COLLOQUIA IN MEMBRANE TRANSPORT

Venue: Department für Medizinische/Pharmazeutische Chemie
1090 Wien, Althanstraße 14 (UZA II), Hörsaal 7

(Harald Sitte, Tel.: (01) 4277-64123, harald.sitte@meduniwien.ac.at, Gerhard Ecker: +43-1-4277-551 10, gerhard.f.ecker@univie.ac.at)

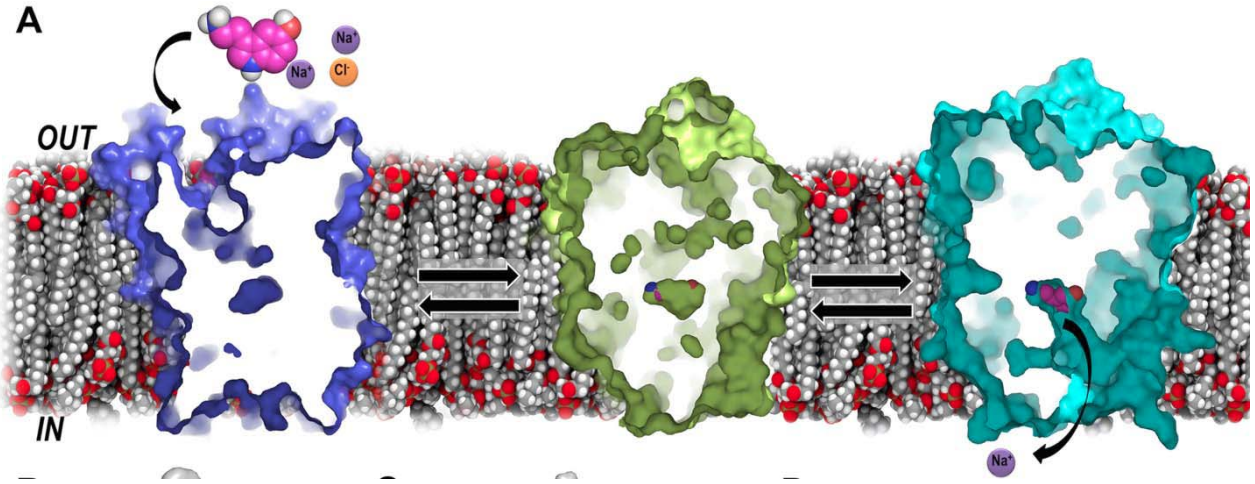
Friday 11.05.2012 15:00 s.t. Birgit Schiott (host: Gerhard Ecker)

Department of Chemistry and iNANO
Aarhus University
Langelandsgade 140
8000, Aarhus C
Denmark

"Molecular modeling of the human serotonin transporter and the leucine transporter – ligand binding and transport dynamics"

Birgit Schiott (birgit@chem.au.dk)

Abstract.
The serotonergic system utilizes serotonin as a neurotransmitter and is involved in the regulation of mood, aggression, anxiety, sleep, appetite, and body temperature.1 A key player in this system is the human serotonin transporter (hSERT) which is also the principal target for antidepressants.2 In recent years the structure of an evolutionary distant bacterial homologue, the leucine transporter (LeuT),3 has advanced the structural understanding of hSERT and related proteins.4 However, some functional findings for LeuT5 are contradicting the findings from mammalian neurotransmitter transporters.6 This inspired us to undertake a modeling studies aiming at producing models for the binding of the endogenous substrate serotonin (5-HT)7 as well as other ligands8 to hSERT and at studying the dynamics of the proteins during transport.9 In the talk, I will present our results from docking studies of several ligands to hSERT and from MD simulations of hSERT and LeuT revealing some characteristics of the transport mechanism.



Cut-through section of hSERT from the side. Left: outward-facing snapshot (blue), Middle: referencehomology model in in occluded state (green), Right: Inward-facing conformation of hSERT revealed during MD simulation. These three structures expose the different stages occurring during transport in hSERT.

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