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ROUNDTABLE AT PAW2007

Neutron trends and perspectives in biophysics

One evening during the "Proteins At Work 2007" workshop, which was held in Perugia on May 28 to 30th, the participants gathered in the lecture room to debate the current state and foreseeable future of neutron scattering to study dynamics in biophysics. Chairs were turned around into a truly round-table configuration (minus the table) and a (turned off) wireless microphone served as a "talking stick"—the person holding it claiming the opportunity to speak without being interrupted. The stick was passed around and all of the about 40 participants had their say. All active in biophysics, most were from physics backgrounds with biologists and physical chemists also well represented. Interestingly diverse views were expressed, but a clear consensus emerged that the field would profit greatly from increased contact with the biology community, and a greater integration with other biophysical methods in order to profit from and participate in the exciting current developments in the life sciences. A special effort should be made, therefore, to overcome traditional physics–biology, interdisciplinary communication barriers. In the particular case of experimental molecular dynamics, new approaches should be found to illustrate the relevant quantitative results in a clear, easily understood and evocative way for the non-specialist. The chairman listened and took notes. This is his summary.

Since the first experiments on myoglobin, neutron scattering experiments to study protein dynamics focused mainly on a few model systems and on water, and with good success are unravelling the physics involved in the processes. This is ongoing work, which is now extended to the exploration of the effects of confinement and crowding in conditions more similar to those in the cytoplasm. It is important work because it develops the tools and establishes the general and fundamental aspects of protein dynamics and its environmental dependence. The focus on a few model systems arose from sample availability. The biological slant on the dynamics problem, however, is to understand specific function, i.e. what makes proteins different rather than what they have in common. The difficulty is simply that biologists work with very small amounts of material, usually grossly insufficient for a neutron experiment. Some groups that have close contact with biology have managed nevertheless to overcome this difficulty by choosing appropriate problems to study, making the effort to prepare the material needed or developing approaches to work on whole cells (for which the necessary quantity to make good samples is easily available). At the Perugia meeting about 80% of the talks dealt with the physics of model systems with 20% on biological questions. The field should aim at a better balance. The power of deuterium labelling for the study of complex systems was recalled. The key is, of course: to develop close contacts with biological laboratories that are active in the relevant fields.

A number of biological system families were evoked, the understanding of which would profit greatly from neutron scattering studies of their dynamics. These include membranes and membrane proteins, structural and fibrous proteins, intrinsically unfolded proteins, the process of protein folding and stabilisation, proteins in their cellular environment, molecular dynamics in the different states of a cell, large molecular machines with a variety of activities…

There is a wealth of biological structural information from high-resolution crystallography, but it is now clear that dynamics on a spread of timescales plays an essential role in biological function. The opening up of the neutron field should not be limited to biology, but also to the other biophysical methodologies that addresses dynamics. This is an important point because the complex problem of molecular dynamics in biology is best addressed by an integrated, complementary, trans-disciplinary approach, rather than a multidisciplinary approach of different specialities with apparently no overlap. Special mention was made of time-resolved techniques that provide snapshots of the structural evolution of a process as it takes place for example as a function of temperature, and of NMR that has known great progress for the study of dynamics and is strongly complementary with neutron scattering, and, of course, of molecular dynamics simulations.

There was a lot of discussion on the difficulties of communication between disciplines, and how important it is to develop ways of conveying relevant quantitative information clearly to non-specialists. The gathering was reminded, however, that biologists are not afraid of mathematics and that they recognise the need and importance of quantification (for example in the fast developing field of systems biology). The question was asked: what do physicists mean when they say biology is complex? A biological system is the current end product of evolution, and if it is there it is because it works. The important points are to keep the focus on understanding biological function, and to identify relevant measurable parameters to help our understanding.

It was decided to establish a network of the neutron biological dynamics community with a web page in order to follow up on the points raised during the roundtable. Groups were encouraged to identify hot topics that would inspire young scientists to enter the field. And perhaps the best conclusion for this summary is to quote the participant who said: "… listen carefully to biologists they have questions."

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