FUNCTIONAL AND FUNCTIONALIZED RED BLOOD CELL MEMBRANES

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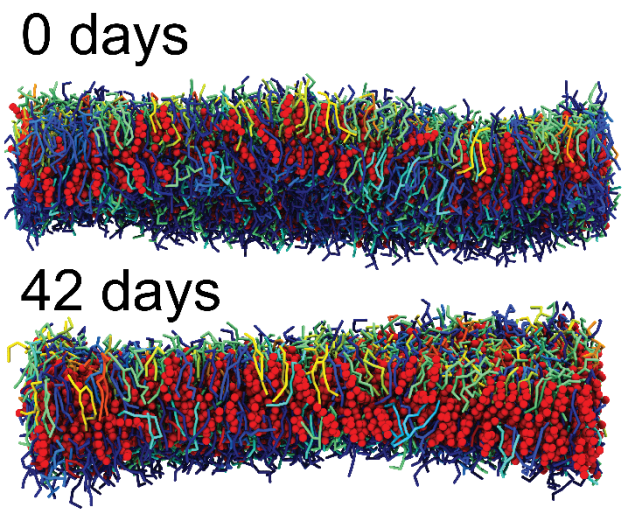

Membranes are an essential building block in cells, and their biophysical properties impact cellular metabolism and functions, such as mobility, division, and vesicle trafficking. Advancements in sample preparation and instrumentation now allow the study of the structure of native biological membranes with an unprecedented resolution [1]. The membrane of red blood cells (RBCs) is of particular interest as these cells are required to undergo deformations when passing through the vascular system, which sets stringent demands on the elastic property of their cell membrane. We isolated the cytoplasmic membrane from human RBCs and measured its bending modulus κ using Neutron Spin Echo (NSE) Spectrometry and X-ray diffuse scattering (XDS). Despite their high cholesterol content of 50 mol%, we find surprisingly small bending rigidities between 2-6 k_BT [2], much smaller than literature values of most single component lipid bilayers. We speculate that this extreme softness results from the presence of highly unsaturated lipids in biological membranes. We also show that this bending rigidity significantly increases during blood storage due to an increased fraction of liquid ordered membrane domains as function of storage time. This effect potentially explains the observed organ dysfunction and the increased mortality in patients who received older blood bags [3].

RBCs are ideal for pharmaceutical applications as they provide access to numerous targets in the human body and superior biocompatibility over synthetic particles. We developed protocols to functionalize RBC membranes to form hybrid membranes [4] that can contain different types of synthetic lipids and proteins. Erythro-VLPs (virus like particles) were designed by embedding the SARS-CoV 2 spike protein into RBC hybrid liposomes that work as COVID vaccine [5]. The platform was also developed as highly selective vehicle for the delivery of antibiotics [6] by encapsulating polymyxin B and conjugating the liposomes with bacterial antibodies. Finally, our start-up company Synth-Med Biotechnology Inc. develops smart, membrane-based biosensors by combining membrane biophysics, an electronic readout and machine learning for the rapid detection of pathogens in food and water.

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