Mechanosensitive channels: a multidimensional approach

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Abstract: Use of computerized instrumentation as well modeling and simulations have been critical in studies of ion channel function and more recently structure. Our research is focused on mechanosensitive channels gated by membrane tension. The functional study of channel gating (opening and closing) begins with sensitive current recordings followed by algorithmic treatment of selected fragments of traces. Kinetic analysis of transitions yields tension response characteristics. This has been done for MscL, the large bacterial mechanosensitive channel, using QuB (SUNY-Buffalo), a suite designed to quantify the kinetic scheme of gating. The data revealed that the channel transition proceeds through a pre-expanded low-conducting state. This permitted us to use the crystal structure of a MscL homolog to build a structural model of E. coli MscL and envision the conformational transitions leading to the open state. The structural analysis helped to design experiments to verify the open conformation and the transition path, which were also supported by molecular dynamic simulations. Characterization of the protein shape and surfaces in terms of dynamic interactions with water and surrounding lipids pose current experimental and computational challenges.