Abstract

Prestin is a member of the solute carrier 26 family of anion transporters. In mammals, Prestin lost the ability to transport anions all together, while gaining a voltage-sensitive membrane expansion function known as electromotility. Almost exclusively expressed in specialized outer hair-cells (OHC) of the cochlea, Prestin is solely responsible for amplifying sound-signals sensed by neighboring inner hair-cells, via the expansion and contraction of the OHC. Recently, we demonstrated that Prestin's electromotive function is intrinsically linked to an incomplete elevator-like transport mechanism which additionally induces an expansion of the transmembrane domain (TMD) in the direction of the membrane plane. However, the mechanism by which Prestin senses the change in trans-membrane potential is a point of stark controversy, due in part to the lack of a clear S4-like voltage sensing domain. Here, we propose to employ all-atom molecular dynamics simulations to identify voltage sensing residues, and to characterize the molecular mechanisms underlying the transduction of electrical potential to mechanical force.