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Dynamic cluster formation, viscosity and diffusion in monoclonal antibody solutions

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Antibodies play a crucial role in the immune response of mammals. Monoclonal antibodies (mAbs) are particularly relevant for therapeutics due to their high specificity and versatility. The pharmaceutical challenge is to formulate highly concentrated mAb solutions to achieve a significant therapeutic effect, while keeping their viscosity below the subcutaneous injectability limit [1], thus rendering their administration to patients less difficult and painful. Since the understanding of macroscopic viscosity requires an in-depth knowledge on protein diffusion and dynamic cluster formation [2,3], we study the self-diffusion of five mAbs (produced and characterized at Lonza AG) in aqueous solution as a function of antibody type, concentration and temperature, by quasielastic neutron scattering (QENS). QENS allows to determine the hydrodynamic mAb cluster size [4] and to probe the internal mAb dynamics. A subset of mAbs was studied using small angle neutron scattering (SANS) to understand the nature of mAb-mAb interactions. Complementary information is provided by MD simulations and rheology measurements. As a reference, we use polyclonal antibodies from bovine serum [5].

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[3] M. Heinen, et al., Soft Matter 8, 1404 (2012).
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[5] M. Grimaldo, et al., J. Phys. Chem. B 118, 7203 (2014).

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