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## RESEARCH INTERESTS

### William S. Price

My research interests lie at the fundamental end of Nanotechnology and Nanobiotechnology, especially molecular dynamics in biological and chemical systems using nuclear magnetic resonance (NMR) imaging (aka MRI) (1), relaxation and pulsed gradient spin-echo NMR diffusion measurements (2). My research has direct applications to a wide range of practical problems including pharmaceutical screening and lithium batteries (3).

Some current areas of interest include:

#### **MOLECULAR MECHANISMS OF IONIC CONDUCTION**

Lithium salt - polymer electrolytes have attracted considerable interest due to their high ionic conductivities ( $10^{-3}$  S cm<sup>-1</sup> or higher) and technologically important applications such as in all solid-state batteries, capacitors and electro chromic window displays. The use of multinuclear PGSE NMR allows the diffusion of all of the species in the conducting polymers (i.e., polymer, anion, cation, solvent) to be measured and thereby affords a much deeper understanding of the underlying conduction mechanisms (4-6).

External collaborators: Prof. Kikuko Hayamizu (Agency of Industrial Science and Technology, Japan) and Dr. Yuichi Aihara (Samsung, Japan)

#### **PROTEIN ASSOCIATION AND CRYSTALLISATION**

Protein self-association is of critical importance in a wide variety of situations, ranging from disease states (e.g., Alzheimer's disease) to protein-based drugs and food processing. Importantly, understanding protein association is fundamental to the development of many areas of bionanotechnology and biomedicine. The delicate nature of associating protein systems severely restricts the techniques available for probing the kinetics of association in such systems. Of these techniques, NMR diffusion measurements show great promise. Theoretical models for aggregation kinetics are also developed and compared to the diffusion data (7-9).

External collaborators: Prof. István Fúro (Royal Institute of Technology, Stockholm, Sweden),

#### **DEVELOPMENT OF FAST NMR DIFFUSION SEQUENCES**

Traditional NMR diffusion measurements take on the order of tens of minutes to complete. This limits the applications of these techniques to systems undergoing rapid change (e.g., protein folding). A major interest in my lab is the development of fast diffusion sequences.

#### **DEVELOPMENT OF BETTER WATER SUPPRESSION TECHNIQUES**

The solvent typically gives rise to an intense resonance in NMR spectra that dwarfs those of the species of interest. Indeed, the solvent resonance is often four or more orders of magnitude larger. The large signal also causes other problems such as radiation damping. Consequently,

suppression of the solvent resonance(s) is required to obtain signals from the solutes (10). We have recently developed two NMR diffusion sequences that are particularly suited for measuring the diffusion of biomolecules in aqueous solution (11, 12).

### **EFFECTS OF MACROMOLECULAR CROWDING ON MOLECULAR ASSOCIATION**

A major problem is that experiments are conducted *in vitro* with environments far different than what occurs *in vivo*. For example, in biological cells, macromolecules typically occupy 20-30% of the total volume. This volume exclusion has profound thermodynamic consequences and can result in rates and equilibria differing by three orders of magnitude from those determined *in vitro*. As well as raising grave questions about the significance of *in vitro* studies, it demonstrates an enormous void in our understanding. In fact, crowding is rarely discussed in biology and biochemical textbooks. From the nanotechnological perspective it represents an untapped resource.

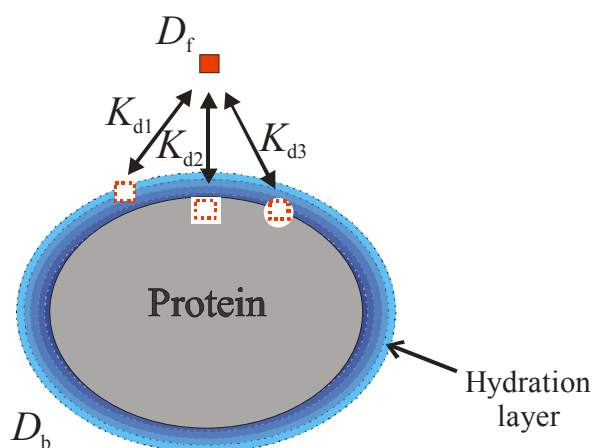
### **THEORETICAL/EXPERIMENTAL STUDIES OF RESTRICTED DIFFUSION IN POROUS MEDIA**

Real materials are often porous in that they are in essence a 'solid' with holes and the boundary conditions are more complex. A porous material is composed of at least two phases: the porous matrix and the pore space which is filled with a liquid or gas. The porous matrix is not necessarily solid in a rigid sense. Examples include biological tissues (e.g., brain), cellulose fibres, ceramics, concentrated emulsions, gels, porous rocks, soil and solid catalysts, and zeolites. Consequently, apart from free solutions, almost all samples of interest come under the porous material category including concentrated macromolecular solutions that will exhibit properties such as obstruction (see below). Most porous substances have a disordered morphology and it is difficult to specify the geometry of the interface between the pore space and the matrix. The transport and thermodynamic properties of fluids in porous media is closely related to the sizes and connectivity of the pores. We are working on NMR sequences and theoretical models for the studies of such systems (13-15).

External collaborators: Prof. Olle Söderman (University of Lund, Sweden).

### **NMR STUDIES OF LIGAND BINDING**

At the simplest level, PGSE measurements can be used to separate non-binding from binding ligands on account of the decrease in the observed diffusion coefficient when a ligand is in fast exchange between being in free solution and being transiently bound to the large (and therefore slowly diffusing) macromolecule. Other studies using a range of drug:macromolecule ratios can be used to determine binding constants. Further, macromolecules have more than one class of binding site for the same drug (e.g., the salicylate – albumin system) and it is pharmacologically important to characterize this type of phenomenon. We are working on more robust diffusion-based approaches to probe ligand binding and developing mathematical models of the phenomena (11, 16, 17).



External collaborators: Prof. Peter Stilbs and Prof. István Fúro (Royal Institute of Technology, Stockholm, Sweden) and Prof. Sergey Traytak (Institute of Applied Mechanics, Russian Academy of Sciences).

#### APPLICATIONS OF NMR MICROSCOPY TO PLANT STUDIES

In collaboration with the National Institute of Agrobiological Resources (Ministry of Agriculture, Japan), I have been applying NMR microscopy to non-invasively study freezing injury in plants (e.g., azalea flower buds, conifer leaf buds etc.) (18, 19).

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