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Structural models and surface equation of state for pulmonary surfactant monolayers

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Abstract

A simple surface equation of state is proposed to describe π-A isotherms of pulmonary surfactant monolayers. The monolayer is considered as undergoing three characteristic states during the compression: the disordered liquid-expanded (LE) state, the ordered liquid-condensed (LC) state and the collapse state. Structural models of pure protein (SP-B and SP-C) monolayer are proposed to interpret the behavior characteristics of monolayer in the states. The area, A_{LC}, is defined as an instantaneous LC-state area when the monolayer is under the complete LC state. The area, A_t, is defined as a transition area from the ordered LC state to the collapse state. And the collapse pressure, π_{max}, is defined as the maximum surface pressure that the monolayer can bear before collapse. The ideal equation of state is revised by A_{LC}, A_t and π_{max}, and a new equation of state is obtained, which is applicable for pure components of pulmonary surfactant. The theoretical π-A isotherms described by the equation of state are compared with the experimental ones for SP-B, SP-C, DPPC and DPPG, and good agreements are obtained. The equation of state is generalized to protein–lipid binary mixtures by introducing mixing rules. The predicted π-A isotherms agree with the experimental ones for various pulmonary surfactant components and the average deviation is about 9.2%.

Keywords: Surface equation of state; Pulmonary surfactant; Surfactant protein; Structural model

1. Introduction

Pulmonary surfactant (PS) is a complex mixture of approximately 90% lipids and 10% proteins present at air–liquid interface of lungs. The main function of PS is to reduce the surface tension at the alveolar air–liquid interface in order to avoid alveolar collapse at the end of expiration and to facilitate the work of breathing [1]. The deficiency or inactivation of PS in premature infants is responsible for respiratory distress syndrome (RDS), which is a major cause of neonatal morbidity and mortality [2]. Therefore, the studies on the action mechanism and molecular biology of PS components have clinical importance.

The surfactant lipids mainly include saturated dipalmitoylphosphatidylcholine (DPPC) and phosphatidylglycerol (PG), where DPPC is the most abundant (40 wt.% of PS) and the most surface-active component [3]. DPPC is an amphiphilic molecule that can generate ordered films and pack tightly to reduce the surface tension to less than 1 mN/m [4]. The very low surface tension value enables the alveolar space to contract during expiration without collapse. Besides, other phospholipids, such as dipalmitoylphosphatidylglycerol (DPPG), can help DPPC facilitate the re-spreading of monolayer [5].

There are four specific surfactant proteins: hydrophilic SP-A and SP-D, hydrophobic SP-B and SP-C. SP-B and SP-C are two small proteins synthesized by the alveolar type II epithelial cells, accounting for approximately 1% to 2% (wt) of total PS [6]. SP-B is a disulphide-linked homodimer composed of two 79-residue polypeptide chains. As a member of the saposin-like family, SP-B is the only protein which is a hydrophobic covalent dimer [7,8]. SP-C is a 35-residue lipopeptide expressed only in lung tissue and is one of the most hydrophobic polypeptides so far known [8]. SP-B and SP-C have been implicated as important contributors to the surface activity of PS. SP-B can enhance the surface tension-reducing properties of PS films, the rate of adsorption and surface spreading of phospholipids [3]. Similarly, SP-C can interact with

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phospholipids and promote the phospholipids to be absorbed to the monolayer surface. And SP-C is more effective in promoting the reinsertion of lipids squeezed out of the surface monolayer during the compression [4]. In order to understand the breathing process and function of PS in a deeper way, it is necessary to learn more details about structural properties of PS monolayers, as well as the effect of SP-B/SP-C.

Another important point to understand the breathing process is the determination of surface tension of the alveolar surface in vivo, because surface tension or surface pressure is one of the most important characteristics for the surface behavior of PS. Most studies on surface pressure (π) ~ area (A) isotherms for insoluble surfactant monolayers were focused on the phase transition from a fluid phase of low density (liquid-expanded or LE phase) to a condensed phase (liquid-condensed or LC phase) [9]. Some surface equations of state for describing π-A isotherms have been proposed by Israelachvili [10], Fainerman [11], Ruckenstein [9,12], Zeng et al. [13]. For example, Fainerman et al. assumed that the monolayer was in the formation of two-dimensional aggregates and an equation of state was theoretically derived to describe the main phase transition between the gaslike and the condensed phases, however, the equation is complex in form and limited in the practical use. The surface equation of state proposed by Ruckenstein et al. could be used to interpret the LE–LC phase transition. They treated the monolayer as a two-dimensional mixture consisting of LC domains, disordered molecules in the LE state, and free sites, however, only pure phospholipid monolayers were studied. All of these equations [9–13] only had good agreements in pure monolayers, and the mixtures were not taken into account, especially the protein–lipid mixtures. Furthermore, they didn't consider about the relations between structural properties of PS components and surface features of surfactant monolayer. In this paper, structural models of pure protein monolayer are suggested, and a new simple surface equation of state is derived based on the structural models. The surface equation of state is applicable for both pure components and binary mixtures of PS.

2. The structural models of pure protein monolayer

2.1. The structural model of pure SP-C monolayer

The three-dimensional structure of SP-C molecule in chloroform/methanol solutions has been determined by NMR spectroscopy [14]. SP-C is composed of a short palmitoylated N-terminal region and a valyl-rich α-helical transmembrane domain. The N-terminal eight residues are conformationally disordered and haven't determined yet. The C-terminal α-helix encompassing residues 9–34 is nearly ideal helix geometry with a length of 3.7 nm and it is very rigid and hydrophobic [8]. It was showed that SP-C α-helix situated in a DPPC monolayer made a 20° tilt angle to the interface [15]. Based on the SP-C structure above, a structural model of pure SP-C monolayer is proposed as follows:

(1) At low surface pressure, the monolayer is in a disordered LE state with large free space among SP-C molecules (Fig. 1 (a)-I).
(2) In the compressing process, the monolayer turns to an ordered LC state, where SP-C molecules are in good order and close together. The N-terminal residues are compressed into the underside of the surrounding C-terminal of α-helix (Fig. 1(a)-II). There exists LE–LC transitional state in the compression, and a LE–LC plateau is showed in the sketch of π-A isotherm (Fig. 1(c)). For pure protein monolayer, it is difficult to get the LE-LC plateau from the experimental π-A isotherms (see Fig. 4), while it is easy for pure lipid monolayer (see Fig. 3). When the monolayer is under the complete LC state, an area, A_{LC}, is defined as an instantaneous LC-state area per "residue" (where "residue" denotes an amino acid residue of protein or a phospholipid

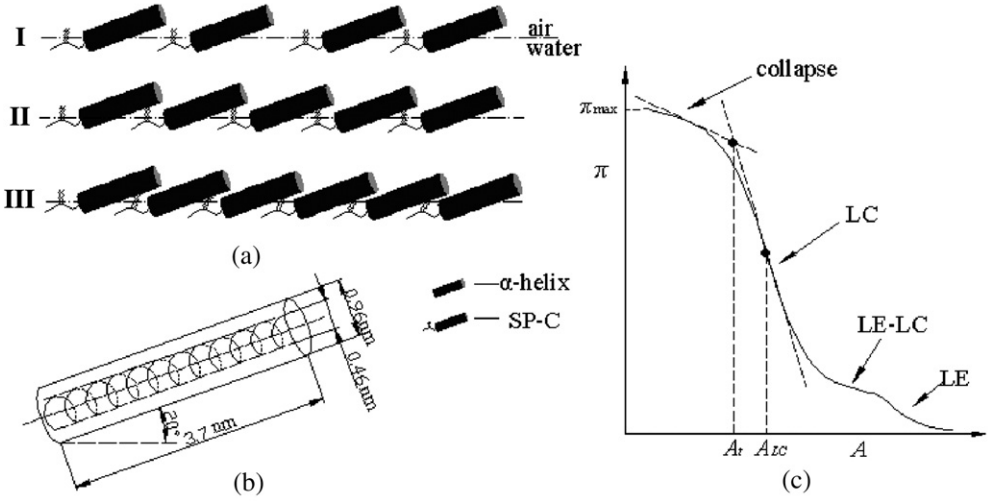

Fig. 1. (a) The structural model of pure SP-C monolayer in the compression. (I) The disordered LE state, (II) The ordered LC state, (III) The collapse state. (b) The structural analysis of α-helix in SP-C molecule. (c) Sketch of π-A isotherm of protein or lipid monolayer. A_{LC} is the instantaneous LC state area. A_t is the transition area. π_{max} is the maximum surface pressure.