

Publication

An iris diaphragm mechanism to gate a cyclic nucleotide-gated ion channel

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Cyclic nucleotide-gated (CNG) ion channels are non-selective cation channels key to signal transduction. The free energy difference of cyclic-nucleotide (cAMP/cGMP) binding/unbinding is translated into mechanical work to modulate the open/closed probability of the pore, i.e., gating. Despite the recent advances in structural determination of CNG channels, the conformational changes associated with gating remain unknown. Here we examine the conformational dynamics of a prokaryotic homolog of CNG channels, SthK, using high-speed atomic force microscopy (HS-AFM). HS-AFM of SthK in lipid bilayers shows that the CNBDs undergo dramatic conformational changes during the interconversion between the resting (apo and cGMP) and the activated (cAMP) states: the CNBDs approach the membrane and splay away from the 4-fold channel axis accompanied by a clockwise rotation with respect to the pore domain. We propose that these movements may be converted by the C-linker to pull the pore helices open in an iris diaphragm-like mechanism.

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