Experimental report

12/09/2016

Proposal: 8-03-844 **Council:** 10/2014

Title: Towards a fuller understanding of protein lipid interactions

Research area: Chemistry

This proposal is a new proposal

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Samples: aqueous solutions (~2m) of tetramethylammonium chloride and model hydrophobic species such as propanol

Instrument	Requested days	Allocated days	From	To
D4	6	3	01/08/2015	06/08/2015

Abstract:

Recently we used neutron scattering data acquired on D4C to reveal significant shortcomings in the molecular dynamics forcefields for ions. Here we will extend this study to include an ion of critical importance in biological systems- tetramethylammonium.
The tetramethylammonium occurs in almost all biological systems, however arguably its most important role is in the head groups of phosphatidylcholines bilayers. Its interaction with membrane proteins is currently a topic of great scientific data.
We will use neutron scattering data acquired on D4C alongside molecular dynamic modelling to examine aqueous interactions of the tetramethylammonium ion with water and other solutes of biological relevance. Specifically this data will be acquired using the technique of neutron scattering with isotopic substitution (NDIS) on the non-exchaneable hydrogens on the tetramethylammonium ion. This data will then be combined with the technique of internal coordination number concentration invariance (ICNCI) to yield information about the solute-solute interactions of this ion.

Experimental report on proposal 8-03-844

Towards a fuller understanding of protein lipid interactions

Our goal in this experiment was to examine the tetramethylammonium ion by neutron scattering. The tetramethylammonium ion is particularly well suited for the method of neutron diffraction with isotopic substitution (NDIS) as it contains 12 identical non-exchangeable hydrogens that can be substituted for deuterium. In practice this means that merely a 2 molal D_2O solution of tetramethylammonium chloride yields a first order NDIS function with almost 150mb of contrast.

$$\Delta S(Q) = 88.3\ S_{HsubHex}(Q) + 39.2\ S_{HsubO}(Q) + 6.5\ S_{HsubC}(Q) + 2.3\ S_{HsubN}(Q) + 2.3\ S_{HsubCl}(Q) + 6.1\ S_{HsubHsub}(Q)$$

Our first objective in this experiment was to study the hydration of the tetramethylammonium ion. This motif is interesting due to the ubiquitous nature of this motif in biochemistry, most notably in the headgroup of phosphocholine lipids.

Our second objective was to study how this motif interacted with tertiary components added to the system. These components were chosen due to their solubility and their structural similarities to general biological motifs. Glucose was chosen to represent the sugars. Acetone was chosen as a simple proxy for ketone/ amide groups. Pyridine was chosen to represent aromatic groups and tetrahydrofuran was chosen to represent small aliphatic groups. While it is good to perform these experiments in D_2O (due to the low coherent scattering cross section of deuterium), more information is obtained if the experiments are also performed in H_2O.

Total scattering patterns were obtained on all the samples as set out in the proposal.
2m *h*TMACl D_2O, 2m *d*TMACl D_2O
2m *h*TMACl H_2O, 2m *d*TMACl H_2O
2m *h*TMACl D_2O 2m THF, 2m *d*TMACl D_2O 2m THF
2m *h*TMACl H_2O 2m THF, 2m *d*TMACl H_2O 2m THF
2m *h*TMACl D_2O 2m Pyridine, 2m *d*TMACl D_2O 2m Pyridine
2m *h*TMACl H_2O 2m Pyridine, 2m *d*TMACl H_2O 2m Pyridine
2m *h*TMACl D_2O 2m Acetone, 2m *d*TMACl D_2O 2m Acetone
2m *h*TMACl H_2O 2m Acetone, 2m *d*TMACl H_2O 2m Acetone
2m *h*TMACl D_2O 2m Glucose, 2m *d*TMACl D_2O 2m Glucose
2m *h*TMACl H_2O 2m Glucose, 2m *d*TMACl H_2O 2m Glucose

This data was then corrected for multiple scattering and absorbtion before the first order NDIS functions ($\Delta S(Q)$ were calculated in H_2O and D_2O (Figure 1).

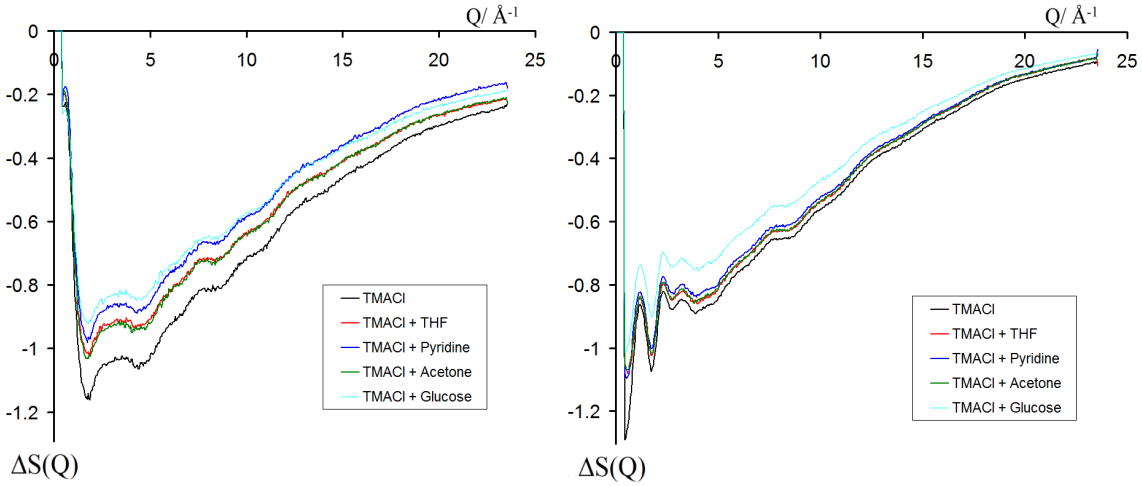

Figure 1. Shown left is the first order NDIS function ΔS(Q) measured in H_2O, and right is shown the same functions but measured in D_2O for each of the solutions in this study.

The second phase of this project is to perform molecular dynamic simulations on the systems that were studied in this experiment. These will be compared to the neutron scattering data to assess the accuracy of these force fields, and if the forcefields are providing a good fit to the experimental data, the simulations will be used as an interpretive aid for the neutron scattering data.

We are currently in the process of performing these simulations and finishing the analysis.