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Propositions

Accompanying the thesis

Single-molecule studies of the conformational dynamics of ABC proteins

Marijn de Boer

1. Proteins are inherently dynamic. Hence, to better understand the functional mechanism of proteins, experimental methods should be used that provide dynamic information.
2. The general view that substrate-binding proteins (SBPs) of ABC importers exist in two conformations (i.e., open and closed) may hold for some SBPs, but others can acquire many more conformations. (Chapter 2 and 5)
3. In contrast to the ‘Venus-flytrap’ mechanism of ligand binding by the SBP: not every ligand induces closing of the SBP and some SBPs close without ligand. (Chapter 2, 4 and 5)
4. Not only the correct SBP conformation is needed for transport by ABC importers, but also the conformational dynamics of the ligand-SBP complex play a role. (Chapter 2 and 6)
5. Developing inhibitors that target the SBPs of ABC importers has been suggested to be a promising strategy against pathogenic bacteria (*Tanaka, K.J. et al. 2018*). However, the inhibitory effect would depend strongly on the blocked process, e.g., blocking the opening of the SBP would be more efficient than blocking the docking of the SBP onto the transporter. (Chapter 3)
6. The protein ABCE1 adopts many conformations due to the asynchronous movement of the two ATP binding sites. (Chapter 7)
7. The spontaneous conformational changes in SBPs, ABCE1 and other proteins influence the conformational equilibrium when a ligand is bound as well as the affinity between the protein and the ligand. (Chapter 8)
8. The unique power of single-molecule methods is that dynamic properties of molecules can be measured under equilibrium conditions.