Structural proteomics: from the molecule to the system

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Over the next few years, structural proteomics will grapple with the problem of visualizing increasingly elaborate structures, from the atomic details of protein structures up to subcellular structures and the whole cell. A recent EU workshop addressed the question of what experimental and theoretical approaches, technologies and infrastructures this will demand.

An EU workshop entitled "The Direction of Structural Proteomics—From the Molecule to the System" was held on 13–15 November 2006 in Skåvsjöholm, Sweden. The meeting was sponsored by the European Commission (EC) in conjunction with the Forum for European Structural Proteomics (FESP) (http://www.ec-fesp.org). FESP is a Specific Support Action established by the EC, which was assigned a mandate to make recommendations for strategic policy in structural biology and structural proteomics (SB/SP) in Europe over the next five to ten years. For this purpose, FESP is conducting surveys and site visits and, toward the end of this year, will issue a series of reports that will present its recommendations.

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The meeting brought together a body of 40 experts. They included not only structural biologists involved in structural proteomics consortia and other cooperative endeavors in Europe, Japan and the US, but also biochemists, biologists and policy makers. These included three senior representatives of the EC itself, the director of the Department of Ventures and Initiatives of the Wellcome Trust and the director of the US National Institutes of Health Protein Structure Initiative (PSI), as well as a representative of the pharma and biotech industry.

The workshop was constructed as a series of thematic sessions and panels, each involving brief presentations from invited scientists that were followed by extensive discussion. In the informal framework established, this formula worked very well, with discussions continuing into the evening. One set of sessions covered all technologies connected with SB/SP, from X-ray crystallography, NMR and bioinformatics, through EM and protein production, to molecular dynamics and mass spectroscopy (MS). Speakers were asked to consider the directions of development of these areas both in content and in terms of requirements for equipment and infrastructure. Other sessions dealt specifically with issues of policy, management and infrastructure, and a third set addressed the interface between the SB/SP community and other scientific communities, primarily biochemists and biologists. Topics addressed at this latter level included such issues as target selection for structure analysis and the ways in which SB/SP can have an impact on unraveling fundamental cellular processes, thus bridging the gap between atoms and tissues.

Several important issues emerged, the first being that the equipment required to carry out NMR, MS and EM studies, in particular, is becoming increasingly sophisticated and, consequently, expensive. Few, if any, individual laboratories will be able to afford such instruments, and it will most likely be necessary to establish, or to coordinate and reinforce, appropriate national or pan-European centers. It was also clear that support for synchrotron and NMR facilities on a Europe-wide level is vital for maintaining the competitiveness of the European structural biology community.

Structural proteomics is part of larger proteomics and genomics efforts that are generating immense amounts of very diverse data. Processing, archiving, integrating and disseminating these data is regarded as a major challenge for the future. It is crucial that current and future data archives be put on a reliable financial basis that will ensure stability and continuity and will permit them to improve their invaluable services to a large community of researchers in the life sciences.

It was notable that many presentations referred to cutting-edge studies that required the use of complementary methods in order to go forward. Thus, much effort needs to be invested in interfacing between the various SB/SP techniques.

As already perceived by the administrators at the EC who are planning the 7th Framework Programme, a wide interdisciplinary chasm

exists between the SB/SP community and, in particular, other biologists, such as systems biologists and developmental biologists, molecular biologists and geneticists, and immunologists. Because they speak rather different dialects, it is not obvious how the many biologists who lack a biochemical background can fully benefit from the wealth of three-dimensional protein structures that structural biologists and the structural proteomics consortia shower upon them. Serious thought must be given to bridging this gap, for instance by carefully designed training programs and integrated projects in which both structural biologists and other biologists participate and, thus, can interact and collaborate. The EC has already begun funding such interdisciplinary projects, and the scientific officers who attended the workshop indicated that they intend to increase such funding through programs focused on the development of technologies, large-scale data gathering and systems biology.

An issue of which the European scientists are well aware is the enormous power of the high-throughput (HTP) techniques developed in the US PSI and in Japan. The general feeling at the meeting was that it is essential for European science to implement these HTP approaches, albeit by adapting them to mesh with the hypothesis-driven research traditionally done in Europe at the target-selection level. For example, if one wished to solve a difficult membrane protein structure, HTP methods would make it possible to screen a large series of functionally related proteins so as to find candidates that would be well expressed and thus might produce diffracting crystals.

It was the feeling of the members of FESP, and of the EC officer with whom the workshop was organized, that it had indeed fulfilled their expectations, inasmuch as it provided them with ample food for thought that they will have to digest thoroughly *en route* to formulating their recommendations. However, from the presentations and discussions, there also emerged a clear picture of increasing synergy between scientists belonging to the various disciplines within the structural biology community, and a realization that SB/SP methodologies must be efficiently harnessed to benefit life sciences as a whole. It was also clear that structural biologists are increasingly aware that their discipline can play a vital role in going from the molecule up through the cell and on to the organism. Fostering the interaction of structural biologists with other biologists is thus crucial, and making their data readily accessible to these other biologists is a key issue that must be seriously addressed.