Investigating Ammonium Transport Mechanisms in AmtB and RhCG by Molecular Dynamics Simulations

Membrane proteins of the ubiquitous Amt/Rh family mediate the transport of ammonium. Despite the availability of different X-ray structures that provide many insights on the ammonium permeation process, the molecular details of its mechanism remain controversial. Functional experiments on plant ammonium transporters and rhesus proteins suggest a variety of permeation mechanisms including the passive diffusion of NH3, the antiport of NH4+/H+, the transport of NH4+, or the cotransport of NH3/H+. The X-ray structures have revealed that the pores of the prokaryotic AmtB and the eukaryotic RhCG proteins share a similar architecture suggesting that they might both catalyze the diffusion of NH3. However, molecular mechanics simulations of both proteins reveal that small differences in the pore lining residues might actually alter the properties of the pore. We notably find that the pore of the AmtB transporter can stabilize water molecules at much greater extent than the pore of RhCG. The possible presence of water molecules in the pore lumen of AmtB opens the door to alternative permeation mechanisms, notably involving the co-transport of H+. We discuss the possible permeation mechanisms in both the AmtB and RhCG proteins in light of some recent functional studies, and illustrate how closely related proteins can support quite different mechanisms.