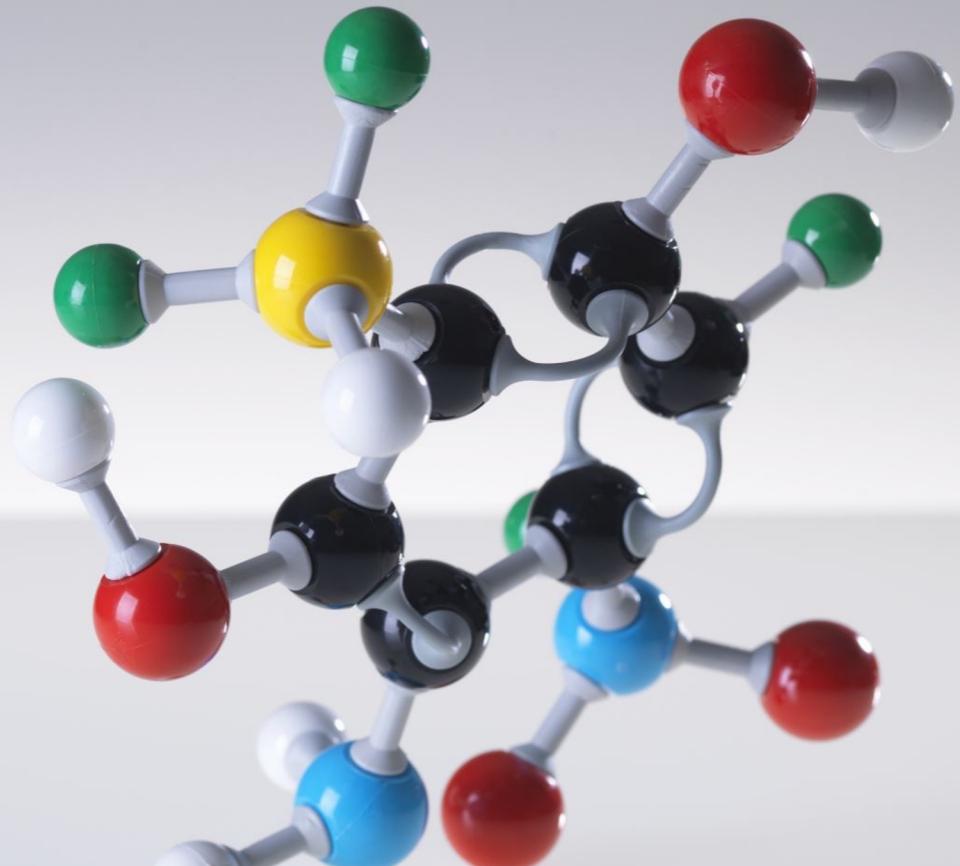


INTRODUCTION TO MOLECULAR DYNAMICS

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MOTIVATION



Using **Statistical Mechanics**, we can accurately model properties of big, simple non-interacting systems.



Using **Quantum Calculations**, we can accurately compute properties of small interacting systems.



Molecular Dynamics will act as a middle ground, allowing us to compute properties of big interacting systems, but with a little less accuracy than the previous methods.

WHAT IS MOLECULAR DYNAMICS?

- Instead of directly exploring the phase space like in statistical mechanics, we will follow the time evolution of the system.
- For ergodic systems these two approaches are equivalent.
- The time evolution is achieved by integration of the Newton equation of motion:

$$\frac{d^2 \mathbf{r}_i}{dt^2} = \frac{1}{m} \mathbf{F}_i$$

INTEGRATING NEWTON EQUATION



It is not possible to find analytical solutions for the newton equation of complex systems with hundreds of particles.



We must resort to numeric solutions.



We will evaluate the properties of the system in a set of discretized time-steps.



There are different integration algorithms that can be used.

THE SIMPLE (AND WRONG) INTEGRATION ALGORITHM

- We are going to discretize the time in steps of value Δt .
- This value should be small enough for the system to be only slightly different in the next time step

$$\frac{dr_i(t)}{dt} = v_i(t)$$

$$\frac{dv_i(t)}{dt} = \frac{1}{m_i} F_i$$

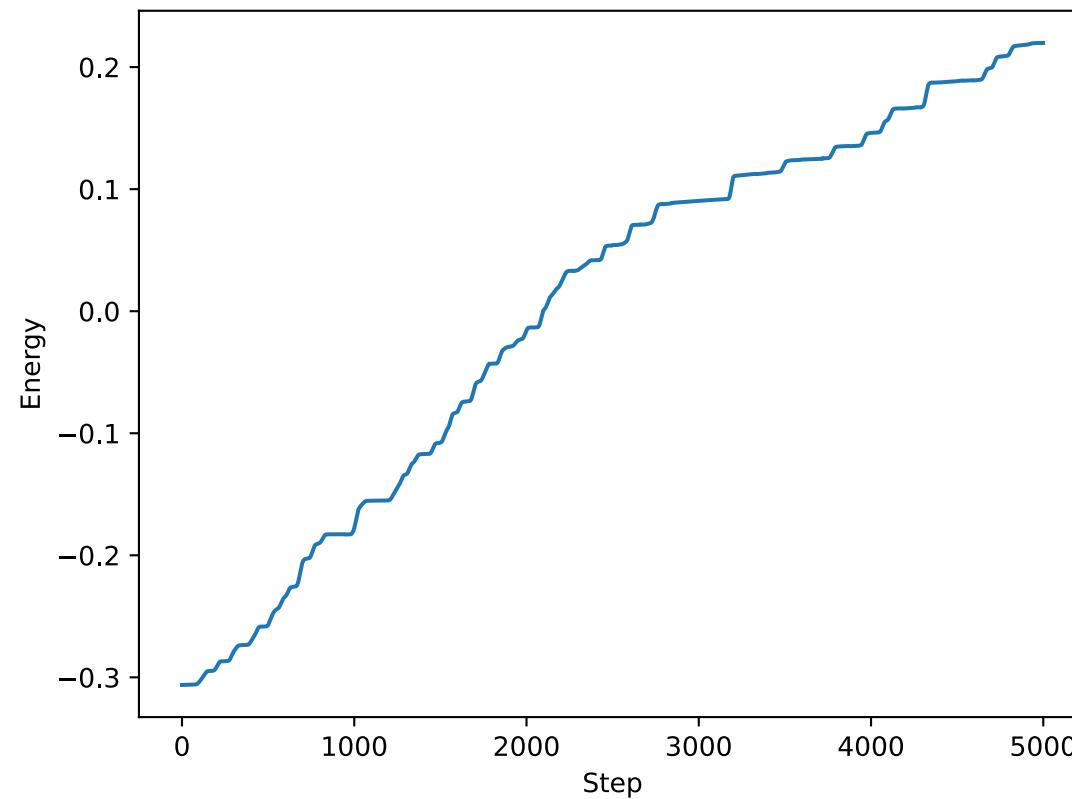


$$r_i(t + \Delta t) = r_i(t) + \Delta t v_i(t)$$

$$v_i(t + \Delta t) = v_i(t) + \frac{\Delta t}{m_i} F_i(t)$$

THE SIMPLE (AND WRONG) INTEGRATION ALGORITHM

- This algorithm presents a drift in energy

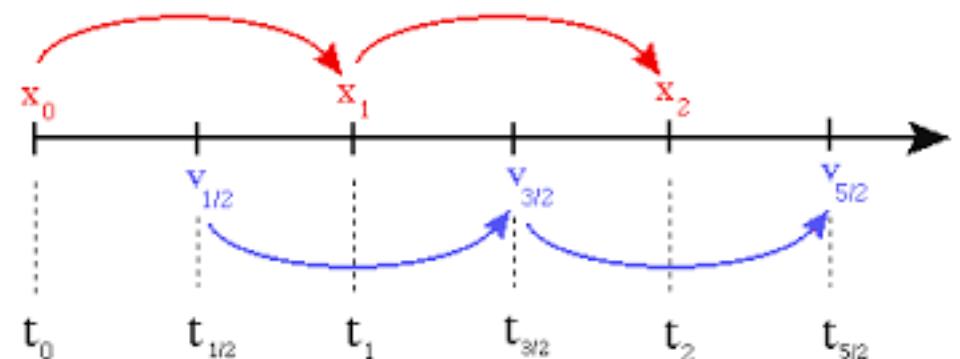


THE LEAP-FROG INTEGRATOR

- A very common algorithm is the Leap-frog integrator.
- Velocities and positions are no evaluated at the same time-steps.
- This algorithm is time-reversible.

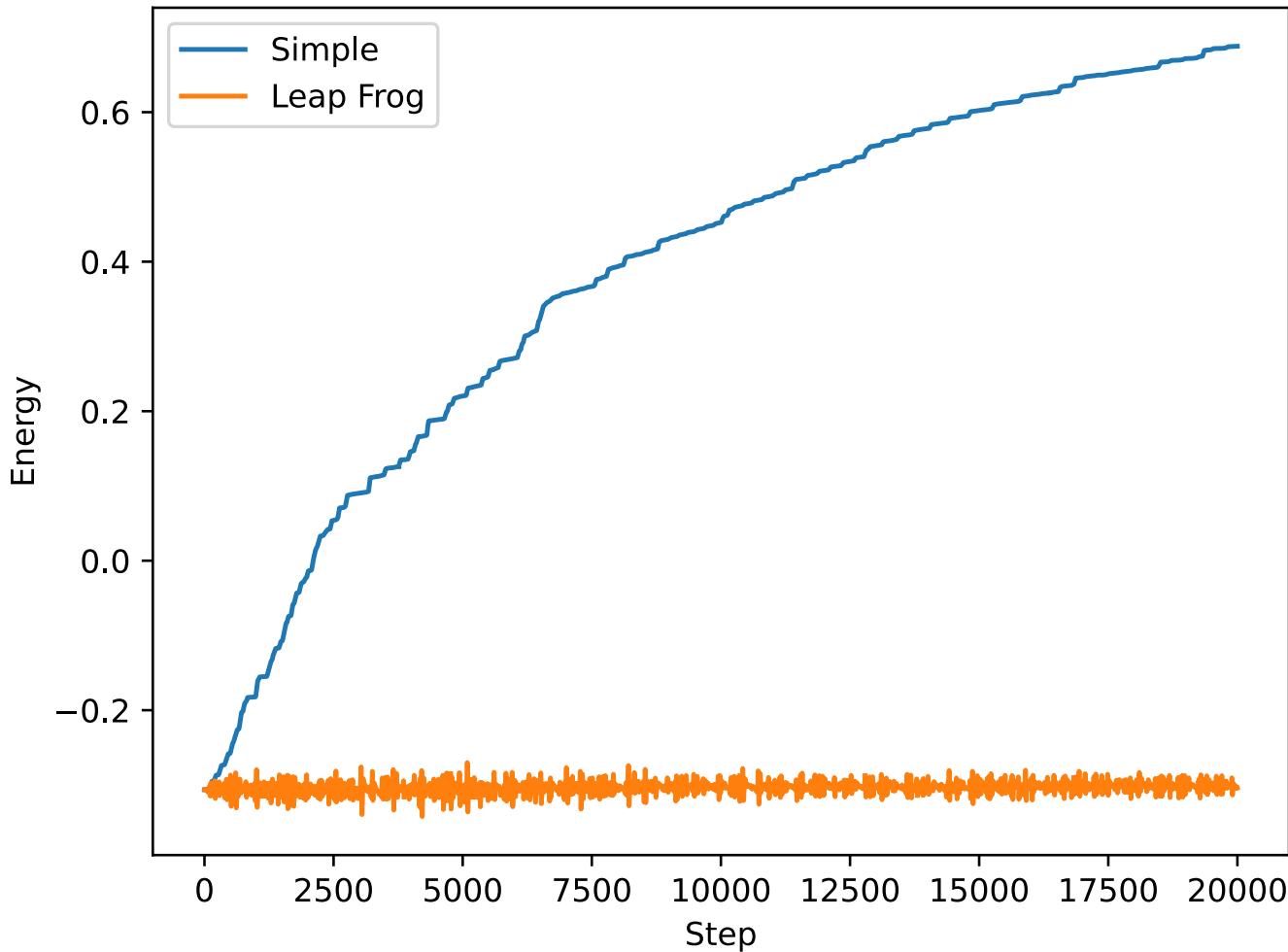
$$v_i(t + \frac{1}{2}\Delta t) = v_i(t - \frac{1}{2}\Delta t) + \frac{\Delta t}{m_i} F_i(t)$$

$$r_i(t + \Delta t) = r_i(t) + \Delta t v_i(t + \frac{1}{2}\Delta t)$$

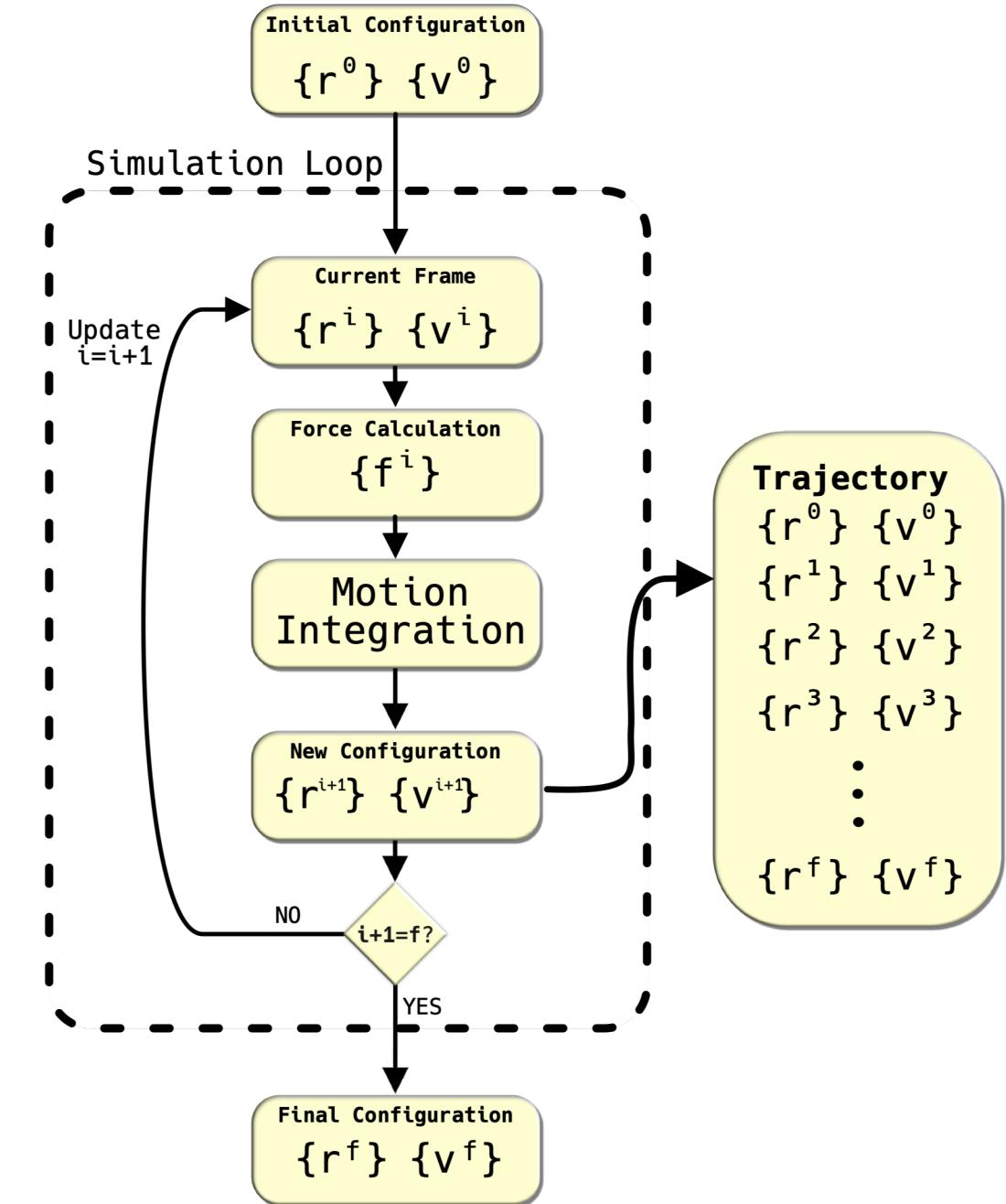


http://www.physics.drexel.edu/~steve/Courses/Comp_Phys/Integrators/leapfrog/

THE LEAP-FROG INTEGRATOR



GENERAL MD- SCHEME



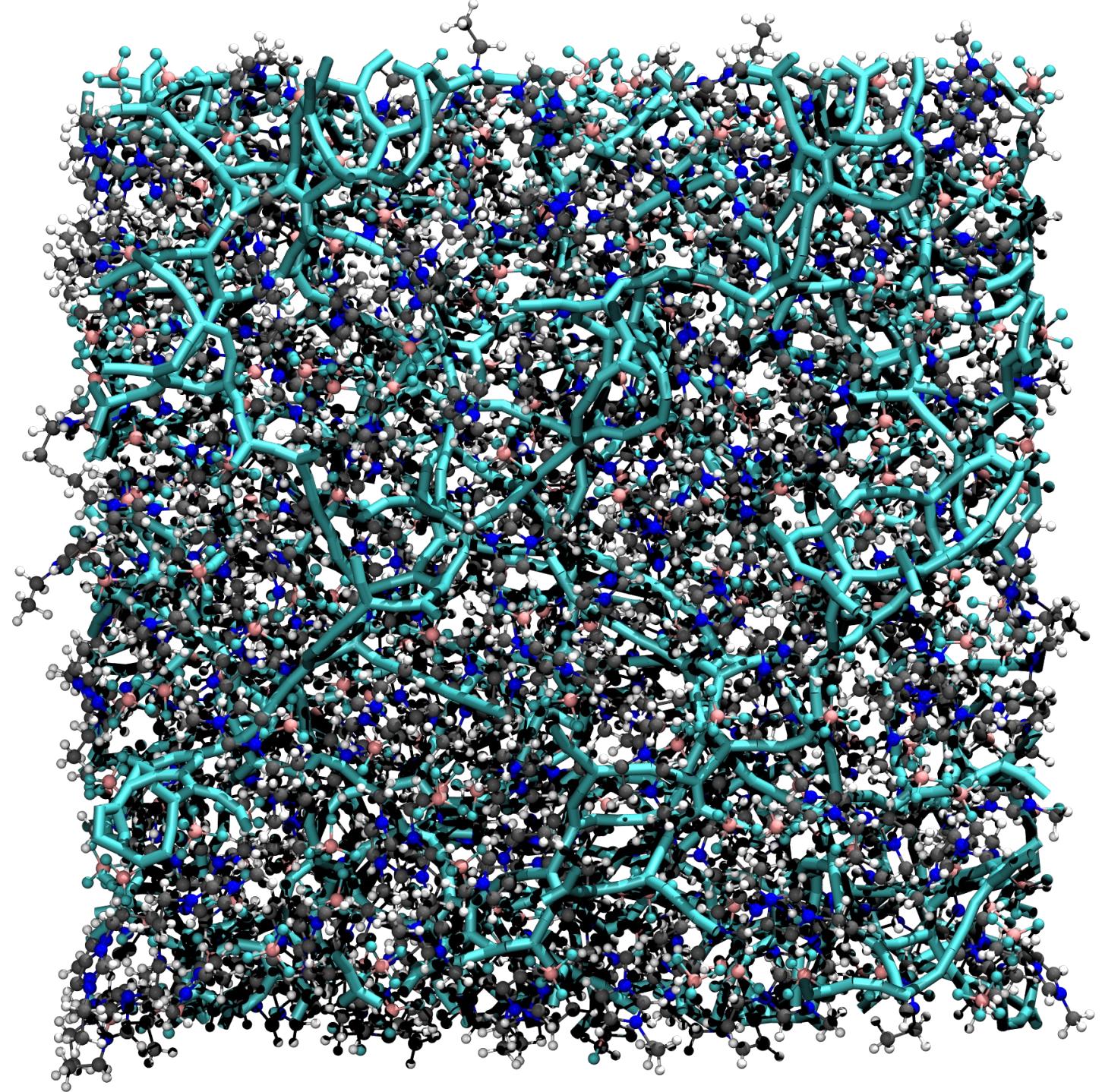
MOLECULAR MECHANICS

Molecular dynamics can be used to simulate a huge variety of systems.

Depending on the origin of the forces (interaction potential) there are different kinds of molecular dynamics.

When using classical approximations for the molecules, we refer to them as “Molecular Mechanics”

Most molecular dynamics simulations are molecular mechanics simulations.



MOLECULAR MECHANICS

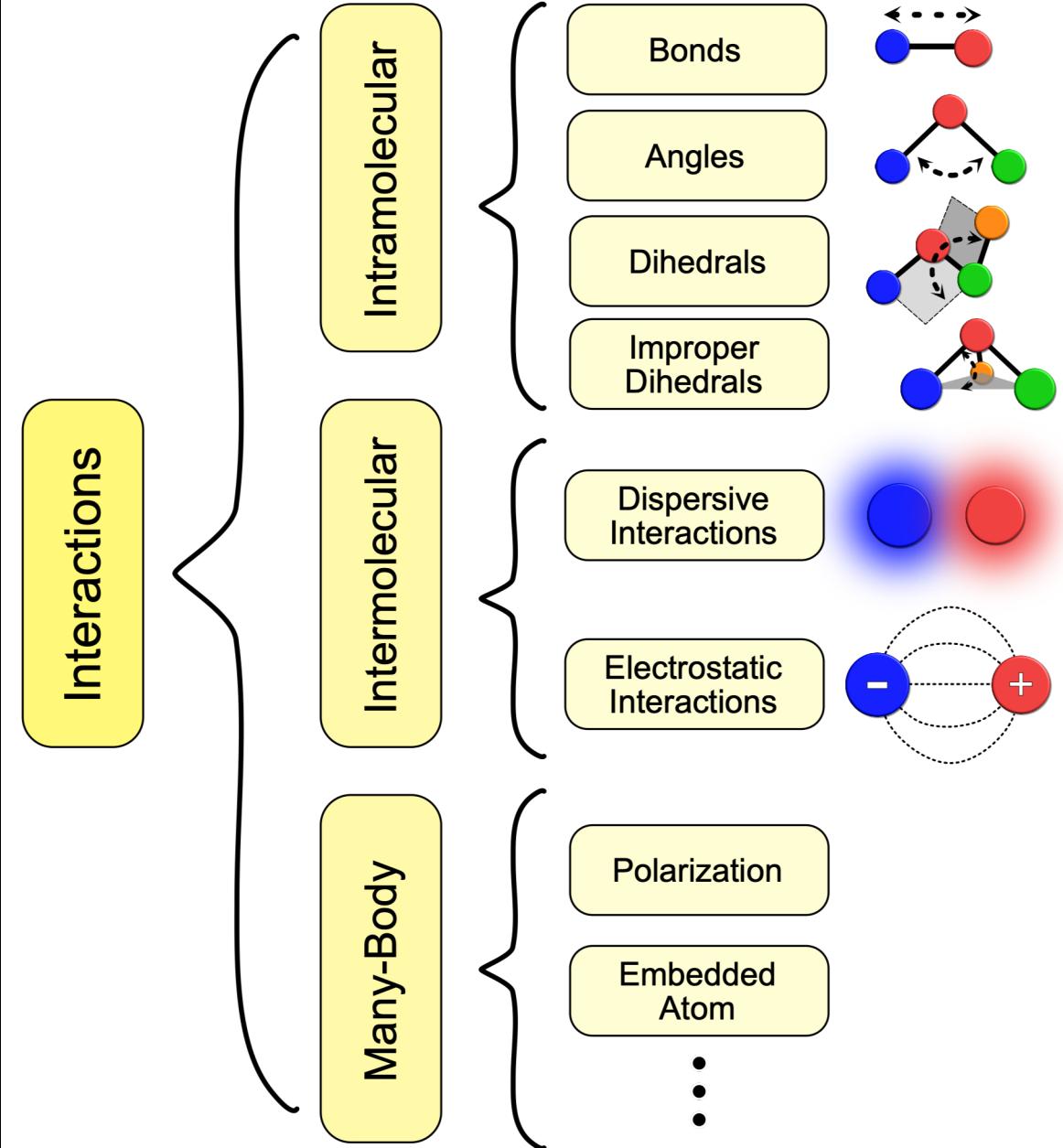
In Molecular Mechanics we only simulate the movement of the nucleus of the atoms.

The electrons are no taken in consideration explicitly.

Charge transfer between atoms/molecules is not (usually) possible.

Molecules and their geometry are pre-fixed before the calculation.

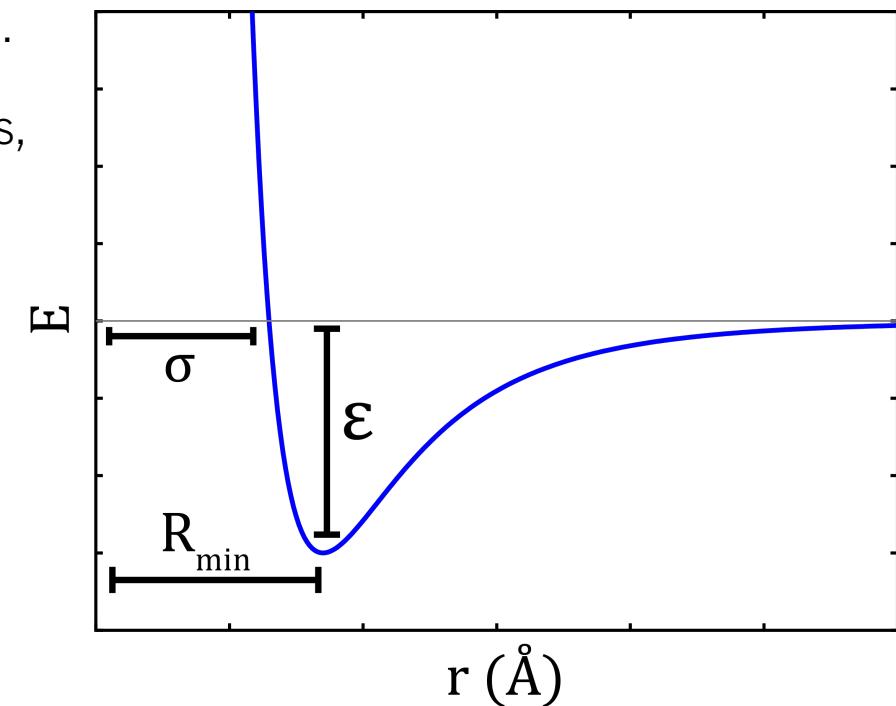
INTERACTION IN MOLECULAR DYNAMICS



DISPERSIVE FORCES

- Due to London dispersive forces, everything is *sticky* at the nano-scale. We model this stickiness with a $-r^6$ term.
- At very short distances, atoms are similar to hard spheres, with repulsive core. We model this repulsive core with a $+r^{12}$ term.
- This model is called a Lennar Jones 12-6 potential.

$$E = 4\epsilon \left[\left(\frac{\sigma}{r} \right)^{12} - \left(\frac{\sigma}{r} \right)^6 \right]$$



COULOMB FORCES

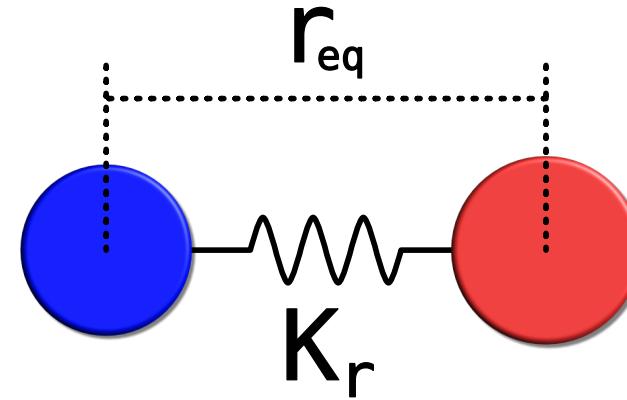
- Coulomb forces are computed using the usual coulomb potential.
- Atoms are assigned atomic charges that are usually constant during the simulation.

$$E = \frac{1}{4\pi\epsilon_0} \frac{q_i q_j}{r_{ij}}$$

BONDS

- Bonds between atoms are usually represented as harmonic oscillators.

$$E = \frac{1}{2}K_r(r - r_{eq})^2$$

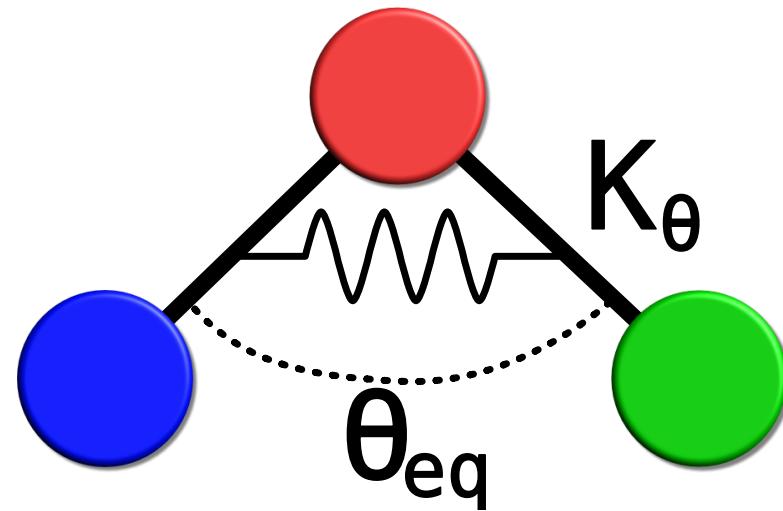


- Bonds with hydrogen atoms are usually considered as rigid bonds due to their quantum nature.

ANGLES

- Angles are also usually considered as harmonic oscillators.

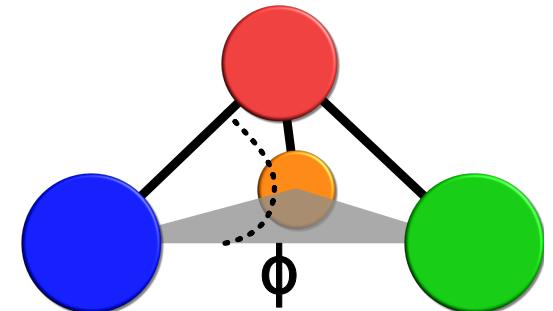
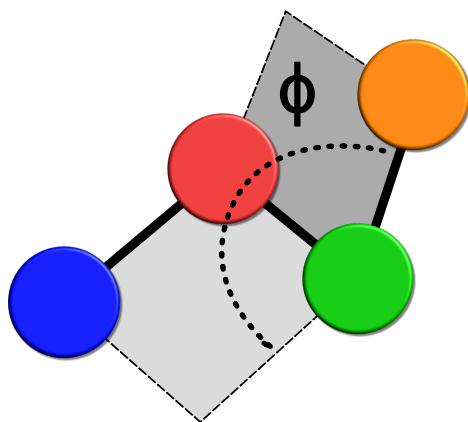
$$E = \frac{1}{2}K_\theta(\theta - \theta_{eq})^2$$



DIHEDRAL ANGLES

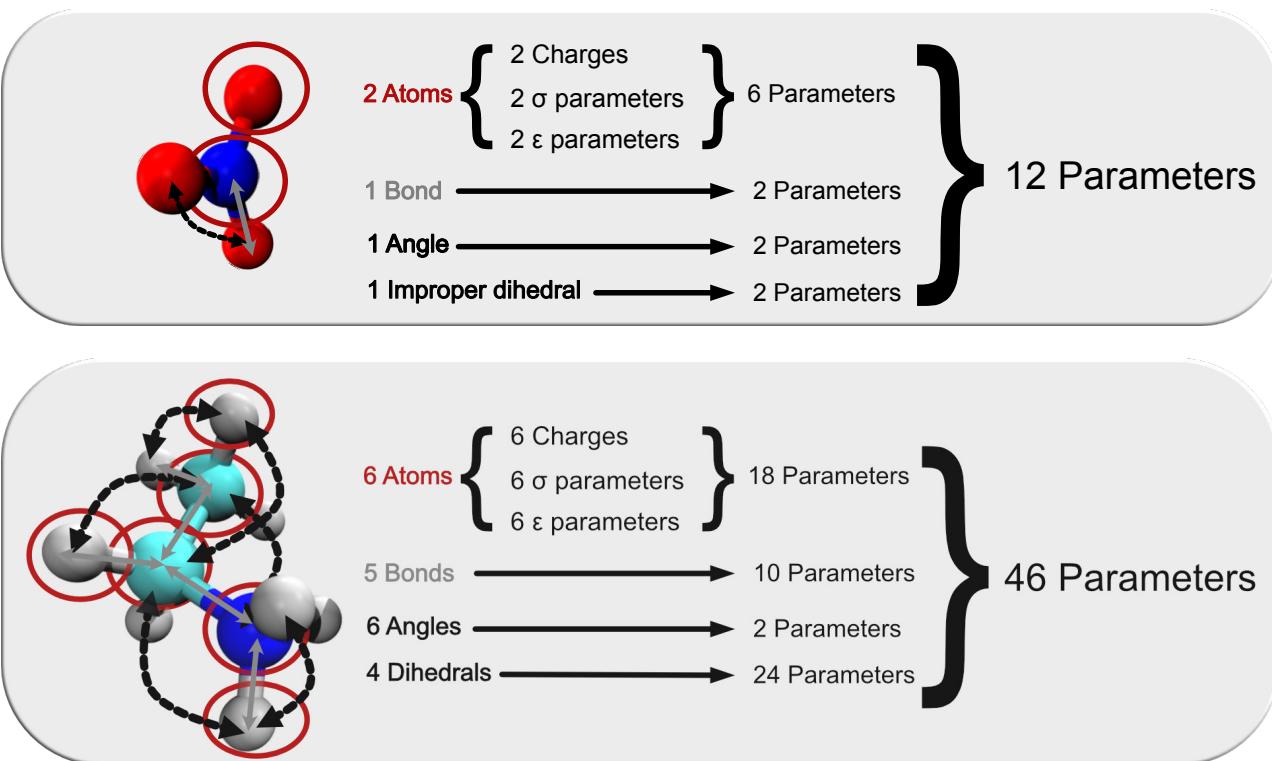
- The dihedrals are usually represented as a cosine series expansion (similar to a Fourier expansion).
- There are several functional forms, but most of them are equivalent

$$E = \sum_{i=1}^3 \frac{V_i}{2} [1 + (-1)^{i+1} \cos(i\phi + f_i)]$$



FORCE FIELD AND TOPOLOGY

- The combination of the model of the interactions is known as the Force Field
- When the specific values for a given molecule are given it is known as the topology of the molecule.
- The topology for a given molecule may have a lot of parameters.
- These parameters are usually obtained from quantum calculations of isolated molecules.

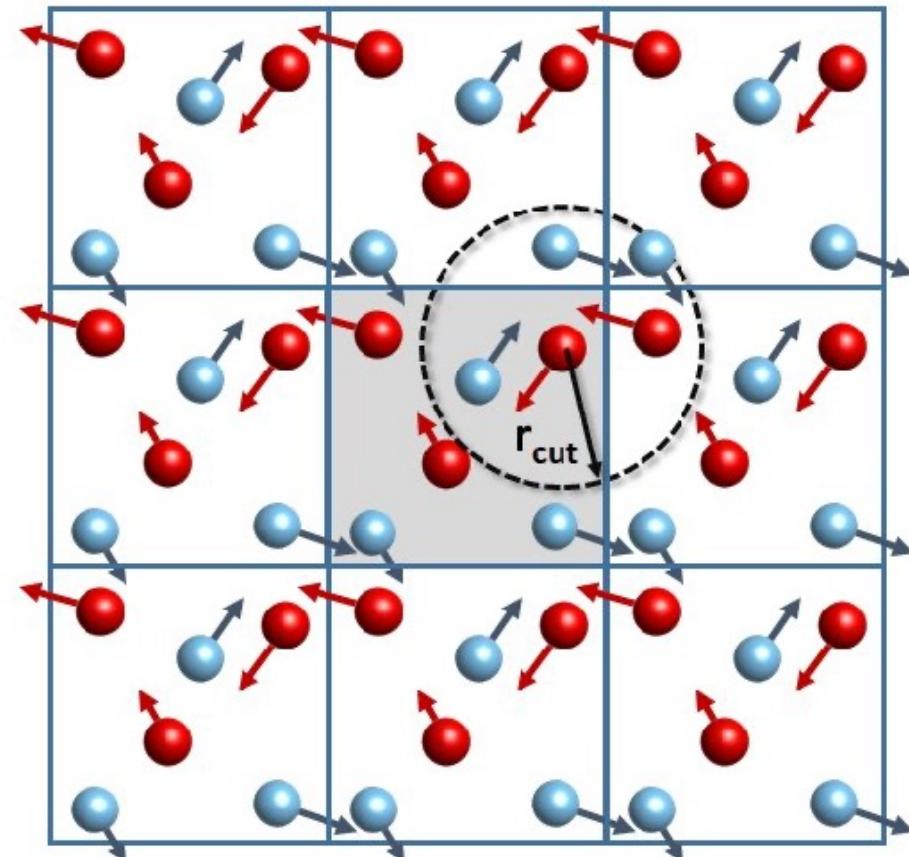


REMOVING BORDER EFFECTS

- Usually, we are not interested in the properties of our system surrounded by vacuum, but their bulk properties.
- These bulk properties must be computed far enough from interfaces.
- The usual way to accomplish this is by implementing *periodic boundary conditions* (PBC).
- These PBCs allow us to simulate an infinite system.

PERIODIC BOUNDARY CONDITIONS

- We model our system as a cube.
- Particles that exit our simulation cube by one side, enter again by the opposite side.
- Inter-particle distances are computed using the shortest route between particles.
- This effectively creates infinite copies of our system.



COMPUTING REPLICA INTERACTIONS

- Due to the infinite replicas of our system, we must find a way to compute the interactions due to dispersive and coulomb potentials.
- For the dispersive interactions we can set a cutoff radius, and we will only compute the interactions with the particles inside that cutoff.
- For the Coulomb potential it is not possible to do that as the potential has infinite range.
- Coulomb interactions are computing in the Fourier space:
 - Ewald Summation
 - Particle Mesh Ewald (PME)
 - Particle- Particle Particle-Mesh (P^3M)
 - Fast Multipole Method (FMM)

HEATING UP: SIMULATIONS IN THE NVT ENSEMBLE

- Molecular Dynamics simulations without modifications are performed in the NVE ensemble.
- If we want to perform simulations in the NVT ensemble we must add a thermostat.
- There are several options for thermostat, the most common are:
 - Berendsen 
 - Nose-Hover 
 - Bussi-Donadio-Parrinello (V-rescale) 

EXAMPLE: V-RESCALE THERMOSTAT

- The V-rescale thermostat scales the velocities of all the particles in the system in order to obtain the correct temperature.
- Includes a random term to properly describe the temperature fluctuation of the thermodynamic ensemble.
- It takes as argument the desired kinetic energy (K) and a relaxation time (τ)

$$\lambda = \left[1 + \left(\frac{\bar{K}}{K} - 1 \right) \frac{\Delta t}{\tau} + 2 \sqrt{\frac{\bar{K}}{K N_f \tau}} W(\Delta t) \right]^{1/2}$$

Scaling Factor 

Relax the system to the target temperature (kinetic energy) 

Random fluctuations around the target temperature 

Gaussian Random Number Generator 

UNDER PRESSURE

- Simulations in the NPT ensemble (necessary to find equilibrium densities) can be achieved by adding a barostat.
- The barostats scale the positions of the center of mass of all the molecules in the simulation box as well as the size of the simulation box.
- There are also several that are commonly used:
 - Berendsen 
 - Parrinello-Rahman 
 - Nose-Hoover 
- Berendsen barostat is useful for relaxations when the initial configuration is far from equilibrium but should not be used for computing properties.

ANALYZING THE RESULTS

- The result of a molecular dynamics simulation is a collection of positions, velocities (and forces) of every atom in each time-step.
- This collection of datum is usually called the trajectory of the system.
- Usually, some thermodynamic quantities are also computed during the simulation (potential energy, total energy, pressure, volume, temperature, ...). However, it is possible to recover this values from the positions and velocities of the atoms.
- Equilibrium thermodynamic properties can be computed by averaging the values obtained during the simulation.
- Other structural and dynamic properties can be computed by performing statistical analysis of the trajectory.

$$y = g(x)$$

Second Lines

Tangent
line
T

$$x+h$$

EXAMPLES

$$\text{AMPLES} \quad f(x) = \lim_{h \rightarrow 0} \frac{(x+h)^2 - x^2}{h}$$

$$= \lim_{h \rightarrow 0} \frac{x^2 + 2xh + h^2 - x^2}{h}$$

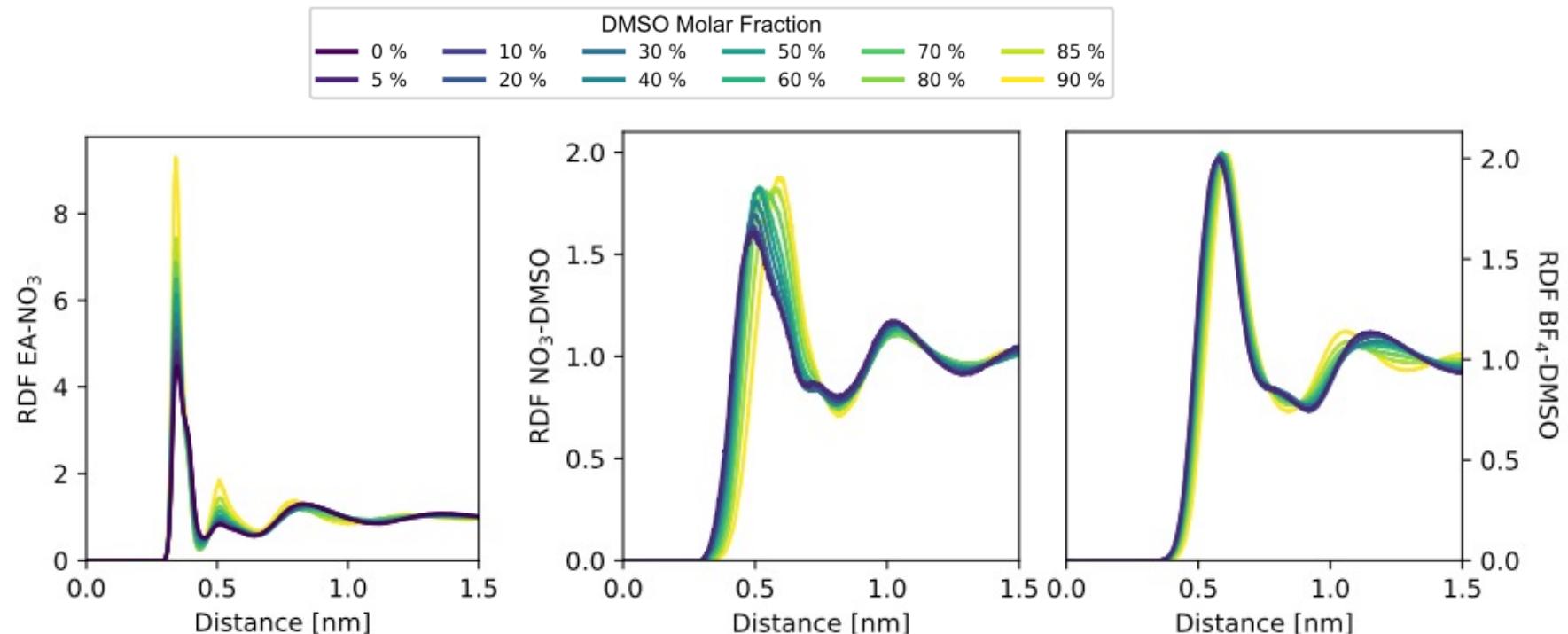
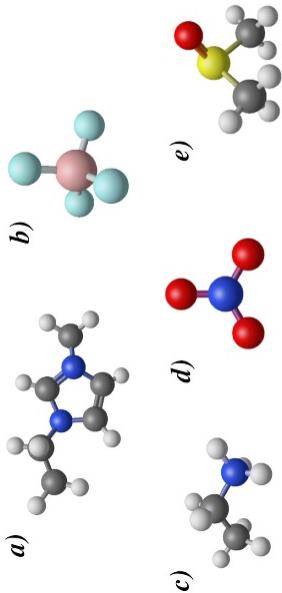
$$= \lim_{h \rightarrow 0} \frac{2xh + h^2}{h}$$

RADIAL DISTRIBUTION FUNCTION

$$RDF_{ab}(r) = \frac{V}{N_a N_b} \sum_{i=1}^{N_a} \sum_{j=1}^{N_b} \langle \delta(|\mathbf{r}_i - \mathbf{r}_j| - r) \rangle$$

- Measures the density of type “b” particles at a distance “r” of a particle of type “a”.
- The values are normalized to the random distribution density.
- The location of the peak is related to the coordination distance.
- The height of the peak is related to the energy of interaction.

<https://doi.org/10.1016/j.molliq.2022.119188>

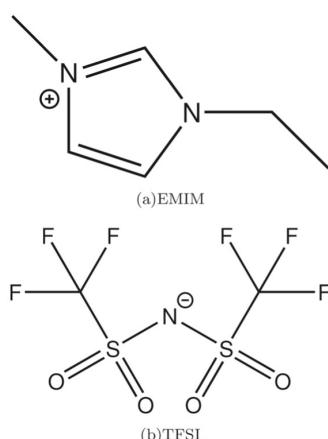


MEAN SQUARED DISPLACEMENT

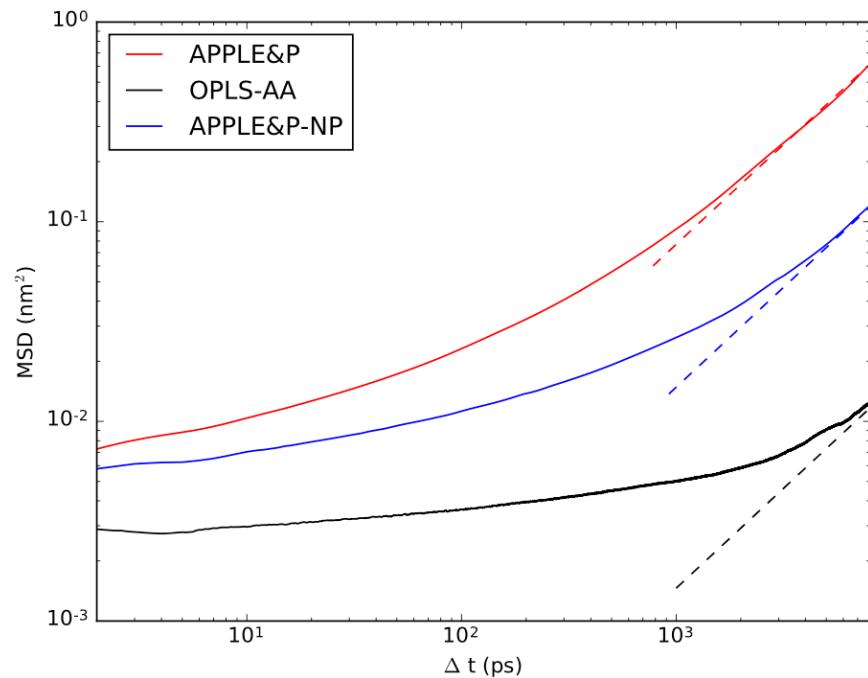
$$MSD(\Delta t) = \left\langle (r_i(t + \Delta t) - r_i(t))^2 \right\rangle$$

$$D = \lim_{\Delta t \rightarrow \infty} \frac{MSD(\Delta t)}{6\Delta t}$$

- Measures the diffusion of the system.
- May present 3 regimes:
 - Ballistic: $MSD \propto t^2$
 - Subdiffusive (only for some systems): $MSD \propto t^a$ with $a < 1$
 - Diffusive: $MSD \propto t$
- The diffusion coefficient of the system is related to the slope of the MSD at long times.



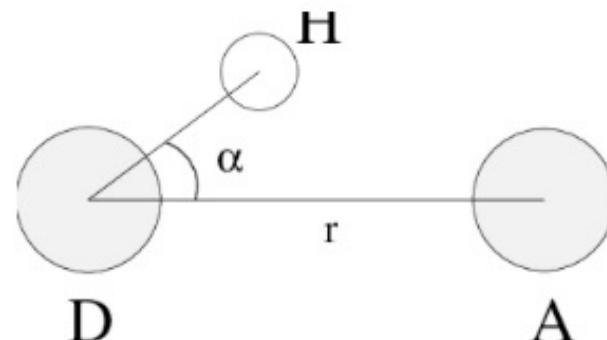
The Journal of Chemical Physics 146, 124503
(2017); doi: 10.1063/1.4978943



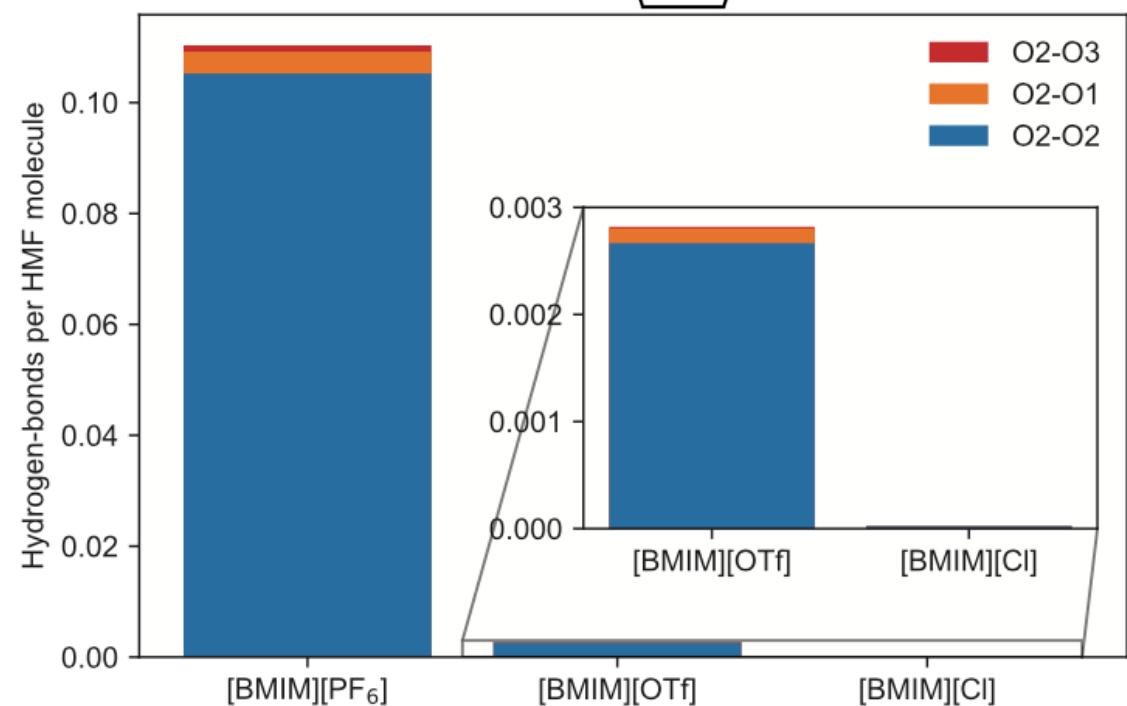
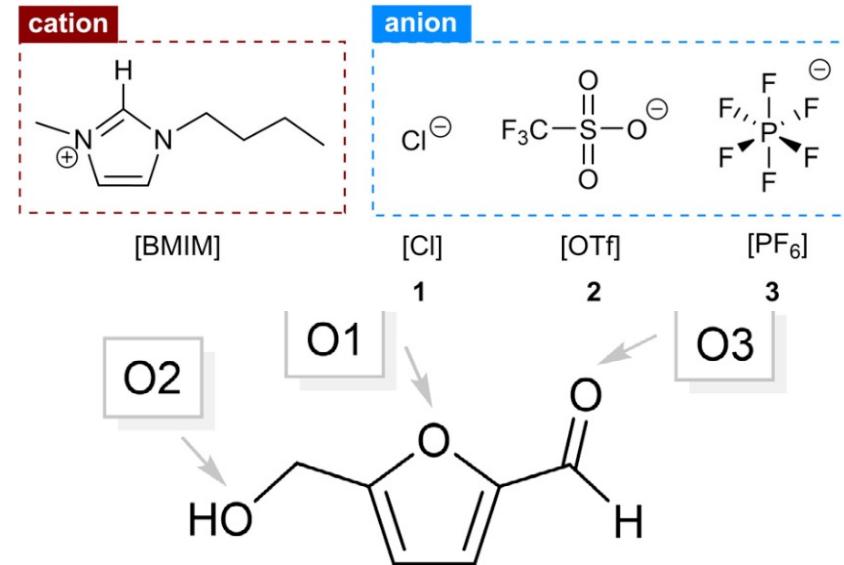
HYDROGEN BONDS

- Hydrogen Bonds can be calculated by using a geometric criteria.

$$\begin{aligned} r &\leq r_{HB} = 0.35 \text{ nm} \\ \alpha &\leq \alpha_{HB} = 30^\circ \end{aligned}$$



<https://manual.gromacs.org/current/reference-manual/analysis/hydrogen-bonds.html#fig-hbond>

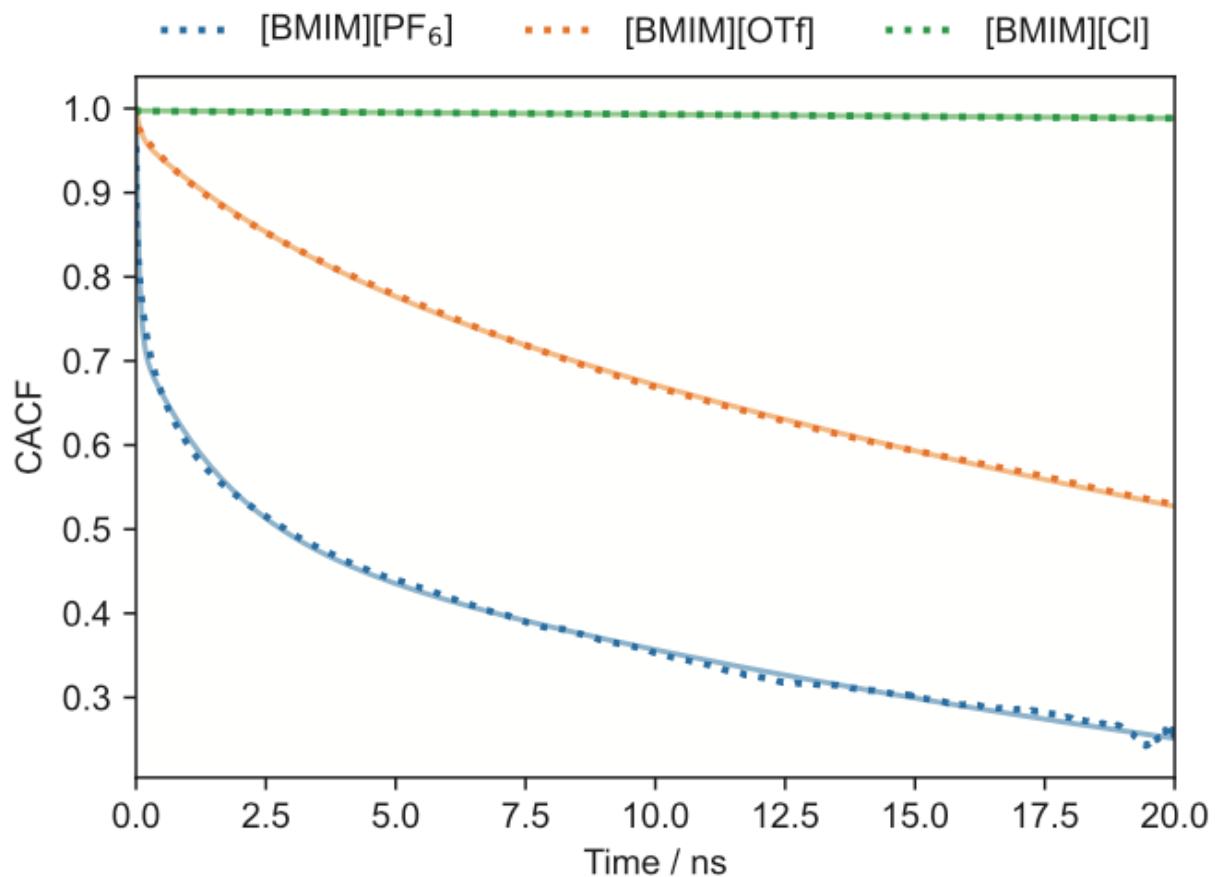


SOLVATION COMPLEX LIFETIME

$$CACF(\Delta t) = \frac{\langle \Theta_{ij}(t)\Theta_{ij}(t + \Delta t) \rangle}{\langle \Theta_{ij}(t)\Theta_{ij}(t) \rangle}$$

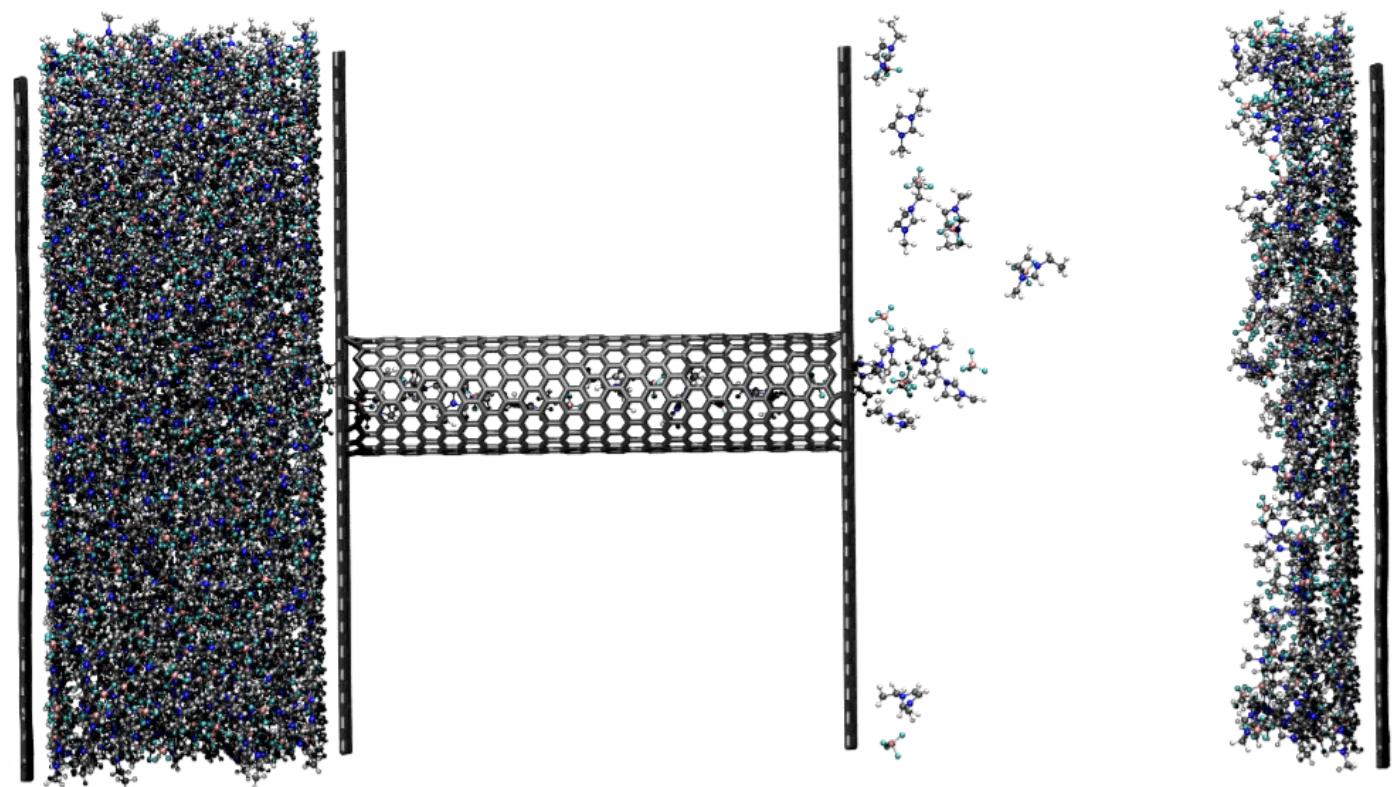
$$\Theta_{ij}(t) = \begin{cases} 1 & \text{if } r_{ij} < r_c \\ 0 & \text{else} \end{cases}$$

- Allow us to quantify how stable are the solvation complex that appear in the simulations.

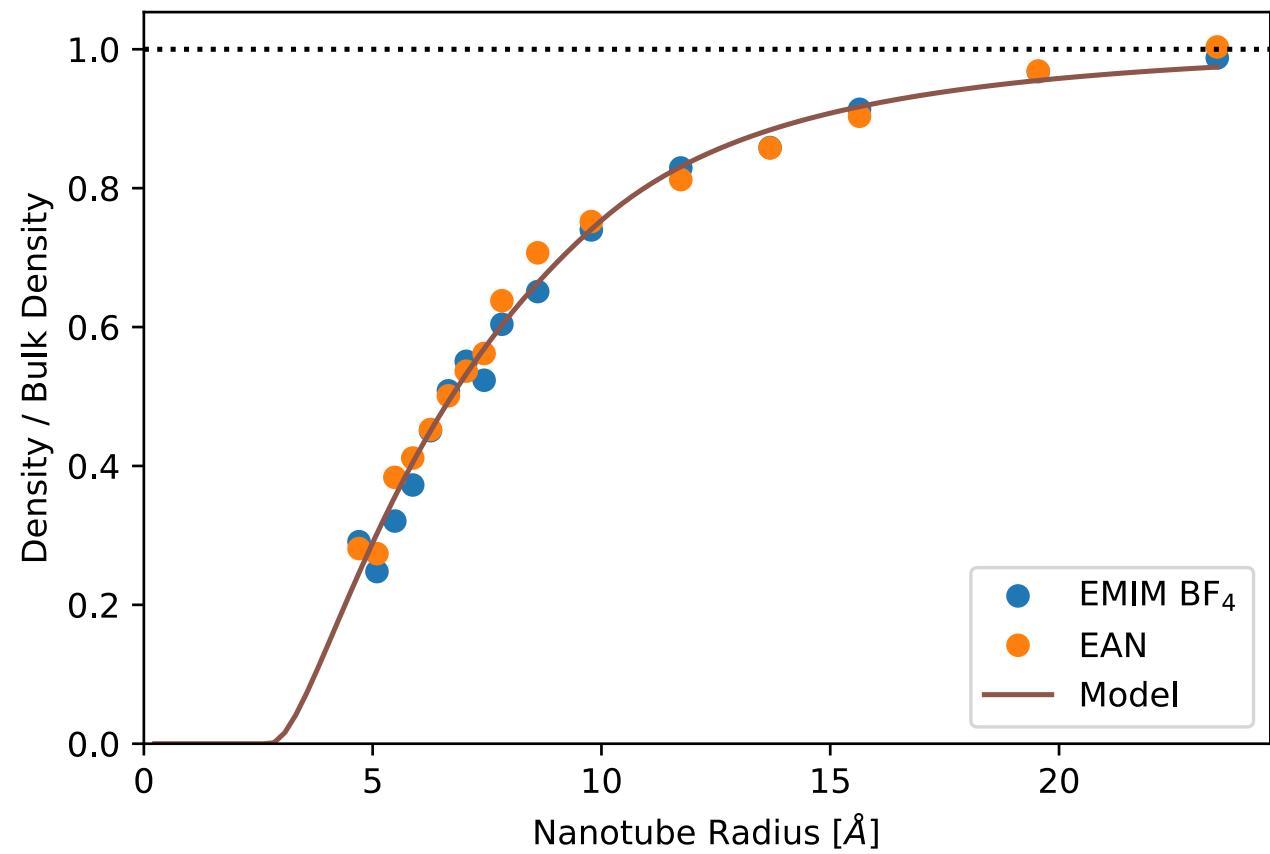
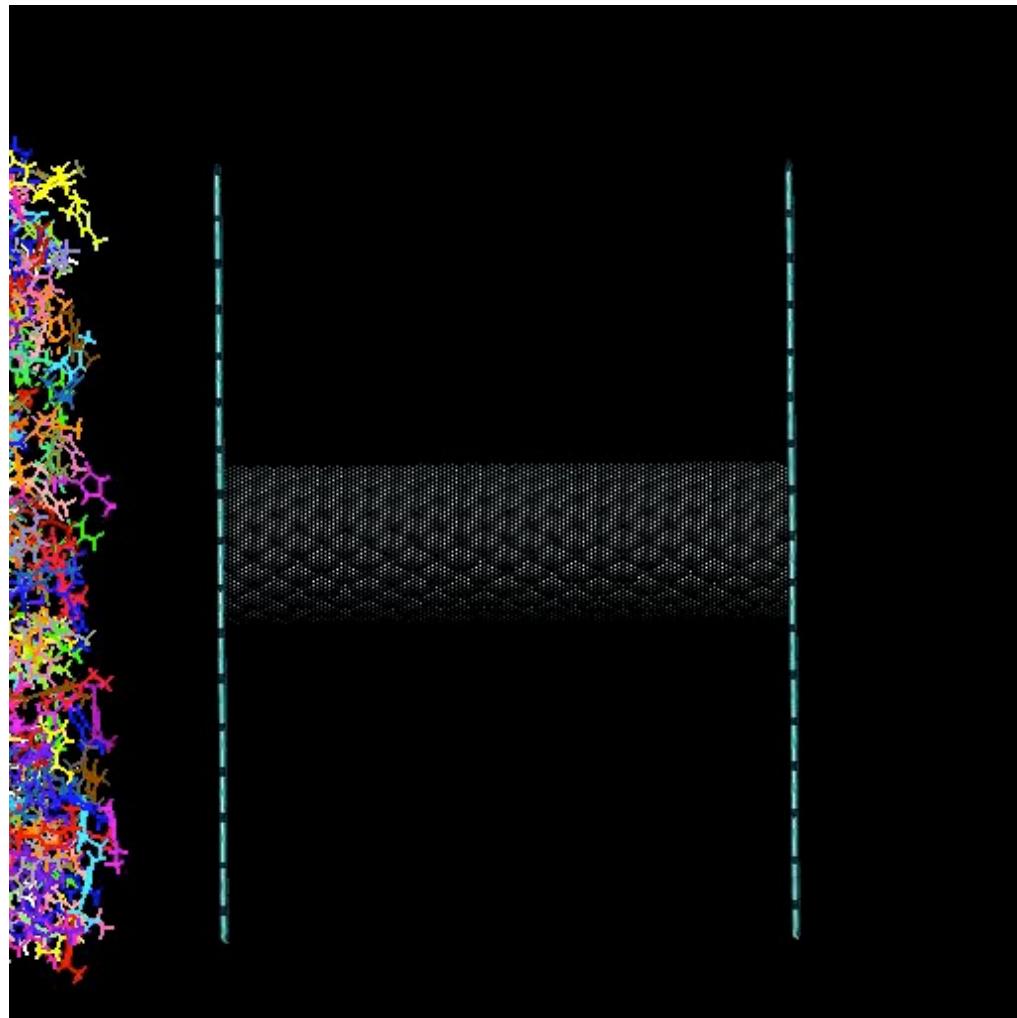


FILLING STRUCTURES

- One of the advantages of MD simulations is their versatility.
- We can easily add external potentials such as an electric field or, in this case, a constant pressure exerted on a graphene wall.



FILLING STRUCTURES



WHAT CAN WE USE FOR MD SIMULATIONS?

GROMACS

- Very fast simulations
- Lots of post-processing tools
- Beginners Friendly
- Not easy to modify the source code

LAMMPS

- Slower performance than GROMACS
- Does not include almost any post-processing.
- Error-prone when not used to its configuration.
- Easy to extend the source code to include custom modules