Simulations with MM Force Fields

Monte Carlo (MC)
and
Molecular Dynamics (MD)
Video II.vi
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We often draw in 1D, but we’re hiding a lot.
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

Increasing the efficiency of searching for the global minimum is an active area of research
Some Common Search Strategies
(Optimization Techniques)

1. Systematically search all coordinates.
   IMPOSSIBLE! $\sim N^{100}$ (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 Molecular Dynamics and Metropolis Monte Carlo Techniques
Phase Space — 1D Harmonic Oscillator

No two trajectories in phase space can cross. A system is either periodic or it samples all of phase space in an ergodic fashion.

Phase point defined as
\[ \mathbf{r} = (q,p) \]

generalized for \( N \) particles as
\[ \mathbf{r} = (q_{1x}, q_{1y}, q_{1z}, p_{1x}, p_{1y}, p_{1z}, \ldots, q_{Nx}, q_{Ny}, q_{Nz}, p_{Nx}, p_{Ny}, p_{Nz}) \]
Are you following the true phase-space trajectory sufficiently accurately? Small steps are necessary (about 0.5 fs not unusual)
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Are you following the true phase-space trajectory sufficiently accurately? Small steps are necessary (about 0.5 fs not unusual)
Integrating over Phase Space

$$\langle \Xi \rangle = \frac{\int_{PS} \Xi(r)P(r)dr}{\int_{PS} P(r)dr}$$

Expectation values are dictated by the relative probabilities of being in different regions of phase space

$$P(r) = e^{-E(q,p)/k_B T}$$

$$Q = \int_{PS} P(r)dr$$

Key point: Don’t waste time evaluating $\Xi(r)$ if $P(r)$ is zero.

Difficulty: Phase space is $6N$-dimensional. If you only want to sample all possible combinations of either positive or negative values for each coordinate (i.e., hit every “hyperoctant” in phase space once), you need $2^{6N}$ points!
Metropolis Monte Carlo:

Generates a thermal population of geometries such that \( n(\mathbf{r}_1)/n(\mathbf{r}_2) = \exp\left(-[U(\mathbf{r}_1)-U(\mathbf{r}_2)]/k_B T\right) \)

Method.
1. Propose “move” \( \mathbf{r}_1 \to \mathbf{r}_2 \)
2. “Accept” move if (i) \( U(\mathbf{r}_1) < U(\mathbf{r}_2) \)
   (ii) \( \exp \left[-(U(\mathbf{r}_1)-U(\mathbf{r}_2))/k_B T\right] > \text{random} \# \in [0,1] \)
3. Else “reject”

So, now \[ \langle \Xi \rangle = \frac{1}{M} \sum_{i=1}^{M} \Xi_i(\mathbf{r}_i) \]
Simulated Annealing

Start at high temperature, then decrease temperature slowly with time.

If cooling infinitely slow, may find GM

High T

Medium T

Low T

T=0

“Time”
Molecular Dynamics (MD)

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 \( \mathbf{F} = m\mathbf{a} = -\frac{dU(\mathbf{r})}{d\mathbf{r}} \)

Need \( \mathbf{r}(0), \mathbf{v}(0), U(\mathbf{r}), \frac{dU}{d\mathbf{r}} \)

\( \mathbf{r}(t=0) \)

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

Again, \( \Xi(\mathbf{r}) \) is conserved

\( \Xi(\mathbf{r}) \) from temperature (randomly distributed)
Occasional Quenches

Remove kinetic energy.
Slide from the current geometry
down the steepest slope
(better, conjugate gradient)

Requires first (often second) derivatives.
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Integrating over Phase Space

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Expectation values are dictated by the relative probabilities of being in different regions of phase space

\[ P(r) = e^{-E(q,p)/k_B T} \quad Q = \int_{PS} P(r)dr \]

Key point: Don’t waste time evaluating \( \Xi(r) \) if \( P(r) \) is zero.

Difficulty: Phase space is \( 6N \)-dimensional. If you only want to sample all possible combinations of either positive or negative values for each coordinate (i.e., hit every “hyperoctant” in phase space once), you need \( 2^{6N} \) points!
Nota bene: the standard deviation in an expectation value is not (necessarily) an error, but may instead be a manifestation of dynamical variation.
Molecular Dynamics

Simulation yields $r(t)$, $v(t)$, $U(r(t))$, correlation functions

- Dynamic structure (e.g. does reaction happen?)
- Transport properties
  (D, viscosity, etc)
Molecular Dynamics

Using “tricks” can be made to run at:

• constant $T$,
• constant $P$,

or combinations thereof.

(Keywords: Statistical mechanical ensemble; heat bath; thermostats; pistons)
“Tricks” in Simulations, continued…

Problem!
Too few solvent molecules!

The solvent sees vacuum, not bulk.

Adding more solvent molecules increases computational effort!
Periodic Boundary Conditions
Make the system thinks it’s larger than it really is.
Problem with MD and Monte Carlo "Quasi-Ergodic" Sampling Problem

However, all these wells are thermally accessible

Solution 1
Nature’s Solution
Run t→∞
What method to use?

MD needs smooth derivatives

MC needs no derivatives

MD needs global updates

MC can use local updates

MC lends itself to simple models

However, MC has no sense of time!
So, What Method To Use?

For equilibrium problems, Monte Carlo is a good first pass.

- **Length Scale**
  - $10^{-10}$ m
  - $10^{-8}$ m
  - $10^{-6}$ m
  - $10^{-4}$ m

- **Time Scale**
  - $10^{-12}$ S
  - $10^{-8}$ S
  - $10^{-6}$ S

- **Equation**
  - $H\psi = E\psi$
  - $F = Ma$
  - $\exp(-\Delta E/kT)$
So, What Method To Use?

For time-dependent problems, MD is the only way.
So, What Method To Use?

Large problems may need a combination of quantum chemistry, Molecular Dynamics, Monte Carlo, and continuum approaches.

- Time Scale
  - $10^{-6}$ S
  - $10^{-8}$ S
  - $10^{-12}$ S

- Length Scale
  - $10^{-10}$ m
  - $10^{-8}$ m
  - $10^{-6}$ m
  - $10^{-4}$ m
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Key point: Don’t waste time evaluating \( \Xi(r) \) if \( P(r) \) is zero.

MC/MD \[ \langle \Xi \rangle = \frac{1}{M} \sum_{i=1}^{M} \Xi_i(r_i) \]