

S3b amino acid residues do not shuttle across the bilayer in voltage-dependent Shaker K⁺ channels

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In voltage-dependent channels, positive charges contained within the S4 domain are the voltage-sensing elements. The "voltage-sensor paddle" gating mechanism proposed for the KvAP K⁺ channel has been the subject of intense discussion regarding its general applicability to the family of voltage-gated channels. In this model, the voltage sensor composed of the S3b and the S4 segment shuttles across the lipid bilayer during channel activation. Guided by this mechanism, we assessed here the accessibility of residues in the S3 segment of the Shaker K⁺ channel by using cysteine-scanning mutagenesis. Mutants expressed robust K⁺ currents in *Xenopus* oocytes and reacted with methanethiosulfonate ethyltrimethylammonium in both closed and open conformations of the channel. Because Shaker has a long S3-S4 linker segment, we generated a deletion mutant with only three residues to emulate the KvAP structure. In this short linker mutant, all of the tested residues in the S3b were accessible to methane