Experimental report

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Proposal: 8-03-807 **Council:** 4/2014

Title: Towards a Fuller Understanding of Salt-Bridges in Proteins

Research area: Biology

This proposal is a new proposal

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Samples: Ammonium Acetate, Guanidimium Acetate, Sodium Acetate, Tetramethylammonium acetate and acetic acid solutions

Instrument	Requested days	Allocated days	From	To
D4	5	4	11/09/2014	16/09/2014

Abstract:

Recent studies have cast doubt on the validity of salt bridge forcefields widely used in molecular dynamics. D4C remains one of the few instruments that can structurally examine this problem. The goal of this experiment is to acquire data that can be used to assess the validity of the protein force fields for salt bridges. This will be done by measuring first order neutron scattering differences on various aqueous acetate solutions. Isotopic substitution (H/D) will be performed on the acetate ions, with this ion being used as a proxy for the anionic part of the salt bridge. Similar experiments will the be performed with different counterions (chosen as proxies for the cation part of the salt bridge). This data, combined with molecular dynamics simulations of the same systems will allow for an accurate assessment of the validity of the protein forcefields and allow greater structural insight into these systems.

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The object of the proposed experiment was to obtain structural data on aqueous systems that could yield an insight into salt bridges in biological systems. Salts of acetic acid were chosen as a topic of study as they closely represent the side chains of both glutamic and aspartic acid (the two common anionic amino acids, and the negative half of salt bridges). The cations ammonium and guanidinium were chosen as proxy mimics of the amino acid side chains of lysine and arginine respectively. The tetramethyl ammonium cation was also examined as a proxy for the choline head group of lipids. In total, solutions of LiAc, NaAc, KAc, GdmAc, NH_4Ac and TMAAc were studied.

Total scattering patterns were measured on H and D substituted acetate solutions. The first order neutron diffraction with isotopic substitution (NDIS) function was then obtained from these two data sets. The NDIS function contains the structure of nuclei around the substituted nuclei. This NDIS function was obtained firstly in H_2O and secondly in D_2O. From these measurements it is possible to obtain just the structure of the exchangeable hydrogens in the system around the substituted nuclei. Further by comparison of the first order difference with the ammonium and guanidinium counter-ion it is possible to see how the solvation of the acetic acid ion varies with the cation. Similar comparisons can be done with the other data sets.

Data was acquired on all the relevant solutions, as well as on the empty bell jar, the empty cell, and vanadium standard. All the total scattering data was corrected for multiple scattering and absorbtion effects. From each H and D substituted acetate solution a first order NDIS function was calculated (see figure 1).

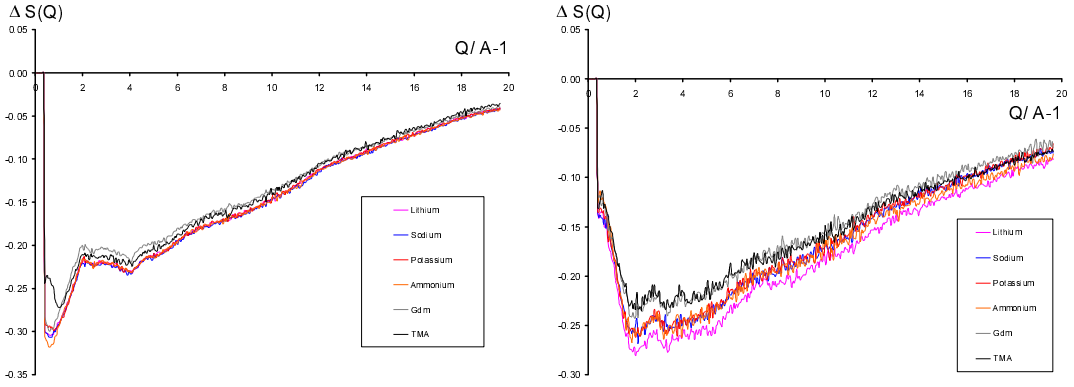

Figure 1. Shown on the left are the first order NDIS difference (H/D substituted acetate) in D_2O, and shown on the left are the same functions for the H_2O solutions. In each case the concentration of the acetate ion is 2 molal.

This data will now be used in conjunction with molecular dynamics simulations to gain an insight into the relevance of these measurements.