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PREFACE

Neutrons in biology: Institut Laue – Langevin, 4–7 September 2005

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The Neutrons in Biology satellite meeting of the Montpellier IUPAB-EBSA Biophysics Congress was held at the Institut Laue – Langevin (ILL) in Grenoble, France, from the 4th to 7th September. It was the first such meeting in recent years, renewing a tradition started in the 1970s at Brookhaven National Laboratory, USA, and a good opportunity to assess past and present achievements in the field and to discuss future developments. The advantages of neutron radiation for the study of molecular structure are based on the fact that they are scattered with similar power by different elements. They can distinguish between hydrogen (H) and its isotope deuterium (D), and they are highly penetrating and non-destructive, thus allowing studies on buried systems. Neutron diffraction experiments at high resolution locate protons in crystal structures even when they are disordered, and at low resolution provide a unique insight into the internal organisation of complex structures by using H-D labelling of the macromolecules or solvent. Neutrons of wavelength in the Ångström range, and their associated energy, exactly match the length and time scales of thermal excitations in condensed matter, making neutron radiation a perfectly suited probe for the experimental study of molecular dynamics in biological macromolecules.

The neutron landscape is now very different from that of 30 years ago. When the ILL user programme started in 1973, neutron diffraction data had been collected from Vitamin B12 at Harwell in the UK, neutron protein crystallography was being developed in Brookhaven to locate protons, biological membranes were studied on dedicated diffractometers in Harwell and Brookhaven, and small angle neutron scattering was applied to solve the quaternary structure of the ribosome. The variety of instruments on high flux beams at ILL significantly extended the range of biological systems and space-time windows covered by the method, and results quickly followed. Now, the ILL remains the most powerful neutron source with the largest instrument park for applications in biology. However, other neutron facilities have introduced instrumentation to make possible certain biological experiments. A new facility has recently become operational near Munich, and next generation pulsed sources are being built in the USA and Japan. The European neutron scattering community is making a strong argument for the building of the European Spallation Source, which should provide a major increase in beam intensities and open up new fields of study. Despite an apparently long list of neutron sources, biology projects are in practice quite restricted because of the strong competition between the different scientific areas for neutron beam time. Considering this, the recent publication record for neutrons in biology is quite impressive.

The Grenoble meeting covered all aspects of the field: high and low-resolution crystallography, small angle scattering, fibre diffraction, membrane diffraction and reflectometry, energy resolved scattering for the study of molecular dynamics. In order to favour cross-disciplinary scientific discussion, the decision was taken not to dedicate oral presentation sessions to specific methodologies, but to have representative talks from

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the different aspects in each session. This led to lively discussion and cross-fertilisation of ideas. Highlights included the location of active site protons in human aldose reductase, a target enzyme for diabetes treatment [1], the solution of the subunit assembly and topology of the Type 1 restriction-modification complex involved in bacterial protection against foreign DNA [2], a complementary X-ray and neutron reflectometry study on the mechanism of cell adhesion by using model membranes at interfaces [3], the determination of the hydrogen bonding pattern and thermal behaviour of cellulose I-alpha and I-beta thus establishing an understanding of the conversion between the two forms [4], the measurement of the thermal fluctuations of protein and RNA in living bacteria to provide a rigidity map of the cell interior and establish the dynamic dimension of adaptation in extremophile organisms [5].

A round-table on 'Sources and Resources' brought forwards the understated role of neutrons in modern structural biology and their power to solve important problems in the post genome sequencing era. Despite significant progress in biochemical and biophysical methods for the deciphering of the large protein and protein-nucleic acid assemblies that constitute the basis of most cellular functions, we still have a lot to learn. Neutrons, and especially small angle scattering methods based on contrast variation, are ideally suited to the study of dynamic macromolecular assemblies. This was demonstrated decades ago by, for example, studies of the interactions between aminoacyl-tRNA synthetases and tRNA [6]. It was work ahead of its time, because crystal structures of the components were not then available. Now, there are more than 32,500 structures in the protein data bank, and in many cases we have high-resolution models of the interacting components in protein assemblies. The round table resulted in a consensus for a concerted action to set up programmes for solution studies of dynamic macromolecular assemblies. The programmes will require a proactive approach on the part of the neutron sources to make available the necessary measuring time on the instruments. As a first step in this direction, EuroBioSANS, an informal association of biological small angle scattering scientists at the different European neutron sources, has been set up to emphasise that for biology studies the sources were not in competition but complementary in making available the best possible environment for successful work in this field.

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