Dynamic protein structure: from protein disorder to membrane pores

Our work focuses on aspects of dynamic and heterogeneous protein conformations and assemblies, using an integrated structural approach based on "native" mass spectrometry, ion mobility, and surface mapping techniques in combination with electron microscopy, SAXS and other biophysical methods. We will briefly introduce the different mass spectrometry-based Structural Proteomics approaches, and highlight the type of data which they can generate, and how they can be integrated with other structural information and with computational models.

Specifically, we are going to show recent results on the detection and characterization of intrinsic disorder in proteins, including alpha-synuclein and the apoptosis-related BAX protein. A range of folding states, from disordered to compact, are characterized and interpreted using molecular dynamics approaches. These data link the conformational state of the protein with their association into larger oligomers, which are believed to be able to form membrane pores. We use detergent micelles, lipid bilayers (bicelles) and nanodiscs for both native MS and covalent labelling of exposed parts of the protein, and apply these techniques to various different ion channels including the mechanosensitive channel of large conductance (MscL). Using covalently attached, charged ligands inside the MscL channel, we can mimic the effect of mechanical pressure on the surrounding membrane and characterize various opening states using ion mobility-MS, electron microscopy, EPR spectroscopy and other biochemical and computational methods, in the absence of lipids.

Frank Sobott *obtained his PhD at the Goethe University in Frankfurt/M (Germany) in 2000 in Physical and Theoretical Chemistry. After working with Dame Carol Robinson at Oxford and Cambridge, he returned in 2004 to Oxford in order to take up posts in the Structural Genomics Consortium, the Centre for Integrative Systems Biology and the Centre for Gene Function, and he retains a visiting professorship in the Biochemistry Department there. At the end of 2009, he moved to the University of Antwerp in Belgium where he heads the Biomolecular & Analytical Mass Spectrometry group and coordinates the Center for Proteomics, with the title of Francqui Research Professor (2011-14).*

His research focuses on the structural analysis of noncovalently bound, supramolecular systems and functional assemblies of biomolecules. The group is developing new methods and instrumentation for the analysis of multi-component, heterogeneous and dynamic assemblies based on mass spectrometry, ion mobility and associated techniques. The group applies these tools in a highly interdisciplinary context to research questions from chemistry, biology and medicine.