



## News

### FUTURE ACCESS TO NEUTRON FACILITIES: A STRATEGY FOR THE UK

The Council for the Central Laboratory of the Research Councils (CCLRC) was asked in 2005 by the Minister for Science and Innovation, Lord Sainsbury, to lead a review entitled "Future Access to Neutron Facilities: A Strategy for the UK". The conclusions to this consultation with neutron user community, stakeholders and international experts has now been published a PDF format of the report can be found at the following links. [Future access to neutron sources: A strategy for the UK \(PDF, 2MB\)](http://www.isis.rl.ac.uk/aboutIsis/Future_access_to_neutron_sources.pdf)



[[http://www.isis.rl.ac.uk/aboutIsis/Future\\_access\\_to\\_neutron\\_sources.pdf](http://www.isis.rl.ac.uk/aboutIsis/Future_access_to_neutron_sources.pdf)]

## Spotlight

### NSG - Willis prizewinner 2006 Dr Giovanna Fragneto



The Neutron Scattering Group of The Institute of Physics and the Faraday Division of the Royal Society of Chemistry have

established a Prize for outstanding neutron scattering science. The prize is named in honour of the founding

chairman of the Neutron Scattering Group, Professor B T M Willis and is awarded annually.

The 2006 prize was awarded by Professor Willis to Dr Giovanna Fragneto at the annual Neutron and Muon Beam Users Meeting, NMUM at Warwick University in March.

### NEUTRONS & CELL MEMBRANES



Dr Giovanna Fragneto

ILL, 6, rue Jules Horowitz  
BP 156 - 38042 Grenoble Cedex 9  
France. email: [fragneto@ill.fr](mailto:fragneto@ill.fr)

Membranes are ubiquitous in living material and carry out highly specialised functions. They surround both cells (plasma membranes) and organelles within cells and represent the surface through which interaction occurs with the outside world. Cell membranes consist mostly of lipids and proteins although sterols are other important constituents that, for example, can make up to 20 wt. % of the lipid composition of plasma membranes. Lipids are amphiphilic molecules consisting of a hydrophilic head and hydrophobic double chains (saturated and un-saturated). They form a continuous bilayer, which acts as a barrier to water soluble molecules and provides the framework for the incorporation of membrane proteins.

Scientists have been well aware for a long time of the importance of lipid structural properties for understanding functional mechanisms at membrane surfaces and studies on lipid bilayers have proliferated in the 70s and 80s. In the last few years we have witnessed the revival of this classical approach for mimicking cell membranes. This is due mainly to the availability of a certain number (although still low) of membrane protein structures, that have elucidated some of the mechanisms happening at cell surfaces, and to the advent of new or improvement of existing structural techniques enabling studies of single bilayers with a fraction of nanometer resolution.

A biologically relevant model membrane should have a composition that matches the lipid content of the real cell

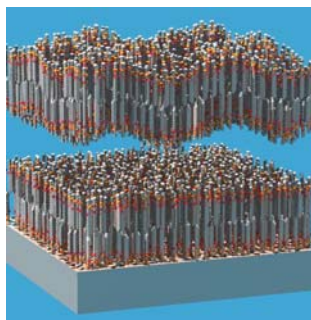
membrane under investigation; it should be highly hydrated (ideally it should lie in aqueous environment); it should interact with other biological species and be free enough to allow for movements, both out of plane, since the bilayer position fluctuates, and in plane, as in real membranes the molecules freely diffuse within the bilayer. In practice, compromises are usually made to accommodate for experimental difficulties and scientific choices.

Phospholipids present a variety of different phases as temperature is changed. Going from high to low temperature, they overcome the fluid to gel phase transition at a temperature commonly known as  $T_m$  (melting temperature). While in the fluid phase,  $L$ , lipid chains are in a liquid-like conformation and mobile in the lateral direction, in the gel phase,  $L'$ , chains are stiffer. For some lipids, just below  $T_m$ , there is the so-called ripple phase,  $P$ , where the lamellae are deformed by a periodic modulation. In nature bilayers are fluid, but the fluidity of the bilayer is not always a necessary prerequisite for function.

Several models for membranes consisting of phospholipid bilayers have been developed and characterised over the years. A good deal of structural work and studies of the various lipid phases has been done using either multilamellar vesicles or stacked bilayers. More recently monolayers at the air/water interface or supported bilayers at the solid/water interface have attracted the interest of scientists since they allow for the study of one or few monomolecular layers and detailed information can be obtained in selected parts of the layers.

The focus of my work in recent years has been the study of supported bilayers characterised with reflectivity techniques using either neutron beams or synchrotron radiation, as well as studies of interactions of these bilayers with cholesterol, peptides, proteins, enzymes, cationic lipoplexes, etc

Supported lipid bilayers can be deposited on solid substrates in various ways. Well defined structures can be obtained with modified Langmuir troughs and the so-called Langmuir-Blodgett or Langmuir-Schaeffer techniques. A major advantage of this model for membranes is the fact that the bilayer is immersed in aqueous solution and that information on a single bilayer can be obtained.



Artist view of a supported double bilayer

A major inconvenient of single adsorbed bilayers is their strong interaction with the solid substrate (mainly

electrostatic), which can change the lipid phase behaviour and does not allow for studies of the translocation of peptides or proteins through the bilayer. For this reason different systems are being developed where the bilayer interaction with the substrate is screened by another layer consisting of either polymers, polyelectrolites, self-assembled monolayers as well as lipids.

We have succeeded in the preparation of stable and reproducible double bilayers, in which the second bilayer floats at 20-30Å on top of the first one (see Figure 1). This system has made it possible to perform reflectivity studies on a highly hydrated, accessible and fluctuating bilayer, where the composition of each leaflet can be chosen separately. It has proved to be very useful to probe bilayer-bilayer interactions, and showed to be stable after inclusion of cholesterol as well as of charges in water and in the bilayer, so that interactions with other molecules relevant for biology studies can be determined in physiological buffer.

Neutron and x-ray specular reflectivity allow for the determination of the structure of matter perpendicular to a surface or an interface. Specular reflectivity is very sensitive to thin layers (down to a few Ångstroms) or small changes within layers. It requires well-defined samples very flat and with roughness as small as possible.

For high-resolution studies, the use of synchrotron beams (high intensity and low divergence) is necessary. Neutron reflectivity is more widely used for the investigation of buried interfaces. For soft-matter systems the major advantage over synchrotron radiation is that neutrons are non-destructive. High resolution can be obtained for aqueous systems when it is possible to measure the reflectivity profiles of the same sample with different  $H_2O/D_2O$  contents and different deuterium labelled components at the interface.

Neutron specular reflectivity studies of double bilayers have enabled the determination of structural changes occurring at the lipid gel to fluid phase transition and the values of the swelling of the water layer between the two bilayers have been used to calculate theoretically the bending modulus of the bilayers in both phases. A series of phospholipids have been used mainly phosphocholines with saturated double chains with number of carbon atoms per from 16 to 20. In agreement with literature data and theoretical predictions, a minimum of the bending modulus was found around the main phase transition for all species. This was the first time the determination was possible with the same sample in the two lipid phases. The same study has been carried out with double bilayers containing 1 to 10% mol:mol cholesterol and it was shown that increasing amounts of cholesterol lead to an increase of the roughness of the layers accompanied by a decrease of the fluctuations around the lipid phase transition.

Synchrotron radiation specular and off-specular data were the collected for the first time on supported single and double phospholipid bilayers in water. The spatial resolution is much better than from similar work with neutrons (max  $q$  measured was  $10 \text{ nm}^{-1}$ ) nevertheless work with neutrons results complementary since it

enables a better determination of the composition of the layers (in particular the water content within the bilayer). The interfacial structure and fluctuations were determined. The first adsorbed layer does not contribute to the scattering signal. The presence of the silicon substrate and water medium leads to a low signal, but the floating bilayer presents large fluctuations that facilitate data analysis. Not only fluctuations in height, but also in density and thickness, were detected and analysed.

By fitting the data within a model of thermal fluctuations, it was possible to determine the value of the bilayer tension and rigidity modulus. Results indicate values of the tension constant over the two examined lipid phases and equal to 0.1mN/m and bending modulus of about 300  $k_B T$  in the gel phase and 10-30  $k_B T$  in the fluid phase, where  $k_B$  is the Boltzmann constant and  $T$  the temperature. Perspectives of this work include the possibility of detecting how adsorbed peptides or proteins correlate with the bilayer fluctuations in position, density, thickness, and possibly lipid composition. Joint X-ray (for resolution) and neutron (for composition) investigations could be sensitive to the overall shape, orientation and position of the protein itself. The position and orientation of peptides, which are more difficult to detect because small, in principle can be determined as well.

Several collaborations are in progress involving the use of the reflectometer D17 at the ILL to look at the interaction of lipid bilayers with different biological systems. These include the study of the structure at cell surfaces of the Neural Cell Adhesion Molecule: a parallel neutron and x-ray study supported one of the two adhesion mechanism found in the literature and helped the interpretation of the switching mechanism from adhesive to non adhesive induced by ionic strength in the presence of polysialic acid (D. Leckband, et al.). Another example is the study of the structure of the translocation domain of Diphtheria toxin at different pHs with lipid bilayers, the insertion mechanism being pH dependent (V. Forge et al.). The fate of the hydrolysis products after the action of the enzyme phospholipase  $A_2$ , ubiquitous in the human immune system, on supported bilayers was determined (H. Wacklin et al.). Neutron reflectivity is also being used to determine the interactions of lipid:DNA complexes, used in gene therapy, with a model cell membrane comprising a supported phospholipid bilayer. The effect of different additives to cationic vesicles interacting with the membrane suggested that the rate of exchange of lipid between the lipid:DNA complexes and cell membranes may play a key role in determining the transfection efficiency of cationic lipid:DNA complexes (J. Lawrence et al.).

Structural determination is an important pre-requisite to understand function. There is a great variety of phenomena happening at membrane surfaces and the availability of high flux neutron reflectometers and 3<sup>rd</sup> generation synchrotron beams will be of enormous importance for structural characterisations in the fraction of nanometer scale.

NSG is a joint subject group of Institute of Physics and the Royal Society of Chemistry and represent the interests of Neutron Scattering community.

## Prize

### *Neutron Scattering Group – Willis prize*

Nominations for the 2007 prize should be forwarded to Professor Don McKPaul.

[D.M.Paul@warwick.ac.uk](mailto:D.M.Paul@warwick.ac.uk)

## Conference Report

*NPNMS 2006*



This year's New Perspectives in Neutron and Muon Science meeting was held at Warwick University on the 30th and 31st March, immediately after the Neutron and Muon Users Meeting. It provided an opportunity for around 25 young researchers to meet and present their work to one another.



Talks were given on a wide range of topics including frustrated magnetism, structural glasses, microemulsions, and residual stress in superconductors. Pete Dowding's invited talk on the industrial use of neutrons to investigate surfactants added to fuels was well received. A social event was held in the Graduate Bar of the Warwick Student Union, whose free T-shirts offer proved popular. The meeting closed with the prize for the best talk being presented to Antonios Konstantopoulos, from Manchester University, for his talk on the 'Characterization of octapeptide systems using Neutron Scattering'.

The programme committee of *Nicola Wilson (chair), Sarah Rogers, Anna Rodriguez, and Peter Baker* would



like to thank the Neutron Scattering Group for funding the meeting, Emma Barney for assistance during the meeting, and Pete Dowding for his talk.

## ICNS 2005 SYDNEY, AUSTRALIA

Arthur Lovell, Helen Walker, Ross Springell



The eighth International Conference on Neutron Scattering took place in Sydney in November/December 2005. It was the first occasion on which this quadrennial meeting has been held in the Southern Hemisphere but it is timely as Australia has a growing neutron scattering community and is currently building its first neutron facility. There was major representation from the 4500-strong European scattering community including five from UCL's CMMP group. The conference was a chance to explore the many cross-discipline successes of the technique, current research and future directions.

The conference setting would certainly take some effort to better: the Sydney Convention Centre lies in the redeveloped Darling Harbour. With a necessary day free prior to the start of the conference to fight our body clocks and reel in some of that sleeping that I don't do on planes, we discovered that Sydney was lively and inviting, with one of the greatest natural settings in its huge harbour and ocean beaches. And that it was cold and wet!

The conference was opened by singing and dancing representatives of two Aboriginal peoples from New South Wales. The sheer breadth of topics presented and discussed demonstrated the universality of neutrons as a condensed matter probe. Up to three or four sessions took place simultaneously so inevitably it was not possible to attend everything of interest. Among the presentation highlights were Open University's Lyndon Edwards' talk on structural integrity through neutron-based residual stress measurements, demonstrating a use for neutrons in expert legal testimony, and Gabriel Aeppli of CMMP who delivered a well-received keynote talk on the use of neutrons for nanotechnology. The heads of other international scattering facilities gave often entertaining resumés of their construction and improvement work – it is an exciting time as new neutron sources are being built in Japan and the US, a second target station at ISIS in the UK, and of course the new Australian source, OPAL.

We presented our work in two poster sessions. With over 800 abstracts received, it was fortunate there was a lot of space! It was a great opportunity to speak to others about their research and we met those involved in similar work to us including some very famous names in neutrons. We collected some handy contacts and met some old friends, as well as making new ones throughout the week.

One of the highlights of the meeting was a tour of OPAL, situated at the Australian Nuclear Science and

Technology Organisation (ANSTO) site at Lucas Heights. This is some 30km from central Sydney. Security was tight: only a few weeks before, an alleged plot to attack Oceania's sole nuclear reactor on the site had (allegedly, okay) been foiled. OPAL, due to come on stream in 2007, will use a replacement reactor as a neutron source. The Australians, with exhilarating abandon, have decided to name all their instruments after antipodean icons and ignore gloriously the chance to squeeze painful acronyms out of them. So: Echidna, Platypus, Wombat and so on. Only Koala, a QUAsi-LAue Diffractometer, holds vaguely to tradition.

Unfortunately none of them are constructed yet, so a little imagination was in order as we walked around the huge hall. We were able to see inside the empty space where the reactor will be, and mock-ups for the beam guides and instrument flooring. The facility once operational will be open to all users via peer-reviewed access but travel expenses may deter those from further afield. Nevertheless it was great publicity for the Australian community.

The conference dinner took place on a sunset cruise about the harbour. The top deck was filled with scientists taking refuge from the main course and a zillion photos. On the final day of the conference awards were presented, including to one of us (RS), who had won one of four Gen Shirane memorial prizes for his poster presentation on U-Fe multilayers. We thanked the organisers for their great hospitality which ensured a successful and enjoyable meeting. As the conference ended the sun was out and we had a few days to explore the city in the pre-Christmas heat!



*A Waiting boarding for dinner*

We are grateful for financial assistance from the IoP Neutron Scattering Group and UCL to make our attendance possible.



*Stephen Shapiro presents Ross with his prize*

## What's on

For a comparative up-to-date list of International & National conferences and other meetings please follow the link at **NSG web pages**.

<http://groups.iop.org/NS/NSG.htm>

### The SAGAMORE XV International Conference on Charge Spin and Momentum Densities



**August 2006**  
**Warwick University**

Please contact: Prof Pam Thomas  
(Tel: +44 (0)2476523354)  
P.A.Thomas@warwick.ac.uk

### Student Bursaries are available

### Neutrons and X-rays as probes of Condensed matter a celebration of the work of Professor Roger Cowley



**Oxford**  
**June 30<sup>th</sup> – July 1<sup>st</sup>, 2006**

Please contact: Dr J P Goff  
[jpgoff@liv.ac.uk](mailto:jpgoff@liv.ac.uk)

Tel: +44(0) 151 794 3418

## Contact

### NSG home page

<http://groups.iop.org/NS/NSG.htm>

**Editor:** A. Zarbakhsh, Queen Mary, University of London.

Contributions for the next issue:

Please e-mail to

[a.zarbakhsh@qmul.ac.uk](mailto:a.zarbakhsh@qmul.ac.uk)

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