Experimental report

06/05/2017

Proposal: TEST-2214 **Council:** 10/2012

Title: Exploring diffusion and internal dynamics of protein

Research area:

This proposal is a new proposal

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Samples: Lysozyme protein
Dendrimers
Monclonal Antibody
partially deuterated L64

Instrument	Requested days	Allocated days	From	To
IN15	6	6	12/07/2013	19/07/2013

Abstract:

Studying Hierarchical Cluster Formation in Concentrated Monoclonal Antibody Formulations

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Monoclonal antibody (mAb) based therapeutic drugs have been the fastest growing sector of the biopharmaceutical industry. Understanding and controlling the viscosity of concentrated mAb formulations are very important for the productions and delivery methods. In order to understand the viscosity change of one mAb, which is named mAbG, in different solvent conditions, D33 is used to measure the solutions structures of mAbG with different concentrations and at different salt conditions. Some of SANS patterns of mAbG are shown in Figure 1. By analyzing the data carefully, it is observed that by adding salts (50mM Na_2SO_4), it can cause mAbG to form dimers. The fitting results also indicates that the dimer form extended structures. Further SANS analysis show that there is an attraction between these dimers so that the large transient protein network can be formed in concentrated protein solutions that can cause the dramatic increase of the viscosity.

We also studied the short-time self-diffusion coefficients shown in Figure 2. Our results indicate that adding salts drive the formation of dimers consistent with the results obtained by SANS data. As a result, the moving unit of proteins moving inside the solutions after adding salts can be considered to be dimers. These dimers form large loosely connected network.

Hence, combining with D33 (SANS) and IN15 (NSE), we have a comprehensive physical picture of the microstructure and dynamics of mAbG protein solutions. Our study together with other experimental information has been published in 2016.[1]

Reference:

[1] Godfrin PD, Zarraga IE, Zarzar J, Porcar L, Falus P, Wagner NJ, Liu Y: **Effect of hierarchical cluster formation on the viscosity of concentrated monoclonal antibody formulations studied by neutron scattering**. *The Journal of Physical Chemistry B* 2016, **120**:278-291.

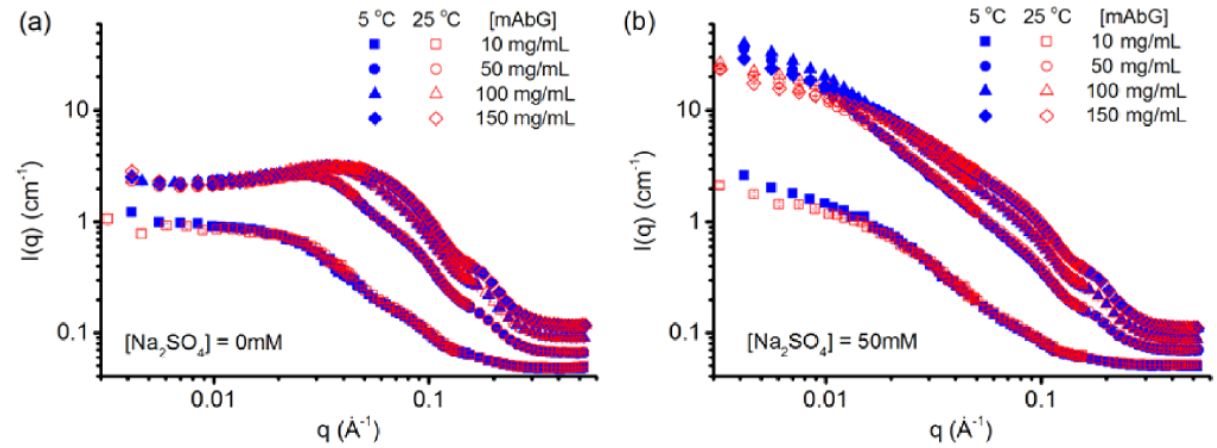

Figure 1. SANS data of mAbG at different concentrations without additional salts (a) and with 50mM Na_2SO_4 (b). The results are published in Ref. [1].

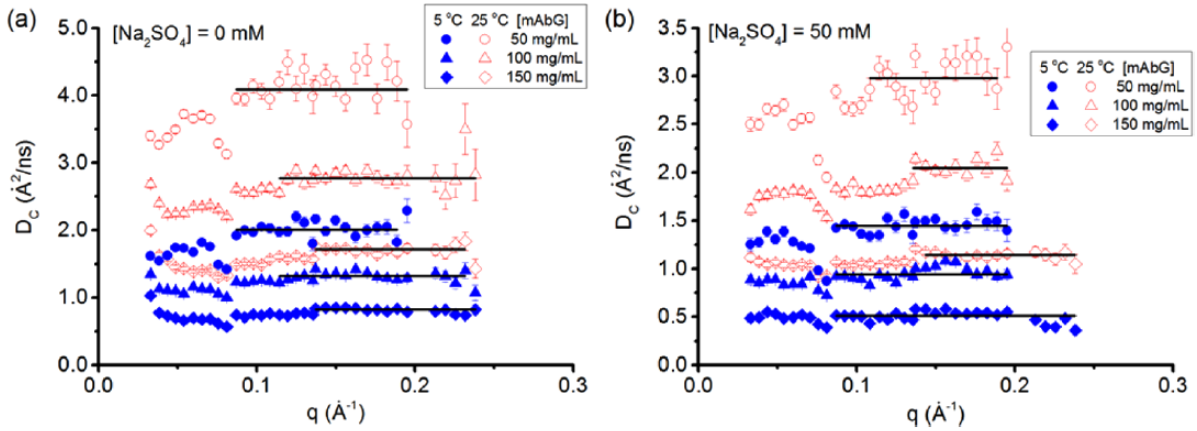

Figure 2. Short-time diffusion coefficients of mAbG at different concentrations without additional salts (a) and with 50mM Na_2SO_4 (b) measured by IN15. The results are published in Ref. [1].