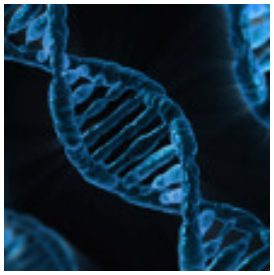

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KEYNOTE 9 - Role of shape anisotropy in interpreting small angle X-ray scattering (SAXS) studies on concentrated protein solutions

Tuesday 5 June 2018 14:40 (40 minutes)

There is a need for achieving high protein concentration liquid formulations of antibody therapeutics to meet patient dose requirements. Predicting the concentrated solution behaviour requires understanding how to map protein-protein interactions on simplified models, which account for the relative contributions from repulsive and attractive forces, shape and interaction anisotropy, and any effects due to intra-molecular flexibility. The overall aim here is to examine applicability and limitations of spherical versus anisotropic-shaped models for proteins in describing the thermodynamic properties and structure of concentrated solutions as probed by small angle X-ray scattering experiments on solutions of a monoclonal antibody or albumin. We show that an ellipsoidal versus spherical model provides an improved description for the excluded volume contribution to the thermodynamic properties and solution structure in concentrated albumin solutions. Molecular simulations of a three bead model for the antibody molecule, which is capable of reproducing generic features in the effective structure factor profile, indicates contributions from intra-molecular correlations can only be separated out for q values corresponding to characteristic separations greater than a protein diameter. Nevertheless fitting to integral equation calculations of the spherical structure factor over this limited q-range can still discriminate between steric-only models and models including an electrostatic repulsive potential with physically realistic charge parameters providing evidence that spherical models are accurate for interpreting longer-ranged repulsive forces.

Author: Prof. CURTIS, Robin (University of Manchester)

Presenter: Prof. CURTIS, Robin (University of Manchester)

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