Topics in Advanced Biological Science アドバンス生命理学特論

Gating without swinging:

a two-channel model of hair-cell mechanotransduction with membrane-mediated cooperativity

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Sound-induced vibrations of the inner ear stretch tip links between stereocilia of hair cells and open mechanotransduction ion channels. Channel opening in turn relaxes the tip links. The classical gating-spring model ascribes this gating compliance to the conformational change of a single MET channel upon gating, known as the gating swing. To reproduce the experimental data, however, the magnitude of the gating swing must be comparable to, or even greater than, the size of a typical ion channel. Experimental evidence indicates that each tip link is associated on average with two channels, and that the lipid bilayer modulates their gating, although it is not clear how. We present a new model of mechanotransduction with two mobile channels per tip link, which gate cooperatively due to elastic forces within the membrane. The relative motion of the channels upon their cooperative opening and closing produces the required change in tip-link extension. The model quantitatively reproduces the main physiological properties of hair-cell mechanotransduction—such as gating compliance, twitch and negative stiffness—using only realistic parameters. Furthermore, it provides a framework in which to understand other as yet unexplained phenomena of hair-cell mechanics, such as the flick, a voltage-driven hair-bundle motion. Our model proposes for the first time a physiological function for the bilayer-mediated cooperativity between mechanosensitive ion channels in a vertebrate sensory system.

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