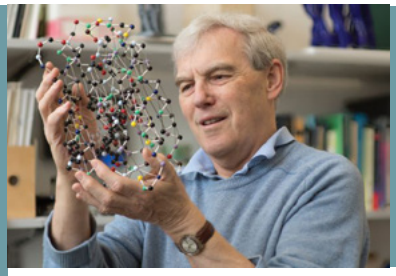
INTERNATIONAL SOLVAY INSTITUTES BRUSSELS

2017 International Solvay Chair in Chemistry



Professor Richard Henderson

Cambridge University, UK

Programme

Inaugural Lecture: Monday 20 March (4 - 5 P.M., Solvay Room)

The cryoEM revolution in structural biology

Structural biology has historically been dominated by X-ray crystallography and nuclear magnetic resonance (NMR) spectroscopy, which are incredibly powerful methods. Over 100,000 structures have been determined, with atomic coordinates deposited in the protein data bank (PDB). In the last few years, single particle electron cryomicroscopy (cryoEM), which does not require crystallisation or isotope labelling, has experienced a quantum leap in its capability, due to improved electron microscopes, better detectors and better software, and this is revolutionising structural biology. Using the technique invented by Jacques Dubochet and his colleagues, a thin film containing a suspension of the macromolecules of interest is plunge-frozen into liquid ethane at liquid nitrogen temperature, creating a frozen-hydrated sample in which individual images of the structures can be seen in many different orientations. Subsequent computer-based image analysis is then used to determine the three-dimensional structure, frequently at near-atomic resolution. I will show examples of some recent structures, and discuss remaining barriers to progress. CryoEM is already a very powerful method, but there are still many improvements that can be made before the approach reaches its theoretical limits.

FOR THE INAUGURAL LECTURE, COFFEE AND TEA WILL BE SERVED AT 3.45 P.M. AND DRINKS AT 5.00 P.M. IN FRONT OF THE SOLVAY ROOM

Lecture 1: Monday 27 March (4 - 6 P.M., Solvay Room)

Key milestones in development of electron cryomicroscopy (cryoEM)

In this lecture, I will track the different strands of research that came together to create the current enthusiasm for cryoEM. These were the development of the plunge-freezing method by Dubochet at EMBL in the 1980s, early work on frozen protein crystals by Taylor & Glaeser in the 1970s, the development of single particle computer programs on negatively stained ribosomes by Frank & van Heel, as well as the trajectory of research at the MRC-LMB in Cambridge, initiated on helical assemblies by DeRosier & Klug, icosahedral viruses by Crowther and two-dimensional crystals by Unwin & Henderson, right up to more recent developments on direct electron detectors and new programs such as Frealign by Grigorieff and Relion by Scheres.

INTERNATIONAL SOLVAY INSTITUTES BRUSSELS

2017 International Solvay Chair in Chemistry

Lecture 2: Tuesday 28 March (4 - 6 P.M., Solvay Room)

Electron microscopy hardware and software for structural biology

As important as the conceptual and practical developments in cryoEM during the last 10 years or so, have been the steady improvements in electron microscope instrumentation (hardware) and computer programs (software). I will describe in this lecture the current status of everything from the electron sources (field emission guns), through stable columns, cold stages and vacuum systems, to new detectors that are approaching but not yet reaching perfection. Alongside this, others have developed superb computer programs that are making the practise of cryoEM possible even for beginners and those who only want to use it as one technique among many.

Lecture 3: Wednesday 29 March (4 - 6 P.M., Solvay Room)

Sample and specimen preparation for cryoEM

Typical structural biology research projects begin with initial biochemical characterisation of an important specimen, with the goal of answering some key biological or medical question, possibly involving the mechanism of action or the identification of a binding site on a particular macromolecular complex or individual molecule. There are many steps between such initial explorations and the successful determination of a high-resolution structure that answers the initial question. In this lecture, I plan to cover some of the keys steps, the barriers that need to be overcome and the pitfalls to avoid, on the way to a reliable structure determination.

Lecture 4: Thursday 30 March (3 - 5 P.M., Solvay Room)

CryoEM: future perspective

Although cryoEM is already a very powerful method, there are many improvements that still can be made before the approach reaches its theoretical limits. In this final lecture, I will discuss the underlying theory, the fundamental limitation to the power of the method due to radiation damage, and the remaining barriers to progress. Once these problems have been overcome and generic, practical solutions have been developed, single particle cryoEM and the closely related cryoET (electron cryotomography method) may become the dominant method in structural biology.

SOLVAY ROOM
Building N.O. 5th Floor
Université Libre de Bruxelles
Campus Plaine - Boulevard du Triomphe
Access 2- 1050 Brussels

www.solvayinstitutes.be