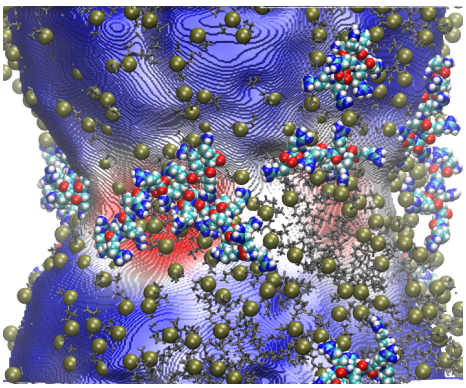

Lipidator Tools

Initial Release Version 1.0

Manual

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Contents

Chapter 1

Features

The lipidator toolkit features implementations of the ReGiS method, the Director fluctuation method and the height fluctuation method to obtain bending and tilt moduli of lipid membranes and surfactants. All methods provide fully automatic fitting and formatted data output. In particular the ReSiS method is designed to support

- arbitrary membrane geometries
- arbitrary cells
- localized moduli
- curvature measurement and visualization

The other methods require square membrane patches with the membrane normal in the z direction. Future updates are likely to lift this requirement. In addition we provide a visualization tool (testcube), that uses advanced ReSiS output to create Gaussian cube files for surface mapping of curvature, tilt and other advanced visualization options.

Chapter 2

Installation

2.1 Requirements

The toolkit requires BOOST C++, Eigen 3 and CMAKE 2.8 to build. By default it assumes the Eigen3 headers in /usr/include/eigen3. The distribution also comes with a copy of KissFFT 1.3. It builds with GNU C++, but other C++ compilers may also work. It also requires OpenMP, which is installed by default on modern computers. After downloading the sourcecode, you may simply build it using

```
cmake .

make
```

The file CMakeLists.txt controls linking and library search options.

Chapter 3

Usage

The standard usage of the tools resis, director and height is

```
toolname trajectory.xtc library.ldx index.ndx [Advanced]
```

Available tools are RESIS, DIRECTOR and HEIGHT. These implement the ReSIS, director fluctuation and height fluctuation methods respectively.

3.1 Necessary Files

In order to use the Lipidator Toolkit, you therefore need a trajectory file in GROMACS xtc format, and index file containing the lipids you are interested in and most importantly a lipid director library. XTC files are standard GROMACS output. The tool gmx trjconv is freely available and capable of converting other formats to xtc.

3.1.1 Preparing the Index file

The index file has the format

```
[ Lipidtype ] .
n1 n2 n3 n4 n5 n6 ...
...
[ Lipidtype2 ]
m1 m2 m3 m4 m5 m6 ..
...
[ Lipidtypen ]
...
```

The atom indices n and m are the first atoms of your lipids. The *Lipidtype* is the name of your lipid, e.g. $DOPE$ as found in the director library. This file can easily be prepared using the GROMACS make_ndx command. You may choose to type it yourself as well. An efficient way of preparing the index file is to use the molecular information from a gro or pdb file. Here is an example for DOPE, where the first atom in the molecule has the type NH3.

```
gmx make_ndx -f conf.gro -o out.ndx
a NH3
name 3 DOPE
del 2
q
```

The del command is used to to remove the groups, especially the automatically generated DOPE groups, that contains all of the molecule's atoms.

Please pay attention that your index file does not contain other groups with the same name

3.1.2 Preparing the Library File

À typical libid library file has the following appearance:

```
#POPE
[P][1]
11 P 19 C 22 C 24 C 31 C 33 C 36 C 83 C
[CHAIN1][2]
73 C 76 C 79 C 116 C 119 C 122 C
[C2][3]
19 C 22 C 24 C 31 C 33 C 36 C 83 C 39 C 86 C 73 5.0 76 5.0 79 5.0
    116 5.0 119 5.0 122 5.0


#ANOTHERLIPID
....
```

A lipid is defined by its name, preceded by a hash # sign. In the next line groups are defined in square brackets. The first square bracket assigns a name, the second assigns a group. The meaning of these groups is

1. Headgroup
2. Tail
3. Surface Atoms

The director is defined as a normalized vector from the center of mass of the headgroup atoms to the tail atoms. It is possible to give several groups to be mapped into either head or tail. The surface is interpolated through the center of the surface atoms.

Do not forget to leave two empty lines after each lipid

After each line defining a group (square brackes) a list of atoms has to be provided. These atoms are relative to the first atom in the lipid, which is defined as 1. The list is made up of pairs. The first element is the atom index and has to be integer, whereas the second value can either be an element name, or a floating point number. An element name will automatically be converted to the molar mass of the correponding element. The name of the lipid in the index file and in the library file have to be identical. Please see advanced options on guidelines to define your own lipid libraries.

3.2 Advanced Usage

Extending the Lipid Library

The format of the lipid library has been discussed in the previous section. Here we provide some guidelines for extending the lipid library. To extend the lipid library the reader should first define a transferable standard for choosing atoms

to compute the director from and adhere to them as far as possible. Options the center of mass of the last three carbon atoms for the tail and phosphate, c2 for the head.

As a second, and much more sensitive step the surface atoms have to also be chosen. This turns out to require some tuning in most cases. We propose the following criteria for a good surface definition

- The Resulting Gaussian in the calculation of the tilt divergence should be centered at zero
- The distribution should be symmetrical
- The surface should be close to the dividing surface of the membrane, usually located around the C2 atoms
- The average curvature and gaussian curvature should be zero in a flat bilayer
- Ideally, there should be a recipe to create surface atoms for other lipids of the same forcefield
- Ideally, the results should be consistent between different methods
- The entropy corrected tilt distribution should also be Gaussian

Fulfilling all of these criteria is not always easy. We recommend having a look at our library files and we welcome the submission of improved surface and director definitions, especially for more lipids and forcefields and will publish them on our webpage with attribution.

3.2.1 ReSIS

So far only the resis tool allows some advanced options. These have to be inserted after the all other options. Currently the following flags are available

w	Activates Monte-Carlo estimate of the Area per lipid
t	Detailed output
c	Wraps trajectory back into the box (orthorhombic cells only)

The Monte-Carlo estimator is very much experimental and should be used with great care. Contributions are welcome. Detailed output comes in the following format:

```
KG : [Gaussian]  B: [Normal] T: [Tilt] DT: [Splay] Frame [Number] p
     [Position] n [Director] N [Surface Normal]
```

Gaussian	Gaussian Surface Curvature on Lipid (float)
Normal	Normal Curvature on Lipid (float)
Tilt	Tilt vector absolute (float)
Splay	Tilt divergence (float)
Frame	Frame Number (integer)
p	Lipid position, 3 floats
n	Director vector, 3 floats
N	Surface normal vector, 3 floats

We provide the tool testcube as a part of the lipidator toolkit to process the advanced output and create color-coded graphs.

Chapter 4

Output

Each tool provides an output summary to stdout after the analysis finishes. One example is the ReSIS output when using the command line

```
./resis traj.xtc lipidlib.ldx traj.ndx
```

The following summary will be printed to stdout

```
-------------------RESIS-1.0-RELEASE-------------------
(c) C. Allolio Mar  7 2018 14:59:26
-------------------------------------------------------
Published: C. Allolio., A. Haluts, D. Harries
Chem. Phys. 2018
https://doi.org/10.1016/j.chemphys.2018.03.004
-------------------------------------------------------
-------------------RESULTS SUMMARY---------------------
 FILE: dope64.xtc
 Area AVG [A^2]: 4061.75 STDEV: 63.9235 Per Lipid [bilayer]:
    63.4648 +- STDERR(10) 0.0164469 STDEV 0.998805
 Mean Curvature /  Lipid [nm^-1]: -0.000649366
 Gausian Curvature / Lipid [nm^-2]: -0.000131437
Monolayer Bending: kappa 14.8115 kt Offset [nm^-1]: 0
Bilayer Tilt: kappa 25.536 kt/nm^2 Offset: 0
-----------------------END SUMMARY---------------------
```

This output is self explanatory. But in addition we generate the files *dope64.xtc.spl* and *dope64.xtc.itilt* These files contain the curves used for fitting the results in plain text format, readable by xmgrace or gnuplot. Note that the endings are simply appended to whatever the original trajectory file was.

4.0.1 Fourier Fluctuation

The *director* tool will also output a summary and a Fourier spectrum plotting $\langle|\tilde{n}_{\parallel}(q)|^2\rangle$ vs q in a file ending with .brown and another file using $\langle|\tilde{n}_{\perp}(q)|\rangle$ vs q with the ending with .btilt as well as give a twist modulus. The height fluctuation method will create a file ending with .fasth, which contains $\langle|\tilde{h}_{\perp}(q)|^4\rangle$ vs q.

4.0.2 Testcube

The testcube tool can create beautful visualizations using cube files, that can be opened e.g. with VMD or GaussView. It is still under development.