**488b A Molecular Dynamics Investigation of the Surface Activity of Components of Pulmonary Surfactant at the Air/Water Interface**

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Pulmonary surfactant, a mixture of ~90 wt % lipids and ~10 wt % proteins secreted by the type II epithelial cells, is essential for the normal functioning of the lungs during the respiration cycle. It helps lower the surface tension by forming a surface active film at the air/liquid interface thus reducing the effort required for breathing. It also prevents alveolar collapse after expiration. Low amounts of pulmonary surfactant in the alveolar space of neonates results in Respiratory Distress Syndrome (RDS). Deactivation of pulmonary surfactant is also known to exacerbate Acute Respiratory Distress Syndrome (ARDS).

Endogenous pulmonary surfactant is a complex mixture of phospholipids and proteins. Dipalmitoylphosphatidylcholine (DPPC), a major component of the mixture (~40 wt %), can form a tightly packed gel phase at physiological temperatures and reduce the surface tension to near-zero values. The commonly held view with respect to surfactant function is that the surface film is able to withstand high surface pressures after expiration through the enrichment of the film with DPPC. Two possible mechanisms have been proposed for DPPC enrichment viz. selective DPPC adsorption from the underlying subphase that acts as a lipid reservoir to the monolayer and the selective removal or "squeezing out" of other lipid components from the monolayer to the subphase during compression. Both mechanisms are thought to occur. The surfactant protein (SP-B) is thought to play a major role in the surface film refinement.

The importance of DPPC to pulmonary surfactant function has been well documented and as a result, the surface tension-surface concentration relationship (equation of state) of DPPC monolayers at the air/water interface is of significant interest. In the current study, we use the extension of the Langevin piston algorithm proposed by Feller and coworkers to simulate a DPPC monolayer at the air-water interface in the $NP_N\gamma T$ ensemble (Feller, Zhang et al. 1995). In this ensemble, the unit cell dimensions are changed anisotropically; the cell length normal to the interface is varied to maintain a constant normal pressure ($P_N$) and the surface area is varied to maintain a constant surface tension ($\gamma$). We present the equation of state for DPPC monolayers at the air/water interface obtained from atomistic detail molecular dynamics simulations. We also discuss the structure of the monolayer, specifically the orientation parameters and distribution functions that describe the interactions between the hydrophilic headgroup and hydrophobic tails of DPPC, as a function of surface concentration.

The current work is part of a multi-scale modeling approach to the study of the dynamics of pulmonary surfactant during the respiration cycle. As a component of this approach, the equation of state describing the surface tension – surface concentration relationship, thus obtained on the molecular scale, would feed into mesoscopic or coarse-grained studies of the system. A subsequent integration is then proposed with macroscopic simulations of the system.

Feller, S. E., Y. Zhang, et al. (1995), J. Chem. Phys. 103(11): 4613-4621.