FIAS Colloquium

Tuesday, July 7, 2011, 14:30
FIAS, Ruth-Moufang-Str. 1, 60438 Frankfurt am Main
Lecture hall 0.100

**Speaker:** Dr. Lucy Forrest, Max Planck Institute for Biophysics, Frankfurt

**Title:** A role for protein symmetry in moving ions across cell membranes

Transport of small molecules such as neurotransmitters across cell membranes is carried out by specific transport proteins that, for example, couple solute flux to the movement of ions along their concentration gradients. This has been proposed to occur via alternate exposure of the protein’s substrate binding-site to either side of the membrane, requiring at least two distinct conformations of the protein. X-ray crystallographic data for several secondary transporter proteins from diverse families support this hypothesis and provide key insights into specific transport mechanisms. Nevertheless, to date, many of these structures have been solved for only one state in the transport cycle. An intriguing feature of these structures is the presence of internal structural repeats with inverted topologies with respect to the membrane. I will show using computational modelling of three different secondary transporter families that these structural repeats encode two degenerate conformations of the same protein. Experimental support for the models is available in the form of biochemical accessibility measurements, spectroscopic data, and cross-linking studies, as well as of recent X-ray structural data. The implications of these results will be discussed in terms of a general role of inverted-topology repeats – and of symmetry – in the pseudo-symmetric alternating-access mechanism of secondary transport.