Lipid Models for United-Atom Molecular Dynamics Simulations of Proteins

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Introduction

United-atom force fields for molecular dynamics (MD) simulations provide a higher computational efficiency especially in lipid membrane simulations with little sacrifice in accuracy, when compared to all-atom forcefields. Excellent united-atom lipid models are available, but in combination with the depreciated GROMOS 87 protein force field.

The aims of this research were to develop united-atom models of the lipid 1,2-dipalmitoyl-sn-glycero-3-phosphocholine (DPPC), 1,2-dimyristoyl-sn-glycero-3-phosphocholine (DMPC), 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine (POPC) and 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphoglycerol (POPG) for the modern GROMOS96 53a6 force field.

Methods

Molecular dynamics simulations calculate the thermal motions of molecules subjected to the physics-based interaction forces (the “force field”):

\[
\sum_{\text{atom}} k_{\text{bond}} (r - r_0)^2 + \sum_{\text{angle}} k_{\text{angle}} \Phi \theta, \theta_0 + \sum_{\text{torus}} k_{\text{torus}} (1 - \cos \alpha, \beta, \gamma)
\]

The time evolution of the system is calculated from Newton's equations of motions:

\[
\frac{dv}{dt} = \frac{F}{m}
\]

\[
\frac{dr}{dt} = v
\]

Newton's equations

Leapfrog algorithm

Results

• Area/lipid for DMPC (A), POPC (B) and POPG (C) (--- experiment):

• Different atom charges and atom types lead to different results for area/lipid of DPPC:

• Acyl chain order parameters for DPPC3 agree closely with experiment (*):

• Coordination of Na⁺ ions in POPG simulation:

• ErbB-2 transmembrane peptide simulation (RMSD to experimental structure):

Reference: