# Probing Structure and Mobility of Proteins in the Amorphous State at Low Hydration

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The characterization of proteins in the dry state has implications for the pharmaceutical industry, since it provides deeper understanding of the effect of lyophilization on the stability and biological activity of bio-macromolecular drugs. We have performed structural and dynamical analyses on a series of lyophilized and hydrated bio-macromolecules with varying degrees of structural complexity by means of Molecular Dynamics (MD) simulations; the simulated dynamical results being compared to experimental findings obtained from neutron scattering.
In recent years, molecular dynamic simulations (both coarse grain and atomistic) have provided insight into the structure and dynamics of bio-materials that has helped elucidate results from laboratory techniques. However, atomistic simulation of lyophilized proteins is still a challenge since the available force fields, and water molecule topology, used for the modelling must be carefully correlated with experiment. Fortunately, the outputs from Molecular Dynamics simulations, in particular the time and length scales probed, align directly with those accessed by neutron scattering. The method of Quasi-Elastic Neutron Scattering (QENS) can be used to investigate picosecond to nanosecond dynamics of macromolecular species and thus help validate the efficacy of the MD protocols applied [1].
Here we report on the simulated effect of temperature and hydration on the structural features of the proteins, focusing particularly on the predicted changes in secondary structure and radial distribution of solvent molecules. We also present a comparison of the temperature dependence of the mean squared displacement (msd) parameter, obtained by analyzing the MD trajectories, with those resulting from experimental QENS measurements [2,3].
Our simulation protocols have proven themselves to be good starting points for the development of computational methods for the characterization of structural and dynamical properties of lyophilized and hydrated proteins.

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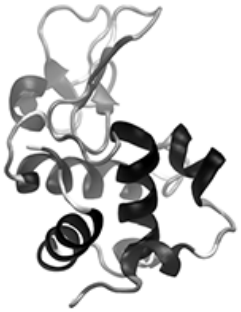

Figure 1.Visual representation of the hen egg white Lysozyme (pdb code: 1AKI) crystallographic structure.

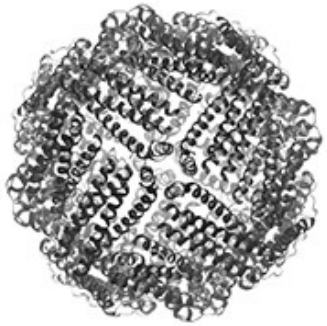

Figure 2. Visual representation of the horse spleen Apoferritin (pdb code: 2W0O) crystallographic structure.

Figure 3. Visual representation of the bovine Insulin (pdb code: 2A3G) crystallographic structure.