FORCE FIELD DEVELOPMENT FOR ATOMIC SIMULATIONS OF LIPID MEMBRANES

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Here we present further development of SLipids (Stockholm Lipids) force field [1,2] with focus on lipids with polyunsaturated fatty acids chains. The strategy previously used for parameterization of lipids with saturated chains was used for polyunsaturated lipids, with strong emphasis on ab-initio computations and using only a limited experimental input.

Polyunsaturated lipids are important components of biological systems. They can be found in different organisms and plants, they are present in large amount in e.g. retina and central neural system and are essential for proper neuronal and retinal function, but were comparatively less studied previously by molecular simulations.

The basic principle: use high quality ab-initio computations where possible.

3 main steps:
1. ab-initio computation of charges for heads and tails in a lipid, with conformational averaging.
2. Fitting Lennart-Jones parameters to density and evaporation heat for smaller fragments.
3. Parametrization of dihedrals: ab-initio computations rotating torsion angle and subsequent validation against structure factors, areas per lipid, NMR order parameters (Gromacs).

Software: Gaussian + RED

Comparison areas per lipid for saturated and polyunsaturated lipids

<table>
<thead>
<tr>
<th>LIPID</th>
<th>P.K.</th>
<th>A.A. (computed)</th>
<th>A.A. (experimental)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DLPC*</td>
<td>333</td>
<td>0.534</td>
<td>0.509</td>
</tr>
<tr>
<td>DMPC**</td>
<td>333</td>
<td>0.509</td>
<td>0.509</td>
</tr>
<tr>
<td>DPPC***</td>
<td>333</td>
<td>0.649</td>
<td>0.671</td>
</tr>
<tr>
<td>DPPC###</td>
<td>333</td>
<td>0.671</td>
<td>0.677</td>
</tr>
<tr>
<td>PC(18:2)</td>
<td>333</td>
<td>0.712</td>
<td>0.714</td>
</tr>
<tr>
<td>PC(18:3)</td>
<td>333</td>
<td>0.671</td>
<td>0.677</td>
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<tr>
<td>PC(18:2)</td>
<td>333</td>
<td>0.712</td>
<td>0.714</td>
</tr>
</tbody>
</table>

Conclusions
The chosen methodology of force field optimization provides simulation results in good agreement with experimental data from X-ray and NMR for lipids with saturated, polyunsaturated and mixed chains. The developed force field SLipids can be further used for predictive simulations of heterogeneous biomembranes to get deep insight into their properties as well as in the field of drug design and other medical applications.

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References: