pymemdyn

Release 2.0

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CHAPTER

ONE

PYMEMDYN VERSION 2.0

PyMemDyn is a standalone *python* package to setup membrane molecular dynamics calculations using the **GROMACS** set of programs. The package can be used either in a desktop environment, or in a cluster with popular queuing systems such as Torque/PBS or Slurm.

PyMemDyn is hosted in github at:

https://github.com/GPCR-ModSim/pymemdyn

You can download any version of **PyMemDyn** by cloning the repository to your local machine using git.

You will need to create a free personal account at github and send and e-mail to: gpcruser@gmail.com requesting access to the code. After request processing from us you will be given access to the free repository.

1.1 Dependencies

GROMACS
Pymemdyn is dependent on GROMACS. Download GROMACS here. Instructions for installation are here.

LigParGen
In order to automatically generate .itp files for ligands and allosterics, the program ligpargen is used. Install using their instructions: https://github.com/Isra3l/ligpargen. Do not forget to activate the conda environment in which you installed ligpargen (conda install py37 if you followed the instructions) before running pymemdyn. In case you are using a bash script, this should be done inside the script. See also "ligpargen_example" in the folder examples.

Testing was done using LigParGen v2.1 using BOSS5.0.

Pymemdyn can also be used without ligpargen installation, but then .itp files containing the parameters for the ligand(s) should be provided.

MODELLER
For replacing missing loops or missing side chains in the protein, MODELLER is used. The download and installation guid for MODELLER are available here.

Queueing system
A queuing system: although not strictly required, this is highly advisable since an MD simulation of 2.5 nanoseconds will be performed. However, if only membrane insertion and energy minimization is requested, this requirement can be avoided. Currently, the queuing systems supported include Slurm and PBS.

1.2 Installation

To install **PyMemDyn** follow these steps:

1. Clone **PyMemDyn** for python 3.7:

```
git clone https://username@github.com/GPCR-ModSim/pymemdyn.git
```

   Make sure to change *username* to the one you have created at github.

2. The previous command will create a *pymemdyn* directory. Now you have to tell your operating system how to find that folder. You achieve this by declaring the location of the directory in a .bashrc file .cshrc or .zshrc file in your home folder. An example of what you will have to include in your .bashrc file follows:

```
export PYMEMDYN=/home/username/software/pymemdyn
export PATH=$PYMEMDYN:$PATH
```

   or if your shell is csh then in your .cshrc file you can add:

```
setenv PYMEMDYN /home/username/software/pymemdyn
set path = ($path $PYMEMDYN)
```

   Notice that I have cloned *pymemdyn* in the software folder in my home folder, you will have to adapt this to wherever it is that you downloaded your *pymemdyn* to.

   After including the route to your *pymemdyn* directory in your .bashrc file make sure to issue the command:

```
source .bashrc
```

   or open a new terminal.

   To check if you have defined the route to the *pymemdyn* directory correctly try to run the main program called pymemdyn in a terminal:

```
pymemdyn --help
```

   You should obtain the following help output:

```
usage: pymemdyn [-h] [-v] [-b OWN_DIR] [-r REPO_DIR] -p PDB [-l LIGAND]
           [--lc LIGAND_CHARGE] [-w WATERS] [-i IONS] [--res RESTRAINT]
           [-f LOOP_FILL] [-q QUEUE] [-d] [--debugFast]

== Setup Molecular Dynamics for Membrane Proteins given a PDB. ==

optional arguments:
  -h, --help            show this help message and exit
  -v, --version         show program's version number and exit
  -b OWN_DIR            Working dir if different from actual dir
  -r REPO_DIR           Path to templates of fixed files. If not provided,
                        take the value from settings.TEMPLATES_DIR.
  -p PDB                Name of the PDB file to insert into membrane for MD
                        (mandatory). Use the .pdb extension. (e.g. -p
                        myprot.pdb)
  -l LIGAND, --lig LIGAND
                        Ligand identifiers of ligands present within the PDB
                        file. If multiple ligands are present, give a comma-
```

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```
                    delimited list.
--lc LIGAND_CHARGE    Charge of ligands for ligpargen (when itp file should
                    be generated). If multiple ligands are present, give a
                    comma-delimited list.
-w WATERS, --waters WATERS
                    Water identifiers of crystalized water molecules
                    present within the PDB file.
-i IONS, --ions IONS  Ion identifiers of crystalized ions present within the
                    PDB file.
--res RESTRAINT       Position restraints during MD production run. Options:
                    bw (Ballesteros-Weinstein Restrained Relaxation -
                    default), ca (C-Alpha Restrained Relaxation)
-f LOOP_FILL, --loop_fill LOOP_FILL
                    Amount of Å per AA to fill cut loops. The total
                    distance is calculated from the coordinates of the
                    remaining residues. The AA contour length is 3.4-4.0
                    Å, To allow for flexibility in the loop, 2.0 Å/AA
                    (default) is suggested. (example: -f 2.0)
-q QUEUE, --queue QUEUE
                    Queueing system to use (slurm, pbs, pbs_ib and svgd
                    supported)
-d, --debug
--debugFast           run pymemdyn in debug mode with less min and eq steps.
                    Do not use for simulation results!
```

3. Updates are very easy thanks to the git versioning system. Once **PyMemDyn** has been downloaded (cloned) into its own *pymemdyn* folder you just have to move to it and pull the newest changes:

```
cd /home/username/software/pymemdyn
git pull
```

4. You can also clone older stable versions of **PyMemDyn**. For example the stable version 1.4 which works well and has been tested extensively again GROMACS version 4.6.7 can be cloned with:

```
git clone https://username@github.com/GPCR-ModSim/pymemdyn.git \
--branch stable/1.4 --single-branch pymemdyn-1.4
```

   Now you will have to change your .bashrc or .cshrc files in your home folder accordingly.

5. To make sure that your GROMACS installation is understood by **PyMemDyn** you will need to specify the path to where GROMACS is installed in your system. To do this you will need to edit the settings.py file with any text editor (vi and emacs are common options in the unix environment). Make sure that only one line is uncommented, looking like: GROMACS_PATH = /opt/gromacs-2021/bin Provided that in your case gromacs is installed in /opt. The program will prepend this line to the binaries names, so calling /opt/gromacs-2021/bin/gmx should point to that binary.

1.3 Modules

1.3.1 Modeling Modules

The following modules define the objects to be modeled.

- **protein.py**. This module defines the ProteinComplex, Protein, Monomer, Dimer, Compound, Ligand, CrystalWaters, Ions, Cholesterol, Lipids, and Alosteric objects. These objects are started with the required files, and can then be passed to other objects.
- **membrane.py**. Defines the cellular membrane.
- **complex.py**. Defines the full complex, protein + membrane. It can include any of the previous objects.

1.3.2 Auxiliary Modules

- **checks.py**. Checks continuity of the protein and composition of the residues.
- **aminoAcids.py**. Contains the amino acids class that defines the 1-letter and three letter codes, along with the number of different atoms per residue.
- **queue.py**. Queue manager. That is, it receives objects to be executed.
- **recipes.py**. Applies step by step instructions for carrying a modeling step.
- **bw4posres.py**. Creates a set of distance restraints based on Ballesteros-Weinstein identities which are gathered by alignment to a multiple-sequence alignment using clustalw.
- **utils.py**. Puts the functions done by the previous objects on demand. For example, manipulate files, copy folders, call functions or classes from standalone modules like bw4posres.py, etc.
- **settings.py** This modules sets up the main environment variables needed to run the calculation, for example, the path to the gromacs binaries.

1.3.3 Execution Modules

- **gromacs.py**. Defines the Gromacs and Wrapper objects. * Gromacs will load the objects to be modeled, the modeling recipe, and run it. * Wrapper is a proxy for gromacs commands. When a recipe entry is sent to it this returns the command to be run.

1.3.4 Executable

- **pymemdyn** The main program to call which sends the run to a cluster.

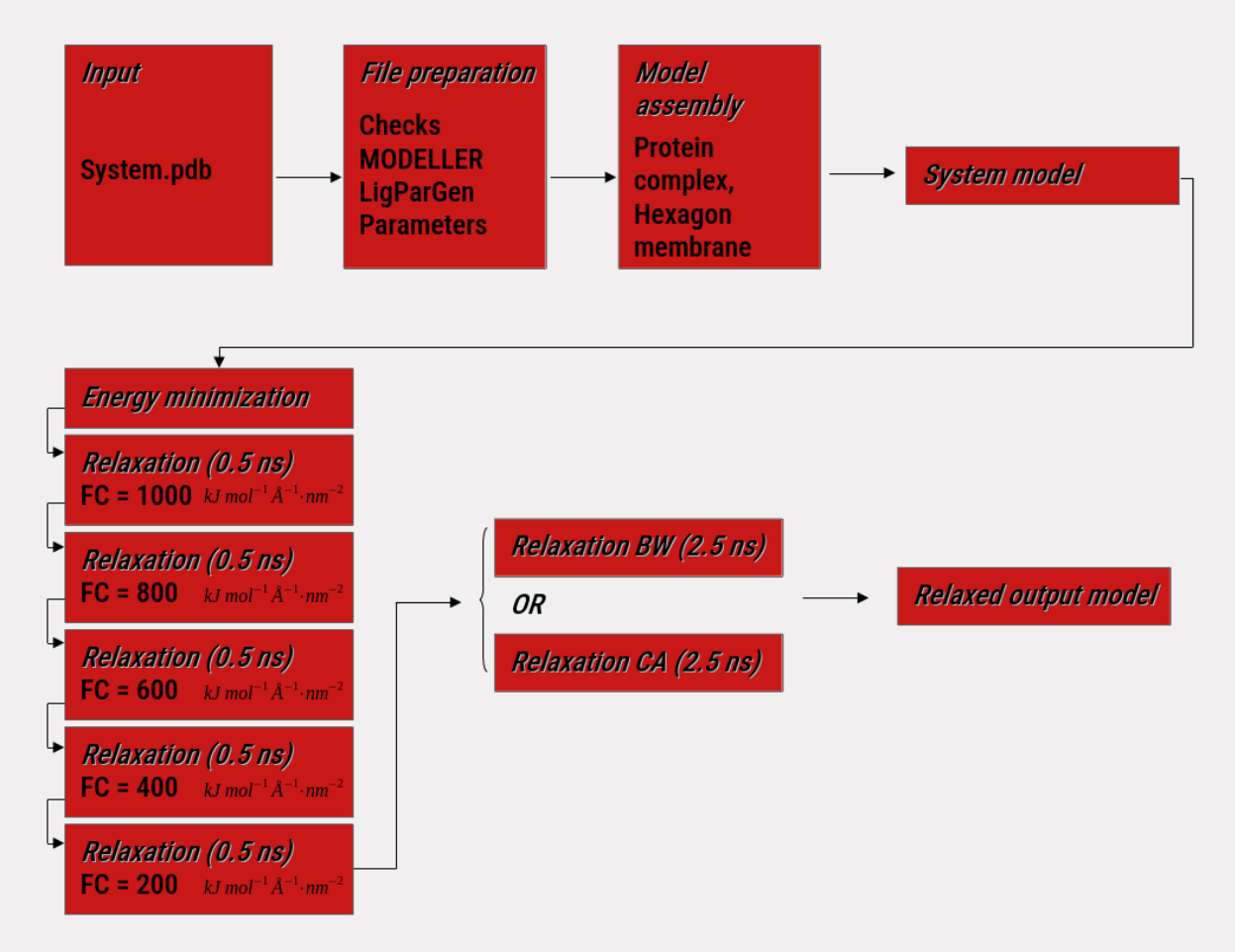
More information about all modules can be found in the Modules chapter.

CHAPTER

TWO

MANUAL

The fully automated pipeline available by using **PyMemDyn** allows any researcher, without prior experience in computational chemistry, to perform an otherwise tedious and complex process of membrane insertion and thorough MD equilibration, as outlined in Figure 1.



In the simplest scenario, only the receptor structure is considered. In such case the GPCR is automatically surrounded by a pre-equilibrated POPC (Palmitoyl-Oleoyl-Phosphatidyl-Choline) membrane model in a way that the TM (Trans-Membrane) bundle is parallel to the vertical axis of the membrane. The system is then soaked with bulk water and inserted into an hexagonal prism-shaped box, which is energy-minimized and carefully equilibrated in the framework of periodic boundary conditions (PBC). A thorough MD equilibration protocol lasting 2.5 ns follows.

But the simulation of an isolated receptor can only account for one part of the problem, and the influence of different

non-protein elements in receptor dynamics such as the orthosteric (primary) ligand, allosteric modulator, or even specific cholesterol, lipid, water or ion molecules are key for a more comprehensive characterization of GPCRs. **PyMemDyn** can explicitly handle these elements allowing a broader audience in the field of GPCRs to use molecular dynamics simulations. These molecules should be uploaded in the same PDB file of the receptor, so they are properly integrated into the membrane insertion protocol described above. Force-field associated files are generated automatically with LigParGen. In addition, it is also possible to perform MD simulations of other membrane proteins, provided that a proper dimerization model exists (i.e., coming from X-ray crystallography or from a protein-protein docking protocol). The ease of use, flexibility and public availability of the **PyMemDyn** library makes it a unique tool for researchers in the receptor field interested in exploring dynamic processes of these receptors.

2.1 Getting started

After you have finished the installation of **PyMemDyn** you can check if the installation has succeeded with:

```
pymemdyn -h
```

This should print the following message:

```
usage: pymemdyn [-h] [-v] [-b OWN_DIR] [-r REPO_DIR] -p PDB [-l LIGAND]
                [--lc LIGAND_CHARGE] [-w WATERS] [-i IONS] [--res RESTRAINT]
                [-f LOOP_FILL] [-q QUEUE] [-d] [--debugFast]

== Setup Molecular Dynamics for Membrane Proteins given a PDB. ==

optional arguments:
  -h, --help            show this help message and exit
  -v, --version         show program's version number and exit
  -b OWN_DIR            Working dir if different from actual dir
  -r REPO_DIR           Path to templates of fixed files. If not provided,
                        take the value from settings.TEMPLATES_DIR.
  -p PDB                Name of the PDB file to insert into membrane for MD
                        (mandatory). Use the .pdb extension. (e.g. -p
                        myprot.pdb)
  -l LIGAND, --lig LIGAND
                        Ligand identifiers of ligands present within the PDB
                        file. If multiple ligands are present, give a comma-
                        delimited list.
  --lc LIGAND_CHARGE    Charge of ligands for ligpargen (when itp file should
                        be generated). If multiple ligands are present, give a
                        comma-delimited list.
  -w WATERS, --waters WATERS
                        Water identifiers of crystalized water molecules
                        present within the PDB file.
  -i IONS, --ions IONS  Ion identifiers of crystalized ions present within the
                        PDB file.
  --res RESTRAINT       Position restraints during MD production run. Options:
                        bw (Ballesteros-Weinstein Restrained Relaxation -
                        default), ca (C-Alpha Restrained Relaxation)
  -f LOOP_FILL, --loop_fill LOOP_FILL
                        Amount of Å per AA to fill cut loops. The total
                        distance is calculated from the coordinates of the
                        remaining residues. The AA contour length is 3.4-4.0
```

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```
                    Å, To allow for flexibility in the loop, 2.0 Å/AA
                    (default) is suggested. (example: -f 2.0)
-q QUEUE, --queue QUEUE
                    Queueing system to use (slurm, pbs, pbs_ib and svgd
                    supported)
-d, --debug
--debugFast         run pymemdyn in debug mode with less min and eq steps.
                    Do not use for simulation results!
```

Don't forget to activate your conda environment if needed.

Now let's say we want to run a system that consists of a membrane protein, two ligands, an ion and some crystallized waters. We need to know a couple of things about the system: the three-letter abbreviations of the ligands, ion and waters, the charge of the ligands. So let's say that in our file we have ligand 1 "LIG", ligand 2 "LIH", ion "NA" and water "POH" and ligand 2 has a charge of -1. Then we can run pymemdyn with the following line:

```
pymemdyn -p file.pdb -l LIG,LIH --lc 0,-1 -i NA -w POH --res ca
```

In case our protein has a missing loop that needs to be filled with Modeller, we can also define the number of Å per AA with -f.

2.2 Running with queues

About 90% of the time you will want to use some queueing system. We deal with queue systems tweaks as we stumble into them and it's out of our scope to cover them all. If you take a look at the source code dir, you'll found some files called "run_pbs.sh", "run_svgd.sh" and so on. Also there are specific queue objects in the source file queue.py we have to tweak for every and each queue. In you want to run your simulation in a supported queue, copy the "run_queuename.sh" file to your working directory, and edit it. E.g. the workdir to run an A2a.pdb simulation in svgd.cesga.es looks like: . .. A2a.pdb run_svgd.sh And run_svgd.sh looks like:

```
\$!/bin/bash
module load python/3.7
module load gromacs/2021
python ~/bin/pymoldyn/pymemdyn -p a2a.pdb
```

Now we just launch this script with:

```
qsub -l arch=amd,num_proc=1,s_rt=50:00:00,s_vmem=1G,h_fsize=1G -pe mpi 8 run_svgd.sh
```

and wait for the results. Note that we launch 1 process, but flag the run as mpi with reservation of 8 cores in SVGD queue.

2.3 Debugging

To also log 'debug'-messages to the log file (log.log), activate the debug mode with –debug:

```
pymemdyn -p proteinComplex.pdb --debug
```

If you are to set up a new system, it is a good idea to just run a few steps of each stage in the equilibration protocol just to test that the pdb file is read correctly and the membrane-insertion protocol works fine and the system can be minimized and does not "explode" during the equilibration protocol (i.e., detect if atom clashes and so on exist on your system).

To do this, use the –debugFast option, like:

```
pymemdyn -p gpcr.pdb -l LIG --waters HOH --debugFast
```

If everythings works fine, you will see the list of output directories and files just as in a regular equilibration protocol, but with much smaller files (since we only use here 1000 steps of MD in each stage). NOTE that sometimes, due to the need of a smooth equilibration procedure (i.e. when a new ligand is introduced in the binding site without further refinement of the complex, or with slight clashes of existing water molecules) this kind of debugging equilibration procedure might crash during the first stages due to hot atoms or LINCS failure. This is normal, and you have two options: i) trust that the full equilibration procedure will fix the steric clashes in your starting system, and then directly run the pymemdyn without the debugging option, or ii) identify the hot atoms (check the mdrun.log file in the last subdirectory that was written in your output (generally eq/mdrun.log and look for "LINCS WARNING"). What if you want to check partial functions of pymoldyn? In order to do this you must edit the file pymemdyn and change:

1. Line 260 comment with "#" this line [that states: run.clean()], which is the one that deletes all the output files present in the working directory.
2. In the last two lines of this file, comment (add a "#") the line: run.moldyn()
3. And uncomment (remove the "#") the line: run.light_moldyn()
4. In the line 153 and within that block (ligh_moldyn) change the lines stating steps = ["xxxx"] and include only those steps that you want to test, which should be within a list of strings.

For the sake of clarity, these have been subdivided in two lines:

```
line 1- steps = ["Init", "Minimization", "Equilibration", "Relax", "CARelax"]
```

Here you remove those strings that you do not want to be executed, i.e. if only membrane insertion and minimization is wished, remove "Equilibration", "Relax", "CARelax" so the line states:

```
steps = ["Init", "Minimization"]

line 2- steps = ["CollectResults"]
```

This only accounts for the preparation of the output files for analysis, so if you only are interested on this stage, comment the previous line. The last assignment is the one that runs. NOTE that you must know what you do, otherwise you might have crashes in the code if needed files to run intermediate stages are missing!

2.4 Output

The performed equilibration includes the following stages:

Table 1: Output

STAGE	RESTRAINED ATOMS	FORCE CONSTANT	TIME
		kJ/(mol A ·nm^2)	ns
Minimization			(Max. 500 steps)
Equil. 1	Protein Heavy Atoms	1000	0.5
Equil. 2	Protein Heavy Atoms	800	0.5
Equil. 3	Protein Heavy Atoms	600	0.5
Equil. 4	Protein Heavy Atoms	400	0.5
Equil. 5	Protein Heavy Atoms	200	0.5
Equil. 6	Venkatakrishnan Pairs /	200 /	2.5 /
Equil. 6	C-alpha Atoms	200	2.5

In this folder you will find several files related to this simulation:

2.4.1 INPUT:

```
- popc.itp              # Topology of the lipids
- ffoplsaa_mod.itp      # Modified OPLSAA-FF, to account for lipid modifications
- ffoplsaabon_mod.itp   # Modified OPLSAA-FF(bonded), to account for lipid modifications
- ffoplsaanb_mod.itp    # Modified OPLSAA-FF(non-bonded), to account for lipid modifications
- topol.tpr             # Input for the first equilibration stage
- topol.top             # Topology of the system
- protein.itp           # Topology of the protein
- index.ndx             # Index file with appropriate groups for GROMACS
- prod.mdp              # Example of a parameter file to configure a production run (see TIPS)
```

2.4.2 STRUCTURES:

```
- hexagon.pdb           # Initial structure of the system, with the receptor centered in the box
- confout.gro           # Final structure of the system (see TIPS)
- load_gpcr.pml         # Loads the initial structure and the trajectory in pymol
```

2.4.3 TRAJECTORY FILES:

```
- traj_pymol.xtc        # Trajectory of the whole system for visualization in pymol. 1 snapshot/100 ps
- traj_EQ.xtc           # Trajectory of the whole system in .xtc format: 1 snapshot/50 ps
- ener_EQ.edr           # Energy file of the trajectory
- load_gpcr.pml         # Script to load the equilibration trajectory in pymol.
```

2.4.4 REPORTS:

In the "reports" subfolder, you will find the following files:

tot_ener.xvg, tot_ener.log	System total energy plot and log
temp.xvg, temp.log	System temperature plot and log
pressure.xvg, pressure.log	System pressure plot and log
volume.xvg, volume.log	System volume plot and log
rmsd-all-atom-vs-start	All atoms RMSD plot
rmsd-backbone-vs-start.xvg	Backbone RMSD plot
rmsd-calpha-vs-start.xvg	C-Alpha RMSD plot
rmsf-per-residue.xvg	Residue RMSF plot

2.4.5 LOGS:

The logger in pymemdyn will write log messages to the file log.log, which is regenerated every run.

In the "logs" subfolder, you will find the log files of mdrun:

eq_{force_constant}.log	log of stages with restrained heavy atoms of the receptor
eqCA.log	log of the stage with restrained C-alfa atoms of the receptor

NOTE ON GROMACS METHODS To integrate the equations of motion we have selected the leap-frog integrator with a 2 femtosecond timestep. Longe-range electrostatic interactions in periodic boundary conditions are treated with the particle mesh Ewald method. We use a Nose-Hoover thermostat with a tau_t of 0.5 picoseconds and a Parinello-Rahman barostat with a tau_p of 2.0. The pressure coupling is semiisotropic, meaning that it's isotropic in the x and y directions but different in the z direction. Since we are using pressure coupling we are working with an NPT ensemble. This is done both in the all-atom restrained steps and in the alpha-carbon atom restrained part. All of these details are more explicitly stated in the Rodriguez et al. [1] publication.

TIPS

NOTE: these tips work for GROMACS version >= 4.5 and < 5.0. For later versions, adjustments are required, but the principle remains the same.

- If you want to configure a .tpr input file for a **production** run, you can use the template 'prod.mdp' file by introducing the number of steps (nsteps), and thus the simulation time, you want to run.

After that, you just have to type:

```
grompp -f prod.mdp -c confout.gro -p topol.top -n index.ndx -o topol_prod.tpr
mdrun -s topol_prod.tpr -o traj.trr -e ener.edr -c confout.gro -g production.log -x traj_prod.xtc
```

- If you want to create a PDB file of your system after the equilibration, with the receptor centered in the box, type:

  echo 1 0 | trjconv -pbc mol -center -ur compact -f confout.gro -o confout.pdb

- If you want to create an xmgrace graph of the root mean square deviation for c-alpha atoms in the 5.0 ns of simulation you can use:

  echo 3 3 | g_rms -f traj_EQ.xtc -s topol.tpr -o rmsd-calpha-vs-start.xvg

- You may want to get a pdb file of your last frame. You can first check the total time of your trajectory and then use this time to request the last frame with:

  gmxcheck -f traj_pymol.xtc echo 1 | trjconv -b 5000 -e 5000 -f traj_pymol.xtc -o last51.pdb

2.5 References

[1] Rodríguez D., Piñeiro A. and Gutiérrez-de-Terán H.
Molecular Dynamics Simulations Reveal Insights into Key Structural Elements of Adenosine Receptors
Biochemistry (2011), 50, 4194-208.

CHAPTER

THREE

MODULES

3.1 Pymemdyn

This is the main script for the pymemdyn commandline tool. In this script the following things are accomplished:

1. Command line arguments are parsed.
2. (If necessary) a working directory is created.
3. (If necessary) previous Run files are removed.
4. A run is done.

3.1.1 Usage

```
usage: pymemdyn [-h] [-v] [-b OWN_DIR] [-r REPO_DIR] -p PDB [-l LIGAND]
            [--lc LIGAND_CHARGE] [-w WATERS] [-i IONS] [--res RESTRAINT]
            [-f LOOP_FILL] [-q QUEUE] [-d] [--debugFast]

== Setup Molecular Dynamics for Membrane Proteins given a PDB. ==

optional arguments:
  -h, --help            show this help message and exit
  -v, --version         show program's version number and exit
  -b OWN_DIR            Working dir if different from actual dir
  -r REPO_DIR           Path to templates of fixed files. If not provided,
                        take the value from settings.TEMPLATES_DIR.
  -p PDB                Name of the PDB file to insert into membrane for MD
                        (mandatory). Use the .pdb extension. (e.g. -p
                        myprot.pdb)
  -l LIGAND, --lig LIGAND
                        Ligand identifiers of ligands present within the PDB
                        file. If multiple ligands are present, give a comma-
                        delimited list.
  --lc LIGAND_CHARGE    Charge of ligands for ligpargen (when itp file should
                        be generated). If multiple ligands are present, give a
                        comma-delimited list.
  -w WATERS, --waters WATERS
                        Water identifiers of crystalized water molecules
                        present within the PDB file.
  -i IONS, --ions IONS  Ion identifiers of crystalized ions present within the
```

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```
                      PDB file.
 --res RESTRAINT      Position restraints during MD production run. Options:
                      bw (Ballesteros-Weinstein Restrained Relaxation -
                      default), ca (C-Alpha Restrained Relaxation)
 -f LOOP_FILL, --loop_fill LOOP_FILL
                      Amount of Å per AA to fill cut loops. The total
                      distance is calculated from the coordinates of the
                      remaining residues. The AA contour length is 3.4-4.0
                      Å, To allow for flexibility in the loop, 2.0 Å/AA
                      (default) is suggested. (example: -f 2.0)
 -q QUEUE, --queue QUEUE
                      Queueing system to use (slurm, pbs, pbs_ib and svgd
                      supported)
 -d, --debug
 --debugFast          run pymemdyn in debug mode with less min and eq steps.
                      Do not use for simulation results!
```

3.2 Run module

class run.Run(*pdb*, **args*, ***kwargs*)

Bases: object

clean()

Removes all previously generated files

moldyn()

Run all steps in a molecular dynamics simulation of a membrane protein

light_moldyn()

This is a function to debug a run in steps

check_dist(*vector1*, *vector2*)

Check distance between protein and all possible ligands (if any). Raise warning is dist > 50

3.3 Protein module

This module handles the protein and all submitted molecules around it.

class protein.System(***kwargs*)

Bases: object

split_system(***kwargs*)

class protein.ProteinComplex(**args*, ***kwargs*)

Bases: object

setObjects(*object*)

Sets an object.

getObjects(*object*)

set_nanom()

Convert dimension measurements to nanometers for GROMACS

class protein.Protein(**args*, ***kwargs*)

Bases: object

check_number_of_chains()

Determine if a PDB is a Monomer or a Dimer

calculate_center()

Determine center of the coords in the self.pdb.

class protein.Monomer(**args*, ***kwargs*)

Bases: object

class protein.Oligomer(**args*, ***kwargs*)

Bases: Monomer

class protein.CalculateLigandParameters

Bases: object

create_itp(*ligand: str*, *charge: int*) → None

Call ligpargen to create gromacs itp file and corresponding openmm pdb file. Note that original pdb file will be replaced by opnemm pdb file.

Parameters

- pdbfile – string containing local path to pdb of molecule. In commandline -i.
- charge – interger charge of molecule. In commandline -c.
- numberOfOptimizations – number of optimizations done by ligpargen. In cmdline -o.

Returns

None

Writes itp file and new pdf file to current dir. old pdb is saved in dir ligpargenInput. unneccessary ligpargen output is saved in dir ligpargenOutput.

add_h(*ligand*)

lpg2pmd(*cofactor*, *index*, **args*, ***kwargs*)

Converts LigParGen structure files to PyMemDyn input files.

Original files are stored as something_backup.pdb or something_backup.itp.

class protein.Compound(**args*, ***kwargs*)

Bases: object

This is a super-class to provide common functions to added compounds

check_files(**files*)

Check if files passed as *args exist

calculate_center()

Determine center of the coords in the self.pdb.

correct_resid(*pdb*, *resid*)

Correct the residue id to the specified residue id.

class protein.Ligand(**args*, ***kwargs*)

Bases: Compound

check_forces()

A force field must give a set of forces which match every atom in the pdb file. This showed particularly important to the ligands, as they may vary along a very broad range of atoms

class protein.CrystalWaters(**args*, ***kwargs*)

Bases: Compound

setWaters(*value*)

Set crystal waters

getWaters()

Get the crystal waters

property number

Get the crystal waters

count_waters()

Count and set the number of crystal waters in the pdb

class protein.Ions(**args*, ***kwargs*)

Bases: Compound

setIons(*value*)

Sets the crystal ions

getIons()

Get the crystal ions

property number

Get the crystal ions

count_ions()

Count and set the number of ions in the pdb

3.4 Checks module

In this file multiple checks are defined for the protein.

class checks.CheckProtein(**args*, ***kwargs*)

Bases: object

find_missingLoops()

Check if the residue numbering is continuous, write sequence. If loops are missing, return missingLoc.

find_missingSideChains()

Check all sidechains of amino acids, save missing ones for modeller and remove faulty side chains from pbd.

Returns

list of tuples in the form [(resID, 'ALA')]

make_ml_pir(**kwargs)

make_ml_pr: Modify missing regions and create a MODELLER alignment file (.pir)

Parameters

- work_dir – working directory
- tgt1 – alignment.pir

refine_protein(**kwargs)

Refine protein structure using MODELLER

Parameters

knowns – the .pdb file to be refined

Returns

.pdb file of refined protein

3.5 aminoAcids module

File for amino acid definitions

class aminoAcids.AminoAcids

Bases: object

3.6 Membrane module

class membrane.Membrane(*args, **kwargs)

Bases: object

Set the characteristics of the membrane in the complex.

set_nanom()

Convert some measurements to nanometers to comply with GROMACS units.

3.7 Bw4posres module

Date: June 23, 2015 Email: mauricio.esguerra@gmail.com

Description: With this code we wish to do various task in one module:

1. Translate pdb to fasta without resorting to import Bio.
2. Align the translated fasta sequence to a Multiple Sequence Alignment (MSA) and place Marks coming from a network of identified conserved pair-distances of Venkatakrishnan et al. clustalo –profile1=GPCR_inactive_BWtags.aln –profile2=mod1.fasta -o withbwtags.aln –outfmt=clustal –wrap=1000 –force -v -v -v
3. Translate Marks into properly identified residues in sequence. Notice that this depends on a dictionary which uses the Ballesteros-Weinstein numbering.
4. From sequence ID. pull the atom-numbers of corresponding c-alphas in the matched residues.

class bw4posres.Run(*pdb*, ***kwargs*)

Bases: object

A pdb file is given as input to convert into one letter sequence and then align to curated multiple sequence alignment and then assign Ballesteros-Weinstein numbering to special positions.

pdb2fas()

From pdb file convert to fasta sequence format without the use of dependencies such as BioPython. This pdb to fasta translator checks for the existance of c-alpha residues and it is based on their 3-letter sequence id.

clustalalign()

Align the produced fasta sequence with clustalw to assign Ballesteros-Weinstein marks.

getcalphas()

Pulls out the atom numbers of c-alpha atoms. Restraints are placed on c-alpha atoms.

makedisre()

Creates a disre.itp file with atom-pair id's to be restrained using and NMR-style Heaviside function based on Ballesteros-Weinstein tagging.

3.8 Complex module

class complex.MembraneComplex(**args*, ***kwargs*)

Bases: object

setMembrane(*membrane*)

Set the membrane pdb file

getMembrane()

setComplex(*complex*)

Set the complex object

getComplex()

3.9 Queue module

A multi-producer, multi-consumer queue.

exception queue.Empty

Bases: Exception

Exception raised by Queue.get(block=0)/get_nowait().

exception queue.Full

Bases: Exception

Exception raised by Queue.put(block=0)/put_nowait().

class queue.Queue(*maxsize=0*)

Bases: object

Create a queue object with a given maximum size.

If maxsize is <= 0, the queue size is infinite.

task_done()

Indicate that a formerly enqueued task is complete.

Used by Queue consumer threads. For each get() used to fetch a task, a subsequent call to task_done() tells the queue that the processing on the task is complete.

If a join() is currently blocking, it will resume when all items have been processed (meaning that a task_done() call was received for every item that had been put() into the queue).

Raises a ValueError if called more times than there were items placed in the queue.

join()

Blocks until all items in the Queue have been gotten and processed.

The count of unfinished tasks goes up whenever an item is added to the queue. The count goes down whenever a consumer thread calls task_done() to indicate the item was retrieved and all work on it is complete.

When the count of unfinished tasks drops to zero, join() unblocks.

qsize()

Return the approximate size of the queue (not reliable!).

empty()

Return True if the queue is empty, False otherwise (not reliable!).

This method is likely to be removed at some point. Use qsize() == 0 as a direct substitute, but be aware that either approach risks a race condition where a queue can grow before the result of empty() or qsize() can be used.

To create code that needs to wait for all queued tasks to be completed, the preferred technique is to use the join() method.

full()

Return True if the queue is full, False otherwise (not reliable!).

This method is likely to be removed at some point. Use qsize() >= n as a direct substitute, but be aware that either approach risks a race condition where a queue can shrink before the result of full() or qsize() can be used.

put(*item*, *block=True*, *timeout=None*)

Put an item into the queue.

If optional args 'block' is true and 'timeout' is None (the default), block if necessary until a free slot is available. If 'timeout' is a non-negative number, it blocks at most 'timeout' seconds and raises the Full exception if no free slot was available within that time. Otherwise ('block' is false), put an item on the queue if a free slot is immediately available, else raise the Full exception ('timeout' is ignored in that case).

get(*block=True*, *timeout=None*)

Remove and return an item from the queue.

If optional args 'block' is true and 'timeout' is None (the default), block if necessary until an item is available. If 'timeout' is a non-negative number, it blocks at most 'timeout' seconds and raises the Empty exception if no item was available within that time. Otherwise ('block' is false), return an item if one is immediately available, else raise the Empty exception ('timeout' is ignored in that case).

put_nowait(*item*)

Put an item into the queue without blocking.

Only enqueue the item if a free slot is immediately available. Otherwise raise the Full exception.

get_nowait()

Remove and return an item from the queue without blocking.

Only get an item if one is immediately available. Otherwise raise the Empty exception.

class queue.PriorityQueue(*maxsize=0*)

Bases: Queue

Variant of Queue that retrieves open entries in priority order (lowest first).

Entries are typically tuples of the form: (priority number, data).

class queue.LifoQueue(*maxsize=0*)

Bases: Queue

Variant of Queue that retrieves most recently added entries first.

3.10 Recipes module

This module describes the commandline or python commands for all the phases of pymemdyn. It consists of:

- Init
- Minimization
- Equilibration
- Relaxation
- Collecting results

class recipes.BasicInit(****kwargs*)

Bases: object

class recipes.LigandInit(****kwargs*)

Bases: BasicInit

class recipes.BasicMinimization(****kwargs*)

Bases: object

class recipes.BasicEquilibration(****kwargs*)

Bases: object

class recipes.LigandEquilibration(****kwargs*)

Bases: BasicEquilibration

class recipes.BasicRelax(****kwargs*)

Bases: object

class recipes.LigandRelax(****kwargs*)

Bases: BasicRelax

class recipes.BasicCARelax(****kwargs*)

Bases: object

class recipes.BasicBWRelax(****kwargs*)

Bases: object

class recipes.BasicCollectResults(**kwargs)

Bases: object

class recipes.BasicCACollectResults(**kwargs)

Bases: BasicCollectResults

class recipes.BasicBWCollectResults(**kwargs)

Bases: BasicCollectResults

3.11 Gromacs module

class gromacs.Gromacs(*args, **kwargs)

Bases: object

set_membrane_complex(*value*)

set_membrane_complex: Sets the membrane object

get_membrane_complex()

property membrane_complex

count_lipids(**kwargs)

count_lipids: Counts the lipids in source and writes a target with N4 tags

get_charge(**kwargs)

get_charge: Gets the total charge of a system using gromacs grompp command

get_ndx_groups(**kwargs)

get_ndx_groups: Run make_ndx and set the total number of groups found

get_ndx_sol(**kwargs)

get_ndx_sol: Run make_ndx and set the last number id for SOL found

make_ndx(**kwargs)

make_ndx: Wraps the make_ndx command tweaking the input to reflect the characteristics of the complex

make_topol_lipids(**kwargs)

make_topol_lipids: Add lipid positions to topol.top

manual_log(*command*, *output*)

manual_log: Redirect the output to file in command[“options”][“log”] Some commands can’t be logged via flag, so one has to catch and redirect stdout and stderr

relax(**kwargs)

relax: Relax a protein

run_recipe(*debugFast=False*)

run_recipe: Run recipe for the complex

select_recipe(*stage=''*, *debugFast=False*)

select_recipe: Select the appropriate recipe for the complex

set_box_sizes()

set_box_sizes: Set length values for different boxes

set_chains(**kwargs)

set_chains: Set the REAL points of a dimer after protonation

set_grompp(**kwargs)

set_grompp: Copy template files to working dir

set_itp(**kwargs)

set_itp: Cut a top file to be usable later as itp

set_options(*options*, *breaks*)

set_options: Set break options from recipe

set_popc(*tgt=''*)

set_popc: Create a pdb file only with the lipid bilayer (POP), no waters. Set some measures on the fly (height of the bilayer)

set_protein_height(**kwargs)

set_protein_height: Get the z-axis center from a pdb file for membrane or solvent alignment

set_protein_size(**kwargs)

set_protein_size: Get the protein maximum base width from a pdb file

set_stage_init(**kwargs)

set_stage_init: Copy a set of files from source to target dir

set_steep(**kwargs)

set_steep: Copy the template steep.mdp to target dir

set_water(**kwargs)

set_water: Create a water layer for a box

class gromacs.Wrapper(*args, **kwargs)

Bases: object

generate_command(*kwargs*)

generate_command: Receive some variables in kwargs, generate the appropriate command to be run. Return a set in the form of a string "command -with flags"

run_command(*kwargs*)

run_command: Run a command that comes in kwargs in a subprocess, and return the output as (output, errors)

3.12 Groerrors module

exception groerrors.GromacsError

Bases: BaseException

exception groerrors.IOGromacsError(*command*, *explain*)

Bases: GromacsError

Exception raised with "File input/output error" message

class groerrors.GromacsMessages(*gro_err=''*, *command=''*, *args, **kwargs)

Bases: object

Load an error message and split it along as many properties as possible

e = {'Can not open file': <class 'groerrors.IOGromacsError'>, 'Fatal error:': <class 'groerrors.IOGromacsError'>, 'File input/output error': <class 'groerrors.IOGromacsError'>, 'srun: error: Unable to create job step': <class 'groerrors.IOGromacsError'>}

check()

Check if the GROMACS error message has any of the known error messages. Set the self.error to the value of the error

3.13 Broker module

This is a lame broker (or message dispatcher). When Gromacs enters a run, it should choose a broker from here and dispatch messages through it.

Depending on the broker, the messages may be just printed or something else

class broker.Printing

Bases: object

dispatch(*msg*)

Simply print the msg passed

3.14 Utils module

utils.clean_pdb(*src=[]*, *tgt=[]*)

Remove incorrectly allocated atom identifiers in pdb file

utils.clean_topol(*src=[]*, *tgt=[]*)

Clean the src topol of path specifics, and paste results in target

utils.concat(***kwargs*)

Make a whole pdb file with all the pdb provided

utils.getbw(***kwargs*)

Call the Ballesteros-Weistein based pair-distance restraint module.

utils.make_cat(*dir1*, *dir2*, *name*)

Very tight function to make a list of files to inject in some GROMACS suite programs

utils.make_ffoplsaanb(*complex=None*)

Join all OPLS force fields needed to run the simulation

utils.make_topol(*template_dir='/home/rkupper/apps/pymemdyn/templates'*, *target_dir=''*, *working_dir=''*, *complex=None*)

Make the topol starting from our topol.top template

utils.tar_out(*src_dir=[]*, *tgt=[]*)

Tar everything in a src_dir to the tar_file

3.15 Settings module

This module handles the local settings for pymemdyn on your machine. The settings are mostly paths and run settings.

CHAPTER

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PYTHON MODULE INDEX

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