Structure and dynamics of the periplasmic loop of the MscL mechanosensitive channel studied by electron paramagnetic resonance spectroscopy

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The periplasmic loop of the bacterial mechanosensitive channel of large conductance (MscL) is one of the five structural domains of the channel, which has been suggested to play a significant role in gating of the channel by mechanical force (Ajouz *et al.*, 2000; Maurer & Dougherty, 2003). The structure of the loop has however, not been fully characterised. After the structural details of the MscL transmembrane helices, TM1 and TM2, were determined by crystallography and electron paramagnetic resonance (EPR) spectroscopy (Chang *et al.*, 1998; Perozo et al., 2001), a model of the complete structure of MscL of *E. coli* was proposed (Sukharev *et al.*, 2001). The model provided basis for characterisation of the MscL gating by molecular dynamics (MD) simulations (Gullingsrud *et al.*, 2001). Recent MD simulations (Meyer *et al.*, 2004) suggested further an important role for the periplasmic loop in the MscL channel gating.

Using the methods of cysteine scanning mutagenesis, spin labelling and EPR spectroscopy on MscL reconstituted into liposomes, we carried out an initial study towards characterisation of the structural dynamics of the loop. The EPR spectra recorded from the channel in its closed configuration and in the open state induced by lysophosphatidylcholine (LPC) (Perozo *et al.*, 2002), indicated that significant structural rearrangements in the loop region occurred during channel opening. Our results thus appear consistent with the findings of the MD simulation studies of the structural dynamics of the channel. Future experiments are aiming to provide a complete structure of the periplasmic loop in the open and closed states of the MscL channel, which should allow obtaining a more accurate model of the gating mechanism of this channel.

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