INSTRUCT

an Integrated Structural Biology Infrastructure for Europe




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Introduction

Structural biology is a branch of molecular biology concerned with the molecular structure of biological macromolecules such as proteins and viruses. Resolving a molecule's structure can give us insights into the function of a molecule and eventually lead to potential drug targets. Structural biologists use many different techniques (Figure 1) including X-ray crystallography, nuclear magnetic resonance (NMR) spectroscopy, electron microscopy (EM), light microscopy and a range of other imaging techniques. Whereas these disciplines have traditionally been tackled as single entities, this is no longer sufficient to gain a detailed and quantitative understanding of the dynamic structure and biological context of the cell. Each technique resolves structures at different resolutions, and over the past few years, scientists have recognized the need and advantage of collaborating on projects, integrating several different techniques to resolve a single biological problem in all its complexities.

The future

Over the next few decades, structural biology will face major scientific challenges, and the need to integrate existing techniques and develop emerging technologies, has never been more important. Advances in structural biology will produce other problems and scientists also recognize the need for developments in supporting technologies such as the automation of data collection and structural determination and data management. These challenges are all more than any one lab can manage individually, and coordinating efforts and equipment will be paramount for achieving these goals and pursuing cutting-edge science in Europe. The recent instruction from President Obama to significantly increase the ambition and scope of scientific research in the USA highlights the importance of an equal ambition for INSTRUCT in coordinating a truly integrated link between structural and functional research in Europe.

The project

Coordinated by Prof. David Stuart from the University of Oxford, INSTRUCT is one of the biomedical projects in the European Strategy Forum on Research Infrastructures within the Framework 7 of the EU, and aims to establish an integrated structural biology infrastructure in Europe to support the development of cellular structural biology research. A number of centres across Europe will allow access for scientists to state-of-the-art equipment in core and complementary techniques, thereby opening new scientific horizons in biomedical research. Alongside these scientific challenges, INSTRUCT also plans to advance and disseminate technologies and methodologies, and to train scientists across Europe in using state-of-the-art and newly developed infrastructure. This vision requires a major, long term and focused investment and will revolutionize the way biomedical research is done in Europe. A biological infrastructure on this scale is unprecedented in Europe, but is crucial in order for European science to maintain its competitive edge and play a leading role in such a vital research area. To date, European research has often been hindered by the short-term status of European funding. Securing a long-term investment will enable

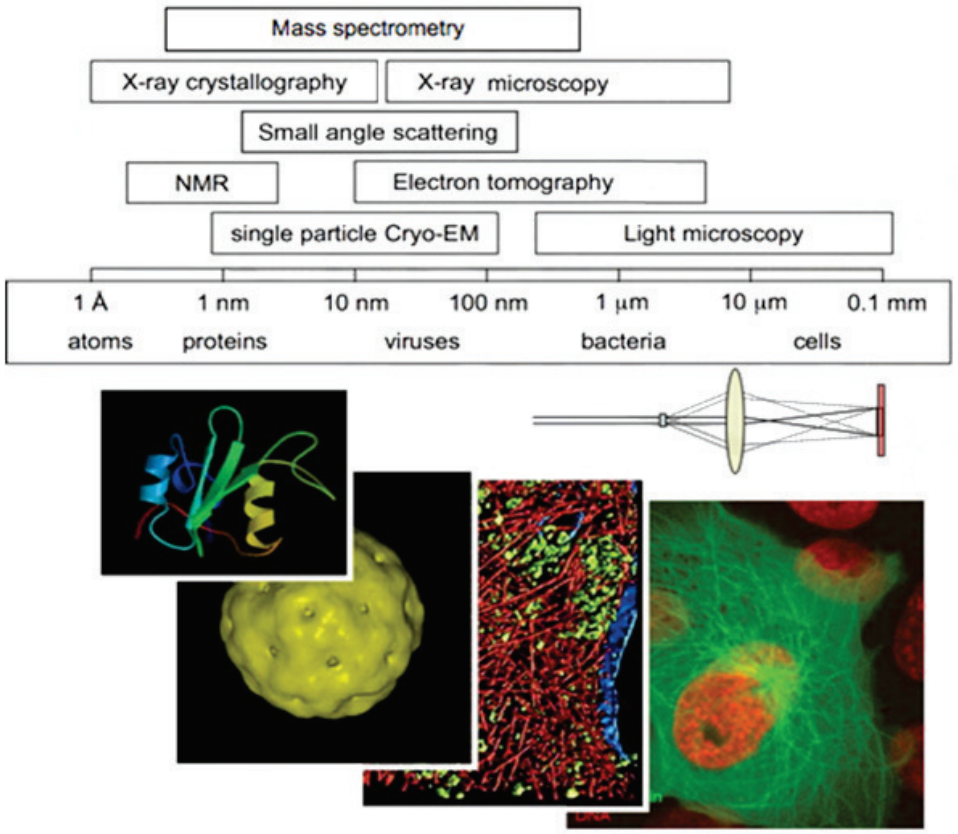

Figure 1. An overview of structural biological techniques showing the range of sizes of molecules studied by each method (Source: Cyttron, Leiden University).

the planning of more ambitious, larger scale and more complex projects.

The preparatory phase

INSTRUCT has just entered the second half of its preparatory phase, which began in April 2008. INSTRUCT will establish a Pan-European infrastructure based on core centres of scientific excellence, reinforced by associate centres with complementary expertise. Each core centre will provide access to cutting-edge equipment such as platforms for protein production, crystallization, mass spectrometry, biophysical methods, NMR, light microscopy and computational methods. Key activities during the preparatory phase have been to develop mechanisms for establishing and maintaining this infrastructure. National user groups have also been established and have met to discuss and compile the requirements of their nations researchers. This input is of great importance in making decisions about the structure of INSTRUCT, especially in terms of establishing guidelines for access and considering national and associate centres. In several countries, unprecedented numbers of scientists have worked together to generate a vital flow of information and ideas.

Identifying bottlenecks

Within the preparatory phase, several of the scientific working groups have been working on feasibility studies to identify bottlenecks in production and to increase efficiency where possible. Several studies have already produced results including workpackage 14.7 which is working on the co-expression of baculovirus systems. In a paper recently published online in Nature methods [1], Acembl, a versatile and automatable system for protein-complex expression in Escherichia coli is presented with the aim of aiding multiprotein complex production for structural and function studies. Other studies include the development of a NMR cryo probe, development in electron microscopy and the automation of eukaryotic expression systems with the development of small volume concentrators. With these techni-

cal developments, the resolution level of structural biology research can be further refined.

The coordination of data management is already an important issue and will continue to be so into the future. With several labs across Europe producing and gathering data, a concise and consistent storage and management of the data will be increasingly vital. Following an extensive feasibility study, researchers have identified PiMS as the management storage of choice and are developing it to make it as user friendly as possible for use across the INSTRUCT community. This will include an online version for labs without the financial means to buy the software, allowing increased data sharing across Europe. Several successful training and dissemination events have already taken place, and the number of participating and interested organizations is rising.

Ties with industry

Another important part of the INSTRUCT vision has been the increased contact and communication with industry. Forging close ties with industry will promote the commercialization of innovative technologies developed within INSTRUCT, and strengthen European industrial competitiveness, in particular Biopharma and Agrochem companies.

Ensuring a smooth transition

To permit a smooth transition to the construction and operational phases, a framework for governance and a mechanism for defining participants has to be clarified. Furthermore, a financial and legal framework is being built to allow major funding bodies to work together to provide a coherent infrastructure with European-wide access. At the time of going to press, the number of affiliated countries is 20, but interest is growing and as the success of the recent annual meeting in Florence shows, researchers from across Europe see and appreciate the need for an integrated infrastructure of structural biology to take biomedical research in Europe to the next level.

References

1. Bieniossek C, Nie Y, Frey D, Olieric N, Schaffitzel C, Collinson I, Romier C, Berger P, Richmond TJ, Steinmetz MO, Berger I (2009) Automated unrestricted multigene recombineering for multiprotein complex production. Nat Methods May 3.

BIOmics Hands-On Workshop

August 30 to September 4, 2009
Weizmann Institute of Science
Rehovot, Israel

http://ispc.weizmann.ac.il/biomics/

The International BIOmics Training & Education Center in Bioinformatics, Proteomics & Functional genomics (BIOmics) announces its first Hands-On Workshop on August 30 to September 4, 2009 at the Weizmann Institute of Science, Rehovot, ISRAEL.

The Workshop is intended for graduate students, postdocs and researchers from academia and industry.

At the Workshop, participants will hear talks from Israeli and international experts and gain first hand experience with:

- high throughput technologies,
- next-generation sequencing,
- viewing molecules in 3D,
- predicting protein–ligand interactions,
- tools for gene ontology;
- approaches for studying whole-genome genetic variation.

Hands-on sessions are limited to 20 participants.

Fellowships are available for attendees from academia, courtesy of the Israel Commission for UNESCO. With your application, let us know whether you will need a fellowship.

The registration deadline is **July 31, 2009**

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