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Voltage Sensor in Voltage-gated ion channels FRANCISCO BEZANILLA, Institute for Molecular Pediatric Science. University of Chicago — Voltage-gated ion channels are intrinsic membrane proteins that play a fundamental role in the generation and propagation of the nerve impulse. Their salient characteristic is that the probability of the ion channel of being open depends steeply on the voltage across the membrane where those channels are inserted. Thus, in a membrane containing many channels, the ionic conductance is controlled by the membrane potential. The voltage exerts its control on the channel by reorienting intrinsic charges in the protein, generally arginine or lysine residues located in the 4th transmembrane segment of the channel protein, a region that has been called the voltage sensor. Upon changing the membrane potential, the charged groups reorient in the field generating a transient current (gating current). The properties of the gating current may be studied with a small number of channels to infer the operation of the sensor at the single molecule level by noise analysis or with a large number of channels to infer the details of the energy landscape the sensor traverses in opening the pore. This information is global in nature and cannot pinpoint the exact origin of the charge movement that generates the gating current. The movement of physical charges in the protein has been inferred with site-directed mutagenesis of the charged residues to histidine that allows the study of proton accessibility. The actual movement has been studied with fluorescence spectroscopy, fluorescence resonance energy transfer. The combined information of site-directed mutagenesis, gating currents, fluorescence studies and emerging crystal structures have started to delineate a physical representation of the conformational changes responsible for voltage sensing that lead to the opening of the conduction pore in voltage-gated ion channels.

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