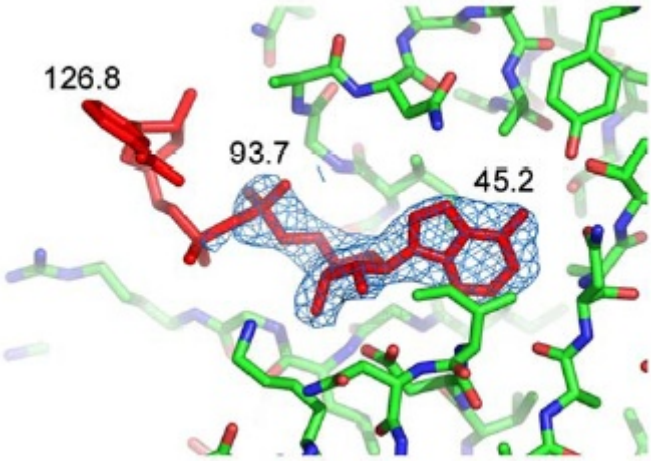
Part of K^+ Transporter is a Squashable Ring



The RCK domain of the KtrAB K^+ transporter: multiple conformations of an octameric ring.

R. A. Albright, J.-L. V. Ibar, C. U. Kim, S. M. Gruner, and J. H. Morais-Cabral
Cabral Group, Yale University

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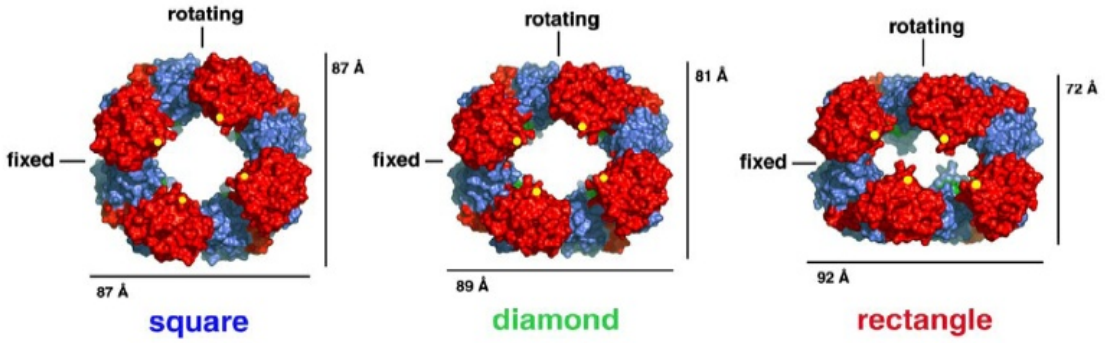
Some eukaryotic and many prokaryotic potassium channels are regulated by RCK (Regulating the Conductance of K^+) domains, making these domains critical to K^+ homeostasis in many cells. Binding of a ligand such as NADH to an RCK domain causes the associated channel to open. How does this happen? To help answer this question, crystal structures have been determined for several RCK domains. In each structure, RCK's are assembled into dimers, and the dimers are combined to form higher oligomers. However, the arrangement of dimers in the crystals appeared quite different, leading to conflicting models for the functional oligomer. The present study by the Morais-Cabral group was designed to resolve this conflict.

Several different crystal types of KtrA, an RCK domain which is part of the KtrAB ion transporter, were studied, at CHESS and NSLS, and 5 structures were determined. Each structure contains rings of 8 RCK monomers (4 dimers), but the shape of the rings varies from a symmetrical "square" form through intermediate "diamonds" to a "rectangular" form. One form can be transformed into another by changing the angle relating the two monomers in a dimer. This is accommodated by modifying half of the dimer-dimer interfaces in the ring (the "rotating" interfaces in the figure). Examination of earlier RCK structures revealed octameric rings in all of them; crystal contacts between rings had obscured their significance.



Different conformations of the KtrA octameric ring, in structures found in crystals grown under slightly different conditions. Each ring is composed of 4 dimers, where each dimer consists of a red and a blue monomer. The "fixed" dimer-dimer interface is similar in all 3 cases, while the "rotating" interface is quite different. The ligand (NADH, ATP, or other similar species) is shown in green, and the yellow dots are markers to follow the motion of a particular residue in going from one form to another.

The crystal structures were determined with various adenine-containing ligands bound to the protein. In order to see the ligand clearly, high-pressure cryocooling was used to stabilize it in a single position. Maps showed a well-defined adenine ring, in a flipped position relative to the model from an earlier KtrA structure, with weaker density for the rest of the ligand. Without pressure-cooling, ligand placement was unclear. The identity of the ligand had negligible effect on the surrounding protein.

Biochemical experiments indicate that the complete KtrAB complex contains two KtrB monomers in addition to an octamer of KtrA; KtrB is a membrane protein that forms the actual ion channel. The authors propose that interactions with KtrB cause the rectangular form of the KtrA ring to be favored until a ligand binds; binding leads to a change in the dimer hinge angle and a resulting transition to the square form, and this transition leads to an opening of the ion channel.