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X25

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Protein Crystallography

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Publications:
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Visualizing the Conduction of Potassium Ions in Cell Membranes

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Biological cells are surrounded by membrane bilayers. These membranes contain hydrophobic proteins that are critical for a variety of cellular functions. One important class of membrane proteins is known as ion channels, which allow cations and/or anions to pass through the membrane. Ion channels are particularly important in neurobiology, where electric currents transmit information over large distances.

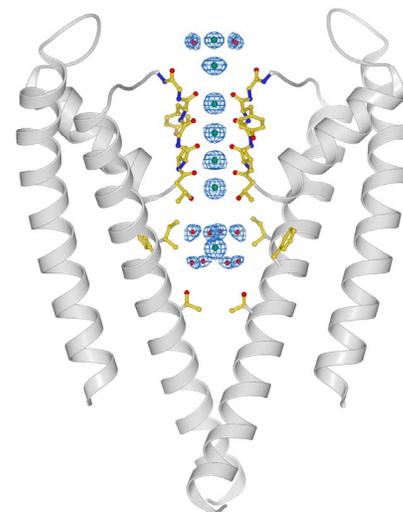
Potassium channels control the electric potential across cell membranes by catalyzing the rapid, selective diffusion of potassium ions. The basic ion permeation pathway within this class of proteins involves the ion conduction pore, which has a water-filled cavity roughly in the middle of the membrane, and a narrow selectivity filter near the extracellular side. The cavity is apparently designed to keep a K^+ ion in a fully hydrated state, and the selectivity filter is designed to catalyze the dehydration, transfer and re-hydration of K^+ ions. In order to determine the mechanism of ion transport through the potassium channel, a high-resolution structure of the protein, potassium ions, and water molecules is necessary.

It is notoriously difficult to determine the structure of membrane proteins because their hydrophobic nature generally makes it hard to obtain them in large quantities and to crystallize them satisfactorily. Thus, only a small number of high-resolution membrane-protein structures are known to date. In recent years, a new approach to crystallizing membrane proteins has been

developed that involves the use of antibody fragments to mediate important crystal lattice contacts and promote crystallization.

Using this method, crystals of the bacterial potassium channel, KcsA, were obtained and diffracted up to 2.0\AA at Beamline X25. The high-resolution structure revealed detailed chemistry of ion coordination and hydration in the channel. It shows how the K^+ channel displaces water molecules around an ion at its extracellular entryway, how it holds a K^+ ion in a shell of eight water molecules in its central cavity, and how the selectivity filter mimics the hydration shell around each K^+ binding site. This unprecedented view of a hydrated potassium ion is made possible by the high-resolution data obtained through co-crystallizing KcsA with an antibody fragment.

These detailed mechanistic results reveal valuable information about the mechanism of K^+ conduction in the cell, which is important for neurobiology and understanding neurological disorders. In addition, the success of this method offers important possibilities for membrane protein crystallography in general.



Structure of potassium channel KcsA at 2.0\AA resolution. Two diagonally opposed subunits of the tetrameric channel are shown in ribbon representation. Residues forming the selectivity filter and residues facing the central cavity are shown in ball-and-stick representation. The electron density map covers the potassium ions (green spheres) along the ion pathway and water molecules (red spheres) in the vicinity.