

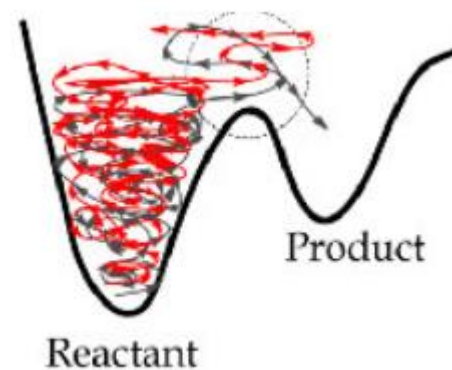
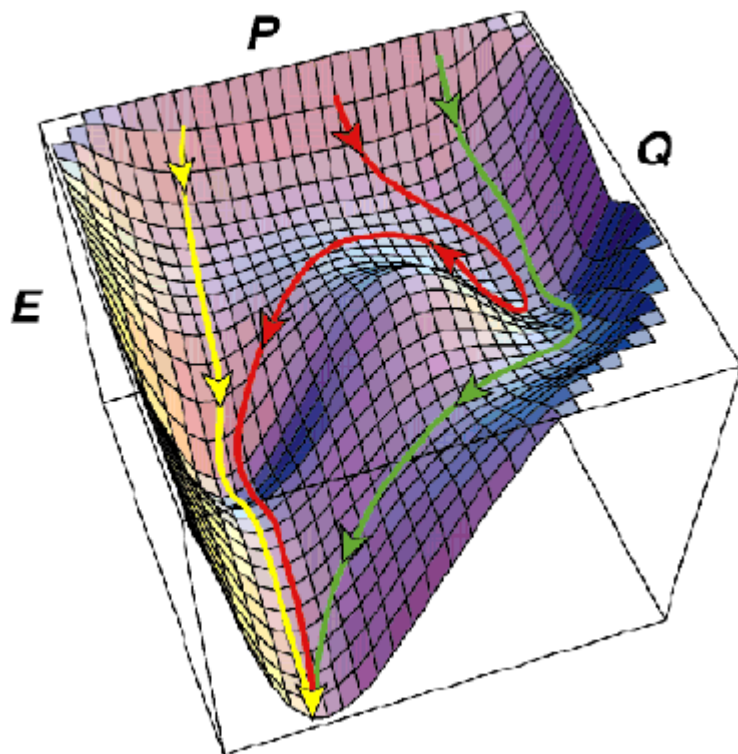
Materials design and selection for circular economy

Mod. 2 Design and selection of functional molecules and materials
for sustainable synthesis and circularity

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Was all clear?

<https://www.wooclap.com/LEZ22023CE>



In 1D a lot of information is lost!

Moving on the surface.....

Many problems in computational chemistry can be formulated as an **optimization of a multi-dimensional function**.

Optimization is a general term for finding stationary points of a function, i.e. points in which the first derivative is zero.

In most cases, stationary points are minima (all positive second derivatives). In some cases, the desired point is a first-order saddle point (the second derivative is negative in one direction and positive in all the others).

Most optimization methods determine the nearest stationary point. The minimum with the lowest energy is called **the global minimum**, while the others are referred to as **local minima**.

The lowest point on the Energy Landscape is the most stable point
(**Global minimum**)

- At absolute zero a system in thermal equilibrium must be at its global minimum, but we all know that even at this temperature the molecule probabilistically samples a range of different structures (zero point vibrational energy)
- Increasing the efficiency of searching for the global minimum is an active area of research

Possible conformations for linear alkanes $\text{CH}_3 (\text{CH}_2)_{n+1} \text{CH}_3$ (supposing 3 energy minima for rotation along each C-C bond)

n	Possible conf. 3^n	Time (1s=1conf)
1	1	3 s
5	243	4 min
10	59049	16 hours
15	14348907	166 days

Some Common Search Strategies (Optimization Techniques)

1. Systematically search all coordinates.

IMPOSSIBLE! Size :100, this means $\sim N^{100}$ (or so).

2. Dynamics + “Quench”

Roam over the surface, occasionally sliding down to the nearest local minimum.

3. Simulated Annealing

Heat the system up, and cool very slowly.

4. Evolutionary/Genetic Algorithms

Allow “good” geometries to survive and to share properties, but “bad” ones to die.

#2 and #3 require a discussion of **Metropolis Monte Carlo** and **Molecular Dynamics** Techniques

Monte Carlo

This method starts from a local minimum and new configurations are generated adding a random kick to one or more atoms.

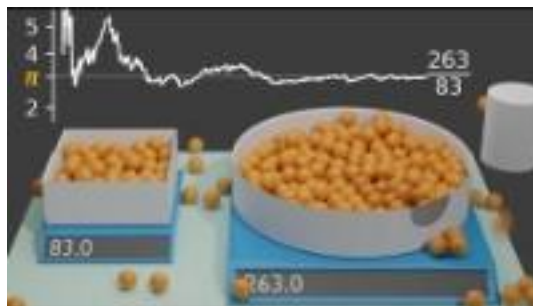
In MC, the new geometry is accepted as a starting point for the next perturbing step if it is lower in energy than the current.

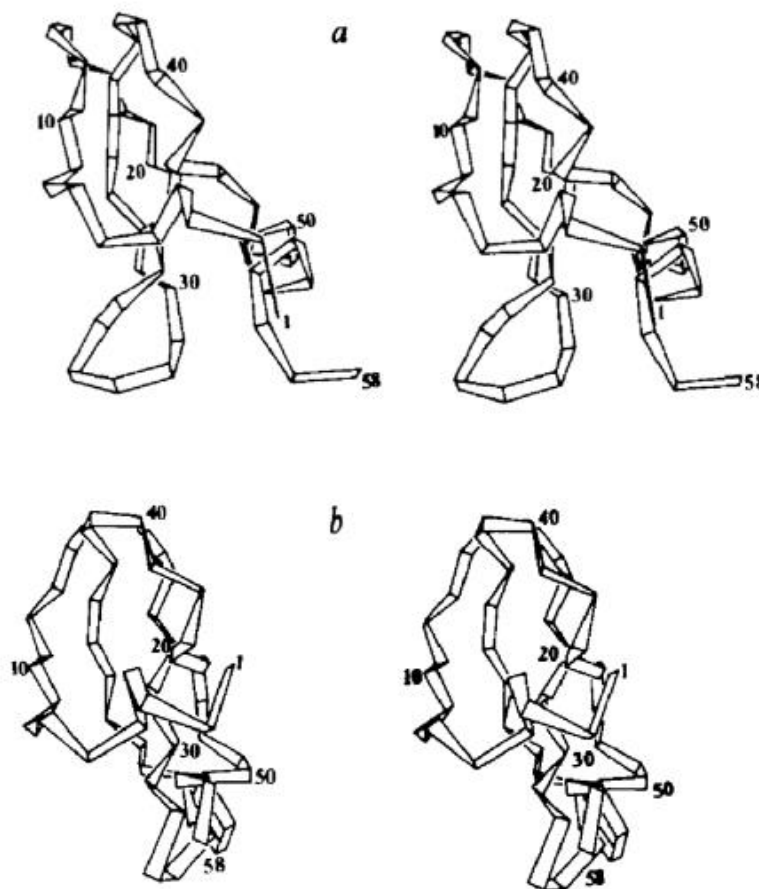
Otherwise the Boltzmann factor $\exp(-\Delta E/k_B T)$ is computed and compared to a random number between 0 and 1.

If it is less, the geometry is accepted, otherwise the next step is generated from the old geometry.

This generates a sequence of configurations from which geometries can be chosen for subsequent minimization.

The step size must be small to have an acceptance ratio of at least 0.5.





Computer simulation of protein folding (1975)

M Levitt, A Warshel

Nature 253:94.

Metropolis Monte Carlo
simulations

2013 NOBEL PRIZE IN CHEMISTRY

Martin Karplus
Michael Levitt
Arieh Warshel



PRESSMEDDELANDE
Press release

9 October 2013

The Nobel Prize in Chemistry 2013

The Royal Swedish Academy of Sciences has decided to award the Nobel Prize in Chemistry for 2013 to

Martin Karplus	Michael Levitt	Arieh Warshel
Université de Strasbourg, France and Harvard University, Cambridge, MA, USA	Stanford University School of Medicine, Stanford, CA, USA	University of Southern California, Los Angeles, CA, USA

"for the development of multiscale models for complex chemical systems"

Université de Strasbourg, France and Harvard University, Cambridge, MA, USA	Stanford University School of Medicine, CA, USA	University of Southern California, Los Angeles, CA, USA
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Molecular dynamics

Solve classical equations of motion from some initial geometry and velocity

$$\mathbf{r}(0) \rightarrow \mathbf{r}(t); \mathbf{v}(0) \rightarrow \mathbf{v}(t)$$

Newton's law $\mathbf{F} = m\mathbf{a} = -dU(\mathbf{r})/d\mathbf{r}$

One needs: $\mathbf{r}(0)$, $\mathbf{v}(0)$, $U(\mathbf{r})$, $dU/d\mathbf{r}$

From temperature
(randomly distributed)

The total energy is conserved, and again the ergodic hypothesis is valid, i.e. we can average

$$\langle \Xi \rangle = \frac{1}{M} \sum_{i=1}^M \Xi_i(\mathbf{r}_i)$$

If you know forces, you can compute acceleration and, with velocity and with a suitably small time step, you can propagate to a new position, calculate new velocity, new force etc...

Removing kinetic energies allows to do molecular mechanics minimization.

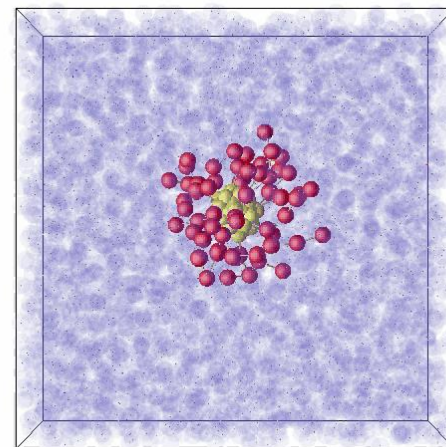
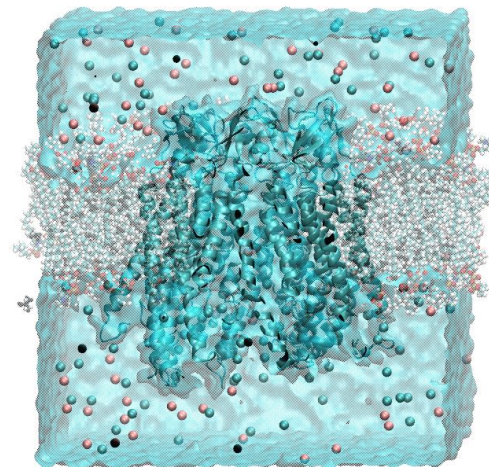
What can we do with MD simulations?

We can simulate time dependent properties

- Protein domain motions
- Small protein folds
- Spectroscopic properties

We can simulate ensemble properties

- Binding free energies
- Drug design
- Biocatalyst design
- Reaction pathways
- Free energy surfaces



What is needed to run a MD simulation?

- A Cartesian representation of the chemical system
- An appropriate potential function
- A propagator to simulate the time evolution
- Efficient numerical algorithms

From equations to code.

For a large number of atoms

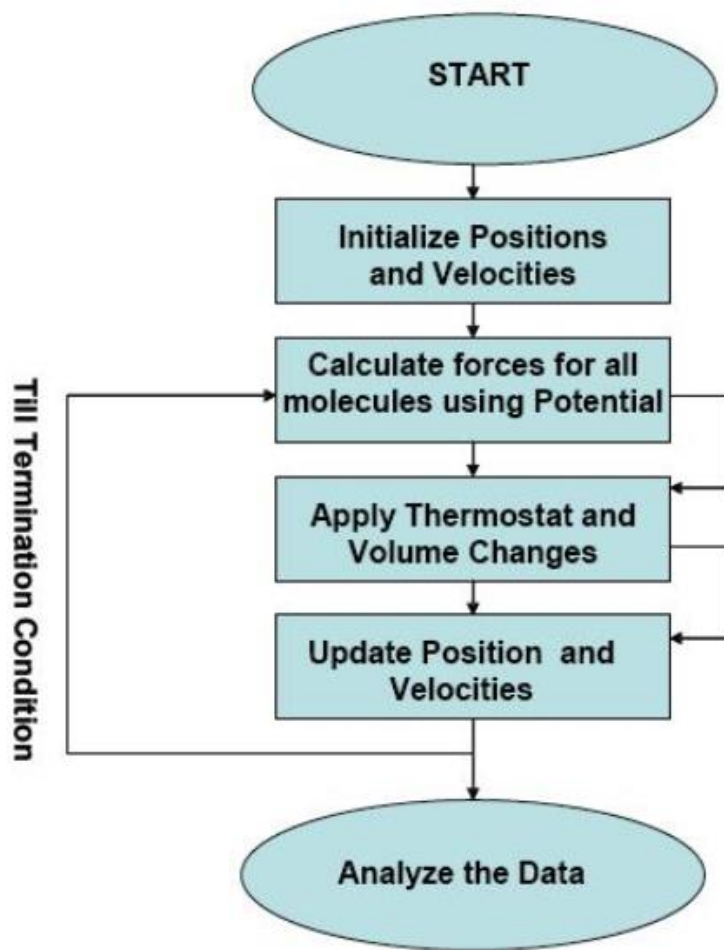


$$V(r^n) = \sum_{\text{bonds}} K_r (r - r_{eq})^2 + \sum_{\text{angles}} K_\theta (\theta - \theta_{eq})^2 \\ + \sum_{\text{dihedrals}} \frac{V_n}{2} [1 + \cos(n\phi - \gamma)] + \sum_{i < j} \left[\frac{A_{ij}}{R_{ij}^{12}} - \frac{B_{ij}}{R_{ij}^6} + \frac{q_i q_j}{\epsilon_r R_{ij}} \right]$$

23 000 atoms = 264 500 000
interactions per step!

For a dt=2fs, we need
500 000 steps to reach 1 ns

The computer code must be
lean and *ultra* efficient

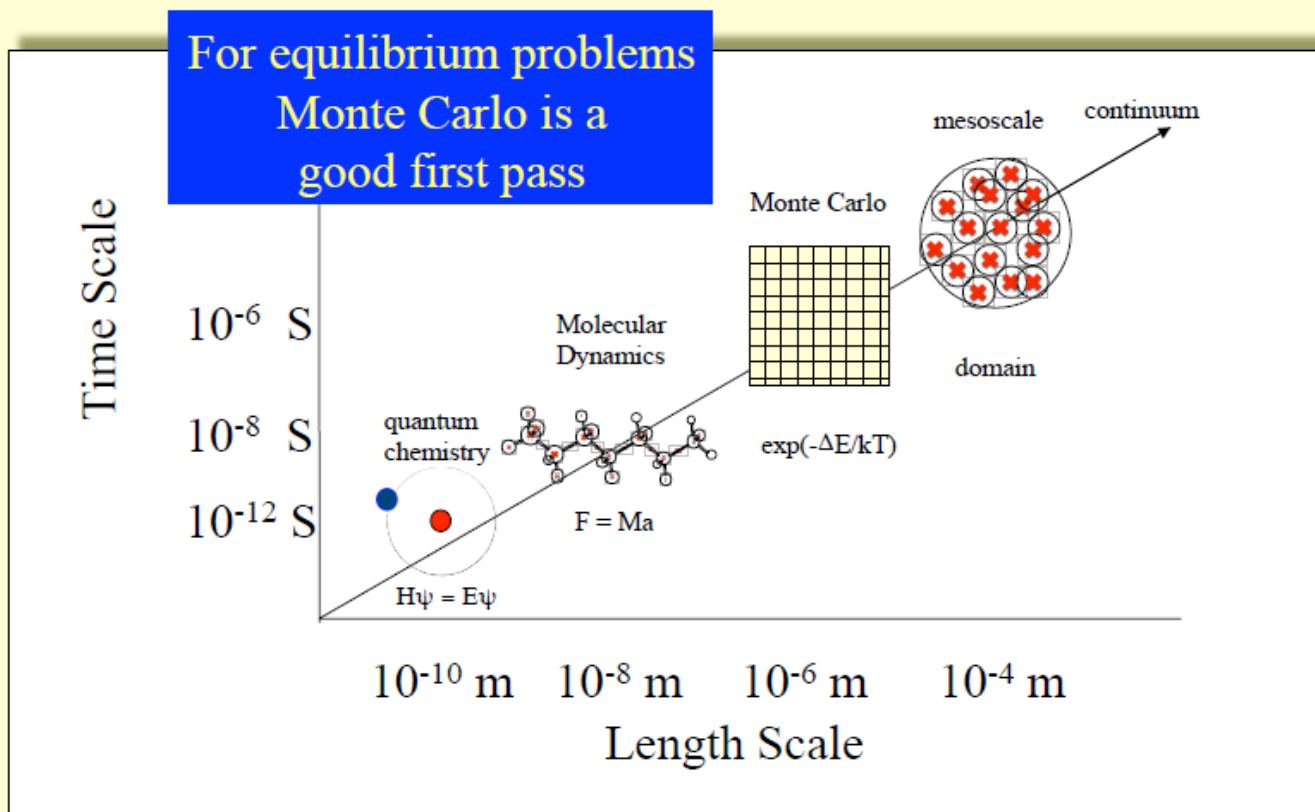


Popular MD Software

- AMBER
- CHARMM
- Gromacs
- LAMMPS
- NAMD

Other More Specialized Packages Also Exist

So, What Method To Use?



For time dependent problems, MD must be chosen!