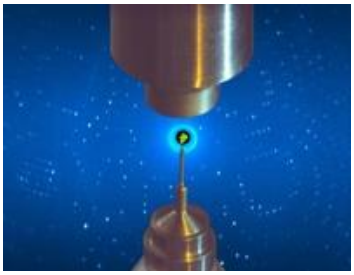

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The structure of KRas at the membrane –simulation and experiment.

Tuesday, 8 June 2021 11:40 (20 minutes)

KRas4B is a membrane-anchored signaling protein and primary target in cancer research. Predictions from molecular dynamics simulations have previously shaped our mechanistic understanding of KRas signaling but disagree with recent experimental results from neutron reflectometry, nuclear magnetic resonance, and thermodynamic binding studies [1]. We compare this body of biophysical data to back-calculated experimental results from a series of molecular simulations that implement different subsets of molecular interactions. Our results show that KRas4B approximates an entropic ensemble of configurations at model membranes, which is not significantly affected by interactions between the globular G-domain of KRas4B and the lipid membrane. These findings promote a model of KRas, in which the G-domain explores the entire accessible conformational space while being available to bind to effector proteins [2].

[1] Van, Q. N. et al. Uncovering a membrane-distal conformation of KRAS available to recruit RAF to the plasma membrane. Proc National Acad Sci 117, 24258–24268 (2020)
[2] Heinrich, F., Van, Q.N., Jean-Francois F., Stephen A.G., Lösche M., Membrane-bound KRAS approximates an entropic ensemble of configurations. Biophys. J. (2021), under review

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