

## Joint DANDRITE & iNANO Topical Seminar

**Friday 20 May 2016**  
12.00 – 13.00

**The iNANO Auditorium (building 1593, basement level, room 012)**  
Gustav Wieds Vej 14, 8000 Aarhus C



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### Life's ups and downs: elevator mechanisms in transporter biology

Secondary transporters use alternating access mechanisms to couple uphill substrate movement to downhill flux of a coupling ion, presenting binding sites alternately to either side of the membrane. Most known transporters utilize a “rocking bundle” motion, where the protein moves around an immobile substrate binding site to regulate ingress. However, one protein, the glutamate transporter homolog  $\text{Glt}_{\text{Ph}}$  translocates its entire substrate binding site vertically across the width of the membrane, a so-called “elevator” mechanism. Here we examine an unrelated transporter, the  $\text{Na}^+$ /succinate transporter VcINDY. With the crystal structure of an inward facing state of VcINDY as a template, we used the “repeat swap” approach to computationally predict the structure of the outward-facing state of the transporter. Our model suggests that VcINDY undergoes a substantial elevator-like movement to transfer its substrate binding site, with a vertical translation of  $\sim 15 \text{ \AA}$  and a rotation of  $\sim 43^\circ$ . Crosslinks formed between three different pairs of introduced cysteine residues, proximate only in the outward-facing state, confirm this large-scale motion. These crosslinks completely inhibit transport, demonstrating that such movement is essential for transport. In contrast, multiple crosslinks across the VcINDY dimer interface preserve transport function, revealing an absence of large scale coupling between VcINDY protomers.

**Host:** Group Leader Poul Nissen, DANDRITE, Aarhus University