

# **Molecular Dynamics (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?**

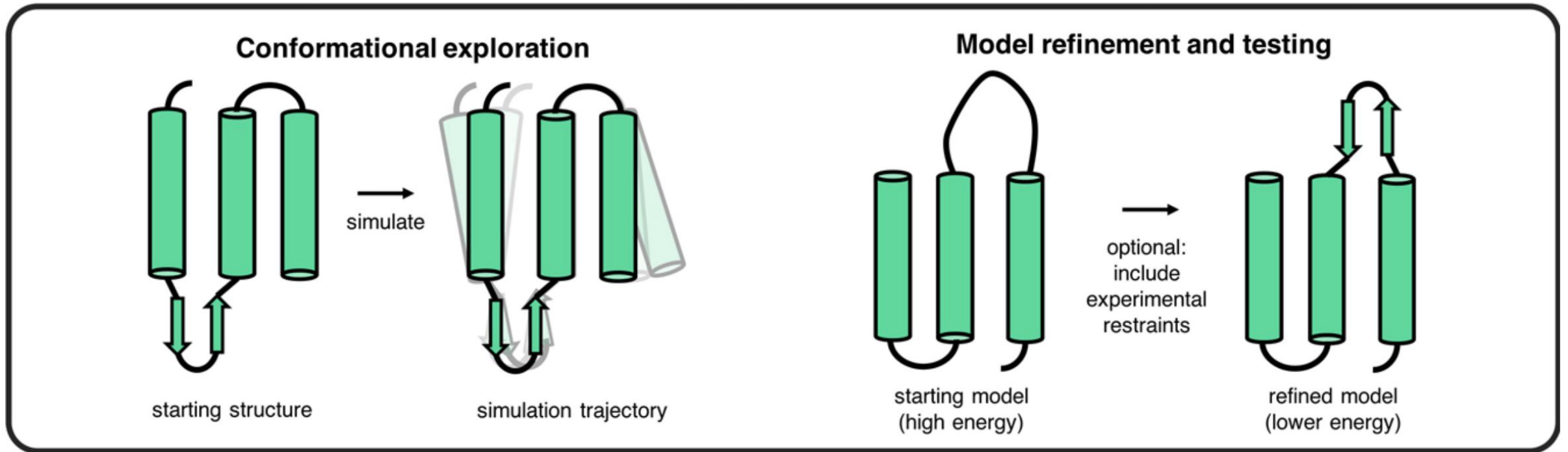
**Molecular dynamics** is a computer simulation method for analyzing the physical movements of atoms and molecules.

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?

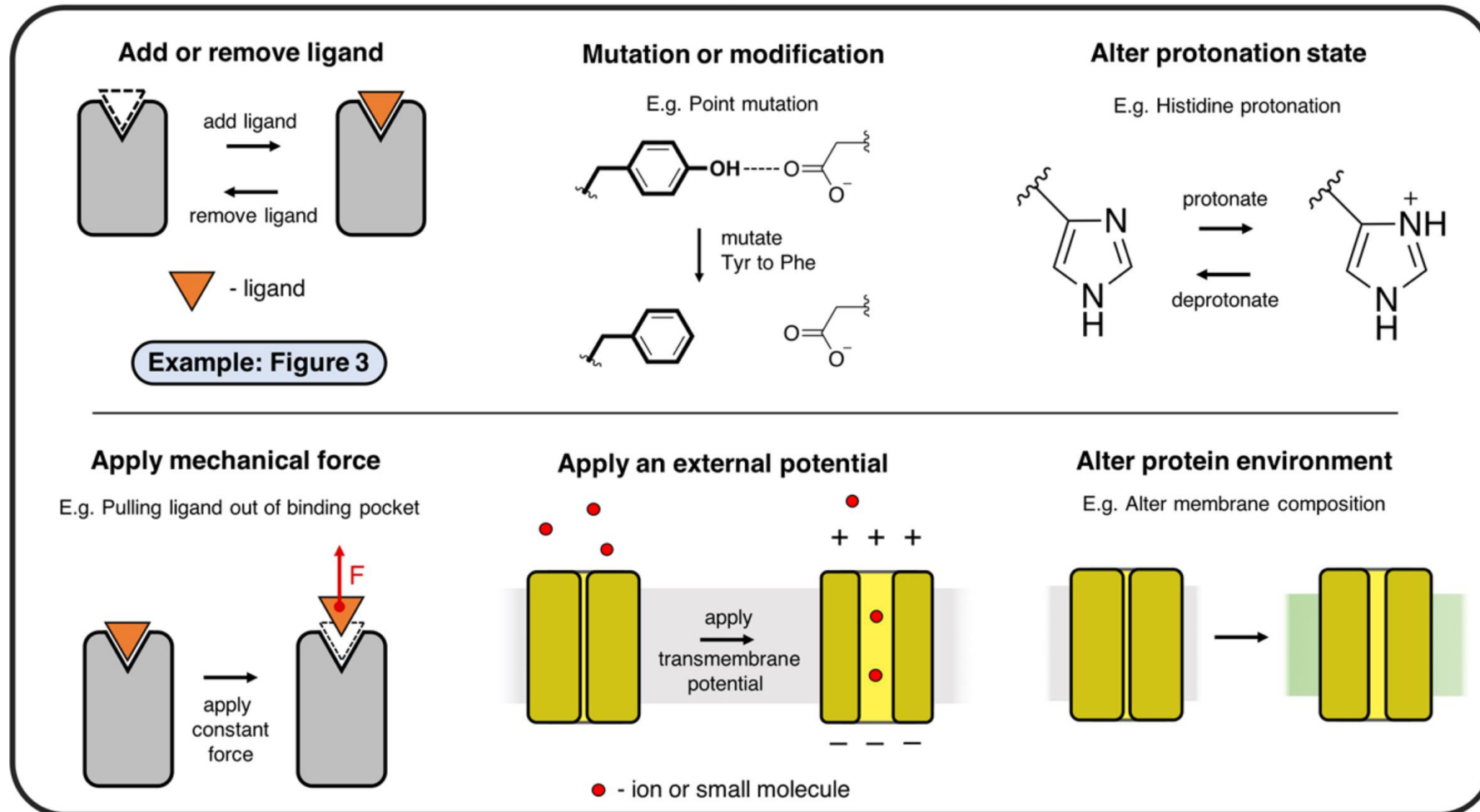
**Structural and dynamic studies:** *Studying conformational flexibility and stability*



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

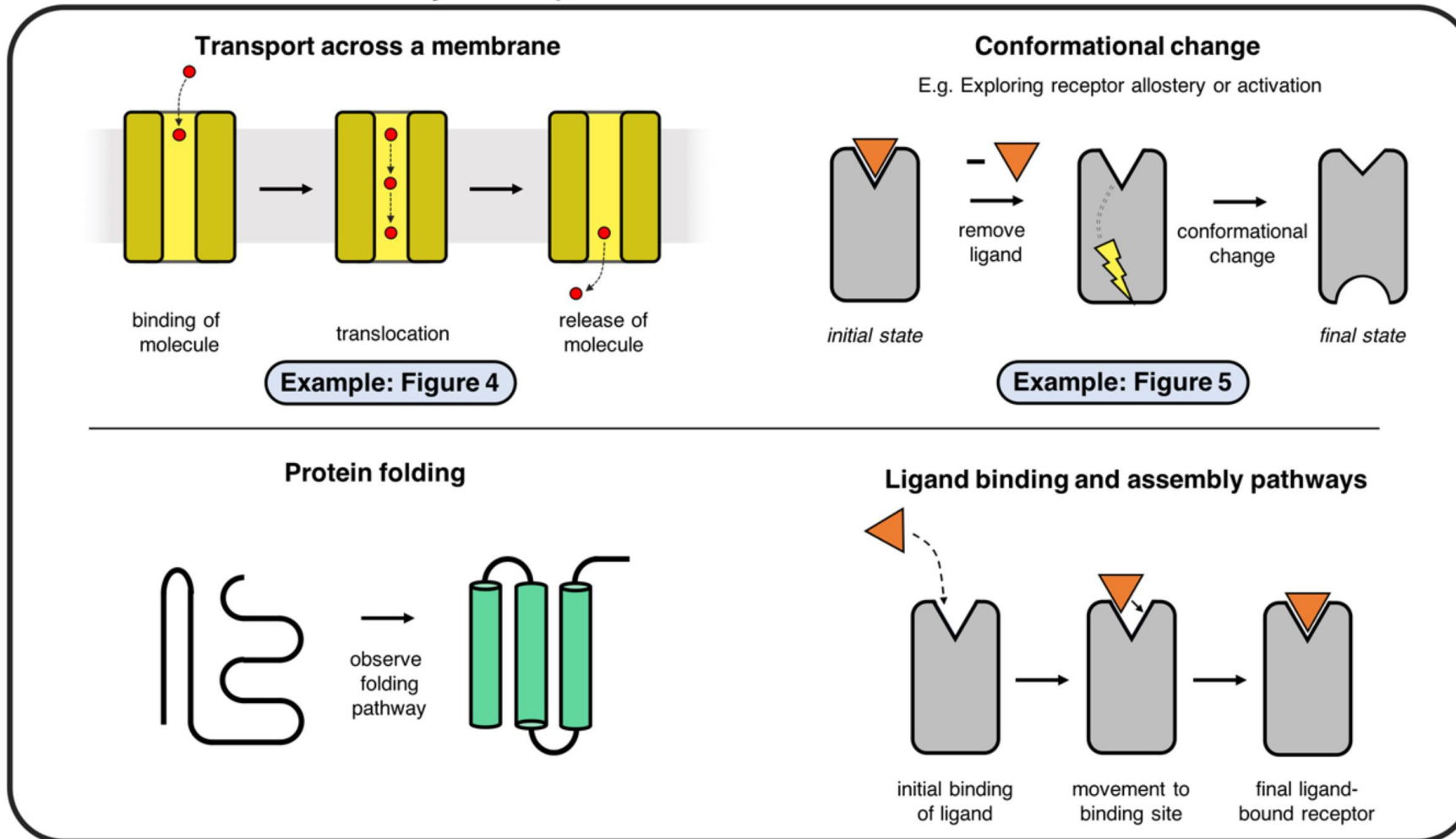
# What information can MD simulations provide?

**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

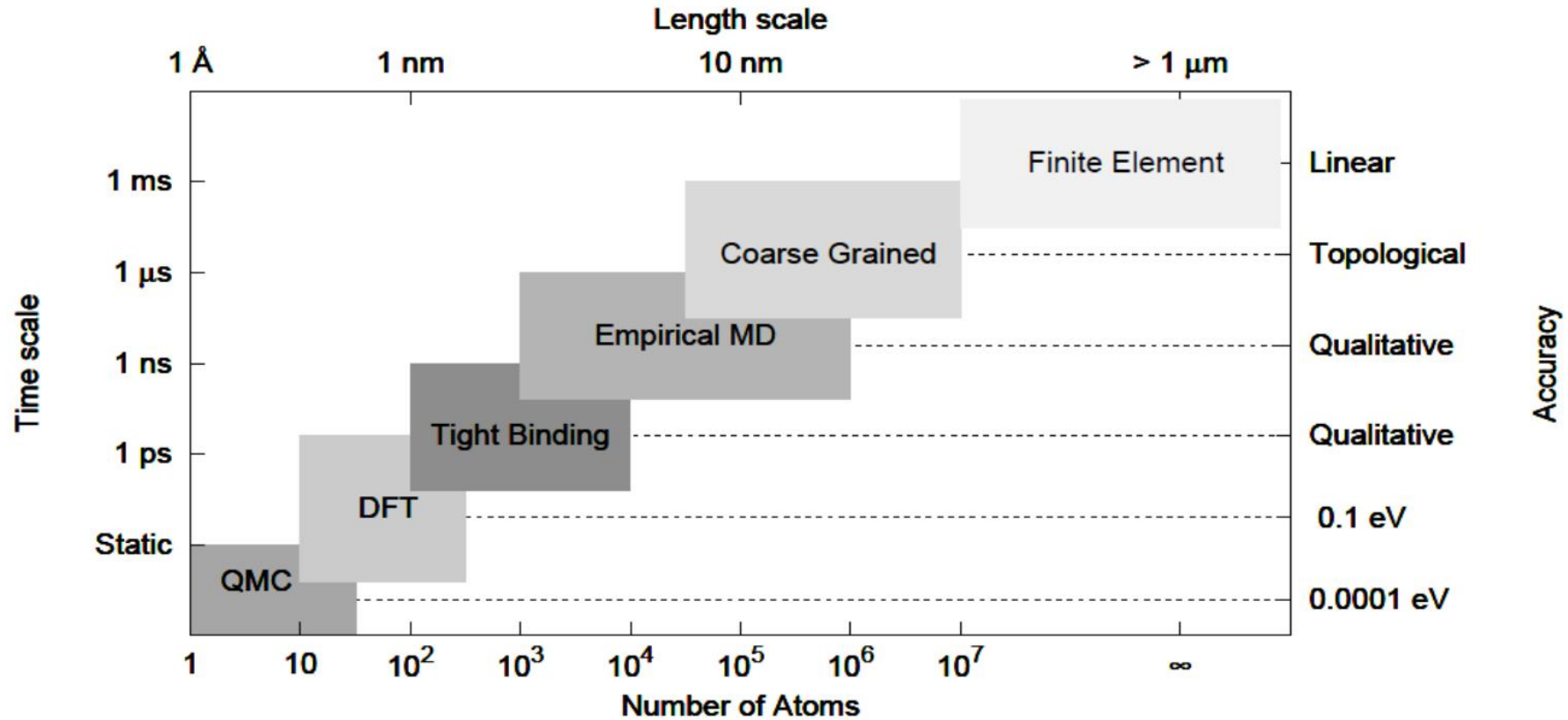
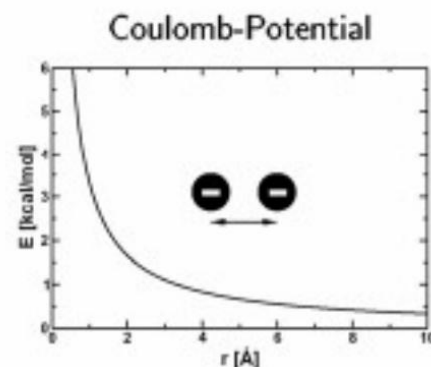
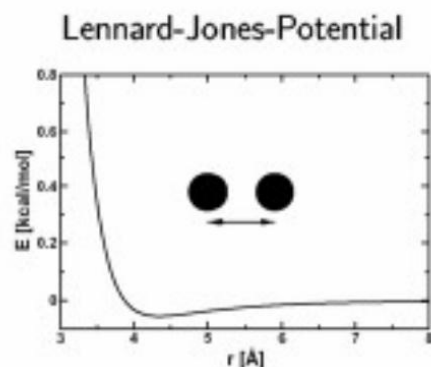
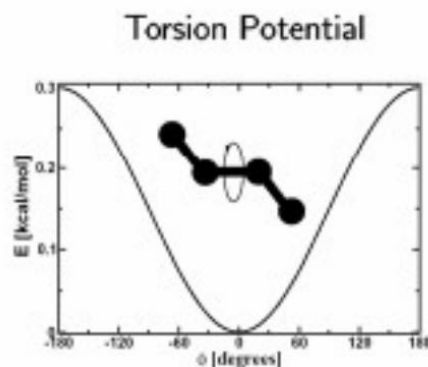
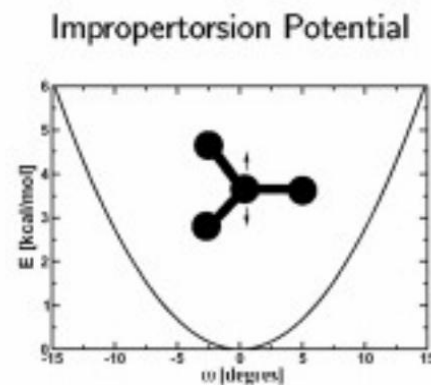
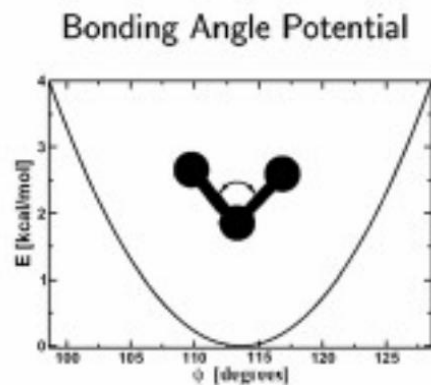
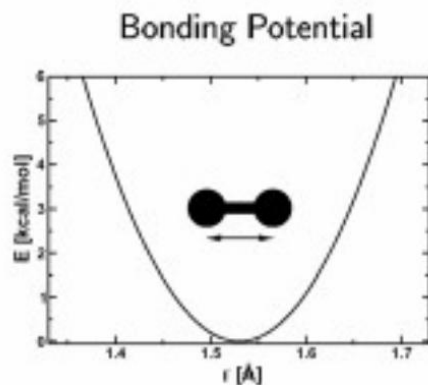


Figure 1. Schematic representation of the range of length- and time-scales accessible to a variety of modelling methods, from quantum Monte Carlo (QMC) for very accurate, very expensive static calculations through to approximate methods such as finite-element modelling.

# A Brief theoretical background of MD



**Classical**  
CHARMM  
AMBER  
GROMOS  
MMFF  
OPLS

**Polarizable**  
CHARMM  
AMBER  
AMOEBA

**Reactive**  
ReaxFF

**Coarse-grained**  
MARTINI

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

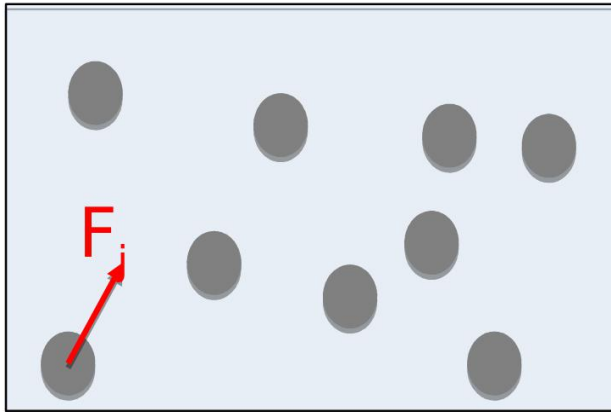
$$+ \sum_\phi k_\phi (1 - \cos(n\phi - \delta)) + \sum_{i < j} 4 \epsilon_{ij} \left[ \left( \frac{\sigma_{ij}}{r} \right)^{12} - \left( \frac{\sigma_{ij}}{r} \right)^6 \right] + \sum_{i < j} \frac{q_i q_j}{r}$$

**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



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

## Verlet algorithm:

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

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

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

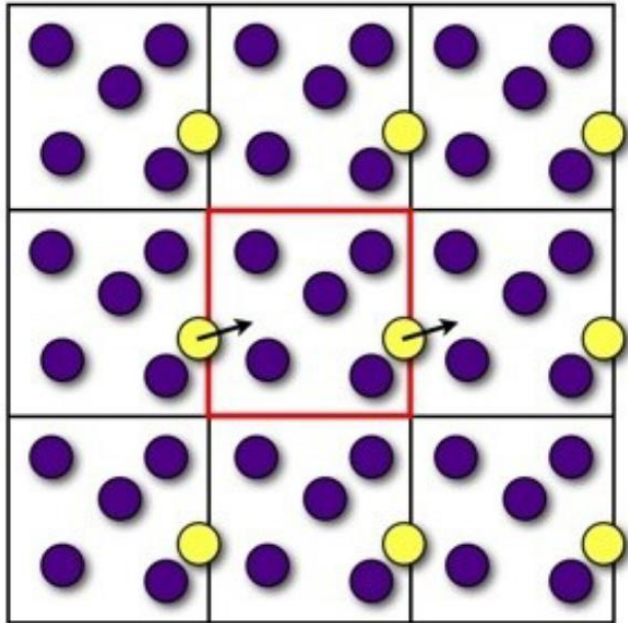
Positions at  $t_0 + \Delta t$  can be computed from actual positions and forces, and previous positions.

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. NAMMD2):

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

The image shows a screenshot of the VMD (Visual Molecular Dynamics) software interface. It consists of three main components:

- VMD Main Window:** A window titled "VMD Main" with a menu bar (File, Molecule, Graphics, Display, Mouse, Extensions, Help) and a table of loaded molecules. The table has columns for ID, T, A, D, F, Molecule, Atoms, Frames, and Vol. The first row shows ID 0, T A D F, Molecule 1L58.pdb, Atoms 1462, Frames 1, and Vol 0. Below the table is a playback control bar with buttons for play, stop, and a slider for speed.
- vmd Terminal Window:** A terminal window titled "vmd" showing the output of the VMD startup process. The output includes information about rendering modes, textures, plugins, and the loading of the 1L58.pdb structure. It reports 1462 atoms, 1330 bonds, and 316 residues. A warning message indicates an unusual bond between residues 97 (protein) and 165 (none). The terminal ends with a copyright notice for STRIPE.
- VMD 1.9.3 OpenGL Display Window:** A large window titled "VMD 1.9.3 OpenGL Display" showing a 3D ribbon representation of the Lysozyme protein structure (PDB: 1L58). The protein is colored in shades of purple, yellow, and blue. A 3D coordinate system is visible in the bottom left corner, with X, Y, and Z axes.

# 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**.

Input Generator
Job Retriever
Force Field Converter
PDB Reader
Glycan Reader & Modeler
Ligand Reader & Modeler
Glycolipid Modeler
LPS Modeler
Nanomaterial Modeler
Multicomponent Assembler
<b>Solution Builder</b>
Membrane Builder
Martini Maker
PACE CG Builder
Polymer Builder
Drude Prepper
Enhanced Sampler
Free Energy Calculator
LBS Finder & Refiner
Ligand Designer
High-Throughput Simulator
PBEQ Solver
Implicit Solvent Modeler
MAP Utilizer
DEER Facilitator
NMR Structure Calculator
Boundary Potential Utilizer
GCMC/BD Ion Simulator

# 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	<b>Astrocyte CHARMM-GUI MD Workflow</b> Run MD simulations based on the input files from CHARMM-GUI at <a href="https://charmm-gui.org">https://charmm-gui.org</a> . Build trajectory.vmd for visualizing results.  <b>Author:</b> Peng Lian <b>Contact:</b> <a href="mailto:biohpc-help@utsouthwestern.edu">biohpc-help@utsouthwestern.edu</a>	<a href="#">▶ Run this Version</a> <a href="#">📖 Documentation</a> <a href="#">⚙️ Developer Information</a>
astrocyte_charmmgui_md - 1.0.0	<b>Astrocyte CHARMM-GUI MD Workflow</b> This workflow performs MD simulation based on the input files generated by CHARMM-GUI( <a href="https://charmm-gui.org/">https://charmm-gui.org/</a> ).  <b>Author:</b> Peng Lian <b>Contact:</b> <a href="mailto:biohpc-help@utsouthwestern.edu">biohpc-help@utsouthwestern.edu</a>	<a href="#">▶ Run this Version</a> <a href="#">📖 Documentation</a> <a href="#">⚙️ Developer Information</a>

**Thanks for your attention!**

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