The Study of 19 Biological Membrane Types Using All-Atom Molecular Simulations
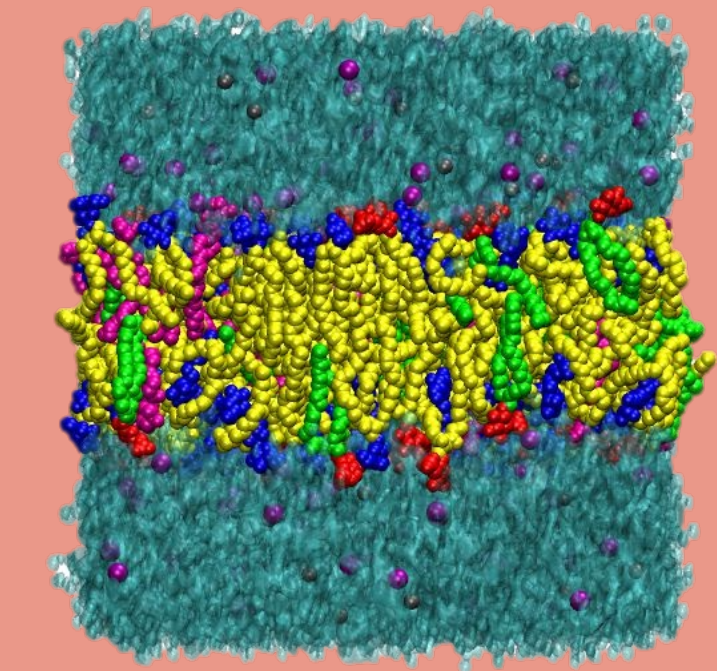
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Introduction

- Molecular Dynamics Simulations are used by scientists to understand biological interactions at an atomic level
- Observations from all-atom simulations can be used to draw conclusions regarding drug development, infection mechanisms, and cellular signaling
- CHARMM-GUI is a free, modular online tool that generates simulation input files which make molecular dynamics simulations more accessible to the scientific community
- A module with predetermined settings for commonly studied membranes would accelerate the work done by visitors of CHARMM-GUI

Dynamic Analysis Results

- **Boxsize Plot** - System size (Angstroms) vs Time (ns)
- **Density Plots** - Plotted density of various membrane components along the z-axis of the system
- **Hydrophobic Thickness** - Measured the size of the hydrophobic region within the membrane system
- **Area per Lipid** - Measured the average area of all of the lipid within the membrane, more pertinent for asymmetrical systems
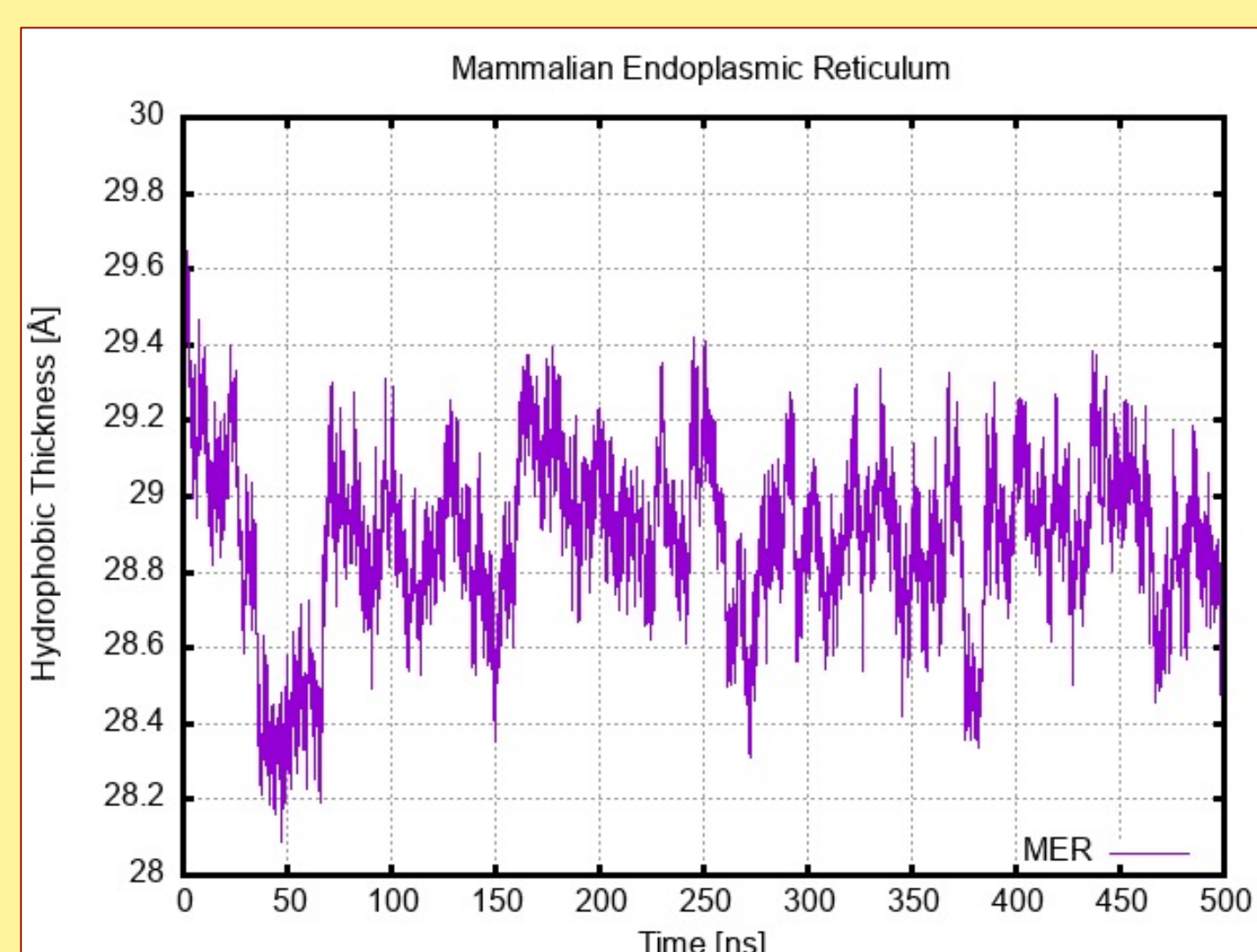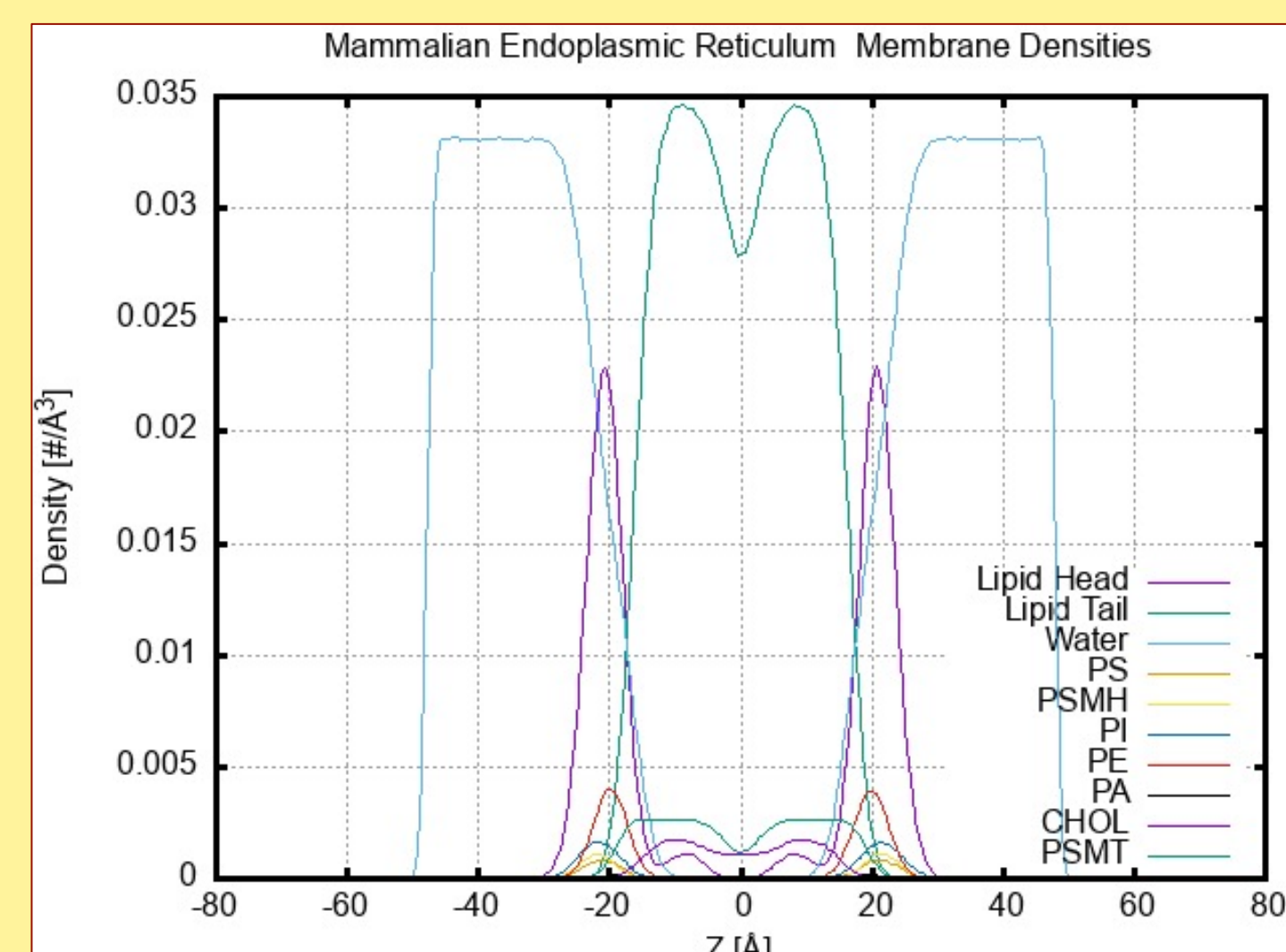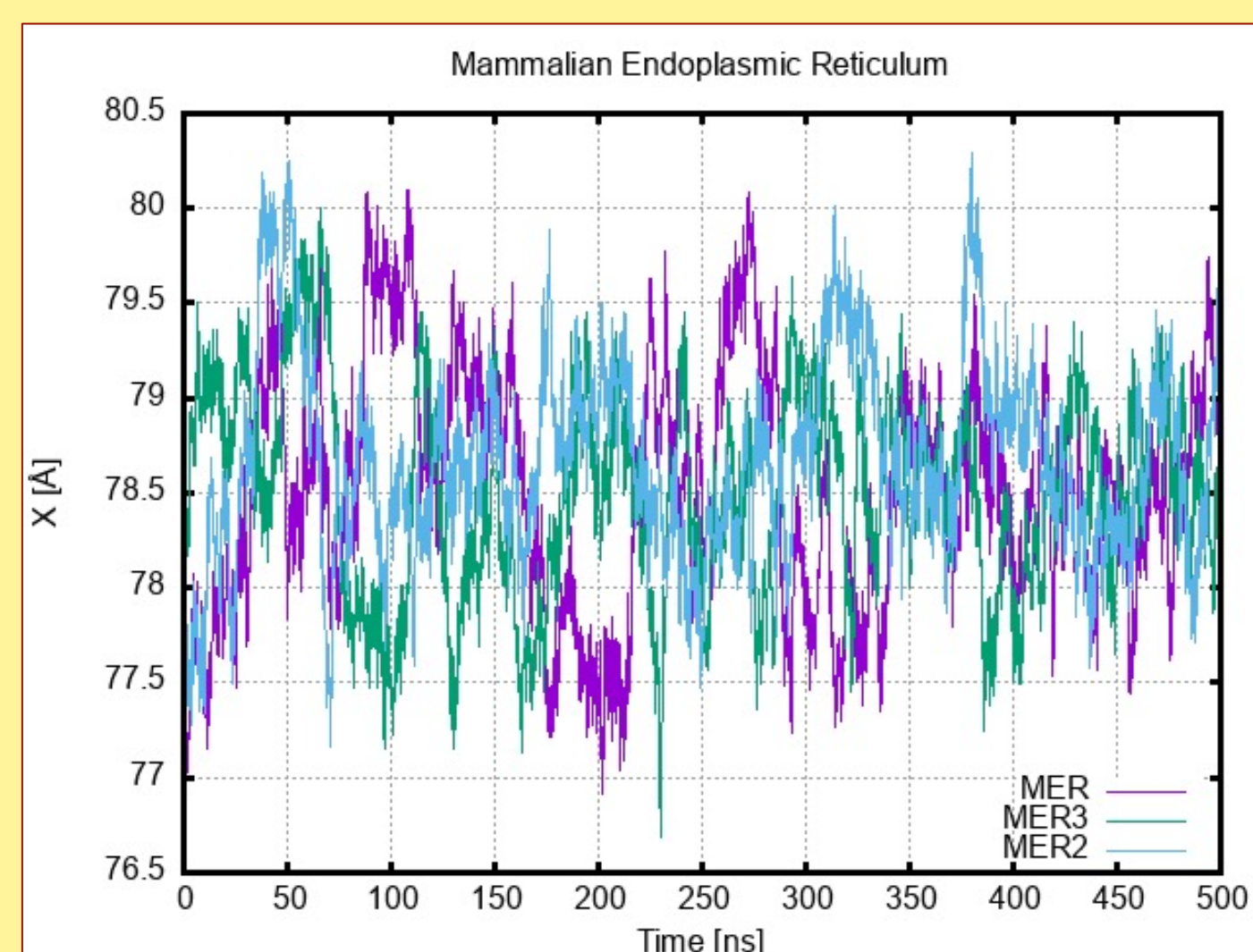
Abstract

Molecular dynamics simulations provide scientists with the ability to observe and analyze the interactions and properties of chemical systems at a molecular level. CHARMM-GUI is an easily accessible online resource that generates input files for the simulation of biological systems. One of the popular modules within CHARMM-GUI for drug development is the bilayer membrane builder. In order to streamline the research process for common membranes, the Im lab has worked on compiling a standardized lipid composition for 19 notable membrane types. The Im lab has since equilibrated and simulated 1000 nanoseconds of each all-atom model as well as conducted dynamic analyses for each of those systems. Once compiled, the data collected will be formatted and made accessible on the CHARMM-GUI website for scientific use.

Membrane Types

- Mammalian Plasma Membrane
- Fungal Plasma Membrane
- Plant/Algae Plasma Membrane
- Archaeal Plasma Membrane
- Bacterial Outer Membrane (G-)
- Bacterial Inner Membrane (G-)
- Bacterial Plasma Membrane (G+)
- Mitochondrial Outer Membrane
- Mitochondrial Inner Membrane
- Mammalian ER
- Fungal ER
- Mammalian Golgi
- Fungal Golgi
- Mammalian Lysosomes
- Plant/Algae Thylakoid
- Cyanobacteria Thylakoid
- Mammalian Endosome
- Plant/Fungal Vacuole

Conclusion and Future Studies

- Once published to CHARMM-GUI, the common membranes module will accelerate molecular dynamic study in the fields of pharmaceuticals and biochemistry.
- Future studies within the Im lab include the development of a triacylglycerol library in the membrane builder module as well as a study on gold nanoparticles in molecular dynamics simulations.

Simulation Workflow

- Lipid selection and system size calculation
  - Rectangular Box Type
  - Length of XY based on 1:1 ratio of lipid components
  - Initial length of Z set to 30 Angstroms

- Component Construction Replacement Method of component distribution
  - .15 M of NaCl distributed via Monte-Carlo simulation

- Component Assembly - Waterbox generation, constructing system

- Equilibration - Force field calculation, energy minimization, and molecular "rest"
  - Temperature set to 300K for plants and yeast, 310.15K for mammals and standard bacteria, 328K for cyanobacteria
  - OpenMM input generation
  - CHARMM36m Force Field

- Production - Stepwise snapshots of molecular motion, generation of images and videos in VMD
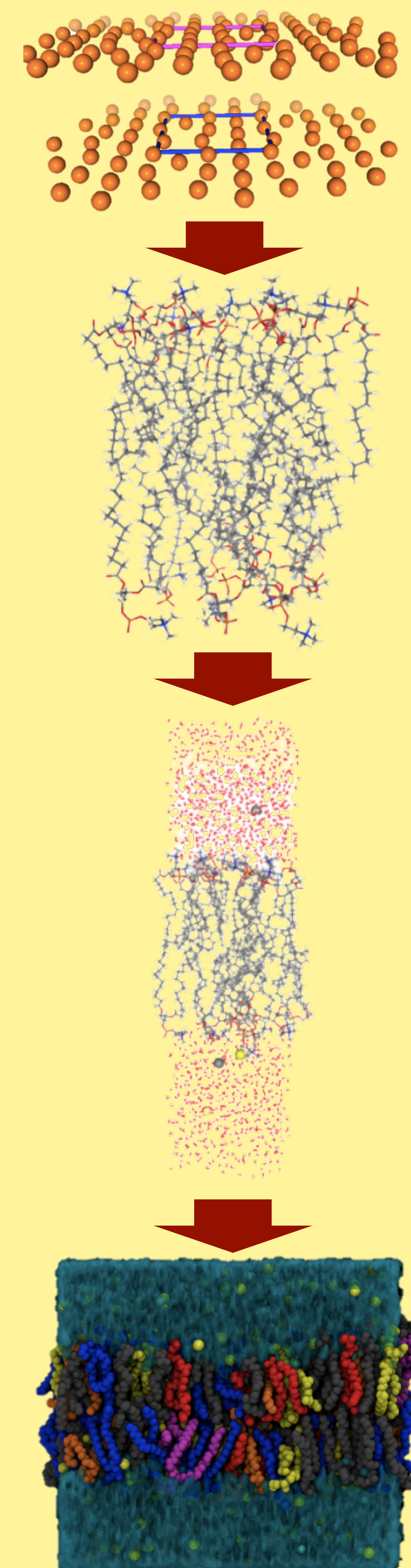
CHARMM-GUI
Effective Simulation Input Generator and More