Mechanism of activation at the selectivity filter of the KcsA K(+) channel

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Potassium channels are opened by ligands and/or membrane potential. In voltage-gated K(+) channels and the prokaryotic KcsA channel, conduction is believed to result from opening of an intracellular constriction that prevents ion entry into the pore. On the other hand, numerous ligand-gated K(+) channels lack such gate, suggesting that they may be activated by a change within the selectivity filter, a narrow region at the extracellular side of the pore. Using molecular dynamics simulations and electrophysiology measurements, we show that ligand-induced conformational changes in the KcsA channel removes steric restraints at the selectivity filter, thus resulting in structural fluctuations, reduced K(+) affinity, and increased ion permeation. Such activation of the selectivity filter may be a universal gating mechanism within K(+) channels. The occlusion of the pore at the level of the intracellular gate appears to be secondary.
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