Dec 23, 2024

Unbiased MD simulations of POPI entry into VPS34KD

DOI
https://dx.doi.org/10.17504/protocols.io.dm6gp9y68vzp/v1

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Protocol Citation: Ainara Claveras Cabezudo, Annan Cook 2024. Unbiased MD simulations of POPI entry into VPS34KD. **protocols.io** https://dx.doi.org/10.17504/protocols.io.dm6gp9y68vzp/v1

Protocol status: Working
We use this protocol and it's working

Created: December 22, 2024

Last Modified: December 23, 2024

Protocol Integer ID: 116785

Keywords: ASAPCRN, molecular dynamics simulations of the kinase domain, unbiased md simulations of popi entry, popi lipid, molecular dynamics simulation, analysis of popi entry, kinase domain, popi entry, vps34kd this protocol, vps34, vps34kd, membrane, catalytic site

Funders Acknowledgements:
Aligning Science Across Parkinson's
Grant ID: ASAP-000350

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 µs 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.