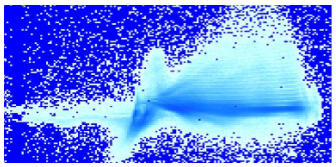

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Probing protein dynamics using XPCS despite radiation damage.

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X-ray Photon Correlation Spectroscopy (XPCS) is a well-established technique to study slow dynamics in disordered materials at nanometer down to angstrom length scales [1]. The method exploits the coherent fraction of the synchrotron radiation and benefits enormously from the recent upgrade of the ESRF source (EBS) [2]. The high degree of coherence opens new avenues for application of XPCS. One of the promising avenues is the study of dynamics in concentrated protein solutions at nearest neighbor distances. Diffusion of proteins on length scales of their own diameter in highly concentrated solutions is essential for understanding biological systems such as a living cell, but its experimental characterization remains a challenge. Our work addresses this problem and discusses the use of X-ray Photon Correlation Spectroscopy at a recently upgraded 4th generation synchrotron source for this purpose. While X-ray radiation damage was generally believed to seriously
threaten the application of XPCS to biological systems, we now present a dedicated experimental and analysis strategy [3] to overcome this obstacle. We report a successful test of this approach to highly concentrated solutions of the eye lens protein alpha crystallin [4], which has previously been established as a model protein exhibiting the classic behavior of hard sphere colloids under these conditions [5]. The thus obtained intrinsic relaxation times for so-called long-time cage diffusion indeed agree with macroscopic measurements of the zero shear viscosity [6]. Our experiments also reveal a complex dependence of the key structural and dynamic properties of the protein solutions on both the total absorbed radiation dose as well as the dose rate. We discuss possible mechanisms responsible for the observed radiation effects and their consequences for future applications of XPCS.

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