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Dilational surface elasticity of spread monolayers of pulmonary lipids in a broad range of surface pressure

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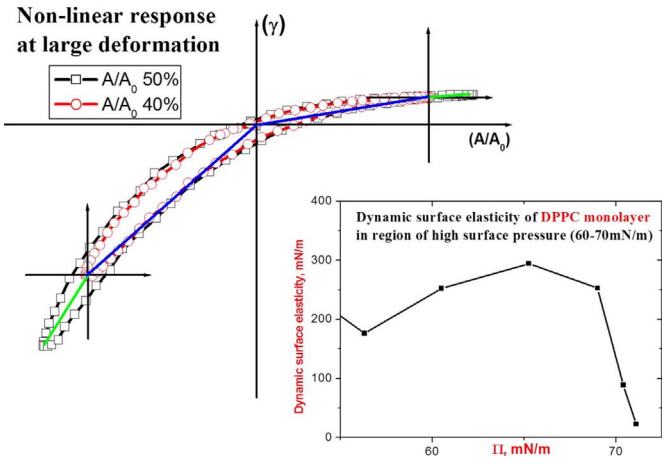
GRAPHICAL ABSTRACT



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ABSTRACT

A new approach to the analysis of nonlinear surface dilational rheological properties was developed with the aim to enlarge the accessible range of surface pressures. The dilational surface elasticity of spread monolayers of DPPC, cholesterol, DMEA and their mixtures was determined in the region of low surface tensions (less than 10 mN/m) corresponding to the state of pulmonary surfactants at the lung interface. The dilational surface elasticity of pure DPPC monolayer proved to be high (~200 mN/m) up to the collapse. The addition of cholesterol, DMEA or their mixture to the DPPC monolayer increased the dynamic surface elasticity, but could decrease significantly the surface pressure of the monolayer collapse if the concentration of additions exceeds an optimal value.

1. Introduction

A thin liquid film of a mixture of natural surfactants covers the surface of lung alveoli and plays a crucial role in the process of breathing [1–4]. The impairment of the functionality of the pulmonary surfactants (PS) can lead to the development of neonatal respiratory distress syndrome [5]. The surfactant replacement therapy, based on the administration of PS extracted from animals, resulted in a decrease

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of the mortality of premature infants. At the same time, the insufficient efficiency and the high cost limit the application of natural PS to the treatment of the acute respiratory distress [6]. The development of a synthetic replacement of PS has to decrease the price and open a new strategy of the drug delivery [4]. However, the insufficient information on the processes in lung alveoli during breathing hinders real progress in the application of synthetic PS and to the best of our knowledge only a few promising attempts have been described so far [7–9].

One usually uses a few functional parameters to characterize the properties of PS at the interface: the equilibrium surface tension, the minimum surface tension under surface compression, the required deformation for achieving lowest surface tension, the area of hysteresis at compression/expansion, the required alveolus index [9–13]. Although the breathing includes permanent surface deformations and the alveolus surface can be far from equilibrium, these functional parameters do not characterize properly the dynamics of the surface layer. The application of the methods of surface rheology can give more relevant information. The intensive investigation of the dilational surface elasticity of spread DPPC monolayers – the main component of PS - showed that the surface elasticity reached very high values at the decrease of surface tension down to 20 mN/m [14–16]. The addition of PS proteins (SP-B and SP-C) to DPPC monolayers decreased the surface elasticity, but improved the rearrangement of components in the surface layer leading to the higher stability under deformations. It has been shown recently that the penetration of solid nanoparticles into DPPC monolayers can induce disordering of the monolayer structure and thereby influence strongly two-dimensional phase transitions [17–19].

Although the dynamic dilational surface elasticity characterizes a dynamic response of the monolayer to the surface dilation, it is usually not considered to be an important characteristic parameter of PS monolayers [3,4,13]. The main reason is probably connected with the problems to determine the dynamic surface elasticity in the systems with extremely low values of the surface tension [1]. Unfortunately, the methods of oscillating bubbles and drops, which are based on the profile analysis, prove to be inappropriate for measurement of the surface elasticity due to the leakage of the film at low surface tension [1]. The oscillating barrier method requires the application of special materials to minimize the leakage [1]. Moreover, the accuracy of these methods decreases at oscillations near the frequency of normal breathing [20]. Measurements of the capillary pressure (pulsating bubble surfactometer) can be used at higher frequencies but they also suffer from leakage. The methods of captive bubble surfactometer and constrained sessile drop are free from problems of leakage but to the best of our knowledge have never been used for measurements of the dynamic surface elasticity [1]. As a result most of the studies of the dilational surface rheology in systems with PS relate to surface tensions higher than 25 mN/m [16].

On the other hand, the breathing process can be characterized by large surface deformations and thereby by a nonlinear response of the surface layer while most of the relations of the surface rheology are based on the assumption that the system response – the surface tension increment - is proportional to the disturbance amplitude [21–24]. Only a few authors considered deviations from the linear behavior of PS monolayers with the increase of deformation [17,25]. The first attempts of the analysis of nonlinear effects in the surface dilational rheology have been published only recently [24,26,27].

This study describes the application of a new modification of the stress decomposition method to the analysis of the dynamic surface properties of PS layers in the case of a non-linear system response. This approach gives a possibility to determine the dilational surface elasticity at low values of the surface tension for spread monolayers of some PS lipids mixtures. Many authors considered spread monolayers of pure DPPC and its mixtures with cholesterol and other lipids to be the simplest models of PS layers and some biomembranes [4,28]. The real mixture of PS is essential more complex and consists of several proteins [1,3]. In this work the dynamic surface properties of the mixture of DPPC, cholesterol and dimyristoyl phosphatidylethanolamine (DMEA) were investigated. The reason is that PS contain also non-phosphocholine zwitterionic lipids, in particularly phosphatidyethanolamine. To the best of our knowledge the mixtures containing DPPC, cholesterol and DMEA have never been investigated so far. The investigation of the surface rheological properties at different levels of deformation gives additional information on the dynamics of PS layers in vitro and can contribute to the understanding of complex physicochemical processes accompanying the breathing. In particular, it turns out that the dependence of the dynamic surface elasticity on surface pressure differs significantly from the corresponding data for the static surface elasticity.

2. Materials and methods

DPPC, cholesterol and DMEA of 99% purity from (Sigma-Aldrich) was used without further purification. Octadecyl dimethylphosphine oxide (PhO) was purchased from Gamma-Service Dr. Schano, Berlin, Germany, with purity required for interfacial studies and used as received.

Chloroform and hexane (Sigma-Aldrich) were purified by distillation. Sodium chloride (Merck) was preliminarily heated in a muffle furnace at about 750 °C for the elimination of possible organic impurities. Sodium phosphate monobasic dehydrate and sodium phosphate dibasic dihydrate (Sigma-Aldrich) were used as received. Water purified by a multicartridge system (Direct-Q) was used in all the experiments.

The spreading solutions of the lipids with the concentration of 1 mg/ml were prepared in chloroform with the required ratios of the lipid components. The aqueous subphase was a phosphate buffer with pH = 7.4 NaCl was used to increase the ionic strength to 0.1 M. The lipid monolayers were spread onto the aqueous subphase in a Langmuir trough by dropwise addition of controlled volumes of the solutions of lipids and their mixtures. PhO was dissolved in hexane for the formation of monolayers on aqueous subphase.

The dynamic dilational surface elasticity was measured by the oscillating barrier method using ISR surface rheometer (KSV NIMA, Finland). The liquid in a Teflon Langmuir trough had a total surface area of 75 × 15 cm^2. The instrument was equipped with two Teflon barriers oscillating symmetrically at given frequencies and amplitudes. The induced oscillations of surface tension were measured by the Wilhelmy plate method. The plate from filter paper had the width of 1 cm and was positioned parallel to the barriers in the middle of the through. The symmetrical movement of the two barriers and location of Wilhelmy plate in the center of through minimized the influence of the shear surface properties. All the measurements were performed at a constant frequency of 0.03 Hz and at different amplitudes of the area oscillations.

3. Method of the analysis of experimental data

In the case of infinitesimal surface compression/expansion one can apply the following relation to describe the corresponding changes of the surface tension ($\Delta\gamma$) [29]:

$$\Delta\gamma(t) = \int_{-\infty}^{t} G(t-\tau)\left(\frac{d\Delta A(\tau)}{A_0 d\tau}\right)d\tau \quad (1)$$

where ΔA is the change of the surface area, A_0 is initial surface area, G is the surface relaxation function and t is the time.

The application of the Fourier transformation to Eq. (1) gives a linear relation between the Fourier transforms of the surface tension ($\Delta\gamma(\omega) = F\{\Delta\gamma(t)\}$), and deformation ($\Delta A(\omega) = F\{\Delta A(t)\}$) [30]:

$$\Delta\gamma(\omega) = \varepsilon(\omega)\frac{\Delta A(\omega)}{A_0} \quad (2)$$