CHARMMANDER

A command-line, CHARMM-GUI based membrane builder.

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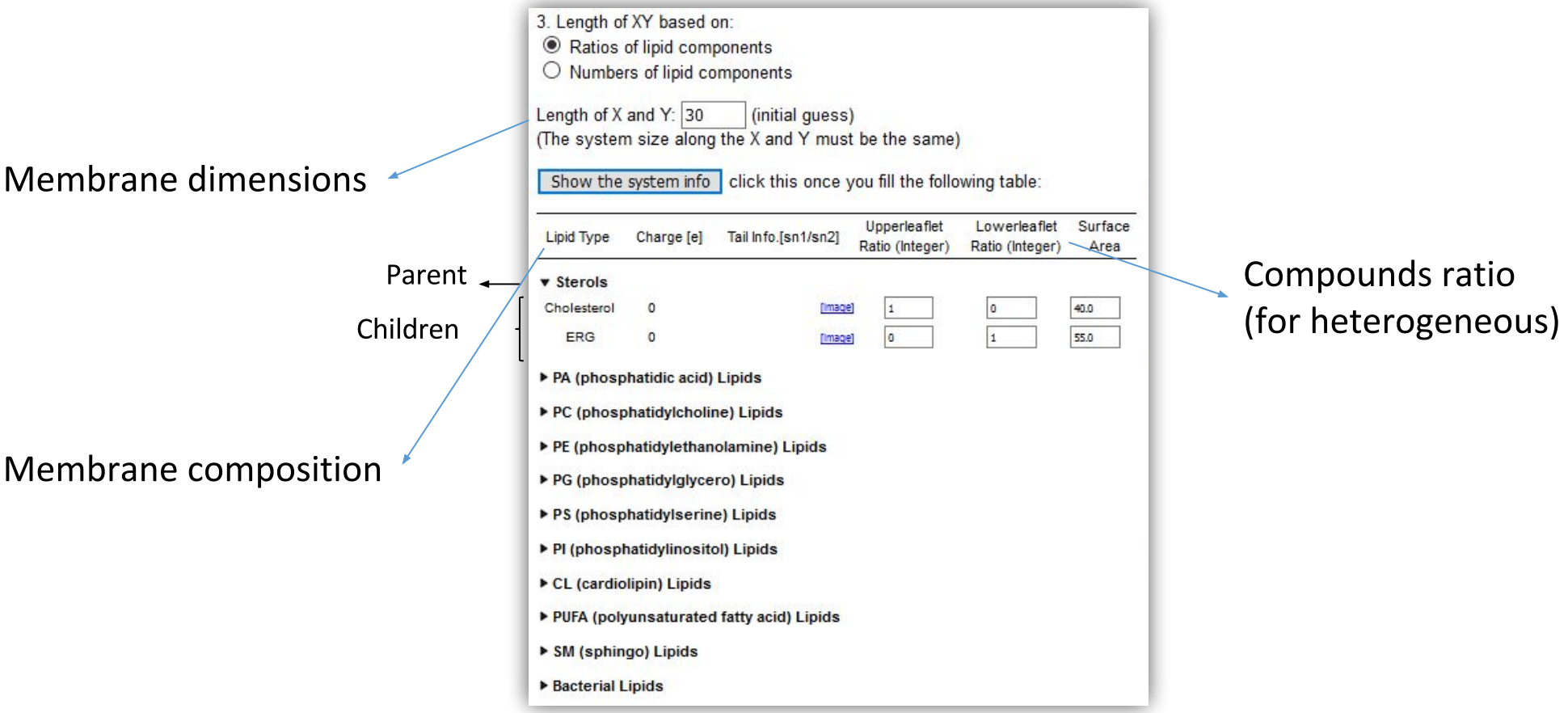
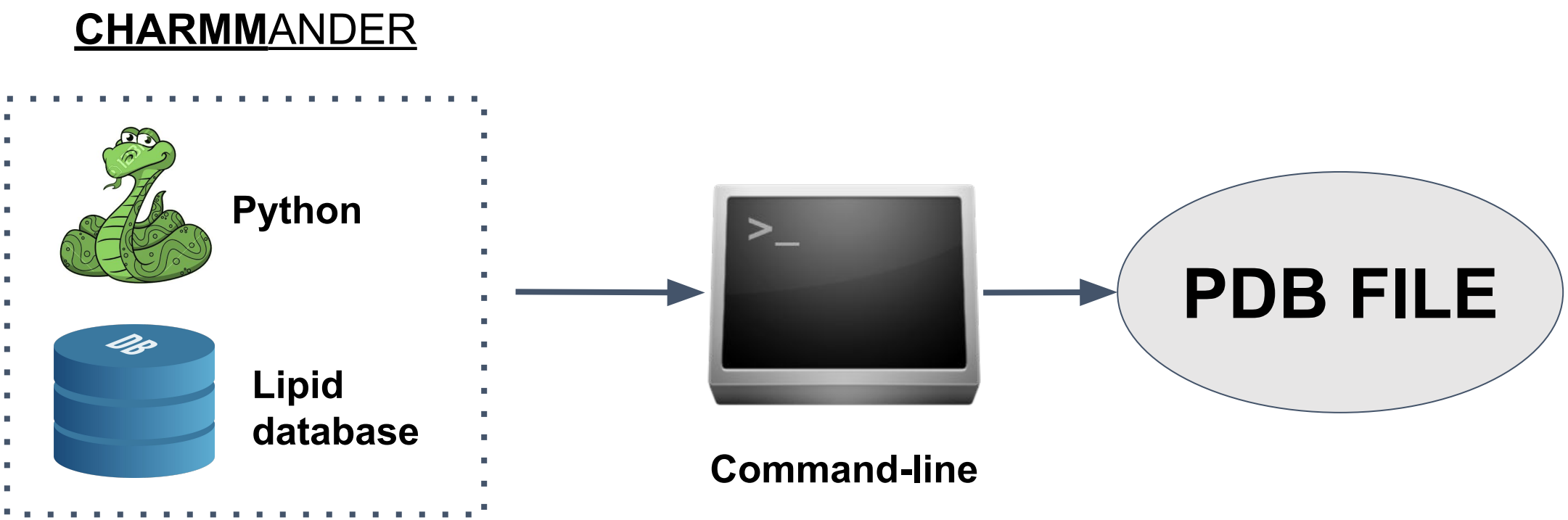
1. Introduction

- CHARMM-GUI Membrane Builder provides a web-based graphical user interface to generate lipid membranes using MD simulations.



2. Objective

- **Project aim**: CHARMM-GUI Membrane Builder → Command-line program



3. Methodology

3.1. Infrastructure

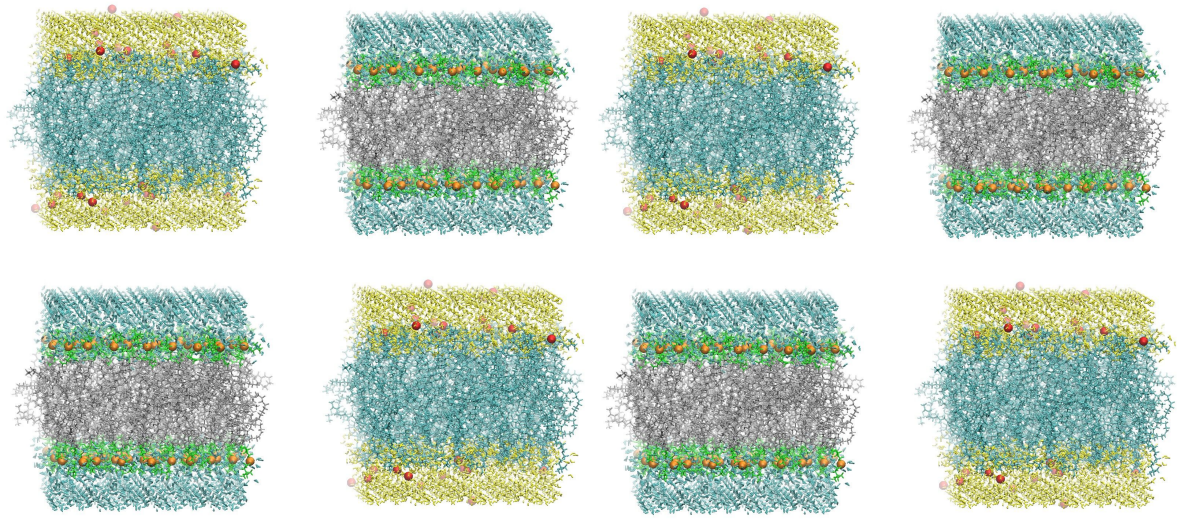
- Database of homogeneous membranes for each lipid, with 30 lipids per leaflet.
- Lipid data dictionaries module:
  - Parent-child relationships
  - Head atom of parent
  - Edge length (sqrSize)
- Main code

3. Methodology

3.1. **Infrastructure:** Database

- Database of **homogeneous** membranes for each lipid (**CRD files**), with 30 lipids per leaflet

Lipid Type	Charge [e]	Tail Info.[sn1/sn2]	Upperleaflet Ratio (Integer)	Lowerleaflet Ratio (Integer)	Surface Area
▸ Sterols					
▸ PA (phosphatidic acid) Lipids					
▸ PC (phosphatidylcholine) Lipids					
▸ PE (phosphatidylethanolamine) Lipids					
▸ PG (phosphatidylglycero) Lipids					
▸ PS (phosphatidylserine) Lipids					
▸ PI (phosphatidylinositol) Lipids					
▸ CL (cardiolipin) Lipids					
▸ PUFA (polyunsaturated fatty acid) Lipids					
▸ SM (sphingo) Lipids					
▸ Bacterial Lipids					
▸ Fatty Acids					
▸ Detergents					



`./db/example_lipid.crd`

3. Methodology

3.1. **Infrastructure:** Lipid data dictionaries

Edge length (sqrSize)

Membrane	Edge Length
Cholesterol	34.641
ERG	40.6202
DLPA	41.4246

Length one edge of the area

Head Atom Parent

Lipid Category	Head Atom
Sterols	O3
PA	P

Separate upper from lower layers

`./lipids_charm_list.py`

3. Methodology

3.1. **Infrastructure:** Lipid data dictionaries

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PA	P

Separate upper from lower layers

Lipid-Category Relationship

Lipid	Lipid category
ERG	Sterols
Cholesterol	Sterols
DLPA	PA

Access to head atom of the child

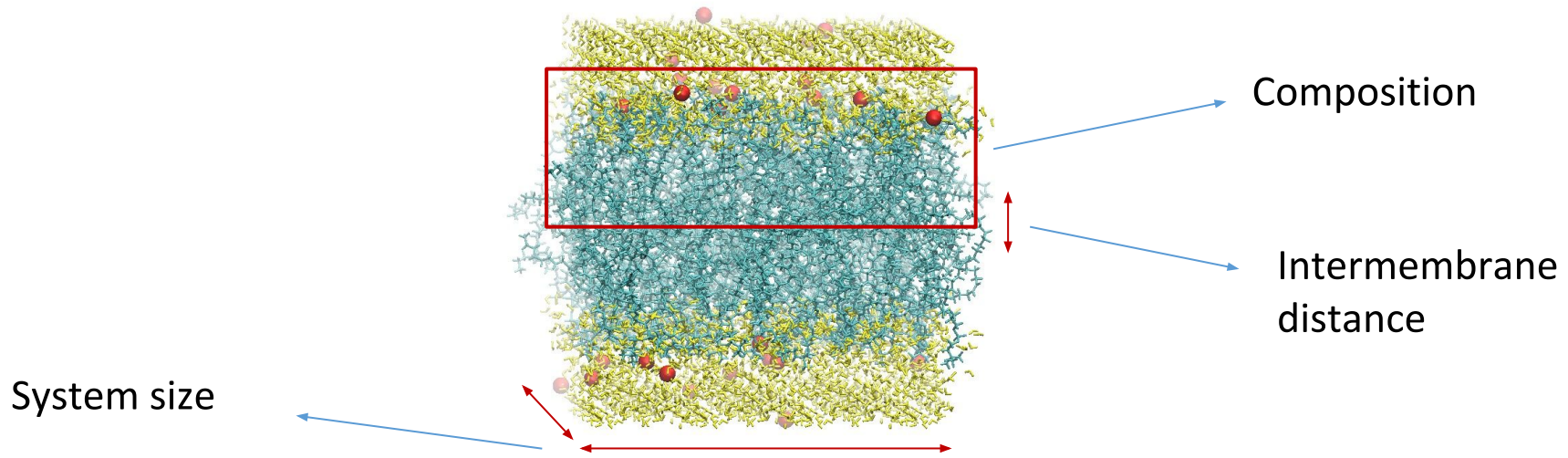
`./lipids_charm_list.py`

3. Methodology

3.2. Main code

- User input.

```
usage: clasif.py [-h] -u UP_LIP [UP_LIP ...] -l LOW_LIP [LOW_LIP ...]
                      -ur UP_RATIO [UP_RATIO ...] -lr LOW_RATIO [LOW_RATIO ...]
                      [-s SYS_SIZE [SYS_SIZE ...]] [-d BET_DIST] [-o OUT_NAME] [-v]
```



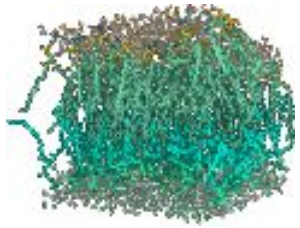
3. Methodology

3.2. Main code

- Selecting membrane template for each leaflet (upper and lower)
  - Main lipid type introduced by user determines the template to select

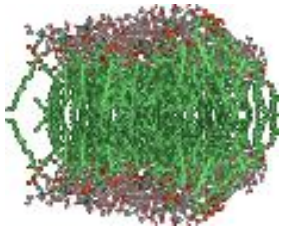
```
python clasif.py -u DGPC DSPS -l DGPC DEPA -ur 1 3 -lr 1 3
```

Major lipid (upper leaflet)



./db/DSPS.crd

Major lipid (lower leaflet)

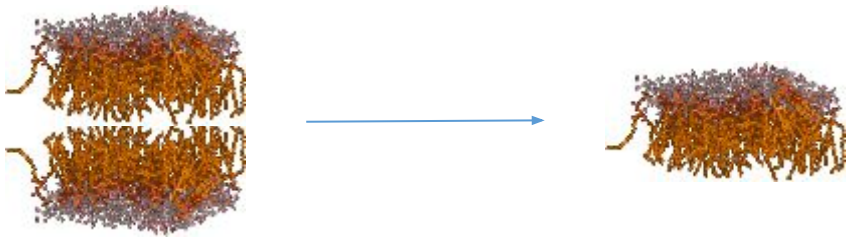


./db/DEPA.crd

3. Methodology

3.2. Main code

- Selecting membrane template for each leaflet (upper and lower)
  - Main lipid type introduced by user determines the template to select
- Reading the correspondent *.crd* template membranes
  - Function that reads the coordinates from the *.crd* file and returns three variables:
    - A molecule object
    - List of residues in upper leaflet
    - List of residues in lower leaflet
- Removing one of the layers from each template



3. Methodology

3.2. Main code

We applied the following pipeline for each leaflet (separately):

- Calculation of current proportions and target proportions (percentage)
- Removal and insertion of lipid
  - Random selection of the residue number that is going to be removed from leaflet
  - Removal of the selected residue
  - Insertion of new lipid
    - New lipids are obtained from the homogeneous membrane templates of the respective lipid
    - **Collisions** are set to TRUE so that the residues that collide are removed from the membrane
- Repeating the 2 previous steps until target proportions are reached

3. Methodology

3.2. Main code

- Creating leaflets of dimensions given by user
  - Taking into account the area of the membrane template and the sizes of the user, repeat the following steps until a square big leaflet is generated (*for* loop):
    - Make copy 1 of leaflet → object molecule to append to
    - Make copy 2 of leaflet → object molecule that will be moved and appended
    - MoveBy the copy *d* units in the X or Y axis
      - *d* is the edge length of the membrane template (retrieved from *sqrtSize* dictionary)
    - Append copy 2 to to copy 1

3. Methodology

3.2. Main code

Finally, the two leaflets are assembled:

- Center both leaflets
- Calculate the vertical size of the largest lipid in both layers
- Move in z axis the lower leaflet by this distance plus the intermembrane distance that the user decides

3. Methodology

3.2. Main code

- Output stored as **PDB file**.
  - Default name (date time) if none provided.
  - User provided.
- Visualization of the output.
  - Optional. Requires VMD installation.

3. Methodology

3.3. Problems found

- Problem 1:

CHARMM-GUI membranes are generated in CRD files (not readable by htmd molecule.py)

  - **Solution**: crd_reader() function → load as molecule objects

3. Methodology

3.3. Problems found

- Problem 2:

molecule.append() method does not output colliding atoms

  - **Solution**: edit molecule.append(mol, **collisions=True**) method → return colliding atoms

3. Methodology

3.3. Problems found

- Problem 3:

Heterogeneous membranes with different composition between layers

  - **Solution**: Separate upper from lower layer (head atoms) and work separately with each one

4. Example of membrane

Choose desired lipids and absolute ratios. **Example**:

python charmmander.py -u SAPA SAPC -l SAPE SAPG -ur 1 3 -lr 3 1 -v -s 200

Sterols

Cholesterol	0	
ERG	0	

PA (phosphatidic acid) Lipids

DLPA	-1	12:0 / 12:0
DMPA	-1	14:0 / 14:0
DPPA	-1	16:0 / 16:0
DSPA	-1	18:0 / 18:0
POPA	-1	16:0 / 18:1
PLPA	-1	16:0 / 18:2
SOPA	-1	18:0 / 18:1
SLPA	-1	18:0 / 18:2
DYPA	-1	16:1 / 16:1
YOPA	-1	16:1 / 18:1
DOPA	-1	18:1 / 18:1
DGPA	-1	20:1 / 20:1
DEPA	-1	22:1 / 22:1
DNPA	-1	24:1 / 24:1

PC (phosphatidylcholine) Lipids

DDPC	0	10:0 / 10:0
DCPC	0	11:0 / 11:0
DLPC	0	12:0 / 12:0
DMPC	0	14:0 / 14:0
DPPC	0	16:0 / 16:0
DSPC	0	18:0 / 18:0
POPC	0	16:0 / 18:1
PLPC	0	16:0 / 18:2
SOPC	0	18:0 / 18:1
SLPC	0	18:0 / 18:2
DYPC	0	16:1 / 16:1
YOPC	0	16:1 / 18:1
DOPC	0	18:1 / 18:1
DUPC	0	18:2 / 18:2
DGPC	0	20:1 / 20:1
DEPC	0	22:1 / 22:1
DNPC	0	24:1 / 24:1

PE (phosphatidylethanolamine)

DLPE	0	12:0 / 12:0
DMPE	0	14:0 / 14:0
DPPE	0	16:0 / 16:0
DSPE	0	18:0 / 18:0
PYPE	0	16:0 / 16:1
POPE	0	16:0 / 18:1
PLPE	0	16:0 / 18:2
SOPE	0	18:0 / 18:1
SLPE	0	18:0 / 18:2
DYPE	0	16:1 / 16:1
YOPE	0	16:1 / 18:1
OYPE	0	18:1 / 16:1
DOPE	0	18:1 / 18:1
DGPE	0	20:1 / 20:1
DEPE	0	22:1 / 22:1
DNPE	0	24:1 / 24:1

PG (phosphatidylglycero) Lipids

DLPG	-1	12:0 / 12:0
DMPG	-1	14:0 / 14:0
DPPG	-1	16:0 / 16:0
DSPG	-1	18:0 / 18:0
PYPG	-1	16:0 / 16:1
POPG	-1	16:0 / 18:1
PLPG	-1	16:0 / 18:2
SOPG	-1	18:0 / 18:1
SLPG	-1	18:0 / 18:2
DYPG	-1	16:1 / 16:1
DOPG	-1	18:1 / 18:1
DGPG	-1	20:1 / 20:1
DEPG	-1	22:1 / 22:1
DNPG	-1	24:1 / 24:1

PS (phosphatidylserine) Lipids

DLPS	-1	12:0 / 12:0
DMPS	-1	14:0 / 14:0
DPPS	-1	16:0 / 16:0
DSPS	-1	18:0 / 18:0
POPS	-1	16:0 / 18:1
PLPS	-1	16:0 / 18:2
SOPS	-1	18:0 / 18:1
SLPS	-1	18:0 / 18:2
DYPS	-1	16:1 / 16:1
YOPS	-1	16:1 / 18:1
DOPS	-1	18:1 / 18:1
DGPS	-1	20:1 / 20:1
DEPS	-1	22:1 / 22:1
DNPS	-1	24:1 / 24:1

Thanks for your attention!

Any question?

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