Molecular Dynamcis (MD) Simulation with BioHPC

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Outline

- What is an MD simulation?
- What information can MD simulations provide?
- A Brief theoretical background of MD
- MD on BioHPC
- CHARMM-GUI Input Generator
- Astrocyte MD workflow

What is an MD simulation?

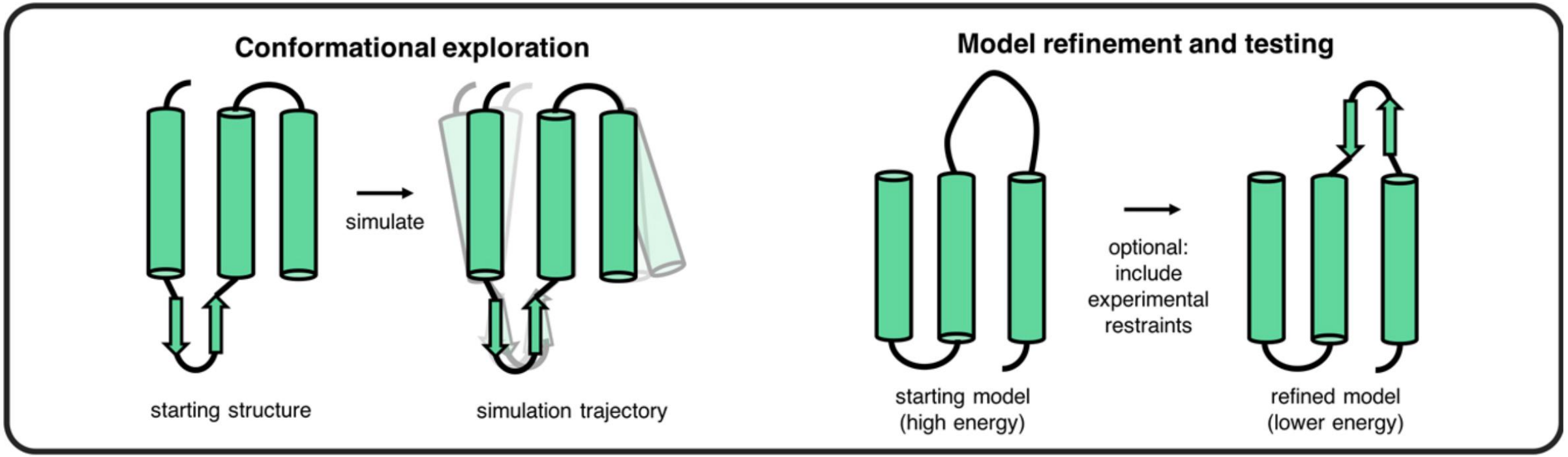
Molecular dynamics is a computer simulation method for analyzing the physical movements of atoms and molecules.

The atoms and molecules are allowed to interact for a fixed period of time, giving a view of the dynamic "evolution" of the system.

In the most common version, the trajectories of atoms and molecules are determined by numerically solving Newton's equations of motion for a system of interacting particles, where forces between the particles and their potential energies are often calculated using interatomic potentials or molecular mechanics force fields.

What information can MD simulations provide?

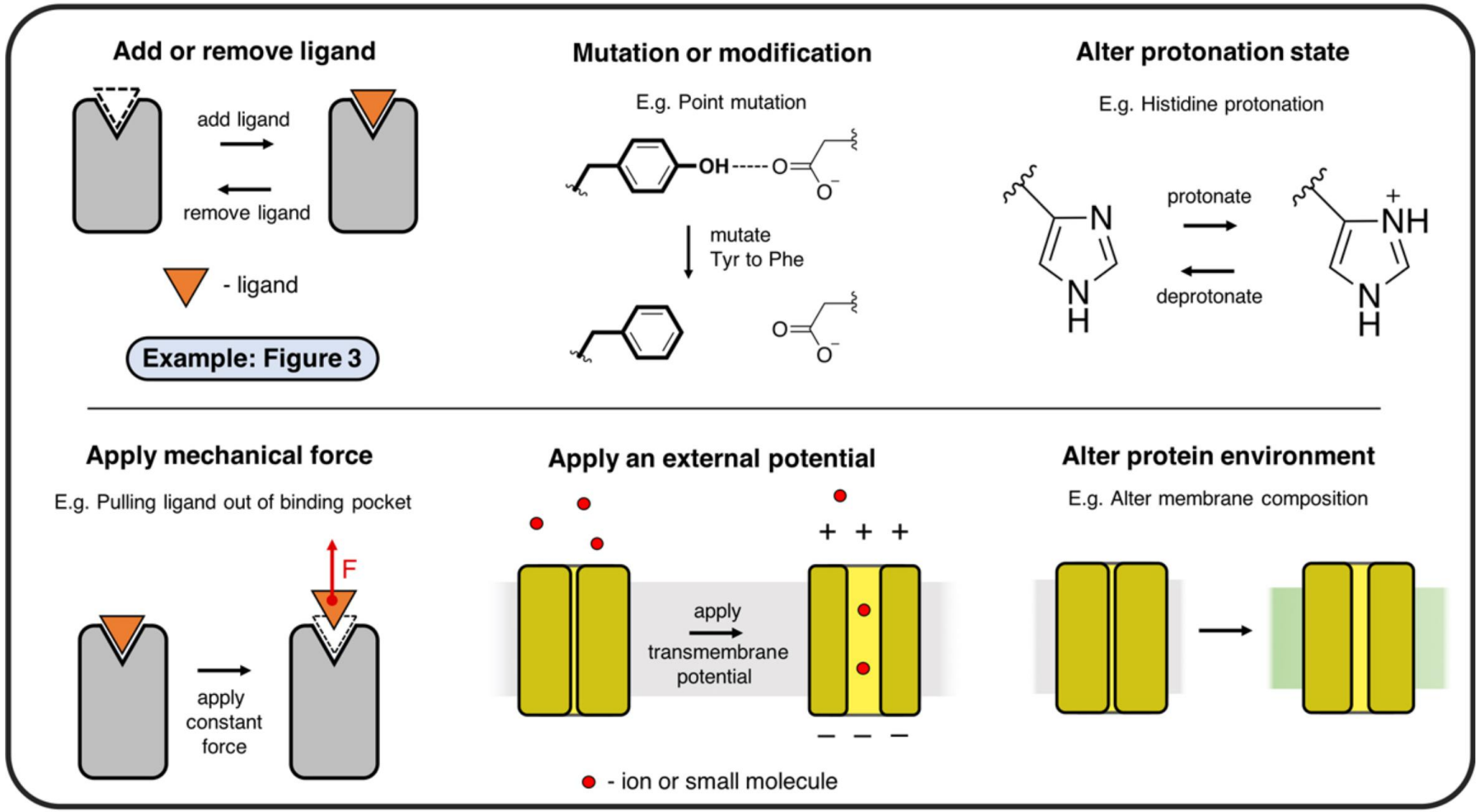
Structural and dynamic studies: *Studying conformational flexibility and stability*



Neuron. 2018 Sep 19; 99(6): 1129–1143. doi: 10.1016/j.neuron.2018.08.011

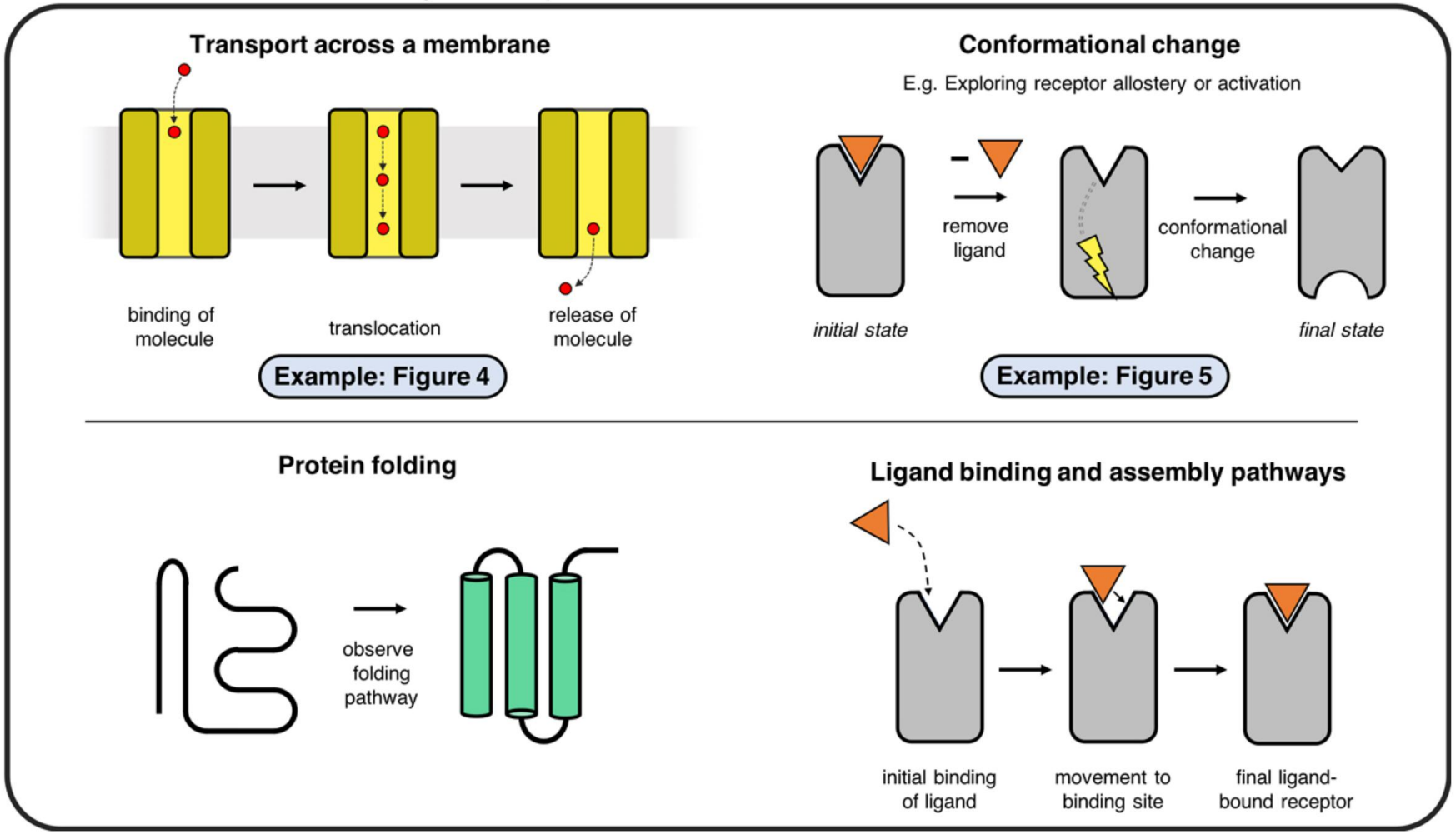
What information can MD simulations provide?

Perturbations: *Observe response following controlled change to system*



What information can MD simulations provide?

Processes: *Observe a dynamic process over time*



A Brief theoretical background of MD

Accuracy vs efficiency of different simulation techniques

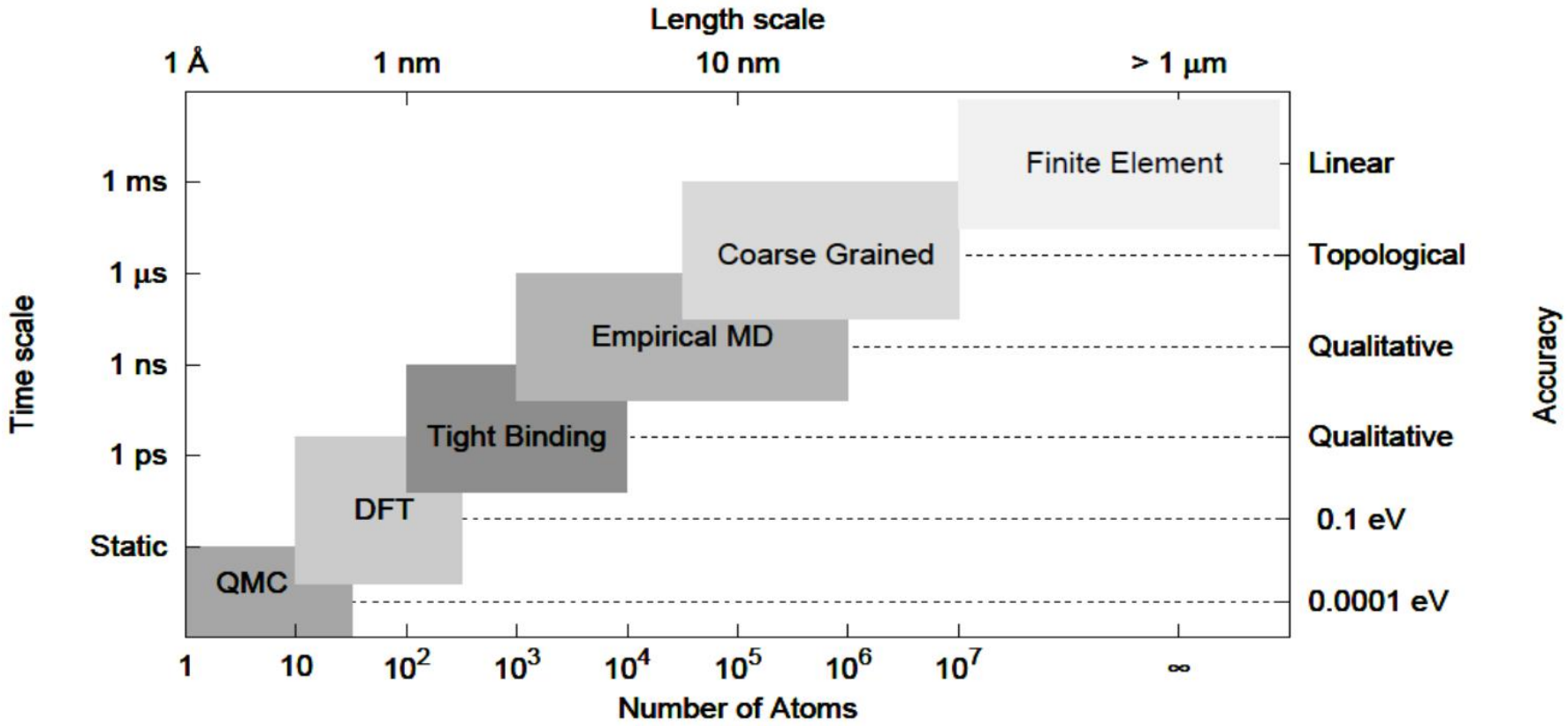
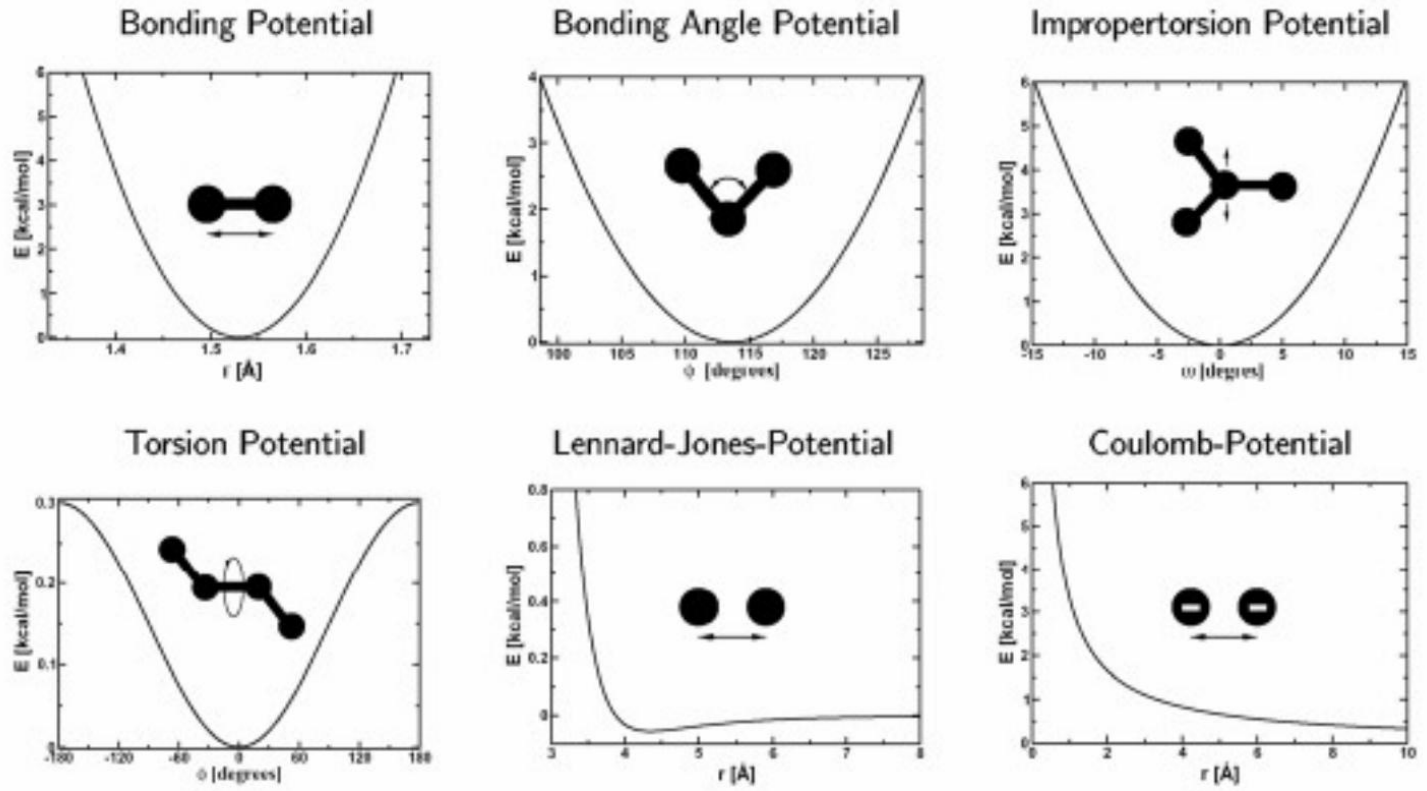


Figure 1. Schematic representation of the range of length- and time-scales accessible to a variety of modelling methods, from quantum Monte Carlo (QMC) for very accurate, very expensive static calculations through to approximate methods such as finite-element modelling.

A Brief theoretical background of MD



$$E = \sum_b k_b(r - r_0)^2 + \sum_\theta k_\theta(\theta - \theta_0)^2 + \sum_\omega k_\omega(\omega - \omega_0)^2$$

$$+ \sum_\phi k_\phi(1 - \cos(n\phi - \delta)) + \sum_{i<j} 4\,\epsilon_{ij}\left[\left(\frac{\sigma_{ij}}{r}\right)^{12} - \left(\frac{\sigma_{ij}}{r}\right)^{6}\right] + \sum_{i<j}\frac{q_i q_j}{r}$$

Classical
CHARMM
AMBER
GROMOS
MMFF
OPLS

Polarizable
CHARMM
AMBER
AMOEBA

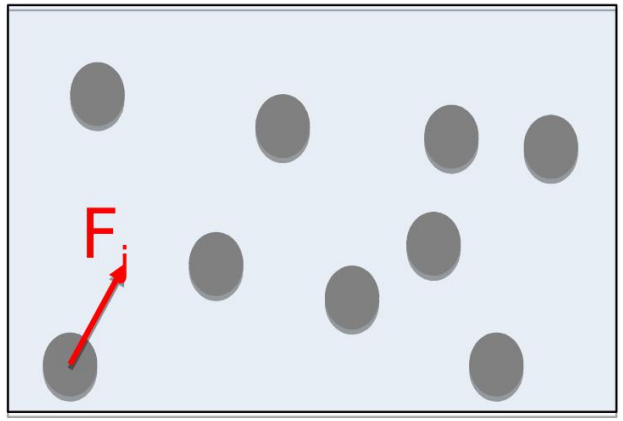
Reactive
ReaxFF

Coarse-grained
MARTINI

Water
TIP3P
TIP4P
SPC

A Brief theoretical background of MD

- Generate a dynamical trajectory by integrating Newton's equations of motion, with suitable initial and boundary conditions



$$\boldsymbol{F}_i = -\frac{\partial U(\boldsymbol{r}^N)}{\partial \boldsymbol{r}_i} = m_i \frac{d^2 \boldsymbol{r}_i}{dt^2}$$

Verlet algorithm:

$$\boldsymbol{r}_i(t_0 + \Delta t) = \boldsymbol{r}_i(t_0) + \boldsymbol{v}_i(t_0)\Delta t + \frac{1}{2}\boldsymbol{a}_i(t_0)\Delta t^2 + \frac{1}{3!}\ddot{\boldsymbol{r}}_i(t_0)\Delta t^3 + O(\Delta t^4)$$

$$\boldsymbol{r}_i(t_0 - \Delta t) = \boldsymbol{r}_i(t_0) - \boldsymbol{v}_i(t_0)\Delta t + \frac{1}{2}\boldsymbol{a}_i(t_0)\Delta t^2 - \frac{1}{3!}\ddot{\boldsymbol{r}}_i(t_0)\Delta t^3 + O(\Delta t^4)$$

$$\boldsymbol{r}_i(t_0 + \Delta t) + \boldsymbol{r}_i(t_0 - \Delta t) = 2\boldsymbol{r}_i(t_0) + \boldsymbol{a}_i(t_0)\Delta t^2 + O(\Delta t^4)$$

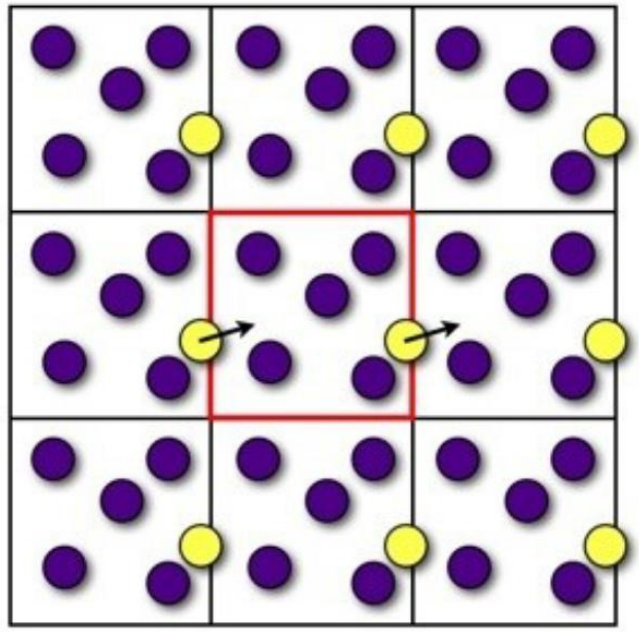
Positions at $t_0+\Delta t$ can be computed from actual positions and forces, and previous positions.

Error is $O(\Delta t^4)$.

Verlet is simple, efficient, stable and reasonably accurate.

A Brief theoretical background of MD

Periodic boundary conditions (PBC)



- To avoid surface effects
- To get bulk properties with a limited number of atoms
- When an atom leaves the cell, it is replacted by another with the same velocity, entering from the opposite cell face
- Beware of artificial periodicity

MD on BioHPC

Software:

```
NAMD/2.11b1/multicore-CUDA
NAMD/2.14/ibverbs-smp-CUDA
NAMD/2.9/ibverbs
NAMD/2.9/multicore

NAMD/2.14/ibverbs
NAMD/2.14/multicore
NAMD/2.9/ibverbs-smp
NAMD/2.9/multicore-CUDA

NAMD/2.14/ibverbs-smp
NAMD/2.14/multicore-CUDA
NAMD/2.9/ibverbs-smp-CUDA

namd/gcc/openmpi/2.12

namd/gpu/2.14
```

```
gromacs/2018.4
gromacs/5.1.4
gromacs/openmpi/plumed/2018.4
gromacs/5.0.4
gromacs/openmpi/5.0.4
gromacs/plumed/2021

amber/12
amber/20
amber/22

openmm/gpu/7.6.0

lammps/2018-12-12
lammps/2020-29-10
lammps/2021-24-06
lammps/2021-25-07
lammps/2021-27-08

desmond-maestro/3.6.1.1
```

MD on BioHPC

Files need to prepare (e.g. NAMD2):

A coordinates file (*.pdb/*.crd)

A topology file (*.psf)

A configuration (*.inp)

Forcefield files (par_*, toppar_*, *.prm, *.inp, *.str)

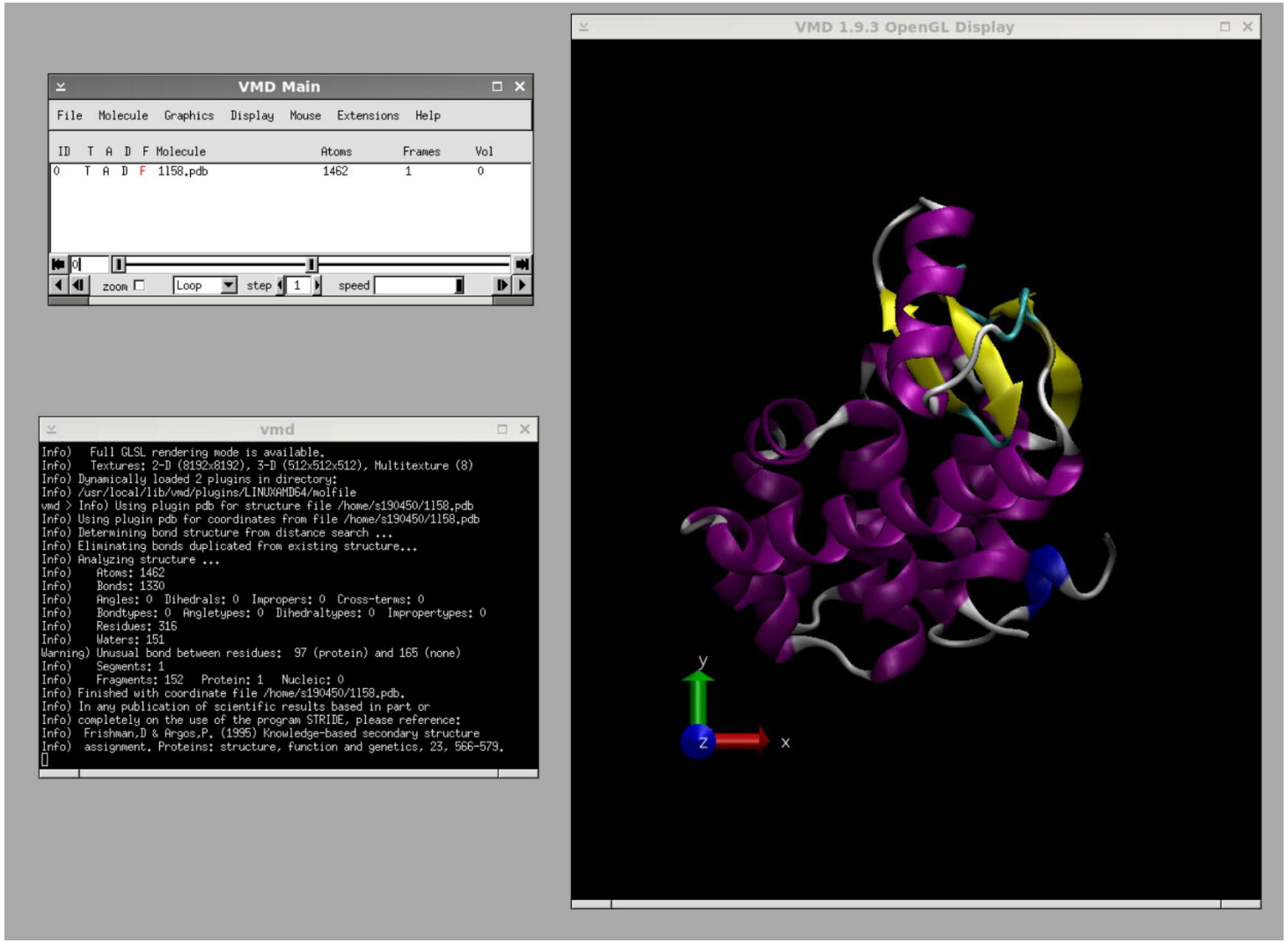
A sbatch script (*.sh)

MD on BioHPC

Prepare files with VMD:

Demonstrate with Lysozyme,

PDB: 1L58



CHARMM-GUI Input Generator

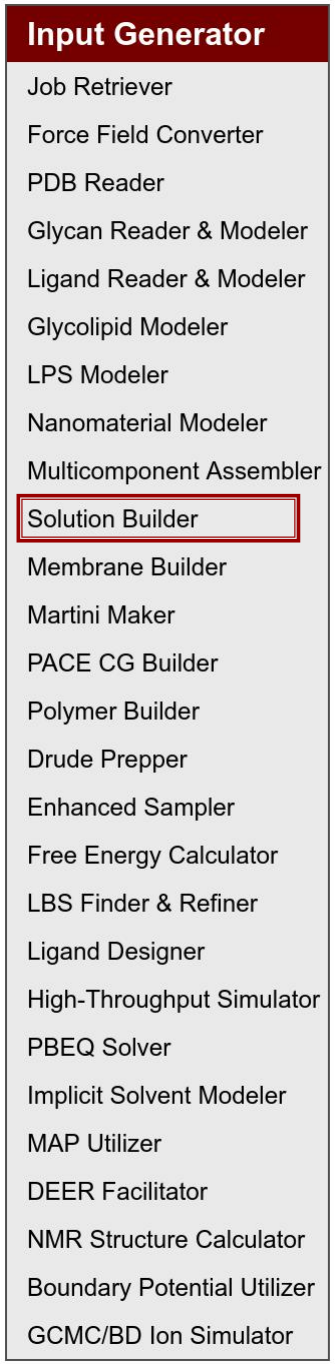
CHARMM-GUI

https://charmm-gui.org

A web-based platform to build complex systems and prepare their inputs with well-established and reproducible simulation protocols.

It supports CHARMM, NAMD, GROMACS, AMBER, GENESIS, Tinker, LAMMPS, Desmond, and OpenMM.

Demonstration with Solution Builder.



Astrocyte MD workflow

Astrocyte CHARMM-GUI MD Workflow

https://astrocyte.biohpc.swmed.edu/workflow/49/view

Demonstration!

Published Versions

Version	Git Tag	
astrocyte_charmmgui_md - 1.1.0	**Astrocyte CHARMM-GUI MD Workflow** Run MD simulations based on the input files from CHARMM-GUI at https://charmm-gui.org. Build trajectory.vmd for visualizing results. **Author:** Peng Lian **Contact:** biohpc-help@utsouthwestern.edu	▶ Run this Version Documentation ⚙ Developer Information
astrocyte_charmmgui_md - 1.0.0	**Astrocyte CHARMM-GUI MD Workflow** This workflow performs MD simulation based on the input files generated by CHARMM-GUI(https://charmm-gui.org/). **Author:** Peng Lian **Contact:** biohpc-help@utsouthwestern.edu	▶ Run this Version Documentation ⚙ Developer Information

Thanks for your attention!

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