Exploring the principles of ion channel gating with viral potassium channels.

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Viral channels are exceptionally small and stable; a perfect model systems to study the very basics of ion transport. One example are the Kcv potassium channels found in algae viruses. Despite having typically less then 100 amino acids per monomer, they closely resemble the mammalian and bacterial K^+ channels in structure and function. With >70 available Kcv isoforms so far, this protein family is an ideal toolkit to study structure/function correlates. We employ mutational studies, bilayer recordings of in vitro expressed protein, kinetic analysis and MD simulation to identify gating mechanisms in this system, two of which I will present.

1.) Despite the lack of a canonical voltage sensor, Kcv_{NH} is a slow outward rectifier, when the cytosolic gate is rendered permanently open by the mutation S77G. By sequence comparison with Kcv_{NTS}, which lacks slow voltage dependence, we have located the responsible gate at the outer pore mouth. Two amino acids in the extracellular turret loop interact with residues in the pore helix and the selectivity filter. Preliminary results suggests a network of hydrogen bonds stabilizing the structure at or near the selectivity filter in a manner similar to that one known from the bacterial channel KcsA.

2.) By comparing two channels with different open probability (Kcv_{NTS} and Kcv_S), we identified a novel mechanism for a cytosolic channel gate. It is formed by merely two amino acids. A serine forms a hydrogen bond with the helix backbone. The resulting slight kink in the helix repositions the adjacent Phe to close the ion pathway. The mechanism is much simpler than the “glycine hinge” known from other K^+ channels, making it a good candidate be transferred in to other proteins.