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Unbiased MD simulations of POPI entry into VPS34KD

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We use this protocol and it's working

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Abstract

This protocol details molecular dynamics simulations of the kinase domain of VPS34 in a membrane containing 15% of POPI lipids and analysis of POPI entry into the catalytic site.



Model Preparation

- 1 Use a conformation obtained of the full PI3KC3-C1 active complex engaged with the membrane as starting structure.
- 2 Isolate the C-terminal region of the VPS34KD catalytic subunit (residues F250-K887).

Membrane Composition

- 3 Retain the membrane composition as in simulations of the full complex, with DOPC (60%), DOPE (20%), DOPS (5%), and POPI (15%).

Simulation Runs

- 4 Perform 1 μ s production runs for ten independent replicates of the simulation system.
- 5 Maintain system pressure at 1 Bar and temperature at 310 °K using the Parrinello-Rahman barostat and velocity-rescaling thermostat.

Electrostatic Interactions

- 6 Treat long-range electrostatic interactions using the smooth particle mesh Ewald method with charge interpolation through fourth-order B-splines.

Analysis

- 7 Monitor the time-resolved distance between the inositol 3'-O of POPI lipids and the gamma phosphate of ATP. For each frame, consider only the closest distance.