

Electrophysiology of bacterial mechanosensitive channels: A path to understanding osmoregulation and drug permeation

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Direct application of the patch-clamp technique to giant bacterial spheroplasts revealed a spectrum of mechano-activated conductances and identified two new families of membrane channels, MscS and MscL. Mechanosensitive channels of small (MscS) and large (MscL) conductance are the major pathways for osmolyte efflux activated by tension in the bacterial cytoplasmic membrane in the event of osmotic downshock. MscL opens at near-lytic tensions, serving as an emergency valve, whereas adaptive MscS opens at moderate tensions, providing fine turgor adjustments. A patch-clamp survey shows that MscL is present at 3x density in *V. cholerae* compared to *E. coli*, yet *Vibrio* is less tolerant to strong down-shocks. Higher number of MscL can be a compensation for some vulnerable traits of *V. cholerae*, including a different set of compatible osmolytes and the geometries of the membrane and the cell wall.

Because mechanosensitive channels sense distribution of lateral pressure in the surrounding lipid bilayer, they can be used as sensors reporting on the asymmetric presence of extrinsic amphipaths in the membrane. Upon testing a series of parabenzoates on excised patches of *E. coli*, we found that right shifts of the MscS activation curve correlate with surface activity and with lateral pressures imposed through intercalation into Langmuir monolayers by the same substances. Similar correlations were found for bacterial autoinducers and their synthetic analogs. Endogenous mechanosensitive channels, therefore, report on lateral pressure perturbations in membranes, and they can track the depth-dependent partitioning of biologically active substances directly into the bacterial membrane, monitoring the process of their permeation.

Biography

Sergei Sukharev earned his Ph.D. in Biophysics from Moscow State University and received postdoctoral training at the Frumkin Institute of Electrochemistry (Moscow) and then at University of Wisconsin-Madison. Currently, he is a Professor of Biology at the University of Maryland and a co-director of the Maryland Biophysics program. He has published more than 60 papers in the field of membrane biochemistry and biophysics and serves as an editorial board member of the Journal of Biological Chemistry.

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