Protein Modeling and Molecular Dynamic Studies of two new Surfactant Proteins

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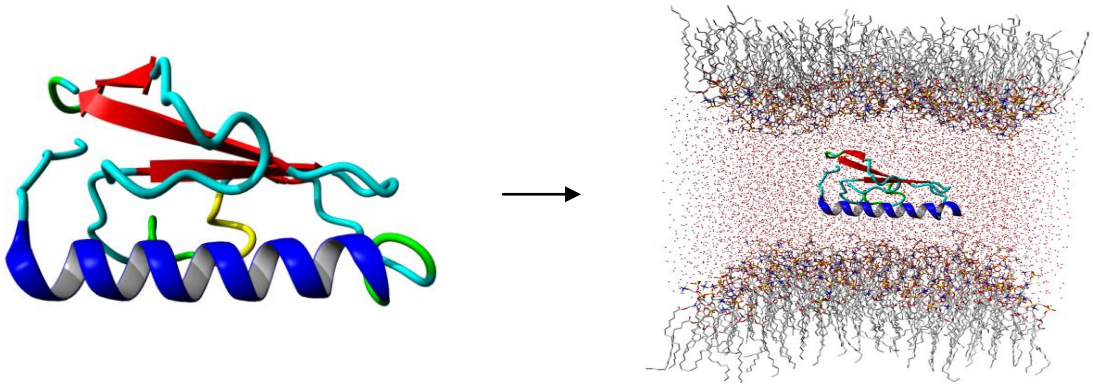
Surfactant proteins are of major importance for the stability and flexibility of lipid layers on air-liquid surfaces like the lung surface or the tear film. They can aid the adsorption of new phospholipids into an existing layer or specifically alter the surface tension of a lipid surface [1]. Furthermore, immunological functions were described for some of the already known surfactant proteins SP-A, SP-B, SP-C and SP-D [2]. For that reason, they are of great interest in the investigation of diseases like the "acute respiratory distress syndrome" (ARDS) or the "dry eye syndrome" (DES). Recently sequences of two new surfactant proteins, called SP-G and SP-H, were identified.



To get insights into the function of SP-G and SP-H, protein structure models were generated for both proteins. These models successfully guided the design of antibodies for the detection and localization of SP-G and SP-H in different human tissues. To verify the stability of the obtained models for further *in silico* experiments, MD simulations in a water box were performed. These were carried out with the GROMACS program package for 50 ns. Since both models showed to be stable they were transferred to a simple lung surface model system, consisting of two dipalmitoylphosphatidylcholine monolayers separated by a water phase. Again, 50 ns MD calculations were performed with GROMACS starting from different orientations of the protein models. During these simulations, it was possible to track the accumulation of the proteins to the lipid layer. Furthermore, the interactions between protein surfaces and lipid head groups could be observed on an atomic scale. The obtained results can give hints for further experimental studies and help to determine the functions of SP-G and SP-H *in vivo*. In addition, future simulations may support the development of new therapies for ARDS and DES.

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[2] E. Crouch, J.R. Wright, *Annu Rev Physiol*, **2001,** *63*, 521-554.