface forces apparatus and AFM for studying the influence of lipid composition and concentrations of MBP on the structure of model lipid bilayers and the interaction forces and adhesion between them [6].

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