Reversible cluster formation in concentrated monoclonal antibody solutions

P. DOUGLAS GODFRIN, University of Delaware, LIONEL PORCAR, PETER FALUS, Institut Laue-Langevin, ISIDRO ZARRAGA, Genentech Inc., NORM WAGNER, University of Delaware, YUN LIU, University of Delaware/NIST — Protein cluster formation in solution is of fundamental interest for both academic research and industrial applications. Recently, industrial scientists are also exploring the effect of reversible cluster formation on biopharmaceutical processing and delivery. However, despite of its importance, the understanding of protein clusters at concentrated solutions remains scientifically very challenging. Using the neutron spin echo technique to study the short time dynamics of proteins in solutions, we have recently systematically studied cluster formation in a few monoclonal antibody (mAb) solutions and their relation with solution viscosity. We show that the existence of anisotropic attraction can cause the formation of finite sized clusters, which increases the solution viscosity. Interestingly, once clusters form at relatively low concentrations, the average size of clusters in solutions remains almost constant over a wide range of concentrations similar to that of micelle formation. For a different mAb we have also investigated, the attraction is mostly induced by hydrophobic patches. As a result, these mAbs form large clusters with loosely linked proteins. In both cases, the formation of clusters all increases the solution viscosity substantially. However, due to different physics origins of cluster formation, solutions viscosities for these two different types of mAbs need to be controlled by different ways.

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