Hydrogen Bond Formation between the Gate and Water Molecules Accelerates Channel Opening of the Bacterial Mechanosensitive Channel MscL

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The bacterial mechanosensitive channel MscL is constituted of homopentamer of a subunit with two transmembrane inner and outer (TM1, TM2) α-helices, and its 3D structure of the closed state has been resolved. The major issue of MscL is to understand the gating mechanism driven by tension in the membrane. To address this question, molecular dynamics (MD) studies have been performed, however, as they do not include MscL-lipid interactions, it remains unclear which amino acids sense membrane tension and how the sensed force induces channel opening. Thus we performed MD simulations for the opening of MscL embedded in the lipid bilayer. In the closed state of MscL, Leu19 and Val23 form a hydrophobic constricted part called gate. Upon membrane stretch, TM2 helices are dragged by lipids and tilted, accompanied by the outward sliding of the crossings. This led to a slight expansion of the gate associated with an exposure of oxygen atoms of the backbone to the inner surface of the gate. This allows water penetration in the gate and formation of hydrogen bonds between water and the exposed oxygen, which in turn weakened the hydrophobic interaction at the crossings, causing a further opening of the gate and water permeation.