

# ***SFB 35 Colloquia in Membrane Transport***

19.03.2010, 15.00: Leseraum Pharmakologie

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### **"Symmetry and the art of transport: a role for inverted-topology structural repeats in neurotransmitter transport"**

Transport of solutes 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 a 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 transporters from diverse families support this hypothesis and provide key insights into specific transport mechanisms. However, to date, most 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 repeats with inverted topologies with respect to the membrane. We have carried out computational modelling using these structural repeats in order to model the opposite conformations of two families of neurotransmitter transporters. Experimental support for these models is provided by biochemical accessibility measurements and cross-linking studies by our collaborators, and by very recent X-ray structural data. The implications for these results will be discussed in terms of a potentially general role of inverted-topology repeats – and of symmetry – in the pseudo-symmetric alternating-access mechanism of secondary transport.