Moving Gating Charges: Comparing Electrostatic Energetics of the S4 Motion of Different Models
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The topology and structure of voltage-gated channels (Gandhi and Isacoff, J. Gen. Physiol. 120:455; Jiang et al., Nature 423:33) has raised interesting questions about the energetics of S4 motion. Two models of how the S4 segment moves in response to a voltage change have been proposed: (1) the 'S4 paddle' of Jiang et al., a +4e charged lipophilic ion that moves from the inner face of the membrane to the outer as the channel is opened; (2) the 'conventional model', in which the charged region of a helical S4 slides perpendicular to a membrane that is thinned locally. Here we present electrostatic computations of these two models of S4 translocation through the membrane electric field. We represent the 'S4 paddle' as 4 positive charges buried at 4.5A intervals along the axis of a 8Ax8Ax22A body that, like the lipid, is assigned a dielectric coefficient of 2. Moving this paddle from the intracellular side through the center of the 35A-thick membrane requires ~150 kT of electrostatic work. For the 'conventional model' of S4 motion, we assume the lipid of the membrane covers 8A of the S4 region, so that up to 2 positive S4 charges can be inside the lipid at a time. (The S4 charges are recessed by 2A from the S4 surface.) In this scenario, favorable conditions for S4 translocation occur if negative countercharges are present in the region where the S4 charges cross the lipid. With 2 such countercharges next to the S4 surface, the electrostatic energy varies in a barrier-well pattern in a range from -10 to +10 kT as the S4 helix is moved across the membrane. This kind of energy profile has been experimentally derived by Sigg et al. (PNAS 100:7611).