**Tutorial for Ligand-Protein simulation**

This is a very basic and simple tutorial to setup a ligand-protein system; all you need to do is to utilize the scripts obtained from **CHARMM-GUI** (whatever the system contains a halogenated ligand or not, the way to build up the system is the same). In this example, one of an easiest way to build the ligand-protein system will be introduced, that is 1) use CHARMM-GUI to build the protein, and then 2) modify the script to add the ligand or ions. The scripts for Drude will be illustrated in the following, while the scripts for the additive are used in a similar approach, and thus not are described here.

**Folders:**

Input scripts for Drude simulations are inside the "4tutorial\_drude" folder

Input scripts for Additive simulations are inside the "4tutorial\_additive" folder

**[ 4tutorial\_drude ]**

Before using the scripts in this folder, you need to generate structures from CHARMM-GUI.

**# 0. Basic usage in CHARMM-GUI**

0-1. Use CHARMM-GUI Solvator to generate protein additive formats (e.g.psf, crd, pdb )

0-2. Use CHARMM-GUI Drude Prepper to build the protein in Drude formats.

Once the those files are generated from CHARMM-GUI, go to **setup-system** folder.

**# 1. Setup-system**

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The setup\_system folder includes the following script

(these scripts are just minor adaptions from charmm-gui's additive scripts; the adaptions include adding "setup warn drude dmass 0.4", "coor sdrude", "coor shake" and change TIP3 to SWM4 these type of commands):

step3.0\_patch.inp

step4.1\_waterbox.inp

step4.2\_ions.inp

step4\_solvator.inp

step5\_pbcsetup.inp

**[Note 1]:** User only need to change the step3.0\_patch.inp to add their ligand.

For example :

read sequence 22U 1

generate 22U first none last none setup warn drude dmass 0.4

OPEN UNIT 1 CARD READ NAME @in/crys\_22u\_h.pdb

READ coor pdb UNIT 1 append

close unit 1

**[Note 2]:** User needs to build their ligand and its toppar stream file; in my case, I built them manually. Note that urrently the bond information for Lonepair is required for NAMD (see toppar/toppar\_22u.str)

**[Note 3]:** The dimension of the boxsize will be written in step4.1\_waterbox.prm

If you want to use the cubic box size:

Please use the following commands in step4.1\_waterbox.inp

calc Xinit = @Lbox

calc Yinit = @Lbox

calc Zinit = @Lbox

To setup systems, just run the above step3.0~step5.inp sequentially. Once the those files are prepared, go to **run\_namd** folder.

**# 2. Run with NAMD**

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The step5\_pbcsetup.psf and step5\_pbcsetup.pdb generated from the setup-system will be used for NAMD.

In **run\_namd** folder, this includes two namd configuration files, which assigned the parameters used for NAMD.

equil.in (for equilibration)

prod.in (for production)

[Note 4] The equil\_restrain.pdb, prod\_restrain\_ca.pdb are the restrained used for this systems, uses could change according to their systems. Besides, the number of steps used in this tutorial are also small, users may need to extend them.

**[ 4tutorial\_additive ]**

The additive files are prepared in the similar approach. Please refer to 4tutorial\_additive folder.

**Note 1:** The ligand's toppar stream file was generated by CGenFF. (see add\_toppar/22u\_lp\_namd.str; currently, the bond information for Lonepair is required for NAMD)

**Note 2:** If the input pdb does not include the lonepair (ex: input/crys\_22u\_h.pdb), you need to add "coor shake" in step3.1.