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Protein Short-Time Diffusion in a Naturally Crowded Environment

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Macromolecular crowding, i.e. the presence of macromolecules at high volume fractions, affects reaction rates and transport processes in the cell. For reliable quantitative models of cellular pathways, the mobility of individual proteins is thus a key information. Often, the protein mobility is modeled by the self-diffusion of colloidal systems. The underlying assumption that neither the shape and size of proteins nor the polydisperse nature of the cytosol matters, has not been checked experimentally so far.
Here, we present a combined experimental-simulational study on the mobility of tracer proteins in cellular lysate [1]. Using quasi-elastic neutron backscattering, we study the mobility of immunoglubulin in deuterated cellular lysate from E.coli. Varying the mixing ratio and volume fraction of protein and lysate, we observe that the immunoglubulin mobility depends on the total volume fraction only. Using Stokesian dynamics simulations, we calculate the mobility of tracers in a model system for the lysate. In the polydisperse lysate, proteins with an average size indeed are slowed down similar to a monodisperse solution of same volume fraction, whereas larger/smaller proteins diffuse slower/faster, respectively. As immunoglubulin is close to the average size, we obtain a consistent picture on the protein mobility in a polydisperse cell-like environment, which is promising for a future quantitative understanding of reaction pathways.
[1] Grimaldo et al. JPCL 2019, 10, 1709

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