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Dynamic cluster formation, viscosity and diffusion in monoclonal antibody solutions

Antibodies play an essential role in the immune response of mammals. Monoclonal antibodies (mAbs) are particularly relevant for therapeutic approaches due to their high specificity and versatility. The pharmaceutical challenge is to formulate highly concentrated antibody solutions to achieve a significant therapeutic effect, while minimizing their viscosity and keeping it under the subcutaneous injectability limit [1], thus rendering the drug 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 of the IgG1 subtype (produced and characterized at Lonza AG) in aqueous solution as a function of the type of antibody and of their concentration, by quasi-elastic neutron scattering (QENS) and small angle neutron scattering (SANS). QENS allows to determine unambiguously the hydrodynamic mAb cluster size [4] and to gain information on the internal mAb dynamics, while SANS has been crucial to obtain information on sample structure and on the nature of interactions occuring among mAb molecules. The instruments employed for data collection are the spectrometer IN16b (ILL) and D11 (ILL).
Complementary information is provided by molecular dynamics (MD) simulations and rheology measurements.
As a reference, we use polyclonal antibody (IgG from bovine serum) solutions [5], thus obtaining a comprehensive picture of mAb diffusion.

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