2/11/2020 Week 5 Module 1
Molecular Mechanics and Molecular Dynamics

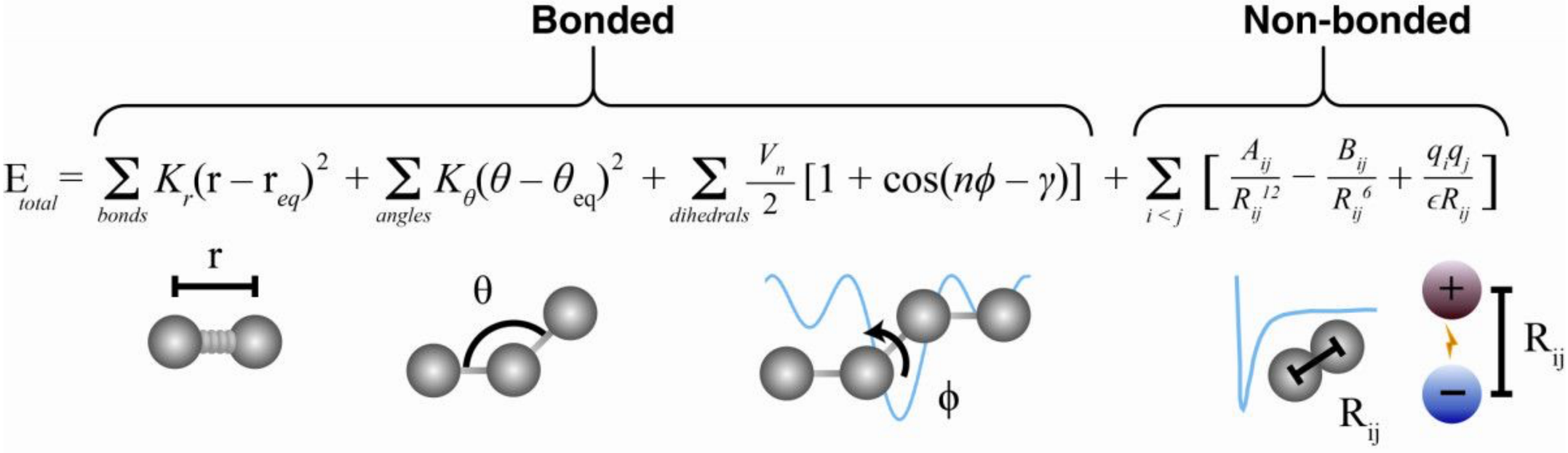
- This module will consist of a
  - mini-lecture on molecular mechanics and molecular dynamics
  - walk-through of a python script to run molecular dynamics with OpenMM
- At the end of this module, you should be able to address these questions:
  - What is molecular mechanics and why do people use it instead of quantum mechanics?
  - Generally speaking, how does a molecular dynamics simulation work?
- You should also be able to run a molecular dynamics simulation of a simple system using OpenMM

What is Molecular Mechanics?

- Quantum mechanics
  - given the coordinates of atomic nuclei, provides the best description of a system's energy
  - computationally expensive and currently infeasible for biomolecules
- Molecular mechanics
  - treats atoms as hard spheres
  - empirical potential energy
- QM/MM
  - treats part of a system with QM and most with MM
  - in many applications, may balance accuracy and computational speed

- See 1st 45 seconds of "An Introduction to Molecular Dynamics" (https://www.youtube.com/watch?v=lLFEqKl3sm4)

Molecular Mechanics Potential Energy



The potential energy of a system can be divided into those caused by interactions between atoms that are chemically bonded to one another and those caused by interactions between atoms that are not bonded. Chemical bonds and atomic angles are modeled using simple springs, and dihedral angles (that is, rotations about a bond) are modeled using a sinusoidal function that approximates the energy differences between eclipsed and staggered conformations. Non-bonded forces arise due to van der Waals interactions, modeled using the Lennard-Jones potential, and charged (electrostatic) interactions, modeled using Coulomb's law.
Taken from Figure 3 of Durrant & McCammon, 2011.

Limitations of Molecular Mechanics

- Less accurate potential energy
- Cannot model bond formation or breaking
- Popular fixed-charge force fields do not account for polarization

What is Molecular Dynamics?

- Add energy to a system modeled by molecular mechanics and simulate its progress with time
- See 0:45 to 2:20 of “An Introduction to Molecular Dynamics” (https://www.youtube.com/watch?v=ILFEqKI3sm4)

- See a separation of alkane and water: https://www.youtube.com/watch?v=xcMSHy3CqXA

General MD Algorithm

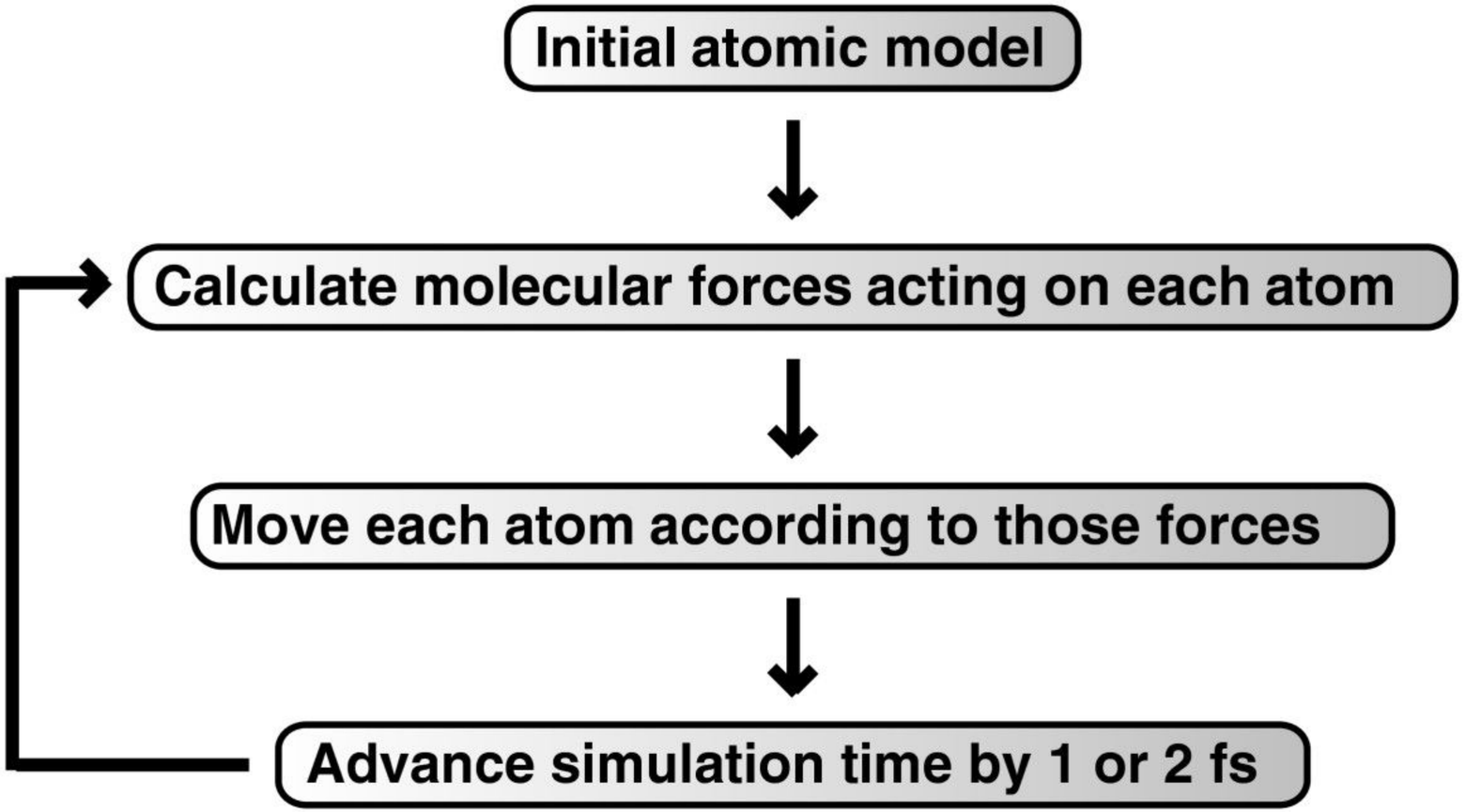


Figure 2 of Durrant & McCammon, 2011

Why do biological molecular dynamics?

- “everything that living things do can be understood in terms of the jigglings and wigglings of atoms” - Richard Feynman

- Check out my molecular dynamics YouTube playlist: https://www.youtube.com/playlist?list=PLYEyeVFrqfAu0ft6sF4vVe5FOEbJYyi_L

Why OpenMM?

- Many choices of software for molecular dynamics
  - https://en.wikipedia.org/wiki/Comparison_of_software_for_molecular_mechanics_modeling
  - https://www.rcsb.org/pages/thirdparty/modeling_and_simulation
- OpenMM is
  - free
  - GPU-accelerated
  - can be used in python scripts/C++ programs

Interactive MD exercise

Review Questions

- What is molecular mechanics and why do people use it instead of quantum mechanics?
- Generally speaking, how does a molecular dynamics simulation work?

References

- Durrant, J. D.; McCammon, J. A. Molecular Dynamics Simulations and Drug Discovery. BMC Biol 2011, 9 (1), 71. https://doi.org/10.1186/1741-7007-9-71, adapted under the CC BY 2.0 license.