

Molecular Dynamics: Methods

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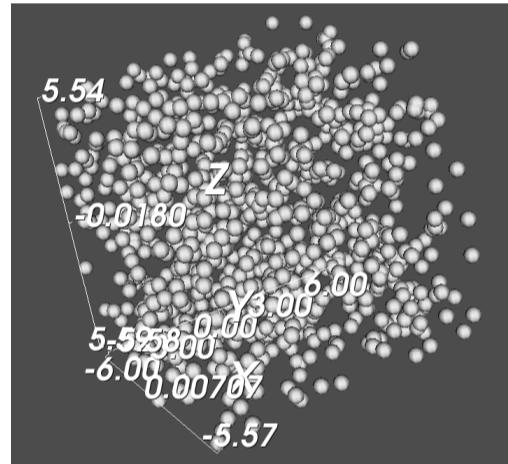
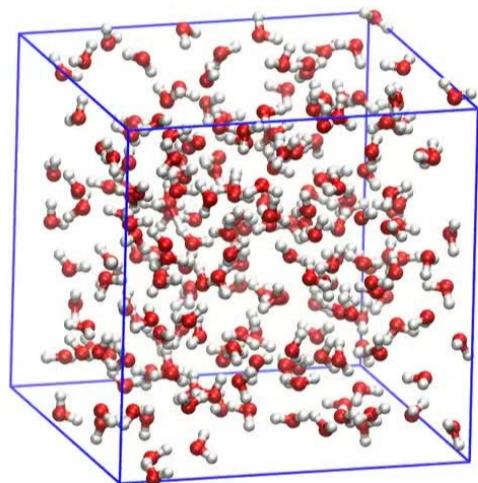
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Overview

What: Molecular Dynamics (MD) offers a general framework to study the movement of molecular structures over time *in silico*.

Why: MD allows us to calculate properties associated with a sample material that would be difficult or even impossible to compute through experiment alone.

How: Models of materials are represented as a set of n particles. At each time step the position and velocity of each particle is updated according to a potential function. The process is repeated for a desired number of iterations.



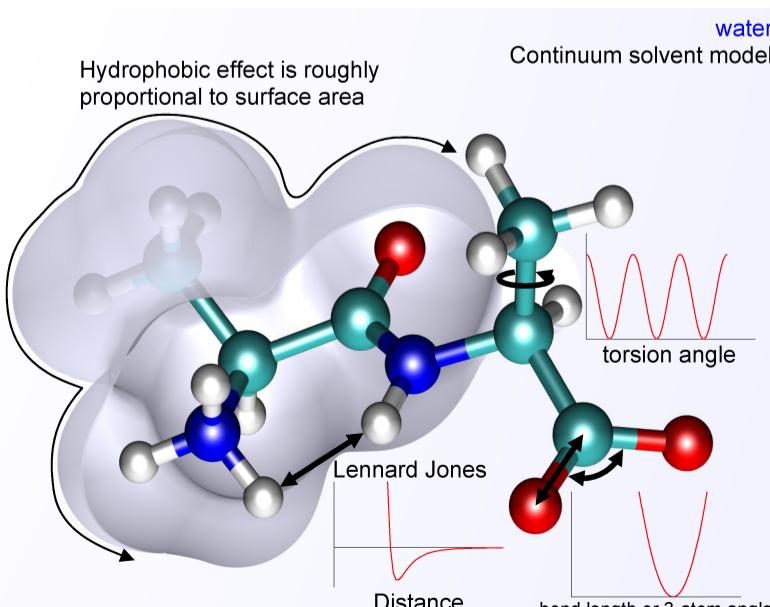
Left: A MD simulation of water at 298 K and 1 atm pressure.

Credit: Christopher Rowley, Wikimedia Commons.

Right: Simple MD simulation based on code from ref [1].

Potential Functions

One of the most important components of a MD simulation is the choice of potential function used. The choice of function is dependant on the structure and composition of the material. For non-bonded interactions a pair potential, such as the **Lennard-Jones** potential is common. For bonded molecules additional terms can be included to account for the effects of covalently bonded atoms such as the dihedral and torsion angles.



Potential functions for the molecule *alanine dipeptide*. Image Credit: Boas F.E. and Harbury P.B. (2007), Wikimedia Commons.

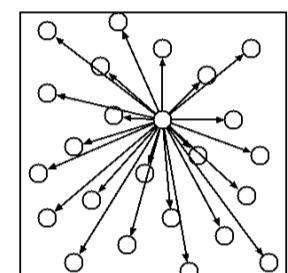
Integrators

The results of a MD simulation will be heavily effected by the choice of integration method. There is a trade off between the time complexity of the integrator and the accuracy of the results. Common choices include:

- **Leapfrog:** have lower memory usage and are suitable for very large scale problems.
- **Predictor-corrector:** are typically better suited to complex, high accuracy problems.

Computing Interactions

In order to compute the potential energy and therefore update the system, the interactions between particles must be computed:



- **All pairs:** simply compares every atom to each other.
- **Cell subdivision:** splits the domain into cells proportional to the interaction range.
- **Neighbourhood lists:** caches a list of neighbours for a particular particle.

Image: Pedro Gonnet, Wikimedia Commons.

Parallelisation & Specialised Hardware

Due to the computational intensity of MD methods calculations are often performed on specialised machines and hardware. The update calculation for a given time step can be parallelised using **domain decomposition**. The simulation domain is split in several regions whose interactions can be computed independently of other regions.

Simplified schematic of the molecular dynamics algorithm

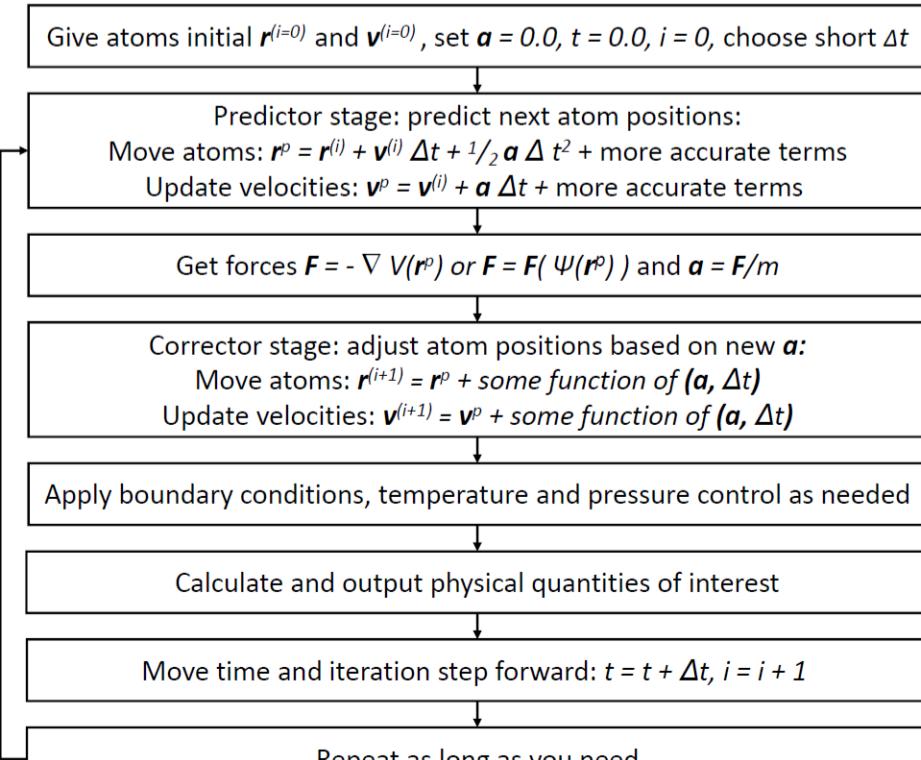


Diagram Credit: Kai Nordlund, Wikimedia Commons.

Molecular Dynamics: Applications

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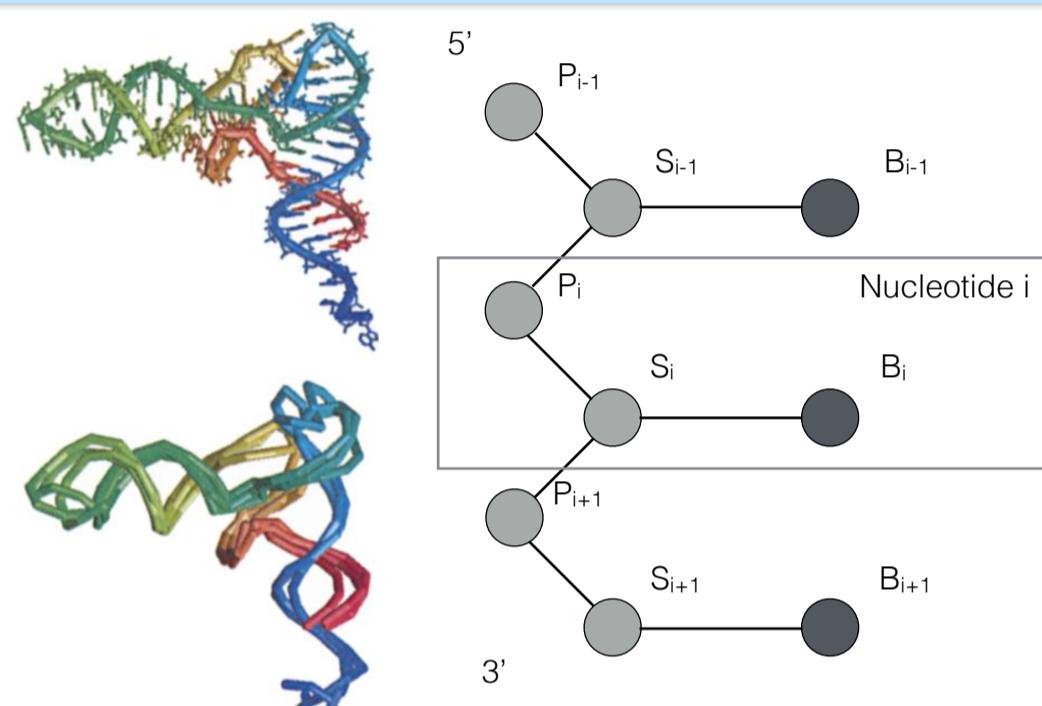
Molecular Dynamics was originally developed to solve problems in computational physics. One of the first notable applications was the simulation of liquid Argon using the Lennard-Jones potential by Rahman in 1964. Since then the technique has developed to have a broad range of application across the sciences. Here are two example applications, one each from the bioinformatics and physics domains, are discussed.

RNA Tertiary Structure Prediction

Predicting the tertiary structure of RNA molecules from a sequence of nucleotides is still an open problem in the field of Bioinformatics. Various approaches have been suggested that attempt to produce an accurate 3D model of folded RNA from both the primary and secondary structure.

Attempts to determine the 3D structure make use of MD in a variety of different forms [3]. Several techniques take a fully atomistic approach where an accurate model of nucleotides is used. These are often limited by their time and space complexity to short sequences of RNA.

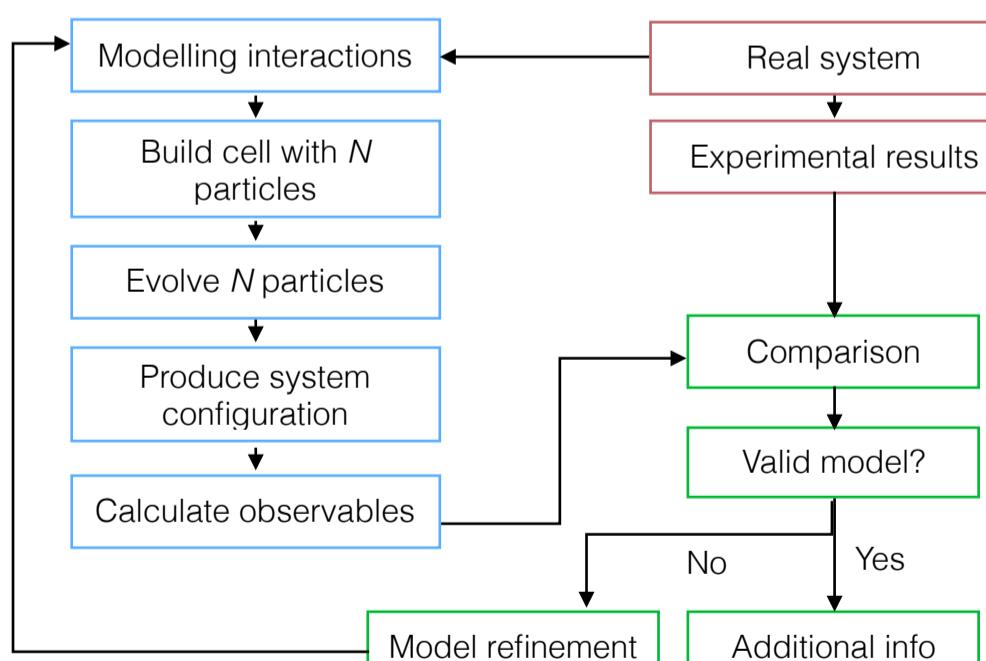
Other approaches make use of a coarse-grained model to simplify the problem. Here chains of nucleotides are often represented as a simple “bead on a string”. MD is also used in combination with other approaches, such as fragment assembly. RNA motifs are “stitched” together using fragment assembly and the final model is further refined using either a fully atomistic or coarse-grained MD simulation.



RNA molecule (top) and the prediction by NAST (bottom).

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Coarse grained “bead on a string” model presented in ref [4] for a chain of RNA. P, S and B represent the Phosphate, Sugar and Base molecules.



MD as a complement to neutron scattering experiments.
Based on diagram from ref [2].

A Complement to Neutron Scattering

Neutron scattering is one of a number of experimental techniques, along with X-ray scattering and NMR, for examining the structure and dynamics of matter at the atomistic level. The pattern of neutron scattering in a diffraction or spectroscopic experiment produces a characteristic signal from which properties of interest can be computed.

Neutron scattering is limited by a number of factors including instrument resolution, cost and access to facilities, and the differentiation of atoms of the same isotopic species.

MD simulations can complement neutron scattering experiments. The results of an experiment can be compared with the same quantities calculated by a MD simulation to verify its accuracy. Then quantities unobtainable from direct experimentation can be computed directly via the verified simulation.

References

1. Rapaport, Dennis C. *The art of molecular dynamics simulation*. Cambridge university press, 2004.
2. Arbe, Arantxa, Fernando Alvarez, and Juan Colmenero. "Neutron scattering and molecular dynamics simulations: synergistic tools to unravel structure and dynamics in polymers." *Soft Matter* 8.32 (2012): 8257-8270.
3. Laing, Christian, and Tamar Schlick. "Computational approaches to 3D modeling of RNA." *Journal of Physics: Condensed Matter* 22.28 (2010): 283101.
4. Ding, Feng, et al. "Ab initio RNA folding by discrete molecular dynamics: from structure prediction to folding mechanisms." *Rna* 14.6 (2008): 1164-1173.