Conformational States of MscS probed by PELDOR

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The heptameric mechanosensitive channel of small conductance (MscS) provides a critical function in Escherichia coli where it opens in response to increased bilayer tension. Three approaches have defined different closed and open structures of the channel, resulting in mutually incompatible models of gating. We have attached spin labels to cysteine mutants on key secondary structural elements specifically chosen to discriminate between the competing models and measured the distances between the labels with an Electron Paramagnetic Resonance (EPR) method called pulsed electron–electron double resonance (PELDOR). The resulting PELDOR spectra of MscS in detergent and within lipid bilayers matched predicted distance distributions for the open crystal structure of MscS. The assignment of MscS as open in detergent by PELDOR was unexpected but is supported by two crystal structures of spin labeled MscS. PELDOR is therefore shown to be a powerful experimental tool to interrogate the conformation of transmembrane regions of integral membrane proteins.