

Dynamics of Membranes and their constituents



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Big Molecules and Small Particles

Modified messenger RNA constitutes a new interesting approach for transient protein expression in different therapies. Based on learnings from DNA delivery the intracellular delivery of such macromolecules remains a challenge. In our work we have prepared so called lipid nanoparticles (LNPs), containing several copies of mRNA in each, using microfluidic mixing. The size of such LNPs can be easily manipulated using different amounts of PEG-ylated stabilizers resulting in rather monodisperse nanoparticles having number-averaged diameters between 50 and 150 nm. In these studies we have been using a erythropoietin mRNA (5-methylcytidine, pseudouridine). The focus of this presentation will be on structural studies using cryo-transmission electron microscopy, small-angle x-ray and neutron scattering for LNPs of different sizes. For the case of neutron scattering using contrast variation is especially informative. We use this information to enable more detailed studies of the LNP internal structure and to tailor the LNP surface composition. Furthermore, we have also performed in vitro cell (human hepatocytes and adipocytes) and in vivo (intravenous and subcutaneous administration) studies measuring both LNP uptake and the concurrent protein expression with the ambition to correlate LNP structure to their biological function.

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