Two stories of membrane protein stability and dynamics: The S4 voltage-sensor and the SecY translocation channel.

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The high sensitivity of voltage-dependent ion channels to small variations in the transmembrane electric potential is due to the motion of charged residues located in the so-called S4 transmembrane (TM) domain. The two reported structures of two K+ voltage-gated (Kv) channels from *archae* (KvAP) and mammalian (Kv2.1) organisms indicate that the Arg residues in S4 are exposed to the lipid membrane during. Recent experiments of translocon-mediated insertion into the endoplasmic reticulum membrane have shown that a polypeptide chain with the sequence of S4 in KvAP can be inserted in the membrane. In the first part of my talk, I will present a model, generated from molecular dynamics simulations, that accounts for the stability of S4 in the lipid membrane environment. The recently determined structure for the SecY protein-conducting channel calls for a model of membrane protein integration based on the ability of a nascent peptide chain to probe both hydrophilic and hydrophobic environments, implying that the lateral gate, formed by two TM domains of the translocation channel, is in a highly dynamical state. In the second part of my talk, I will present our efforts to produce a model of SecY in its active oprn-state and characterize its conformational dynamics.