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Protein short-time diffusion in a naturally crowded environment

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Knowledge of the protein tracer diffusion constitutes a key element to describe intracellular transport, which can be modeled by the self-diffusion in colloid systems. However, it is necessary to test the underlying assumption that neither the protein shape and size nor the polydisperse nature of the cytosol matter. We present a combined experimental and simulation study of the protein tracer diffusion in deuterated E.coli cellular lysate. Quasi-elastic neutron scattering accesses the short-time diffusion of immunoglobulin (IgG) in this lysate. Varying the mixing ratio and volume fraction of IgG and lysate, we observe that this diffusion only depends on the total volume fraction of macromolecules. Stokesian dynamics simulations confirm that when the tracer size agrees with the average size of the polydisperse lysate, these proteins are indeed slowed down similar to a monodisperse solution of same volume fraction. In contrast, larger/smaller proteins diffuse slower/faster, respectively. IgG being close to this average size, we obtain a consistent picture on the diffusion from simulations and experiments. Ongoing investigations with different tracer proteins in lysate as well as binary mixtures of proteins support this colloid picture of the self-diffusion even in such complex polydisperse cell-like environments, which is promising for a future quantitative understanding of reaction pathways in biology.

References:M. Grimaldo et al., *J.Phys.Chem.Lett.* 10, 1719 (2019), andM. Grimaldo et al., *Quart.Rev.Biophys.* 52, e7 (2019)**Acknowledgement:**

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