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Investigations on the kinetics of the liquid-liquid phase separation of myelin basic protein: Combining neutron scattering with imaging techniques

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The myelin basic protein (MBP) is a key player when it comes to the formation of tight membrane wrapping around vertebrate's nerve cells. In physiological conditions, MBP is acting as a glue that stacks multiple myelin layers to build up an insulating sheath which covers axons. To accomplish this task, MBP undergoes a so-called Liquid-Liquid Phase Separation (LLPS) - a property which has recently attracted wide attention in the biological and biophysical community. In a LLPS, two liquid phases with different protein concentrations and physio-chemical properties coexist. Damaged integrity of human MBP and the consequent lack of LLPS capability often results in neurodegenerative diseases such as, for instance, Multiple Sclerosis.

Although the importance of its ability to perform a LLPS is already known, the kinetics of MBP's phase separation are not well studied yet. Hence, we focus on investigations that follow the formation of liquid-like MBP droplets which can be observed when suitable conditions are applied. To examine both the nucleation and the growth of those µm-sized condensates, we combine imaging techniques and (neutron) scattering experiments: Confocal microscopy of labelled MBP has confirmed the phase separation and provided information about the droplet size distribution. These finding we compared to Small Angle Neutron Scattering (SANS) experiments in a q-range of $7 \cdot 10^{-5} - 6 \cdot 10^{-1}$ Å^{-1}. Microfluidic experiments where combined with high-speed camera imaging in order to obtain details about the nucleation kinetics. Complementary, a stopped flow setup was used for Time Resolved (TR-SANS) experiments to support the previous results and to determine the growing droplet size within low second to early minute time-scale in situ. For long term droplet growth, Dynamic Light Scattering (DLS) yielded a $t^{1/3}$-dependent growth which indicates Ostwald ripening as dominating mechanism.

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