

# Coarse-grained Molecular Dynamics Simulations with Membrane Proteins

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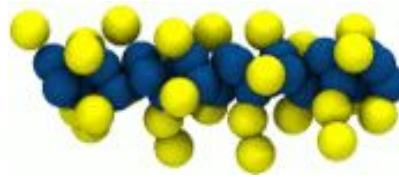


# Molecular Dynamics Simulations

- Molecular dynamics (**MD**) **simulations** as ‘computational microscopes’.
- When computationally modeling biomolecular systems, the **molecular model** (degrees of freedom) can be either:
  - Atomic model (All Atom MD)
  - Models grouping atoms (Coarse-Grained MD)
- The molecular model will depend on the type of properties of interest of the system under study.

# Coarse-Grained MD Simulations

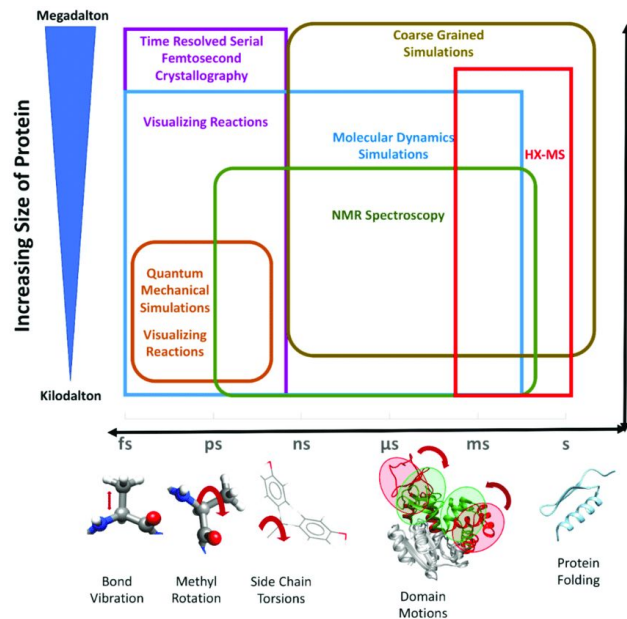
- Coarse-grained models reduce the level of description by grouping all atom types in larger particles.



- The lack of resolution confers **unique properties** to the MD simulations. This comes with advantages and limitations of this type of models.
- Depending on the particular parameters we need to analyse for our study: only AA or CG (usually); or both type of models can be suitable.

# Coarse-Grained MD Simulations

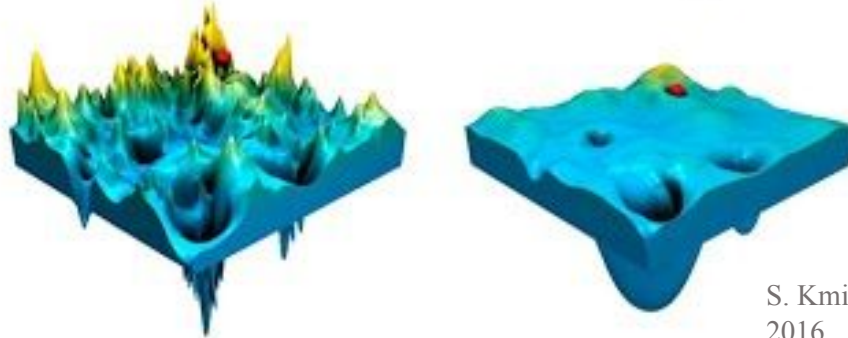
- **Simulation of large systems and long timescales** which are inaccessible to traditional AA simulations.



Srivastava et al.,  
2018

# Coarse-Grained MD Simulations

- **Simulation of large systems and long timescales** which are inaccessible to traditional AA simulations.
- CG simulations show a smoothened potential energy landscape (reduced friction) → In the same simulation time, a CG system can therefore sample more of that energy landscape in a given time of period. → Speed up of the system kinetics. → **The event of study usually occurs in less simulation time** (not well defined).

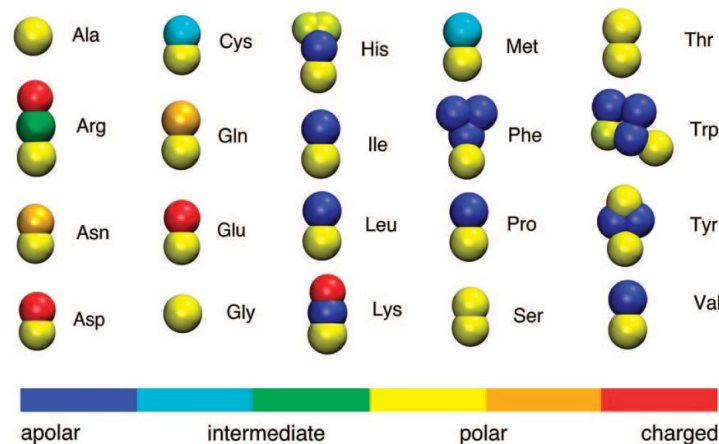


# Coarse-Grained MD Simulations

- **Simulation of large systems and long timescales** which are inaccessible to traditional AA simulations.
- CG simulations show a smoothened potential energy landscape (reduced friction) → In the same simulation time, a CG system can therefore sample more of that energy landscape in a given time of period. → Speed up of the system kinetics. → **The event of study usually occurs in less simulation time** (not well defined).
- This advantages come from a **lack of resolution** → The questions under investigation cannot strongly depend on the lost degrees of freedom.
  - Increase resolution, hybrid systems, backmapping?

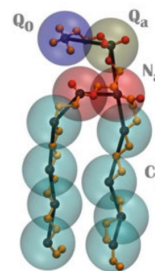
# The MARTINI Forcefield

- 4 to 1 mapping.
  - 4 main types of particle (charged ( $Q$ ), polar ( $P$ ), non-polar ( $N$ ) and apolar ( $C$ )).
  - 18 final bead types or 'building blocks'
- Realistic structural information.
  - Preferred interaction modes
  - Aggregation patterns
  - Lipid-mediated effects
- Speed up of the system kinetics (time scale)
- **Limitations**
  - Resolution
  - Elastic Network
  - Excessive aggregation



Periole and Marrink,  
2013

## DPPC

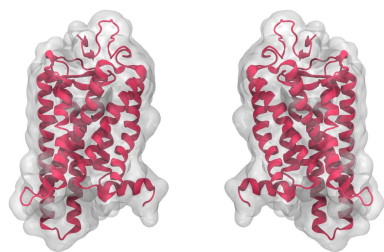


## Water



Monticelli et al.,  
2013

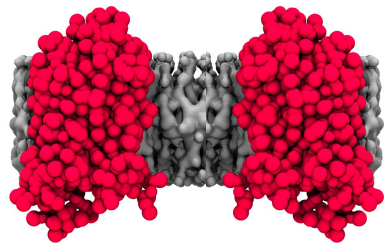
# Today's Protocol



**PDB**  
**(4dkl)**



**CHARMM-GUI**  
(MARTINI MAKER module)



**GROMACS + MARTINI FF**  
(MD simulation package)



**Python**  
(Jupyter notebooks + MD  
Analysis)



**Analysis**



# Generating a CG system using CHARMM-GUI

## CHARMM-GUI

Effective Simulation Input Generator and More

CHARMM is a versatile program for atomic-level simulation of many-particle systems, particularly macromolecules of biological interest. - M. Karplus

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Some [lectures](#), [job postings](#), and [FAQ](#) are now available. See [upload log](#) for update history and [giving](#) for donation. [Contact](#) info is given below.

CHARMM-GUI

About Us

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## Front Page

Since its original development in 2006, CHARMM-GUI has proven to be an ideal web-based platform to interactively build complex systems and prepare their inputs with well-established and reproducible simulation protocols for state-of-the-art biomolecular simulations using widely used simulation packages such as CHARMM, NAMD, GROMACS, AMBER, GENESIS, LAMMPS, Desmond, and OpenMM. The CHARMM-GUI development project has been widely adopted for various purposes and now contains a number of different modules designed to set up a broad range of biomolecular simulation systems in [Input Generator](#). Many original modules were developed as an in-house effort, but we have established close collaborations with the developers of CHARMM and other MD simulation packages for addition of newer modules.

Our philosophy in CHARMM-GUI development is less about providing the nuts and bolts of molecular modeling, but instead focused on helping users to achieve a task, such as building a membrane system or solvating a protein, by providing a streamlined interface. This design principle helps us to think of the workflow critically when designing the interface, which leads CHARMM-GUI to be accessible to users with little experience in modeling tools and remains useful to experts, especially for batch generation of systems. CHARMM-GUI has been used by many researchers, and it is a well-recognized tool in the biomolecular modeling and simulation communities (see [Google Scholar Citations](#)).

The CHARMM-GUI development project is still ongoing. These functionalities are not only based on requests from general users and developers, but also on an emerging need for a unified platform to prepare and execute various advanced simulation approaches that have been developed and will be developed by many developers in diverse simulation communities and packages. CHARMM-GUI will continue to help expert and non-expert researchers from a broader range of the modeling and simulation community to build the complex biomolecular systems of their interest and prepare the input files for any general and advanced modeling and simulation through the large and unique scope of CHARMM-GUI functionality. It will also provide an effective one-stop online resource for the biomedical research community to carry out innovative and novel biomolecular modeling and simulation research.

# Generating a CG system using CHARMM-GUI

## CHARMM-GUI

Effective Simulation Input Generator and More

CHARMM is a versatile program for atomic-level simulation of many-particle systems, particularly macromolecules of biological interest. - M. Karplus

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Some [lectures](#), [job postings](#), and [FAQ](#) are now available. See [upload log](#) for update history and [giving](#) for donation. [Contact](#) info is given below.

### Input Generator

Job Retriever  
PDB Reader  
Glycan Reader & Modeler  
Ligand Reader & Modeler  
Glycolipid Modeler  
LPS Modeler  
Nanomaterial Modeler  
Multicomponent Assembler  
Solution Builder  
Membrane Builder  
**Martini Maker**  
PACE CG Builder  
Drude Prepper  
Free Energy Calculator  
MAP Utilizer  
DEER Facilitator  
NMR Structure Calculator  
PBEQ Solver  
Implicit Solvent Modeler  
Boundary Potential Utilizer  
GCMC/BD Ion Simulator

all atom

coarse-grained

### Input Generator

One easiest way to support CHARMM-GUI is to cite the CHARMM-GUI main paper as well as the papers of the modules used in users' publications. Please see [Citations](#) for details.

Since most modules start with PDB Reader, it is strongly recommended to [read the PDB Reader page](#) and to [see the PDB Reader demo](#) in [Video Demo](#).

- Job Retriever  
Facilitates recovery of jobs, when the Job ID is known
- PDB Reader  
Read a PDB file (RCSB or CHARMM formats) into CHARMM
- Glycan Reader & Modeler  
Read carbohydrate structures from a PDB file into CHARMM and/or model user-specified N-/O-glycan or glycan-only structure(s)
- Ligand Reader & Modeler  
Generate various ligand structures using the CHARMM force field
- Glycolipid Modeler  
Provide various glycolipid structure and PSF files
- LPS Modeler  
Provide various lipopolysaccharide (LPS) structure and PSF files
- Nanomaterial Modeler  
Generate various nanomaterial systems for molecular dynamic simulation
- Multicomponent Assembler  
Combine PSF/CRD of non-membrane molecules into a heterogeneous system
- Solvator  
Solvate globular protein, or generate various shapes of water box
- Solution Builder (new Quick MD Simulator)  
Setup subsequent steps for molecular dynamics simulations of globular proteins

# Generating a CG system using CHARMM-GUI

## Protein/Membrane System

Select Martini Models:

Download PDB File:  Download Source:

Upload **All-atom** PDB File:  No file chosen

PDB Format: ☐ PDB ☐ PDBx/mmCIF ☐ CHARMM

## Membrane Only System

Select Martini Models:

orientations of (OPM) database  
proteins in membranes <https://opm.phar.umich.edu/>

HOME ABOUT OPM SEARCH DOWNLOAD OPM FILES CONTACT US PPM SERVER TMPFOLD SERVER

### Protein Classification

Types (3)  
Classes (11)  
Superfamilies (503)  
Families (981)  
Species (860)  
Localizations (24)  
Proteins (4800)

### Orientalions of Proteins in Membranes (OPM) database

OPM provides spatial arrangements of membrane proteins with respect to the hydrocarbon core of the lipid bilayer. OPM includes all unique experimental structures of transmembrane proteins and some peripheral proteins and men. Each protein is positioned in a lipid bilayer of adjustable thickness by minimizing its transfer energy from water to t. OPM provides structural classification and sorting according to different criteria (Classification). Our calculations are in agreement with experimental studies of 24 transmembrane and 39 peripheral peptides and j. **OPM also provides a few preliminary results of our computational analysis of transmembrane  $\alpha$ -helix as pages).**

Search by PDB ID, author, macromolecule, sequence, or ligands   
Advanced Search | Browse by Annotations

RCSB PDB 199502 Biological Macromolecular Structures Enabling Breakthroughs in Research and Education

PDB-101 EMBL-EBI PDBe PDBj PDB-USA

Structure Summary 3D View Annotations Sequence Sequence Similarity Structure Similarity Experiment

### Transmembrane View

transmembrane regions



### 4DKL

Crystal structure of the mu-opioid receptor bound to a morphinan antagonist

DOI: 10.2210/pdb4DKL/pdb

Classification: [SIGNALING PROTEIN/ANTAGONIST](#)

Organism(s): [Mus musculus](#), [Enterobacteria phage T4](#)

Expression System: [Spodoptera frugiperda](#)

Mutation(s): 3

Deposited: 2012-02-03 Released: 2012-03-21

Deposition Author(s): [Manglik, A.](#), [Kruse, A.C.](#), [Kobilka, T.S.](#), [Thian, F.S.](#), [Mathiesen, J.M.](#), [Sunahara, R.K.](#), [Pardo, L.](#), [Weis, W.J.](#), [Kobilka, B.K.](#), [Granier, S.](#)

Experimental Data Snapshot

Method: X-RAY DIFFRACTION  
Resolution: 2.8 Å  
R-Value Free: 0.275  
R-Value Work: 0.233

wwPDB Validation

3D Report Full Report

Metric	Percentile Ranks	Value
Rfree		0.268
Cispeptide		7
Ramachandran outliers		0
Sidechain outliers		0.8%
RSRZ outliers		3.6%

3D View: Structure | Electron Density | Ligand Interaction

<https://www.rcsb.org/structure/4dkl>

# Generating a CG system using CHARMM-GUI

## Martini Bilayer Maker

PDB Info	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5	STEP 6	JOB ID: 7908217498								
<table><tr><td>Title</td><td>4DKL PDB from OPM database</td></tr><tr><td>PDB ID</td><td>4DKL</td></tr><tr><td>Type</td><td>Protein</td></tr><tr><td>Experimental Method</td><td>Unknown</td></tr></table>								Title	4DKL PDB from OPM database	PDB ID	4DKL	Type	Protein	Experimental Method	Unknown
Title	4DKL PDB from OPM database														
PDB ID	4DKL														
Type	Protein														
Experimental Method	Unknown														

### Model/Chain Selection Option:

Click on the chains you want to select.

Select Model #  ☐ Read all models?

Type	SEGID	PDB ID	Residue ID		Engineered Residues
			First	Last	
<input checked="" type="checkbox"/> Protein	PROA	A	65	617	BF0, SO4, CLR, MPG, 1PE
<input checked="" type="checkbox"/> Protein	PROB	B	65	617	BF0, SO4, CLR, MPG, 1PE
<input type="checkbox"/> Hetero	HETA	A			CL
<input type="checkbox"/> Hetero	HETB	B			CL
<input type="checkbox"/> Water	WATA	A			
<input type="checkbox"/> Water	WATB	B			

CHARMM-GUI uses internal segid format PRO[A-Z] (protein), DNA[A-Z] (DNA), RNA[A-Z] (RNA), and HET[A-Z] (ligands), instead of PDB chain id.

# Generating a CG system using CHARMM-GUI

## Martini Bilayer Maker

Bookmark this [link](#), if you want to comeback to this page

PDB Info

STEP 1

STEP 2

STEP 3

STEP 4

STEP 5

STEP 6

JOB ID: 7908217498

Title 4DKL PDB from OPM database  
PDB ID 4DKL  
Type Protein  
Experimental Method Unknown

### PDB Manipulation Options:

☒ Renaming Engineered Residues: ?

Rename **BF0** to  Leave blank to remove  
Rename **SO4** to  Leave blank to remove  
Rename **CLR** to  Leave blank to remove  
Rename **MPG** to  Leave blank to remove  
Rename **1PE** to  Leave blank to remove

*Residues which CHARMM-GUI does not recognize. As they are not part of the protein, we remove them in this case.*

☒ Terminal charge:

PROA ☐ Charged ☒ Neutral  
PROB ☐ Charged ☒ Neutral

*Protein N- and C- terminus would be charged if we do not neutralize them.*



# Generating a CG system using CHARMM-GUI

## Martini Bilayer Maker

Bookmark this [link](#), if you want to comeback to this page

JOB ID: 7908217498

STEP 1 STEP 2 STEP 3 STEP 4 STEP 5 STEP 6

Original PDB File: [4DKL.pdb](#) (view structure) [download.tgz](#)

Individual Chains: [4dkl\\_proa.pdb](#)  
[4dkl\\_prob.pdb](#)

CHARMM Input: [step1\\_pdbreader.inp](#)

CHARMM Output: [step1\\_pdbreader.out](#)

CHARMM PDB: [step1\\_pdbreader.pdb](#) (view structure)

CHARMM CRD: [step1\\_pdbreader.crd](#)

CHARMM PSF: [step1\\_pdbreader.psf](#)

## Computed Energy:

Please beware of that the computed energy is CHARMM single-point energy and is displayed to make sure all the coordinates are defined.

ENER	ENR	Eval#	ENERgy	Delta-E	GRMS	DIHedrals	IMPRopers
ENER INTERN			BONDS	ANGLES	UREY-b	PRIMO	
ENER CROSS			CMAPs	PMF10	PMF20	ASP	USER
ENER EXTERN			VDWaaLs	ELEC	HBONds		
ENER>	0	2916244.0957	0.0000	142334.2837			
ENER INTERN>	56883.46721	1287.81486	116.27277	5103.98888	84.13379		
ENER CROSS>	144.41320	0.00000	0.0000	0.0000			
ENER EXTERN>	2857771.1042	-5147.0992	0.0000	0.0000			

## Orientation Options: ?

- ☒ Use PDB Orientation This option is suggested for an oriented structure from <http://opm.phar.umich.edu>
- ☐ Align the First Principal Axis Along Z This option is suggested for small helical bundle or homo-oligomer.
- ☐ Align a Vector (Two Atoms) Along Z This option is suggested for an irregular, hetero-oligomer.

## Positioning Options:

- ☐ Rotate Molecule respect to the X axis  Degree
- ☐ Rotate Molecule respect to the Y axis  Degree
- ☐ Translate Molecule along Z axis  Angstrom
- ☐ Flip Molecule along the Z axis

*We can use the orientation of our PDB because we extracted it from the OPM (right orientation inside the membrane).*

# Generating a CG system using CHARMM-GUI

Martini Bilayer Maker

Bookmark this [link](#), if you want to comeback to this page

PDB Info STEP 1 **STEP 2** STEP 3 STEP 4 STEP 5 STEP 6 JOB ID: 7908217498

CHARMM PDB: [step1\\_pdbreader.pdb \(view structure\)](#) [download.tgz](#)

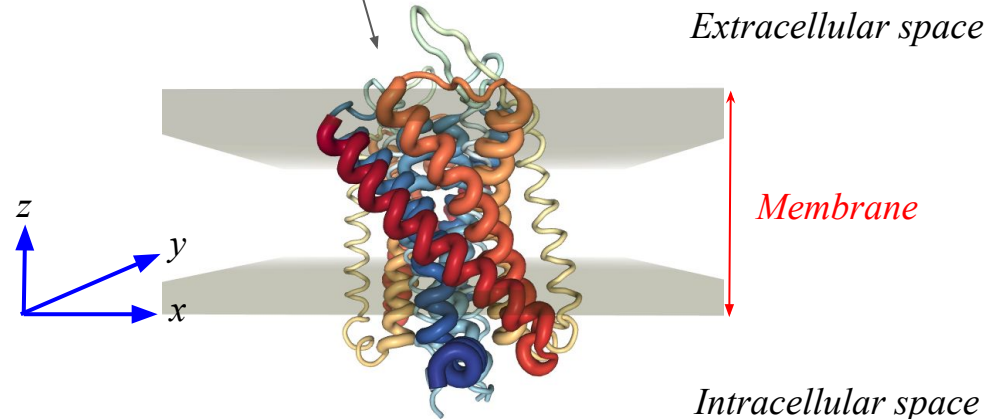
Orientation Input: [step2\\_orient.inp](#)

Orientation Output: [step2\\_orient.out](#)

Oriented PDB: [step2\\_orient.pdb \(view structure\)](#) (please view this structure before you move to the next step)

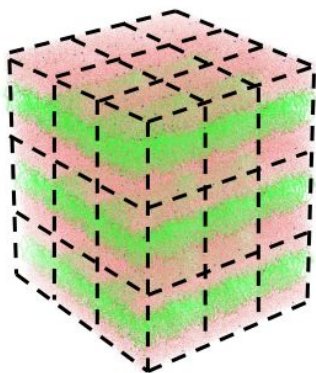
Area Calculation: [step2\\_area.str](#) Calculate cross sectional area of the protein  
[step2\\_area.plo](#) Computed cross sectional area along Z axis  
[step2\\_protein\\_area.str](#) Top/Bottom area of the protein

*Check the orientation in the membrane*



# Generating a CG system using CHARMM-GUI

*In no case, the protein should be able to interact herself with any of the images in the periodic boundary conditions.*



## System Size Determination Options:

☐ Homogeneous Lipid

bilayer building.

"Homogeneous Lipid" option is no longer supported. You can use "Heterogeneous Lipid" option even for homogeneous lipid

☒ Heterogeneous Lipid

1. Box Type: Rectangular

2. Length of Z based on:

☒ Water thickness 15 (Minimum water height on top and bottom of the system)

3. Length of XY based on:

☒ Ratios of lipid components

☐ Numbers of lipid components

Length of X and Y: 120 (initial guess)  
(The system size along the X and Y must be the same)

Show the system info | click this once you fill the following table:

Lipid Type	Charge [e]	Tail Info. [sn1/sn2]	Images	Upperleaflet Ratio (Integer)	Lowerleaflet Ratio (Integer)	Surface Area
------------	------------	----------------------	--------	------------------------------	------------------------------	--------------

### ► Sterols

### ► PA (phosphatidic acid) Lipids

### ▼ PC (phosphatidylcholine) Lipids

DAPC	0	20:4-22:5 / 20:4-22:5	<a href="#">[image]</a>	<input type="text" value="0"/>	<input type="text" value="0"/>	<input type="text" value="76.1"/>
DBPC	0	20:0-22:0 / 20:0-22:0	<a href="#">[image]</a>	<input type="text" value="0"/>	<input type="text" value="0"/>	<input type="text" value="65.4"/>
DFPC	0	18:3 / 18:3	<a href="#">[image]</a>	<input type="text" value="0"/>	<input type="text" value="0"/>	<input type="text" value="77.9"/>
DGPC	0	20:1-22:1 / 20:1-22:1	<a href="#">[image]</a>	<input type="text" value="0"/>	<input type="text" value="0"/>	<input type="text" value="68.5"/>
DIPC	0	18:2 / 18:2	<a href="#">[image]</a>	<input type="text" value="0"/>	<input type="text" value="0"/>	<input type="text" value="76.5"/>
DLPC	0	12:0-14:0 / 12:0-14:0	<a href="#">[image]</a>	<input type="text" value="0"/>	<input type="text" value="0"/>	<input type="text" value="64.1"/>
DNPC	0	24:1-26:1 / 24:1-26:1	<a href="#">[image]</a>	<input type="text" value="0"/>	<input type="text" value="0"/>	<input type="text" value="68.2"/>
DOPC	0	16:1-18:1 / 16:1-18:1	<a href="#">[image]</a>	<input type="text" value="0"/>	<input type="text" value="0"/>	<input type="text" value="69.7"/>
DPPC	0	16:0-18:0 / 16:0-18:0	<a href="#">[image]</a>	<input type="text" value="0"/>	<input type="text" value="0"/>	<input type="text" value="63.0"/>
DRPC	0	22:6-24:6 / 22:6-24:6	<a href="#">[image]</a>	<input type="text" value="0"/>	<input type="text" value="0"/>	<input type="text" value="95.7"/>
DTPC	0	08:0-10:0 / 08:0-10:0	<a href="#">[image]</a>	<input type="text" value="0"/>	<input type="text" value="0"/>	<input type="text" value="60.5"/>
DVPC	0	16:1-18:1 / 16:1-18:1	<a href="#">[image]</a>	<input type="text" value="0"/>	<input type="text" value="0"/>	<input type="text" value="65.6"/>
DXPC	0	24:0-26:0 / 24:0-26:0	<a href="#">[image]</a>	<input type="text" value="0"/>	<input type="text" value="0"/>	<input type="text" value="62.3"/>
DYPC	0	12:1-14:1 / 12:1-14:1	<a href="#">[image]</a>	<input type="text" value="0"/>	<input type="text" value="0"/>	<input type="text" value="61.6"/>
LPPC	0	12:0-14:0 / 16:0-18:0	<a href="#">[image]</a>	<input type="text" value="0"/>	<input type="text" value="0"/>	<input type="text" value="61.4"/>
PAPC	0	16:0-18:0 / 20:4-22:5	<a href="#">[image]</a>	<input type="text" value="0"/>	<input type="text" value="0"/>	<input type="text" value="71.5"/>
PEPC	0	16:0-18:0 / 20:2	<a href="#">[image]</a>	<input type="text" value="0"/>	<input type="text" value="0"/>	<input type="text" value="68.3"/>
PGPC	0	16:0-18:0 / 20:1-22:1	<a href="#">[image]</a>	<input type="text" value="0"/>	<input type="text" value="0"/>	<input type="text" value="65.5"/>
PIPC	0	16:0-18:0 / 18:2	<a href="#">[image]</a>	<input type="text" value="0"/>	<input type="text" value="0"/>	<input type="text" value="67.8"/>
POPC	0	16:0-18:0 / 16:1-18:1	<a href="#">[image]</a>	<input type="text" value="1"/>	<input type="text" value="1"/>	<input type="text" value="68.3"/>

## Calculated Number of Lipids:

Lipid Type	Upperleaflet Number	Lowerleaflet Number
POPC	179	178

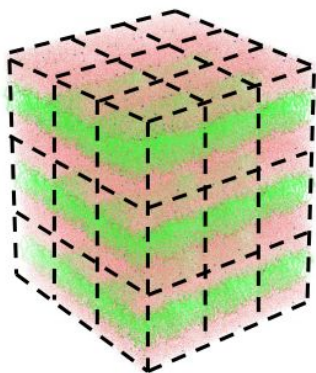
## Calculated XY System Size:

	Upperleaflet	Lowerleaflet
Protein Area	2196.35966	2295.08284
Lipid Area	12225.7	12157.4
# of Lipids	179	178
Total Area	14422.05966	14452.48284
Protein X Extent	38.26	
Protein Y Extent	28.25	
Average Area	14437.27	
A	120.16	
B	120.16	



# Generating a CG system using CHARMM-GUI

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☒ Heterogeneous Lipid

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2. Length of Z based on:

☒ Water thickness 15 (Minimum water height on top and bottom of the system)

3. Length of XY based on:

☒ Ratios of lipid components

☐ Numbers of lipid components

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(The system size along the X and Y must be the same)

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### ► PA (phosphatidic acid) Lipids

### ▼ PC (phosphatidylcholine) Lipids

DAPC	0	20:4-22:5 / 20:4-22:5	[image]	0	0	76.1
DBPC	0	20:0-22:0 / 20:0-22:0	[image]	0	0	65.4
DFPC	0	18:3 / 18:3	[image]	0	0	77.9
DGPC	0	20:1-22:1 / 20:1-22:1	[image]	0	0	68.5
DIPC	0	18:2 / 18:2	[image]	0	0	76.5
DLPC	0	12:0-14:0 / 12:0-14:0	[image]	0	0	64.1
DNPC	0	24:1-26:1 / 24:1-26:1	[image]	0	0	68.2
DOPC	0	16:1-18:1 / 16:1-18:1	[image]	0	0	69.7
DPPC	0	16:0-18:0 / 16:0-18:0	[image]	0	0	63.0
DRPC	0	22:6-24:6 / 22:6-24:6	[image]	0	0	95.7
DTPC	0	08:0-10:0 / 08:0-10:0	[image]	0	0	60.5
DVPC	0	16:1-18:1 / 16:1-18:1	[image]	0	0	65.6
DXPC	0	24:0-26:0 / 24:0-26:0	[image]	0	0	62.3
DYPC	0	12:1-14:1 / 12:1-14:1	[image]	0	0	61.6
LPPC	0	12:0-14:0 / 16:0-18:0	[image]	0	0	61.4
PAPC	0	16:0-18:0 / 20:4-22:5	[image]	0	0	71.5
PEPC	0	16:0-18:0 / 20:2	[image]	0	0	68.3
PGPC	0	16:0-18:0 / 20:1-22:1	[image]	0	0	65.5
PPC	0	16:0-18:0 / 18:2	[image]	0	0	67.8
POPC	0	16:0-18:0 / 16:1-18:1	[image]	1	1	68.3

If we give a X and Y length (in Å) which would generate a system too small for our protein...

## Calculated Number of Lipids:

Lipid Type	Upperleaflet Number	Lowerleaflet Number
POPC	5	4

## Calculated XY System Size:

	Upperleaflet	Lowerleaflet
Protein Area	2196.35966	2295.08284
Lipid Area	341.5	273.2
# of Lipids	5	4
Total Area	2537.85966	2568.28284

Protein X Extent	38.26
Protein Y Extent	28.25

Average Area	2553.07
A	50.53
B	50.53

The system is smaller than the protein extent.

## Calculated Number of Lipids:

Lipid Type	Upperleaflet Number	Lowerleaflet Number
POPC	179	178

## Calculated XY System Size:

	Upperleaflet	Lowerleaflet
Protein Area	2196.35966	2295.08284
Lipid Area	12225.7	12157.4
# of Lipids	179	178
Total Area	14422.05966	14452.48284

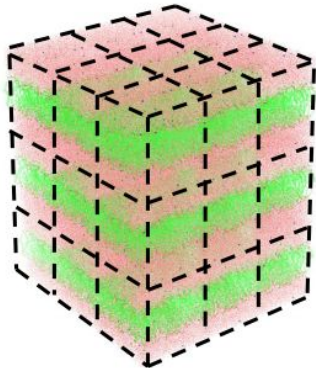
Protein X Extent	38.26
Protein Y Extent	28.25

Average Area	14437.27
A	120.16
B	120.16

Information about the system that will be generated

# Generating a CG system using CHARMM-GUI

In no case, the protein has to be able to interact herself with any of the images in the periodic boundary conditions.



## System Size Determination Options:

☐ Homogeneous Lipid bilayer building. "Homogeneous Lipid" option is no longer supported. You can use "Heterogeneous Lipid" option even for homogeneous lipid

☒ Heterogeneous Lipid

1. Box Type: Rectangular

2. Length of Z based on:

☒ Water thickness 15 (Minimum water height on top and bottom of the system)

3. Length of XY based on:

☒ Ratios of lipid components

☐ Numbers of lipid components

Length of X and Y: 120 (initial guess)  
(The system size along the X and Y must be the same)

Show the system info | click this once you fill the following table:

Lipid Type	Charge [e]	Tail Info. [sn1/sn2]	Images	Upperleaflet Ratio (Integer)	Lowerleaflet Ratio (Integer)	Surface Area
------------	------------	----------------------	--------	------------------------------	------------------------------	--------------

### ► Sterols

### ► PA (phosphatidic acid) Lipids

### ▼ PC (phosphatidylcholine) Lipids

DAPC	0	20:4-22:5 / 20:4-22:5	[image]	0	0	76.1
DBPC	0	20:0-22:0 / 20:0-22:0	[image]	0	0	65.4
DFPC	0	18:3 / 18:3	[image]	0	0	77.9
DGPC	0	20:1-22:1 / 20:1-22:1	[image]	0	0	68.5
DIPC	0	18:2 / 18:2	[image]	0	0	76.5
DLPC	0	12:0-14:0 / 12:0-14:0	[image]	0	0	64.1
DNPC	0	24:1-26:1 / 24:1-26:1	[image]	0	0	68.2
DOPC	0	16:1-18:1 / 16:1-18:1	[image]	0	0	69.7
DPPC	0	16:0-18:0 / 16:0-18:0	[image]	0	0	63.0
DRPC	0	22:6-24:6 / 22:6-24:6	[image]	0	0	95.7
DTPC	0	08:0-10:0 / 08:0-10:0	[image]	0	0	60.5
DVPC	0	16:1-18:1 / 16:1-18:1	[image]	0	0	65.6
DXPC	0	24:0-26:0 / 24:0-26:0	[image]	0	0	62.3
DYPC	0	12:1-14:1 / 12:1-14:1	[image]	0	0	61.6
LPPC	0	12:0-14:0 / 16:0-18:0	[image]	0	0	61.4
PAPC	0	16:0-18:0 / 20:4-22:5	[image]	0	0	71.5
PEPC	0	16:0-18:0 / 20:2	[image]	0	0	65.3
PGPC	0	16:0-18:0 / 20:1-22:1	[image]	0	0	65.5
PIPC	0	16:0-18:0 / 18:2	[image]	0	0	67.8
POPC	0	16:0-18:0 / 16:1-18:1	[image]	1	1	68.3

If we give a X and Y length (in Å) which would generate a system too small for our protein...

## Calculated Number of Lipids:

Lipid Type	Upperleaflet Number	Lowerleaflet Number
POPC	5	4

## Calculated XY System Size:

	Upperleaflet	Lowerleaflet
Protein Area	2196.35966	2295.08284
Lipid Area	341.5	273.2
# of Lipids	5	4
Total Area	2537.85966	2568.28284

Protein X Extent	38.26
Protein Y Extent	28.25
Average Area	2553.07
A	50.53
B	50.53

The system is smaller than the protein extent.

## Calculated Number of Lipids:

Lipid Type	Upperleaflet Number	Lowerleaflet Number
POPC	179	178

## Calculated XY System Size:

	Upperleaflet	Lowerleaflet
Protein Area	2196.35966	2295.08284
Lipid Area	12225.7	12157.4
# of Lipids	179	178
Total Area	14422.05966	14452.48284
Protein X Extent	38.26	
Protein Y Extent	28.25	
Average Area	14437.27	
A	120.16	
B	120.16	

Information about the system that will be generated

In this case we'll use a 100% POPC membrane, but more complex and realistic membranes can be created by combination of lipid ratios.

# Generating a CG system using CHARMM-GUI

## Martini Bilayer Maker

Bookmark this [link](#), if you want to comeback to this page

PDB Info STEP 1 STEP 2 **STEP 3** STEP 4 STEP 5 STEP 6 JOB ID: 7908217498

download.tgz

Oriented PDB: [step2\\_orient.pdb \(view structure\)](#)

System Size Input: [step3\\_size.inp](#)

System Size Output: [step3\\_size.out](#)

System Size: [step3\\_size.str](#)

Packing Simulation: [step3\\_packing.inp](#) Packing Simulation Input  
[step3\\_packing.out](#) Packing Simulation Output  
[crystal\\_image.str](#) Crystal Image  
[step3\\_packing.pol.str](#) Topology File of Pseudo Liquid Spheres  
[step3\\_packing.pdb \(view structure\)](#) Generated Packed System (please view this structure before you move to the next step)

### Determined System Size:

Box Type	Rectangle		
Crystal Type	TETRAGONAL		
System Size	A	120.15518	Dimension along the A (X) axis
	B	120.15518	Dimension along the B (Y) axis
	C	100.178	Dimension along the C (Z) axis
Crystal Angle	Alpha	90.0	Angle between the axis B and C
	Beta	90.0	Angle between the axis A and C
	Gamma	90.0	Angle between the axis A and B
# of Lipids	on Top	179	
	on Bottom	178	
Z Center	-3.196		Center of the system along the Z axis

### System Building Options:

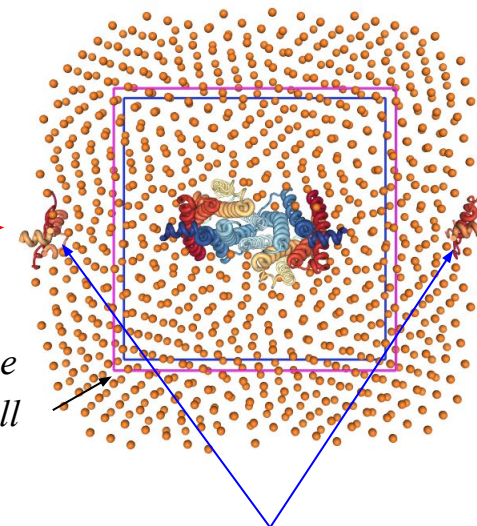
- ☐ Insertion method Build system using insertion method
- ☒ Replacement method Build system using replacement method
- ☒ Check lipid ring (and protein surface) penetration

For this system, insertion method can not be used. Replacement method will be used instead.

### Component Building Options:

- ☒ Include Ions
- ☒ 0.15 M NaCl (ion concentration) Calculate number of ions
- ☐ Add neutralizing ions  
78 positive ions and 102 negative ions will be generated. Note that this is the estimated ion numbers, so the actual ion numbers may differ.
- ☒ Ion Placing Method: Distance

*The squares define  
the system that will  
be generated.*



*Periodic boundary  
images*

# Generating a CG system using CHARMM-GUI

## Martini Bilayer Maker

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PDB Info	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5	STEP 6	JOB ID: 7908217498
<div>Oriented PDB: <a href="#">step2_orient.pdb (view structure)</a></div> <div>Component Input: <a href="#">step4_lipid.inp</a></div> <div>Component Output: <a href="#">step4_lipid.out</a></div> <div>Component Number: <a href="#">step4_components.str</a></div> <div>Component PDB: <a href="#">step4_lipid.pdb (view structure)</a></div>							<a href="#">download.tgz</a>

### Check lipid penetration

The protein surface penetration check finds the lipid tails that go beyond the protein surface, and the lipid ring penetration check detects the lipid tails that pass through the cyclic groups (e.g., cholesterol ring) in the simulation systems. Energy minimization can resolve many of these bad contacts, but one might need to visually check the following lipid molecules to ensure the following contacts are resolved. The user can regenerate the lipid bilayer if necessary.

Protein surface penetration:

No protein surface penetration is found.

Lipid ring penetration:

No lipid ring penetration is found.

### Building Ion and Waterbox

Membrane components are generated. Due to time constraints, we first generate the lipid bilayer then generate ions and the water box. Click "Next Step" to generate ions and the water box.

# Generating a CG system using CHARMM-GUI

## Martini Bilayer Maker

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PDB InfoSTEP 1STEP 2STEP 3STEP 4STEP 5STEP 6

JOB ID: 7908217498

Oriented PDB:  
Component Input:  
Component Output:  
Component Number:  
Generated Waterbox:  
  
Generated Ion:  
  
Component PDB:

[step2\\_orient.pdb \(view structure\)](#)  
[step4\\_lipid.inp](#)  
[step4\\_lipid.out](#)  
[step4\\_components.str](#)  
[step4.2\\_waterbox.inp](#)  
[step4.2\\_waterbox.out](#)  
[step4.2\\_waterbox.crd](#)  
  
[step4.3\\_ion.inp](#)  
[step4.3\\_ion.out](#)  
[step4.3\\_neg.crd](#)  
[step4.3\\_pos.crd](#)  
[step4.3\\_ion.pdb](#)  
[step4\\_lipid.pdb \(view structure\)](#)

[download.tgz](#)

Input file for water box inclusion  
Output file for water box inclusion  
CRD file for the water box  
  
Input file for ion inclusion  
Output file for ion inclusion  
CRD file for the ion  
CRD file for the ion  
PDB file for the ion

### Assemble Generated Components:

Membrane components are generated. Click "Next Step" to assemble those components together.



# Generating a CG system using CHARMM-GUI

## Martini Bilayer Maker

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PDB Info STEP 1 STEP 2 STEP 3 STEP 4 **STEP 5** STEP 6 JOB ID: 7908217498

Lipid PDB: [step4\\_lipid.pdb \(view structure\)](#) [download.tgz](#)  
Assembly Input: [step5\\_assembly.inp](#)  
Assembly Output: [step5\\_assembly.out](#)  
System Information: [step5\\_assembly.str](#)  
Assembled PSF: [step5\\_assembly.psf](#)  
Assembled CRD: [step5\\_assembly.crd](#)  
Assembled PDB: [step5\\_assembly.pdb \(view structure\)](#)

### Determined System Size:

# of Atoms 11905  
Crystal Type TETRAGONAL  
System Size  
A 120.15518 Dimension along the A (X) axis  
B 120.15518 Dimension along the B (Y) axis  
C 100.178 Dimension along the C (Z) axis  
Crystal Angle  
Alpha 90.0 Angle between the axis B and C  
Beta 90.0 Angle between the axis A and C  
Gamma 90.0 Angle between the axis A and B  
# of Lipids  
on Top 179  
on Bottom 178  
# of Water 6139  
# of NA Ion 72  
# of CL Ion 96  
Z Center 0.0 Center of the system along the Z axis

### Equilibration Input Generation Options:

☒ NPT Ensemble

### Dynamics Input Generation Options:

☒ NPT Ensemble

Temperature: 303.15 K

# Generating a CG system using CHARMM-GUI

## Martini Bilayer Maker

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PDB Info

STEP 1

STEP 2

STEP 3

STEP 4

STEP 5

STEP 6

JOB ID: 7908217498

Assembled PDB: [step5\\_assembly.pdb](#) (view structure)

Input Generator Input: [step5\\_input.inp](#)

Input Generator Output: [step5\\_input.out](#)

Crystal Image: [crystal\\_image.str](#)

Equilibration Inputs: [gromacs/step6.0\\_minimization.mdp](#)  
[gromacs/step6.1\\_minimization.mdp](#)  
[gromacs/step6.2\\_equilibration.mdp](#)  
[gromacs/step6.3\\_equilibration.mdp](#)  
[gromacs/step6.4\\_equilibration.mdp](#)  
[gromacs/step6.5\\_equilibration.mdp](#)  
[gromacs/step6.6\\_equilibration.mdp](#)

Production Inputs: [gromacs/step7\\_production.mdp](#)

Minimization Step 0

Minimization Step 1

Equilibration Step 2

Equilibration Step 3

Equilibration Step 4

Equilibration Step 5

Equilibration Step 6

Production Input

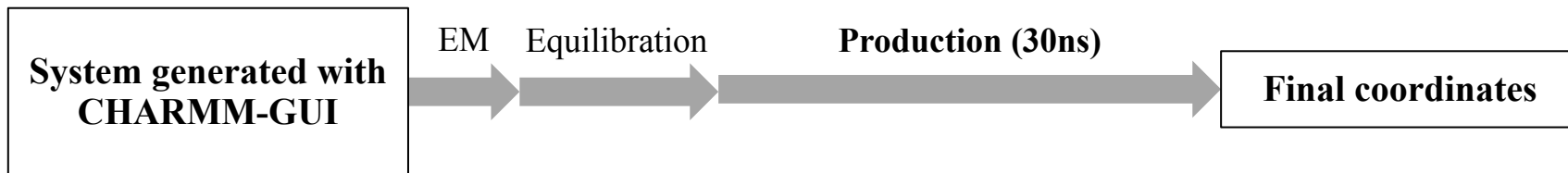
download.tgz

*Download the input files to  
simulate the system using  
Gromacs.*

Please download "download.tgz" to continue equilibration and production simulations.

# CG MD Protocol

GROMACS + MARTINI FF



index.ndx  
PROA\_P.itp  
PROB\_P.itp  
README  
step5\_charmm2gmx.pdb

step6.0\_minimization.mdp  
step6.1\_minimization.mdp  
step6.2\_equilibration.mdp  
step6.3\_equilibration.mdp  
step6.4\_equilibration.mdp

step6.5\_equilibration.mdp  
step6.6\_equilibration.mdp  
step7\_production.mdp  
system.top  
toppar

*To simulate with GROMACS we need:*

**Coordinates (.gro/.pdb)**

**FF + Topologies (.top/.itp)**

**Simulation options (.mdp)**