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Review article

Lipid bilayers supported on bare and modified gold – Formation, characterization and relevance of lipid rafts

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ABSTRACT

Supported lipid bilayers (SLB) comprise a very important set of model systems of biomembranes. In particular, they can be prepared on metallic surfaces such as gold electrodes, which allow a number of electrochemical studies and applications that could not be undertaken with other types of model systems, such as liposome suspensions. Also of special relevance is lipid bilayer composition, especially those combinations of lipids which permit the formation of biologically relevant membrane domains such as lipid rafts. Indeed, membrane domain organization is a crucial feature concerning not only the biophysical properties of the bilayer itself, but also the behavior and bioactivity of membrane-interacting biomolecules. In spite of its relevance, the presence of bilayer domains has not been central in many investigations involving lipid bilayers supported on conductive surfaces. Moreover, air exposed gold surface is hydrophobic, which is not ideally suitable to establish a proper interaction with the lipids polar head group. To overcome such limitation different strategies may be adopted, encompassing the fine tuning of the buffer conditions and previous surface modification by hydrophilic self-assembled monolayer (SAM) or thiolipids. This review will be focused on the formation and characterization of SLB and lipid rafts on gold substrates, illustrating the range of applications of such platforms, with examples of the study of electroactive molecules and the development of new biosensing interfaces.

1. Introduction

Biological membranes are complex structures comprising a great variety of proteins and lipids organized in several time and length scales. According to their functions biomembranes exhibit different protein/lipid ratios and also distinct lipid compositions. In many biophysical studies the use of simplified models composed by a few lipid species, many times incorporating a protein of interest, is required. These membrane model systems have emerged as excellent tools for both basic membrane research and applications, such as drug–membrane interaction and biosensing [1–7]. Lipids can be classified in different groups including phospholipids, sphingolipids, and sterols (Fig. 1a), presenting structures that can differ between organisms, cells and even sub-cellular compartments. The structural and functional diversity of lipids is such that two recent lipidomics initiatives have emerged, and a new classification system for lipid molecules was proposed [8,9]. Also, depending on the polar head groups and the length and unsaturation degree of the hydrocarbon chains, lipids confer distinct properties to the biomembranes. For instance, a single phospholipid bilayer can undergo several thermotropic phase transitions, such as the gel to fluid that occurs at the main transition temperature, T_m. Upon this transition, the bilayer changes from a highly ordered, compact and slow lateral diffusion arrangement (gel) to a disordered one (fluid). These properties are important to be considered when choosing the appropriate model to study a given physical–chemical membrane process. In many steps of the preparation of membrane model systems, including SLBs, a temperature higher than the highest T_m of the lipid mixture used is required. We have observed that under the same conditions that are appropriate for the formation of a planar SLB on gold for a low T_m lipid, tubular structures are formed when using a high T_m lipid [10]. Long-chain, saturated phospholipids are usually in the gel phase at room temperature (Fig. 1a – DPPC, PSM, GM1 and ceramide), whereas unsaturated ones are in the fluid phase (Fig. 1a – DOPC, POPC). An extensive collection of lipid phase transition temperatures can be found elsewhere [11]. By using a binary mixture of lipids from these groups, a bilayer presenting gel/fluid phase coexistence is obtained. These phases are organized into domains sharing some properties with the heterogeneities found in biological membranes [12].

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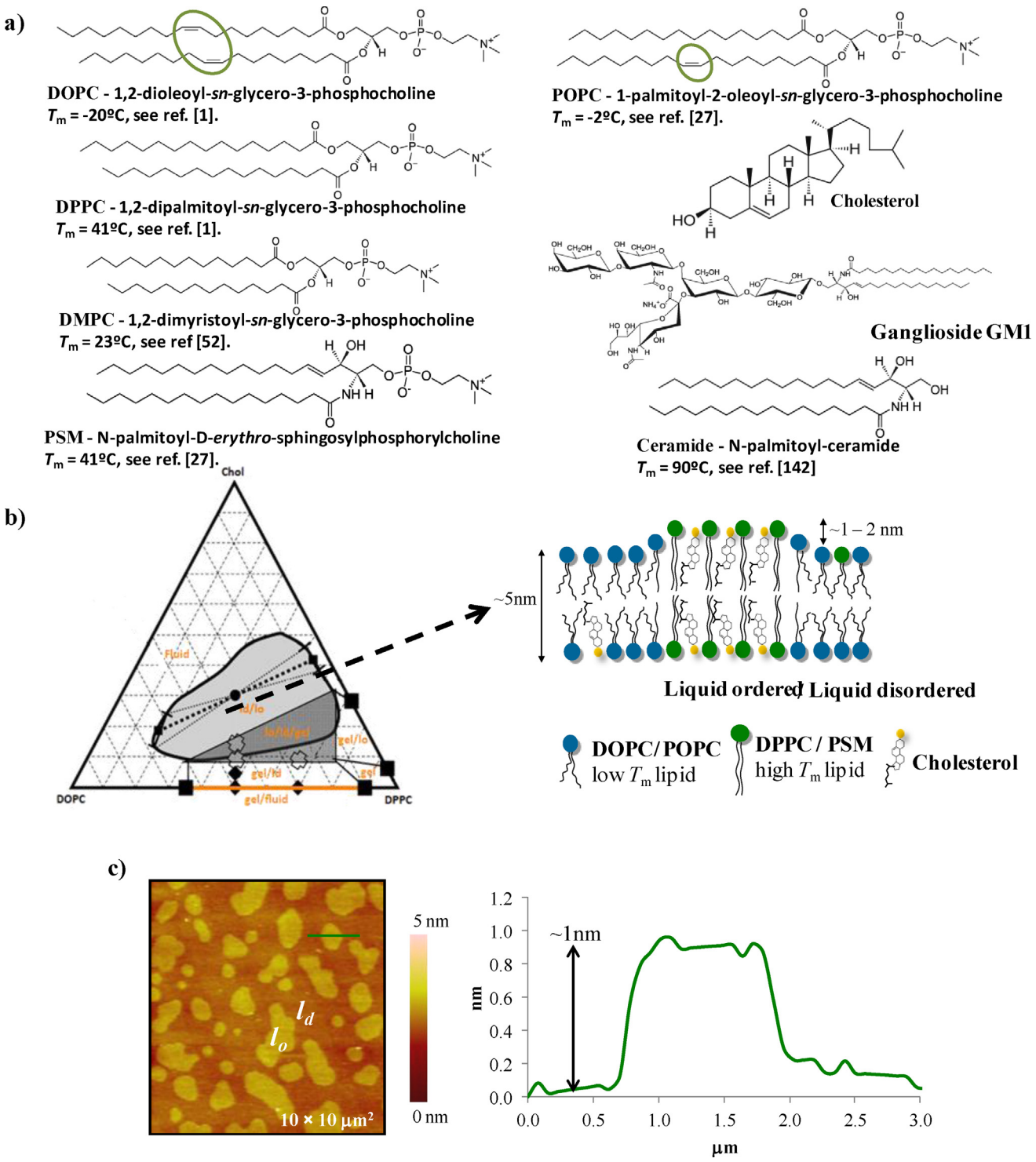

Fig. 1. (a) Structure lipids commonly employed in model systems of biomembranes. (b) Ternary phase diagram at 23 °C of a simple lipid mixture, DOPC/DPPC/cholesterol, that leads to phase coexistence between l_d and l_o (lipid rafts) and the schematic representation of those domains with typical thickness values. The phase diagram was obtained for free-standing bilayers [30]. (c) Tapping mode AFM topographic image in buffer solution of a DOPC/PSM/cholesterol (2:2:1 molar ratio) lipid bilayer formed on mica, where it is possible to distinguish two different lipid phases – thicker l_o domains and the surrounding l_d phase. The topographic profile on the right corresponds to the green line in the image. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

1.1. Lipid rafts: their relevance and how to mimic them

Of particular importance are the lipid domains found in eukaryotic organisms designated as lipid rafts, due to their involvement in many cellular functions, such as intracellular distribution of proteins, signal transduction, and by modulating the activity of membrane proteins [13–16]. These highly specialized structures have been defined as being small (sub-micrometer range), heterogeneous and dynamic domains enriched in cholesterol and sphingolipids [17]. The acyl chains of the lipids enriched in these domains exhibit a higher degree of saturation than the ones in the surrounding membrane and pack tightly with certain sterol molecules [18–20]. In the case of mammalian cells, the presence of cholesterol (Fig. 1a) in these microdomains drives the formation