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Simulating the effects of delipidation on the mechanosensitive channel of small conductance MscS

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The mechanosensitive channel of small conductance, MscS, is a bacterial mechanosensitive channel which activates to relieve hypoosmotic stress. MscS opens in response to membrane tension before transitioning into a non-conducting state in the presence of prolonged stimulus.

Zhang et al. (2021) recently pioneered an experimental method of mimicking membrane tension to obtain a high resolution cryo-EM structure of MscS in a desensitized state. This was achieved through removal of lipids from nanodiscs containing MscS using β-cyclodextrin, resulting in the stretching of the remaining bilayer to cover the same area and thus exerting tension on the embedded protein. There is interest in understanding and validating how gradual lipid removal from a membrane can successfully trigger the opening of mechanosensitive channels. Molecular dynamics simulations are well placed to capture short lived conformations (e.g. the open state), explore the effects of lipid removal on nanodisc behaviour and investigate the movements which allow MscS to transition between functional states.

Here, we use all-atom molecular dynamics simulations to investigate the structural changes which occur in MscS in response to delipidation (to mimic the effect of β-cyclodextrin) and discuss the key roles played by bound lipids associated with these conformational changes.

References

Zhang, Y., Daday, C., Gu, R., Cox, C., Martinac, B., de Groot, B. and Walz, T., 2021. Visualization of the mechanosensitive ion channel MscS under membrane tension. *Nature*, 590(7846), pp.509-514.