

Molecular Simulation and Statistical Mechanics from a Practical Viewpoint

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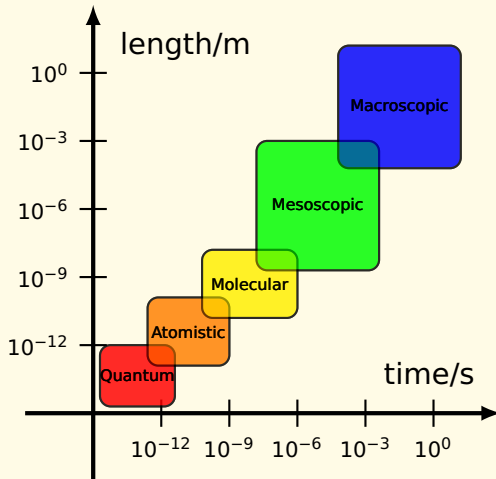
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Outline

- 1 Introduction
- 2 Molecular Dynamics
- 3 Monte Carlo
- 4 Brownian Dynamics and DPD
- 5 How Do We Calculate Things?
- 6 Smarter Monte Carlo
- 7 Free Energies and the Jarzynski Equality

What is Molecular Simulation?

Time and Length Scales

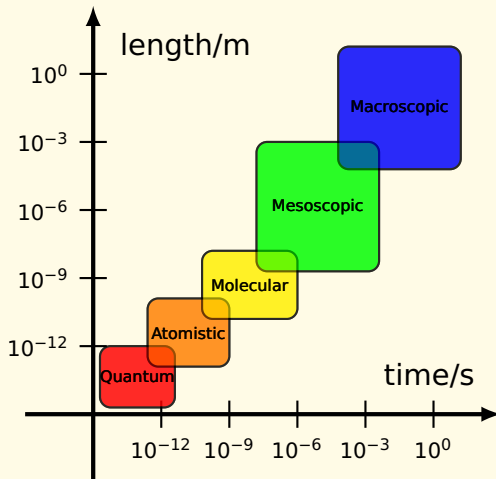


Simulation Methods

- FE** Finite Element Methods
- CFD** Computational Fluid Dynamics
- LB** Lattice Boltzmann
- MPC** MultiParticle Collision Dynamics
- DPD** Dissipative Particle Dynamics
- BD** Brownian Dynamics
- MC** Monte Carlo
- MD** Molecular Dynamics
- CP** Electronic Structure Calculations

What is Molecular Simulation?

Time and Length Scales



Simulation Methods

FE Finite Element Methods

CFD Computational Fluid Dynamics

LB Lattice Boltzmann

MPC MultiParticle Collision Dynamics

DPD Dissipative Particle Dynamics

BD Brownian Dynamics

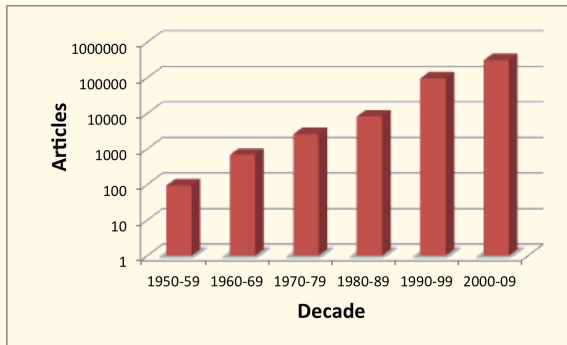
MC Monte Carlo

MD Molecular Dynamics

CP Electronic Structure Calculations

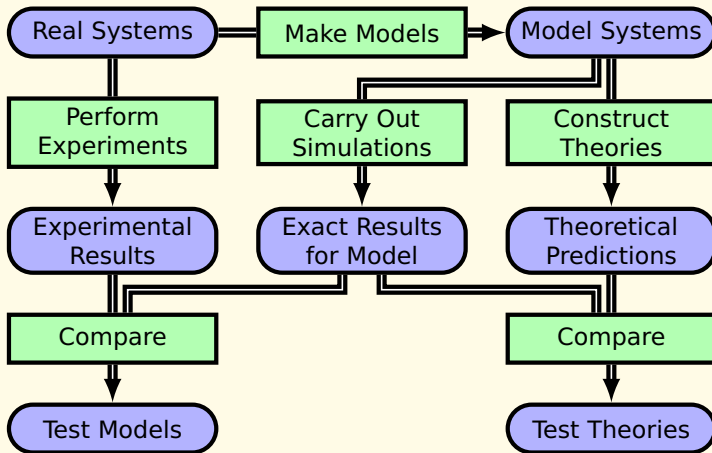
Molecular Simulation Over the Years

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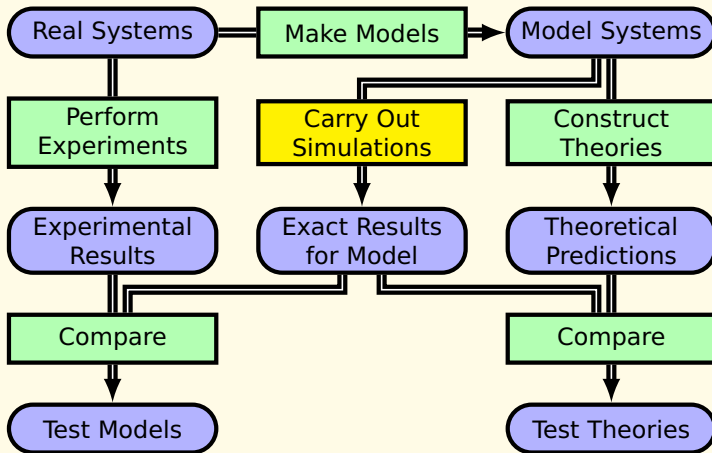


TITLE and TOPIC: Monte Carlo, molecular dynamics, Brownian dynamics, lattice Boltzmann, dynamical density functional theory, Car Parrinello, QM/MC.

Where Are We?

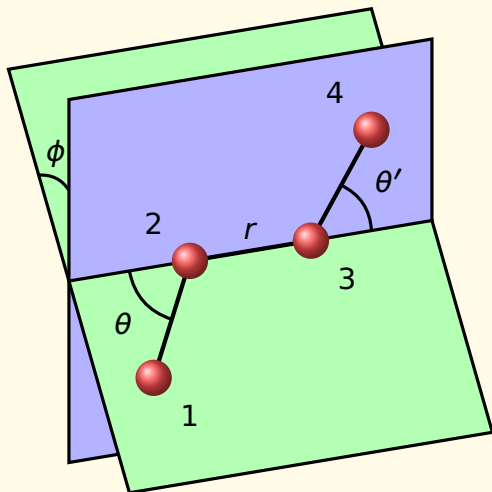


Where Are We?



Molecular Models

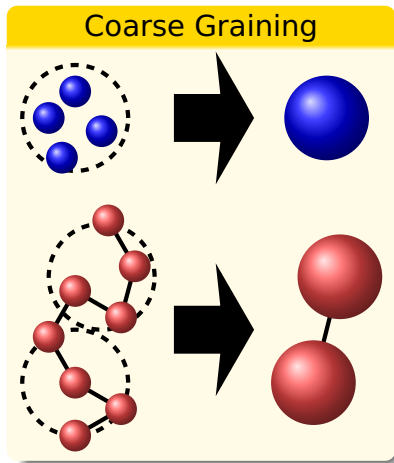
Bond Lengths and Angles



Forces derived from potentials.
Potential energy depends on:

- internal coordinates
 - bond stretching
 - angle bending
 - angle twisting
- non-bonded atom interactions
 - Lennard-Jones
 - electrostatics

Coarse-Grained Mesoscale Models



Treatment of Solvent:

Brownian Dynamics:

often replaced by random forces and friction.

Dissipative Particle Dynamics:

represented by coarse-grained beads.

MultiParticle Collision Dynamics:

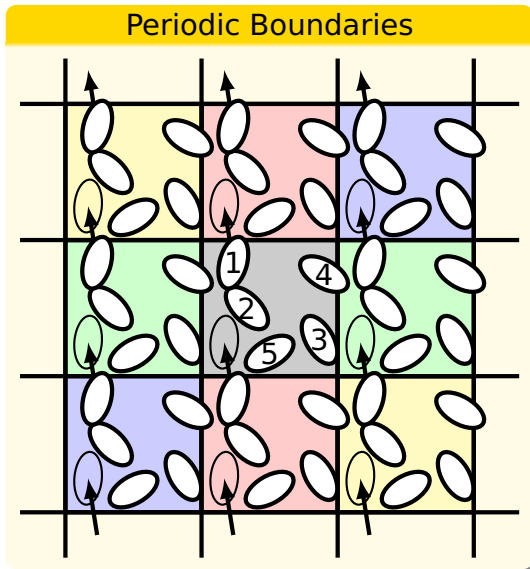
idealized, colliding, particles.

Treatment of Macroparticles:

Usually represented by coarse-grained beads.

- We feed in microscopic information:
 - atomic or molecular coordinates $\mathbf{r} = \{\mathbf{r}_1, \mathbf{r}_2, \dots, \mathbf{r}_N\}$;
 - possibly, conjugate momenta $\mathbf{p} = \{\mathbf{p}_1, \mathbf{p}_2, \dots, \mathbf{p}_N\}$;
 - or, in general, (micro)states \mathbf{r} .
- We compare results with theories or experiments
 - thermodynamic quantities
 - structure
 - phase transitions
 - dynamical properties
- We need to understand some statistical mechanics
 - Distributions of states and how to sample them
 - Finite-size effects
 - Correlation functions in space and time

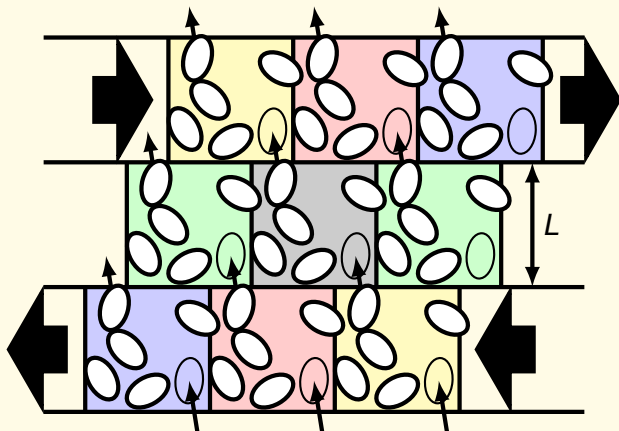
Periodic Boundary Conditions



- Simulation box is cubic.
- Surround cube with replicas.
- Each molecule interacts with nearest image.
- If a molecule leaves the basic simulation box, attention can be switched to the incoming image.

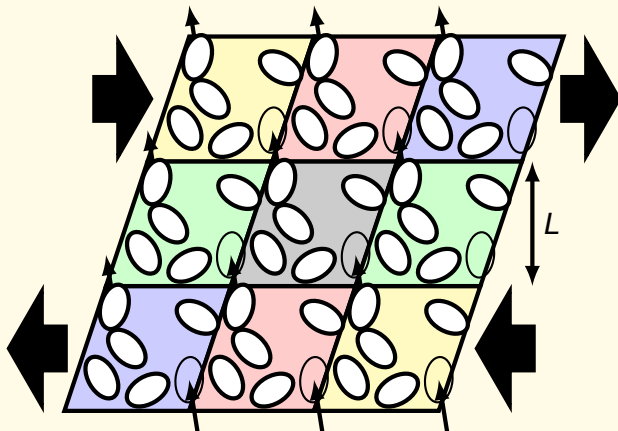
Shear Flow

Lees-Edwards Boundaries



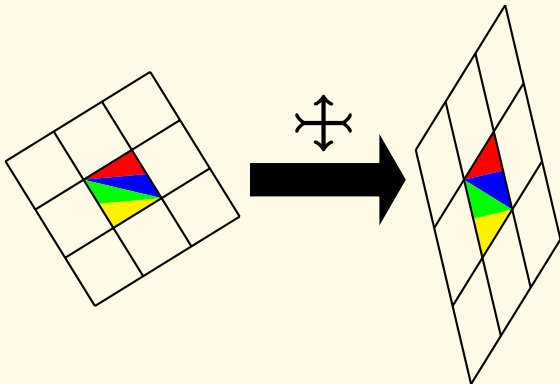
AW Lees, SF Edwards, *J. Phys. C*, **5**, 1921 (1972).

Sheared Boundaries



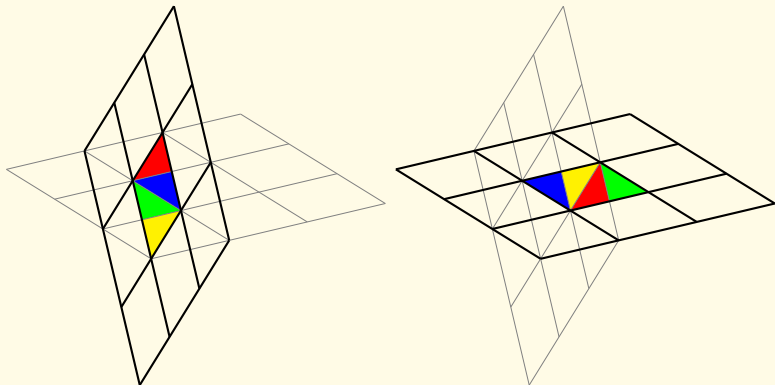
AW Lees, SF Edwards, *J. Phys. C*, **5**, 1921 (1972).

Kraynik-Reinelt Boundaries



AM Kraynik, DA Reinelt, *Int. J. Mul. Flow*, **18**, 1045 (1992).

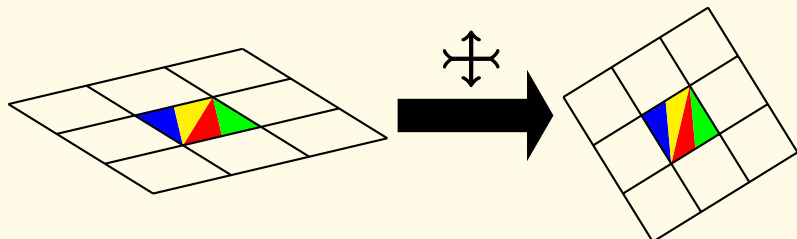
Kraynik-Reinelt Boundaries






AM Kraynik, DA Reinelt, *Int. J. Mul. Flow*, **18**, 1045 (1992).

Planar Extensional Flow

Kraynik-Reinelt Boundaries



-  AM Kraynik, DA Reinelt, *Int. J. Mul. Flow*, **18**, 1045 (1992).
-  BD Todd, PJ Daivis, *Phys. Rev. Lett.*, **81**, 1118 (1998).
-  BD Todd, PJ Daivis, *Molec. Simul.*, **33**, 189 (2007).

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Classical Mechanics

Equations of motion

$$\dot{\mathbf{r}} = \mathbf{p}/m, \quad \dot{\mathbf{p}} = \mathbf{f}, \quad \mathbf{f} = -\nabla U(\mathbf{r})$$

- $K(\mathbf{p}) = |\mathbf{p}|^2/2m$

- $E = H = K + U.$

- A system of coupled ordinary differential equations.
- Can be numerically integrated step-by-step.
- Calculating forces is expensive.
- Wish to make the timestep as large as possible.
 - Hence, simulation algorithms tend to be **low order**;
 - this allows the time step to be increased as much as possible without jeopardizing energy conservation.
- Cannot follow true trajectory for long times t_{run} .
 - Classical trajectories are **ergodic** and **mixing**;
 - trajectories diverge from each other exponentially;
 - however long-term energy conservation is possible.

The MD Algorithm

Velocity Verlet Equations

$$\mathbf{p}(t + \frac{1}{2}\Delta t) = \mathbf{p}(t) + \frac{1}{2}\Delta t \mathbf{f}(t)$$

$$\mathbf{r}(t + \Delta t) = \mathbf{r}(t) + \Delta t \mathbf{p}(t + \frac{1}{2}\Delta t)/m$$

$$\mathbf{p}(t + \Delta t) = \mathbf{p}(t + \frac{1}{2}\Delta t) + \frac{1}{2}\Delta t \mathbf{f}(t + \Delta t)$$

Alternative Form

$$\mathbf{r}(t + \Delta t) = \mathbf{r}(t) + \Delta t \mathbf{p}(t)/m + \frac{1}{2}\Delta t^2 \mathbf{f}(t)/m$$

$$\mathbf{p}(t + \Delta t) = \mathbf{p}(t) + \frac{1}{2}\Delta t (\mathbf{f}(t) + \mathbf{f}(t + \Delta t))$$

- Low-order, easily coded into a program.
- Good energy conservation, stable (see later).

Microcanonical NVE Ensemble

The connection with a thermodynamic potential, the entropy, is made through the distribution of microstates and their density (per unit energy).

Microcanonical Ensemble Equations

Density of states: $\mathbb{W}(E) = \iint d\mathbf{r}d\mathbf{p} \delta(H(\mathbf{r}, \mathbf{p}) - E)$

Entropy: $S = k_B \ln \mathbb{W}$ (Boltzmann)

Distribution: $\varrho_{NVE}(\mathbf{r}, \mathbf{p}) = \mathbb{W}^{-1} \delta(H(\mathbf{r}, \mathbf{p}) - E)$

Average: $\langle A \rangle_{NVE} = \iint d\mathbf{r}d\mathbf{p} \varrho_{NVE}(\mathbf{r}, \mathbf{p}) A(\mathbf{r}, \mathbf{p})$

Almost true for MD; the Verlet algorithm is not exact.

Propagators and Statistical Mechanics

The formalism of Hamiltonian mechanics, Poisson brackets, Liouville operators, leads to

Liouville Equations

$$\frac{dA}{dt} = \frac{\partial A}{\partial \mathbf{r}} \cdot \dot{\mathbf{r}} + \frac{\partial A}{\partial \mathbf{p}} \cdot \dot{\mathbf{p}} = \left(\frac{\partial A}{\partial \mathbf{r}} \cdot \frac{\partial H}{\partial \mathbf{p}} - \frac{\partial A}{\partial \mathbf{p}} \cdot \frac{\partial H}{\partial \mathbf{r}} \right) = (A, H) \equiv iLA$$

$$\frac{\partial \varrho}{\partial t} = -\varrho \left(\frac{\partial \dot{\mathbf{r}}}{\partial \mathbf{r}} + \frac{\partial \dot{\mathbf{p}}}{\partial \mathbf{p}} \right) - \left(\dot{\mathbf{r}} \frac{\partial \varrho}{\partial \mathbf{r}} + \dot{\mathbf{p}} \frac{\partial \varrho}{\partial \mathbf{p}} \right) = -(\varrho, H) \equiv -iL\varrho$$

- Formal solutions $A(t) = e^{iLt}A(0)$, $\varrho(t) = e^{-iLt}\varrho(0)$
- The propagator advances the system in time
- $A(\mathbf{r}_t, \mathbf{p}_t) = e^{iLt}A(\mathbf{r}_0, \mathbf{p}_0)$, where $\mathbf{r}_t = \mathbf{r}(t)$ etc
- Schrödinger/Heisenberg analogy
- $\langle A(t) \rangle = \text{Tr } \varrho A(t) = \text{Tr } \varrho e^{iLt} A = \text{Tr} (e^{-iLt} \varrho) A = \text{Tr } \varrho(t) A$

Trotter Decomposition

$$e^{iLt} = \left(e^{iL\Delta t} \right)_{\text{approx}}^n + \mathcal{O}(n\Delta t^3), \quad \text{where } t = n\Delta t$$

The quantity in parentheses is an **approximate** propagator correct at short timesteps $\Delta t \rightarrow 0$.

Useful approximations arise from splitting $iL = iL_p + iL_r$

Split Propagator

$$iL_p = \dot{\mathbf{p}} \cdot \frac{\partial}{\partial \mathbf{p}} = \mathbf{f} \cdot \frac{\partial}{\partial \mathbf{p}} \quad iL_r = \dot{\mathbf{r}} \cdot \frac{\partial}{\partial \mathbf{r}} = \mathbf{v} \cdot \frac{\partial}{\partial \mathbf{r}}$$

$$\text{drift: } e^{iL_r \Delta t} A(\mathbf{r}, \mathbf{p}) = A(\mathbf{r} + \mathbf{v} \Delta t, \mathbf{p})$$

$$\text{kick: } e^{iL_p \Delta t} A(\mathbf{r}, \mathbf{p}) = A(\mathbf{r}, \mathbf{p} + \mathbf{f} \Delta t)$$

Propagators and the Verlet Algorithm

Symmetric Splitting

$$e^{iL\Delta t} = e^{(iL_p + iL_r)\Delta t} \approx \underbrace{e^{iL_p\Delta t/2}}_{\text{kick}} \underbrace{e^{iL_r\Delta t}}_{\text{drift}} \underbrace{e^{iL_p\Delta t/2}}_{\text{kick}}$$

- For nonzero Δt this is an **approximation** to $e^{iL\Delta t}$ because in general iL_p and iL_r do not commute,
- but it is still exactly time reversible and symplectic.
 - Symplectic (roughly) implies conserving phase space volume $d\mathbf{r}_t d\mathbf{p}_t = d\mathbf{r}_0 d\mathbf{p}_0$.

It is then easy to see that the three successive steps embodied in the above equation, with the above choice of operators, generate the velocity Verlet algorithm.

Propagators and the Verlet Algorithm

- The trajectories generated by the above scheme are approximate, and will not conserve the true energy H .
- Nonetheless, they do exactly conserve a **pseudo-hamiltonian** or **shadow hamiltonian** H^\ddagger
- H and H^\ddagger differ from each other by a small amount, vanishing as $\Delta t \rightarrow 0$.
- This means that the system will remain on a hypersurface in phase space which is close to the true constant-energy hypersurface.

Such a stability property is extremely useful in MD, since we wish to sample constant-energy states.

Example

Consider a simple one-dimensional harmonic oscillator, of natural frequency ω , representing perhaps an interatomic bond in a diatomic molecule. The equations of motion and conserved hamiltonian are

Harmonic Oscillator Equations

$$\dot{r} = p/m, \quad \dot{p} = -m\omega^2 r, \quad H(r, p) = p^2/2m + \frac{1}{2}m\omega^2 r^2$$

For this system, velocity Verlet *exactly* conserves:

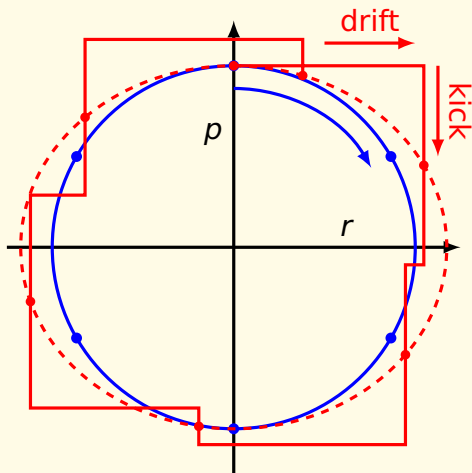
The Shadow Hamiltonian

$$H^\ddagger(r, p) = p^2/2m + \frac{1}{2}m\omega^2 r^2 \left(1 - (\omega\Delta t/2)^2\right)$$

Position of extra term is chosen for convenience.

Example

Harmonic Oscillator



In a **phase portrait**, the simulated system remains on an ellipse

$$H^\ddagger = \text{constant}$$

which differs slightly from the true ellipse,

$$H = \text{constant}$$

for small $\omega\Delta t$
(here $\omega\Delta t = \pi/3$).

Multiple Timesteps

- Suppose there are **slow** \mathbf{F} , and **fast** \mathbf{f} , forces.
- Momentum satisfies $\dot{\mathbf{p}} = \mathbf{F} + \mathbf{f}$.
- Break up Liouville operator $iL = iL_p + i\ell_p + iL_r$:

Multiple Timestep Liouville Operator

$$iL_p = \mathbf{F} \cdot \frac{\partial}{\partial \mathbf{p}}, \quad i\ell_p = \mathbf{f} \cdot \frac{\partial}{\partial \mathbf{p}}, \quad iL_r = \mathbf{v} \cdot \frac{\partial}{\partial \mathbf{r}}$$

$$e^{iL\Delta t} \approx e^{iL_p\Delta t/2} e^{(i\ell_p+iL_r)\Delta t} e^{iL_p\Delta t/2}$$

$$e^{(i\ell_p+iL_r)\Delta t} \approx \left(e^{i\ell_p\delta t/2} e^{iL_r\delta t} e^{i\ell_p\delta t/2} \right)^n$$

- Fast-varying forces computed once per δt .
- Slow forces computed once per $\Delta t = n\delta t$.

Multiple Timesteps

Algorithm

```
p = p + (DT/2)*F
do step = 1, n
  p = p + (dt/2)*f
  r = r + dt*p/m
  f = force(r)
  p = p + (dt/2)*f
end do
F = FORCE(r)
p = p + (DT/2)*F
```

Split interatomic forces into a succession of components covering different ranges.

- Short-range forces change rapidly with time and require a short time step.
- Long-range forces vary more slowly, can use longer time step and less frequent evaluation.

Multiple-time-step algorithms are still under active study, and there is some concern that resonances may occur between the natural frequencies of the system and the various timesteps used in schemes of this kind.

Constant-Temperature Dynamics

How to simulate systems at given T by MD?

Andersen Thermostat

- Periodically reselect momenta at random from the Maxwell-Boltzmann distribution $\mathbf{p} = \sqrt{mk_B T} \mathbf{G}$.
 - \mathbf{G} is a set of Gaussian random numbers, with zero mean, unit variance.
 - $k_B T$ = Boltzmann constant \times temperature
- Like occasional random coupling with thermal bath.
- Resample individual atoms, or entire system.
- Simple to implement and reliable.
- Proven to sample the canonical ensemble
 - if the MD algorithm is accurate!



HC Andersen, *J. Chem. Phys.*, **72**, 2384 (1980).

Constant-Temperature Dynamics

An alternative, deterministic, approach:

Nosé-Hoover Thermostat

$$\dot{\mathbf{r}} = \mathbf{v} = \mathbf{p}/m, \quad \dot{\mathbf{p}} = \mathbf{f} - \xi \mathbf{v}, \quad M\dot{\xi} = |\mathbf{v}|^2 - gk_{\text{B}}T/m$$

- ξ : friction coefficient, allowed to vary in time;
- M is a thermal inertia parameter, determining a relaxation rate for thermal fluctuations;
- $g \approx 3N$ is the number of degrees of freedom.

If the system is too hot (cold), then ξ will tend to increase (decrease) tending to cool (heat) the system.



S Nosé, *Mol. Phys.*, **52**, 255 (1984).



WG Hoover, *Phys. Rev. A*, **31**, 1695 (1985).

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Canonical NVT Ensemble

- Defined by macroscopic variables
 - N (number of atoms), V (volume), T (temperature).
- Distribution is Boltzmann weighted in energy $E(\mathbf{r})$
- Corresponding potential is Helmholtz free energy.

Canonical Ensemble Equations

Partition function:
$$Q = \int d\mathbf{r} e^{-E(\mathbf{r})/k_B T}$$

Helmholtz free energy:
$$F = E - TS = -k_B T \ln Q$$

Boltzmann distribution:
$$\varrho_{NVT}(\mathbf{r}) = Q^{-1} e^{-E(\mathbf{r})/k_B T}$$

Ensemble average:
$$\langle A \rangle_{NVT} = \int d\mathbf{r} \varrho_{NVT}(\mathbf{r}) A(\mathbf{r})$$

Importance Sampling

- We cannot, in general, sum over all the states, or sample enough of them, to calculate \mathbb{Q} or F .
- Instead, sample states with probability $\mathcal{P}(\mathbf{r}) \propto \varrho(\mathbf{r})$
- Select a sequence of states $\mathbf{r}_1, \mathbf{r}_2, \dots, \mathbf{r}_t, \dots$
 - t is a discrete index labelling successive states;
 - step-by-step: t plays the role of time
- Ensemble average converted to an average over t .

Monte Carlo Weighted Averages

$$\langle A \rangle = \int d\mathbf{r} \varrho(\mathbf{r}) A(\mathbf{r}) = \frac{1}{t_{\text{run}}} \sum_{t=1}^{t_{\text{run}}} A(\mathbf{r}_t)$$

The Boltzmann weight appears **implicitly** in the way the states are chosen.

Markov Chain Monte Carlo

Markov Chain **designed** to sample desired distribution.

- $q(\mathbf{r})$ may be treated as a component, labelled by the index \mathbf{r} , of a (very large) column vector \mathbf{e} .
- Label the distribution at each step t : \mathbf{e}_t .
- The **transition matrix** \mathbf{T} has elements $T(\mathbf{r}' \leftarrow \mathbf{r})$ giving the conditional probability of going to state \mathbf{r}' from state \mathbf{r} , for every \mathbf{r}, \mathbf{r}' .
 - Note that sometimes this matrix is defined with the order of indices interchanged.

Ensemble Evolution Equations

$$\mathbf{e}_1 = \mathbf{T}\mathbf{e}_0, \quad \mathbf{e}_t = \mathbf{T}\mathbf{e}_{t-1} = \underbrace{\mathbf{T}\mathbf{T}\cdots\mathbf{T}}_{t \text{ times}}\mathbf{e}_0 = \mathbf{T}^t\mathbf{e}_0$$

Limiting Distribution

- As $t \rightarrow \infty$, $\mathbf{e}_{t+1} = \mathbf{e}_t \Rightarrow \mathbf{T}\mathbf{e} = \mathbf{e}$.
- An eigenvector equation, with eigenvalue 1.
- Equation is **independent** of \mathbf{e}_0 .
- Relates \mathbf{T} to desired equilibrium distribution \mathbf{e} .
- \mathbf{T} must also satisfy $\sum_{r'} T(r' \leftarrow r) = 1$ for all r .

With this condition, the eigenvalue equation becomes

Markov Chain Equilibrium Condition

$$\sum_{r'} T(r \leftarrow r') \varrho(r') = \varrho(r) = \sum_{r'} T(r' \leftarrow r) \varrho(r)$$

This has a simple physical interpretation:

LHS: rate of arrival at state r from everywhere

RHS: rate of departure from state r to everywhere.

We may **guarantee** the truth of the last equation:

Microscopic Reversibility or Detailed Balance

$$T(\mathbf{r} \leftarrow \mathbf{r}')\varrho(\mathbf{r}') = T(\mathbf{r}' \leftarrow \mathbf{r})\varrho(\mathbf{r})$$
$$\Rightarrow \frac{\varrho(\mathbf{r}')}{\varrho(\mathbf{r})} = \frac{T(\mathbf{r}' \leftarrow \mathbf{r})}{T(\mathbf{r} \leftarrow \mathbf{r}')}$$

Familiar to those with a chemistry background:

- Equilibrium constant for a chemical reaction as the ratio of forward and backward rate constants.
- We are choosing the ratio of rate constants in order to give the desired equilibrium constant.

Metropolis Monte Carlo

Express \mathbf{T} as a product for **trial move** and **acceptance**.

$$T(\mathbf{r}' \leftarrow \mathbf{r}) = P_{\text{try}}(\mathbf{r}' \leftarrow \mathbf{r}) \times P_{\text{acc}}(\mathbf{r}' \leftarrow \mathbf{r})$$

Markov chain Metropolis-Hastings Algorithm

- 1 Select new trial state \mathbf{r}' with probability $P_{\text{try}}(\mathbf{r}' \leftarrow \mathbf{r})$
- 2 Accept the new state with probability

$$P_{\text{acc}}(\mathbf{r}' \leftarrow \mathbf{r}) = \min \left(1, \frac{\varrho(\mathbf{r}') P_{\text{try}}(\mathbf{r} \leftarrow \mathbf{r}')}{\varrho(\mathbf{r}) P_{\text{try}}(\mathbf{r}' \leftarrow \mathbf{r})} \right)$$

- 3 Re-count old state with probability $1 - P_{\text{acc}}$.

- If we set $\varrho(\mathbf{r}) = e^{-E(\mathbf{r})/k_B T} \rightarrow$ Boltzmann distribution.
- Often simply choose $P_{\text{try}}(\mathbf{r} \leftarrow \mathbf{r}') = P_{\text{try}}(\mathbf{r}' \leftarrow \mathbf{r})$.
- Don't need to evaluate \mathbf{P}_{try} , just know ratios.

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Langevin Dynamics

In an effort to economize, we replace the solvent (e.g. water) by random and frictional forces acting on the atoms which are of real interest.

Langevin Equation

$$\frac{d\mathbf{r}}{dt} = \mathbf{v} = \frac{\mathbf{p}}{m}, \quad \frac{d\mathbf{p}}{dt} = \mathbf{f} - \xi\mathbf{v} + \sigma\dot{\mathbf{w}}$$

- $\xi\mathbf{v}$ represents frictional forces
 - $\xi = k_B T / D =$ friction coefficient,
 - $D =$ diffusion coefficient,
- $\sigma\dot{\mathbf{w}}$ represents random forces
- $\sigma = \sqrt{2\xi k_B T}$ (fluctuation-dissipation theorem)
- Generates canonical ensemble
 - given an accurate BD algorithm

Random Forces

$\mathbf{w}(t)$ is a set of independent **Wiener** processes. Defined by integrating them over a timestep dt , to define them in terms of a set of independent Gaussian random variables, \mathbf{G} , of zero mean and unit variance.

More Formal Langevin Equation

$$d\mathbf{w} = \int_0^{dt} \dot{\mathbf{w}} dt = \dot{\mathbf{w}} dt = \sqrt{dt} \mathbf{G},$$

$$d\mathbf{p} = \mathbf{f} dt - \xi \mathbf{v} dt + \sigma \sqrt{dt} \mathbf{G}.$$

Various algorithms, based on operator splitting, can be constructed.



B Leimkuhler, C Matthews, *J. Chem. Phys.*, **138**, 174102 (2013).

Brownian Dynamics

At high friction, the relaxation of the momenta can be assumed to occur instantaneously. Setting $d\mathbf{p}/dt = 0$ gives the Langevin equation without inertia.

BD equation of motion

$$\frac{d\mathbf{r}}{dt} = \xi^{-1}(\mathbf{f} + \sigma\dot{\mathbf{w}}) = \frac{D}{k_{\text{B}}T} \mathbf{f} + \sqrt{2D} \dot{\mathbf{w}}$$

Simple BD algorithm

$$\Delta\mathbf{r} = \mathbf{r}(t + \Delta t) - \mathbf{r}(t) = \frac{D}{k_{\text{B}}T} \mathbf{f}(t) \Delta t + \mathbf{R}$$

random displacements $\mathbf{R} = \sqrt{2D\Delta t} \mathbf{G}$

$$\langle \mathbf{R} \rangle = 0$$

$$\langle \mathbf{R}\mathbf{R} \rangle = 2D\Delta t \mathbf{1}$$

For one particle,
if $\mathbf{f} = \mathbf{0}$,

$$\left. \begin{array}{l} \langle \Delta x^2 \rangle \\ \langle \Delta y^2 \rangle \\ \langle \Delta z^2 \rangle \end{array} \right\} = 2D\Delta t$$

Brownian Dynamics with Hydrodynamics

Averaged hydrodynamic interactions appear through a pairwise, separation-dependent, diffusion tensor.

BD algorithm with Hydrodynamics

$$\Delta \mathbf{r} = \mathbf{r}(t + \Delta t) - \mathbf{r}(t) = \frac{\mathbf{D}(t)}{k_B T} \cdot \mathbf{f}(t) \Delta t + \nabla \cdot \mathbf{D}(t) \Delta t + \mathbf{R}.$$

- \mathbf{D} is a $3N \times 3N$ diffusion tensor or matrix
- **Rotne-Prager** form (position dependent)
- Random displacements, \mathbf{R} , is selected from the $3N$ -variate Gaussian distribution with zero means and covariance matrix $\langle \mathbf{R}\mathbf{R} \rangle = 2\mathbf{D}\Delta t$.
- As a consequence, the components of \mathbf{R} are *correlated* with each other.

Dissipative Particle Dynamics

A different kind of stochastic dynamics aims to allow hydrodynamic effects in fluid simulation.

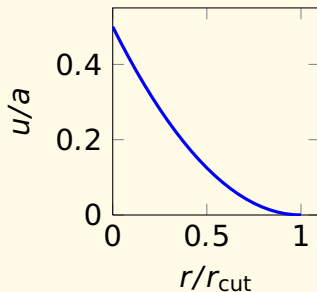
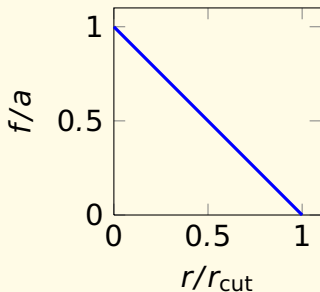
DPD Equations

$$\frac{d\mathbf{r}}{dt} = \mathbf{v} = \frac{\mathbf{p}}{m}, \quad \frac{d\mathbf{p}}{dt} = \mathbf{f}(\mathbf{r}) - \xi\mathbf{V}(\mathbf{r}, \mathbf{p}) + \sigma\dot{\mathbf{W}}(\mathbf{r}, \mathbf{p})$$

- ξ is a friction coefficient.
- The \mathbf{f} are conservative forces.
- The $\xi\mathbf{V}(\mathbf{r}, \mathbf{p})$ are dissipative, frictional forces.
- The $\sigma\dot{\mathbf{W}}(\mathbf{r}, \mathbf{p})$ are random forces.
- Resembles the Langevin equation.

Soft Conservative Forces

DPD Force and Potential



Linear Force Law

$$\mathbf{f}_{jk} = a\phi(r_{jk})\hat{\mathbf{r}}_{jk}, \quad \phi(r) = \begin{cases} 1 - r/r_{\text{cut}} & r < r_{\text{cut}} \\ 0 & r > r_{\text{cut}} \end{cases}$$

Soft Conservative Forces

- Particles represent **regions** of fluid, not individual atoms or molecules.
- Can also be used to build very coarse-grained bead-spring models of polymers, lipids, surfactants, and other amphiphilic molecules.
- Interactions between them are much **softer** than (say) Lennard-Jones potentials.
- The particles can even pass through each other.
- The softer potentials, in turn, mean that much longer time steps ($\sim 1 \times 10^{-11}$ s, 10 picoseconds) may be used than in conventional MD simulations.

Dissipative and Random Forces


Equal and Opposite Pairwise Terms

$$\mathbf{v}_j = \sum_{k \neq j} \phi(r_{jk}) (\mathbf{v}_{jk} \cdot \hat{\mathbf{r}}_{jk}) \hat{\mathbf{r}}_{jk}, \quad \text{where } \mathbf{v}_{jk} = \mathbf{v}_j - \mathbf{v}_k$$

$$\dot{\mathbf{w}}_j = \sum_{k \neq j} \sqrt{\phi(r_{jk})} \dot{w}_{jk} \hat{\mathbf{r}}_{jk} \quad \text{where } w_{jk} = w_{kj}$$

- $w_{jk}(t) = w_{kj}(t)$ are independent Wiener processes.
- Effect of j on k is the negative of the effect of k on j .
- The fluctuation-dissipation theorem is satisfied.
- Dynamics is Galilean-invariant.
- Momentum is conserved.
- This leads to hydrodynamics.

Momentum-Conserving Thermostat

-  CP Lowe, *Europhys. Lett.*, **47**, 145 (1999).
 - A **pairwise** Andersen stochastic thermostat.
 - Alternative to DPD equations: conventional MD,
 - plus momentum-conserving thermostat.

Lowe-Andersen Algorithm

- 1 Advance \mathbf{r} , \mathbf{p} each step using velocity Verlet.
- 2 For selected pairs ij , with probability $P = \nu\Delta t$, update $\mathbf{p}_i \rightarrow \mathbf{p}_i + \Delta\mathbf{p}_{ij}$, $\mathbf{p}_j \rightarrow \mathbf{p}_j - \Delta\mathbf{p}_{ij}$, with

$$\Delta\mathbf{p}_{ij} = \frac{1}{2}m \left[G_{ij}\sqrt{2k_B T/m} - (\mathbf{v}_{ij} \cdot \hat{\mathbf{r}}_{ij}) \right] \hat{\mathbf{r}}_{ij}$$

G_{ij} = Gaussian random, zero mean, unit variance.

Low-Andersen Thermostat

- Periodically reselects the component of the **relative velocity** along $\hat{\mathbf{r}}_{ij}$ from the Maxwell-Boltzmann distribution.
- Can include $\phi(r_{ij})$ in prescription.
- The key parameter is the stochastic randomization frequency ν :
 - high values of ν give effective temperature control, but also a high viscosity;
 - low values of ν give very weak temperature control while allowing the viscosity to be low.

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Canonical Ensemble Temperature

Kinetic and Configurational Temperature

$$k_B T_k = \langle p_{i\alpha}^2 / m \rangle, \quad k_B T_c = \frac{\langle (\partial U / \partial r_{i\alpha})^2 \rangle}{\langle \partial^2 U / \partial r_{i\alpha}^2 \rangle}$$

- $i = 1 \dots N, \alpha = x, y, z$
- Both sides may be averaged over i and α .
- Ensemble-dependent $\mathcal{O}(1/N)$ corrections



JO Hirschfelder, *J. Chem. Phys.*, **33**, 1462 (1960).



LD Landau and EM Lifshitz, *Statistical Physics* (1958).



HH Rugh, *Phys. Rev. Lett.*, **78**, 772 (1997).



BD Butler, *et al*, *J. Chem. Phys.*, **109**, 6519 (1998).

Canonical Ensemble Thermodynamics

Heat Capacity

$$k_B T^2 C_V = \langle E^2 \rangle - \langle E \rangle^2 = \langle \delta E^2 \rangle$$

Different formulae in different ensembles

Pressure

$$PV = Nk_B T - V \left\langle \frac{\partial U}{\partial V} \right\rangle = \underbrace{Nk_B T}_{\text{ideal}} - \underbrace{\frac{1}{3} \left\langle \sum_i \sum_{j \neq i} w_{ij} \right\rangle}_{\text{excess}}$$

- Assuming pairwise additivity $U = \sum_i \sum_{j \neq i} v_{ij}$,
- Defining the virial function $w(r) = r dv(r)/dr$.

Chemical Potential

Excess Chemical Potential

$$\beta\mu^{\text{ex}} = \left(\frac{\partial \beta F^{\text{ex}}}{\partial N} \right) = - \left(\frac{\partial \ln Q_{NVT}^{\text{ex}}}{\partial N} \right) \approx - \ln \left(\frac{Q_{N+1}^{\text{ex}}}{Q_N^{\text{ex}}} \right)$$

Separate the terms in the potential energy which involve the extra particle $U_{N+1} = U_N + \Delta U_{N+1}$.

Widom Test-Particle Formula

$$\begin{aligned} \mu^{\text{ex}} &= -k_B T \ln \int d\mathbf{s}_{N+1} \langle e^{-\beta \Delta U_{N+1}} \rangle \\ &= -k_B T \ln \langle \langle e^{-\beta \Delta U_{N+1}} \rangle \rangle \end{aligned}$$

Average over ensemble and $\mathbf{s}_{N+1} \equiv \mathbf{r}_{N+1}/L$.

How Long to Run?

- Simulation runs are typically short
 - 10^5 – 10^8 MD steps, or $t_{\text{run}} \approx 10^{-9}$ – 10^{-6} seconds
 - Equilibration; has the system reached equilibrium?
 - Production run; how long is long enough?
- Consider system and physical properties of interest.
- Suppose we are interested in a variable $A(\mathbf{r}, \mathbf{p})$.
- Define A such that $\langle A \rangle = 0$, for convenience.

Time Correlation Function

$$c(t) = \frac{\langle A(t_0)A(t_0 + t) \rangle}{\langle A^2 \rangle} = \frac{\langle A(0)A(t) \rangle}{\langle A^2 \rangle} \rightarrow \begin{cases} 1 & \text{as } t \rightarrow 0 \\ 0 & \text{as } t \rightarrow \infty \end{cases}$$

- We assumed that the system is in equilibrium.
- So $c(t)$ is independent of t_0 .

How Long to Run?

Correlation Time

$$\tau = \int_0^{\infty} dt c(t) \quad \text{and sometimes} \quad c(t) \approx \exp(-t/\tau)$$

For good statistics, need run length $t_{\text{run}} \gg \tau$.

- Define finite-time average $\langle A \rangle_t = \frac{1}{t} \int_0^t dt' A(t')$.
- Repeat simulation many times, giving a distribution of results $\langle A \rangle_t$ sampled from an ensemble.
- Denote the ensemble average by $\langle A \rangle = \langle A \rangle_{\infty} = 0$.
- In general $\delta A_t \equiv \langle A \rangle_t - \langle A \rangle \neq 0$.
- Average $\langle \delta A_t \rangle = 0$, but variance $\langle \delta A_t^2 \rangle \neq 0$.

Statistical Errors: Time Averaging

Variance of Time Averages

$$\langle \delta A_t^2 \rangle = \langle A^2 \rangle \times \frac{2}{t} \int_0^t dt' \left(1 - \frac{t'}{t}\right) c(t') \xrightarrow{t \gg \tau} \langle A^2 \rangle \times \frac{2\tau}{t}$$

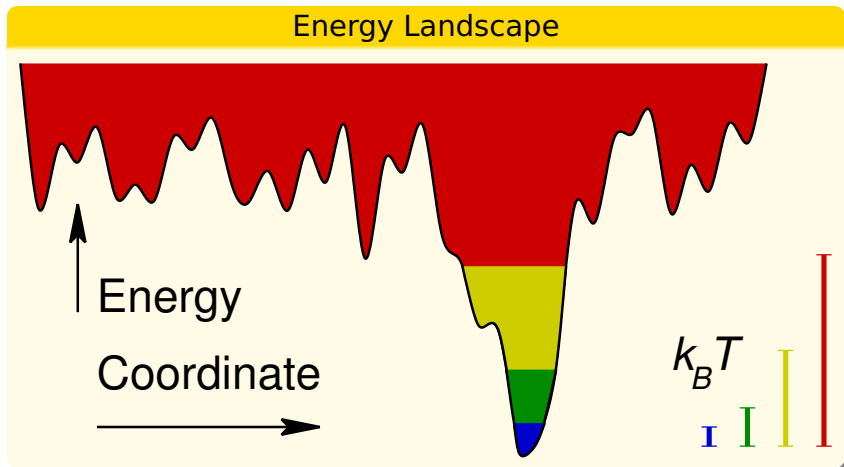
- Statistical error in MD average is inversely proportional to square-root of the run time.
- Also depends on correlation time of the property.
- Average over time t is an average of $\sim t/2\tau$ essentially independent quantities.
- Sampling more frequently than τ does not greatly improve precision.

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Parallel Tempering

How can simulations find and sample the low-energy configurations, without getting trapped in **local** minima?



Parallel Tempering

Two simulations in parallel: $\beta_1 = 1/k_B T_1$, $\beta_2 = 1/k_B T_2$.

- $q_1(\mathbf{r}; \beta_1) \propto e^{-\beta_1 U(\mathbf{r})}$, $q_2(\mathbf{r}'; \beta_2) \propto e^{-\beta_2 U(\mathbf{r}')}$.
- Joint distribution $q_{1\&2} = q_1 \times q_2$
- Introduce a new Monte Carlo move:

Configuration Swap Move

old \rightleftharpoons new

$$(\mathbf{r}; \beta_1) (\mathbf{r}'; \beta_2) \rightleftharpoons (\mathbf{r}'; \beta_1) (\mathbf{r}; \beta_2)$$

$$T(\text{new} \leftarrow \text{old}) q_{1\&2}(\text{old}) = T(\text{old} \leftarrow \text{new}) q_{1\&2}(\text{new})$$

$$\begin{aligned} \frac{T(\text{new} \leftarrow \text{old})}{T(\text{old} \leftarrow \text{new})} &= \frac{q_{1\&2}(\text{new})}{q_{1\&2}(\text{old})} = \frac{q_1(\mathbf{r}'; \beta_1) q_2(\mathbf{r}; \beta_2)}{q_1(\mathbf{r}; \beta_1) q_2(\mathbf{r}'; \beta_2)} \\ &= e^{-(\beta_1 - \beta_2)(U(\mathbf{r}') - U(\mathbf{r}))} \end{aligned}$$

Use this in the Metropolis prescription in the usual way.

Parallel Tempering

- Swap moves are cheap.
- Thermal equilibrium holds.
- Acceptance rates high when temperatures similar.
- Generalizes naturally to a set of temperatures.
- Gives ensemble averages for all the temperatures,
 - and temperatures in between, too!
- Low- T configurations are well equilibrated;
 - frequent swaps with higher- T configurations.
- Sampling deep wells / high barriers possible.
- Can be parallelized.

Smart Monte Carlo

 PJ Rossky *et al.*, *J. Chem. Phys.*, **69**, 4628 (1978).

Brownian-Dynamics-like Trial Move

$$\mathbf{r}' = \mathbf{r} + \beta D \Delta t \mathbf{f} + \mathbf{R}, \quad \mathbf{R} = \sqrt{2D\Delta t} \mathbf{G}, \quad \beta = 1/k_B T$$

$$\mathbf{r}' - \mathbf{r} - \beta D \Delta t \mathbf{f} = \sqrt{2D\Delta t} \mathbf{G} \equiv \sigma \mathbf{G}$$

$$\frac{P_{\text{try}}(\mathbf{r} \leftarrow \mathbf{r}')}{P_{\text{try}}(\mathbf{r}' \leftarrow \mathbf{r})} = \frac{\exp\left\{-\frac{1}{2}|\mathbf{r} - \mathbf{r}' - \beta D \Delta t \mathbf{f}'|^2 / \sigma^2\right\}}{\exp\left\{-\frac{1}{2}|\mathbf{r}' - \mathbf{r} - \beta D \Delta t \mathbf{f}|^2 / \sigma^2\right\}}$$

- $D\Delta t$ determines size of attempted moves
- The \mathbf{P}_{try} ratio corrects for bias in the force direction

Smart Monte Carlo

Replace $D\Delta t$ by $(k_B T/m) \frac{1}{2} \Delta t^2$

Molecular-Dynamics-like Trial Move

$$\mathbf{r}' = \mathbf{r} + \frac{1}{2} \Delta t^2 \mathbf{f}/m + \Delta t \mathbf{P}/m, \quad \mathbf{P} = \sqrt{mk_B T} \mathbf{G}$$

$$\mathbf{r}' - \mathbf{r} - \frac{1}{2} \Delta t^2 \mathbf{f}/m = \sqrt{k_B T/m} \Delta t \mathbf{G} \equiv \sigma \mathbf{G}$$

$$\frac{P_{\text{try}}(\mathbf{r} \leftarrow \mathbf{r}')}{P_{\text{try}}(\mathbf{r}' \leftarrow \mathbf{r})} = \frac{\exp\left\{-\frac{1}{2} \left| \mathbf{r} - \mathbf{r}' - \frac{1}{2} \Delta t^2 \mathbf{f}'/m \right|^2 / \sigma^2\right\}}{\exp\left\{-\frac{1}{2} \left| \mathbf{r}' - \mathbf{r} - \frac{1}{2} \Delta t^2 \mathbf{f}/m \right|^2 / \sigma^2\right\}}$$

$$\text{denominator} = \exp\left\{-\frac{|\mathbf{P}|^2/2m}{k_B T}\right\} = \exp\{-K/k_B T\}$$



PJ Rossky *et al.*, *J. Chem. Phys.*, **69**, 4628 (1978).

Velocity Verlet plus Andersen Thermostat

$$\text{Define } \mathbf{P}' \equiv \mathbf{P} + \frac{1}{2}\Delta t(\mathbf{f} + \mathbf{f}')$$

$$\text{numerator} = \exp\left\{-\frac{|\mathbf{P}'|^2/2m}{k_B T}\right\} = \exp\{-K'/k_B T\}$$

$$\frac{P_{\text{try}}(\mathbf{r} \leftarrow \mathbf{r}')}{P_{\text{try}}(\mathbf{r}' \leftarrow \mathbf{r})} = \frac{\exp\{-K'/k_B T\}}{\exp\{-K/k_B T\}} = e^{-\Delta K/k_B T}$$

$$\begin{aligned} P_{\text{acc}}(\mathbf{r}' \leftarrow \mathbf{r}) &= \min\left(1, \frac{\varrho(\mathbf{r}') P_{\text{try}}(\mathbf{r} \leftarrow \mathbf{r}')}{\varrho(\mathbf{r}) P_{\text{try}}(\mathbf{r}' \leftarrow \mathbf{r})}\right) \\ &= \min\left(1, e^{-\Delta U/k_B T} e^{-\Delta K/k_B T}\right) \\ &= \min\left(1, e^{-\Delta E/k_B T}\right) \end{aligned}$$

Smart Monte Carlo

Molecular Dynamics form of Smart Monte Carlo

- 1 Choose random momenta from Boltzmann distribution
- 2 Apply Velocity Verlet algorithm to advance coordinates and momenta
- 3 Accept or reject using Metropolis on $\Delta E = \Delta K + \Delta U$
- 4 Throw away new momenta and start afresh in next step.



PJ Rossky *et al.*, *J. Chem. Phys.*, **69**, 4628 (1978).



MP Allen, D Quigley, *Molec. Phys.*, **111**, 3442 (2013).

Hybrid Monte Carlo

Re-invented, and significantly generalised.



S Duane, AD Kennedy, BJ Pendleton and D Roweth, *Phys. Lett. B*, **195**, 216 (1987).

- Not restricted to velocity Verlet algorithm.
- The MD algorithm must be strictly time reversible and phase-space-volume-preserving $d\mathbf{r}'d\mathbf{p}' = d\mathbf{r}d\mathbf{p}$.
- Just as valid for long timesteps as for short ones.
- Shorter timestep \Rightarrow smaller $\Delta E \Rightarrow$ higher P_{acc} .
- The time evolution algorithm need not use the same potential energy function as the real system.
 - It could use a similar, but cheaper form.
 - But real ΔE must be used in accept/reject decision.
- Easily-parallelizable version of Monte Carlo.

Free Energies and Probability Distributions

- Consider a general coordinate $Q(\mathbf{r})$, typically some combination of atomic coordinates
 - for example, a bond length
 - but possibly an order parameter
- Can define a free energy $F(Q)$, as usual but subject to the constraint that $Q(\mathbf{r}) = Q$ is fixed.
- This is related to the probability distribution $\mathcal{P}(Q)$ seen in an unconstrained simulation:

Landau Free Energy

$$F(Q) \equiv -k_B T \ln \mathcal{P}(Q) + \text{constant} \quad \mathcal{P}(Q) = \langle \delta(Q(\mathbf{r}) - Q) \rangle$$

- Q is a fixed parameter, while $Q(\mathbf{r})$ is instantaneous value of coordinate during simulation.
- $\delta(Q(\mathbf{r}) - Q)$ is the Dirac delta function.

Umbrella Sampling

To extend the sampling into low-probability regions of the distribution, use non-Boltzmann **weighted sampling** or **umbrella sampling**.



GM Torrie, JP Valleau, *J. Comp. Phys.*, **23**, 187 (1977).

- Include an extra term in the potential $U \rightarrow U - \mathcal{F}$
- Typically $\mathcal{F}(\mathbf{r}) = \mathcal{F}(Q(\mathbf{r}))$
- Sampled distribution now $\rho_W(\mathbf{r}) \propto e^{-(U(\mathbf{r}) - \mathcal{F}(\mathbf{r}))/k_B T}$

Weighted and Corrected Averages

$$\langle A \rangle_W = \frac{\int d\mathbf{r} A(\mathbf{r}) e^{-(U(\mathbf{r}) - \mathcal{F}(\mathbf{r}))/k_B T}}{\int d\mathbf{r} e^{-(U(\mathbf{r}) - \mathcal{F}(\mathbf{r}))/k_B T}}$$

$$\langle A \rangle = \frac{\int d\mathbf{r} A(\mathbf{r}) e^{-U(\mathbf{r})/k_B T}}{\int d\mathbf{r} e^{-U(\mathbf{r})/k_B T}} = \frac{\langle A e^{-\mathcal{F}(\mathbf{r})/k_B T} \rangle_W}{\langle e^{-\mathcal{F}(\mathbf{r})/k_B T} \rangle_W}$$



Barrier Flattening

Weighted Probability Distribution

$$\begin{aligned}
 \langle \delta(Q(\mathbf{r}) - Q) \rangle_W &\propto \int d\mathbf{r} \delta(Q(\mathbf{r}) - Q) e^{-(U(\mathbf{r}) - \mathcal{F}(\mathbf{r}))/k_B T} \\
 &\propto e^{\mathcal{F}(Q)/k_B T} \int d\mathbf{r} \delta(Q(\mathbf{r}) - Q) e^{-U(\mathbf{r})/k_B T} \\
 &\propto e^{\mathcal{F}(Q)/k_B T} \langle \delta(Q(\mathbf{r}) - Q) \rangle \\
 \Rightarrow \mathcal{P}_W(Q) &\propto e^{\mathcal{F}(Q)/k_B T} \mathcal{P}(Q)
 \end{aligned}$$

- Knowing $\mathcal{F}(Q)$ we can convert $\mathcal{P}_W(Q) \rightleftharpoons \mathcal{P}(Q)$.
- But $\mathcal{P}(Q) \propto \exp(-F(Q)/k_B T)$
- $\mathcal{F}(Q) = F(Q) \iff \mathcal{P}_W(Q) = \text{constant}$ (flat distribution)

Barrier Flattening

Iterative Weight Refinement

- 1 $\mathcal{F}(Q) = 0$ to start.
- 2 Sample with effective energy $= U(\mathbf{r}) - \mathcal{F}(Q(\mathbf{r}))$.
- 3 Determine $\mathcal{P}_W(Q)$ over a simulation run.
- 4 Wherever $\mathcal{P}_W(Q) > 0$, $\mathcal{F}(Q) \rightarrow \mathcal{F}(Q) - k_B T \ln \mathcal{P}_W(Q)$
- 5 Repeat steps 2–4 until convergence:

$$\mathcal{F}(Q) \rightarrow F(Q) \quad \mathcal{P}_W(Q) \rightarrow \text{constant}$$

Called **multicanonical**, or **entropic**, sampling

 BA Berg, T Celik, *Phys. Rev. Lett.*, **69**, 2292 (1992).

 J Lee, *Phys. Rev. Lett.*, **71**, 211 (1993).

 BA Berg *et al.*, *J. Phys. Chem.*, **99**, 2236 (1995).

Windows and Umbrellas

- Umbrella sampling can be applied with a succession of potentials which act to localise the sampling in overlapping windows.

$$-\mathcal{F}(Q) = \frac{1}{2}k(Q - Q_i)^2$$

- The results may be combined with the WHAM or MBAR methods



S Kumar et al., *J. Comput. Chem.*, **13**, 1011 (1992).



M Shirts, JD Chodera, *J. Chem. Phys.*, **129**, 124105 (2008).



A Pohorille et al., *J. Phys. Chem. B*, **114**, 10235 (2010).

Density of States Sampling

Efficient MC methods have been developed to map out behaviour of systems over a wide temperature range, including identification of low- E structures.

Thermodynamics from Density of States

density of states: $\mathbb{W}(E) = e^{S(E)/k_B}$

partition function: $\mathbb{Q} = \int d\mathbf{r} e^{-\beta E(\mathbf{r})} = \sum_E \mathbb{W}(E) e^{-\beta E}$

average energy: $\langle E \rangle = \mathbb{Q}^{-1} \sum_E \mathbb{W}(E) E e^{-\beta E}$

heat capacity: $C_V = (\langle E^2 \rangle - \langle E \rangle^2) / k_B T^2$

Density of States Sampling

- $\mathbb{W}(E)$ increases very rapidly with E .
- A **density-of-states simulation** samples states with a probability or weight $\mathcal{P}(E) \propto 1/\mathbb{W}(E)$.
- This covers the entire energy scale uniformly.
- Allows low-energy configurations to exchange with higher-energy ones and vice versa.

Metropolis-like Acceptance Formula

$$P_{\text{acc}}(\mathbf{r}' \leftarrow \mathbf{r}) = \min \left(1, \frac{\mathcal{P}(E(\mathbf{r}'))}{\mathcal{P}(E(\mathbf{r}))} \right) = \min \left(1, \frac{\mathbb{W}(E(\mathbf{r}))}{\mathbb{W}(E(\mathbf{r}'))} \right)$$



FG Wang, DP Landau, *Phys. Rev. E*, **64**, 056101 (2001).

Wang-Landau Sampling

Wang-Landau Algorithm to determine $\mathbb{W}(E)$

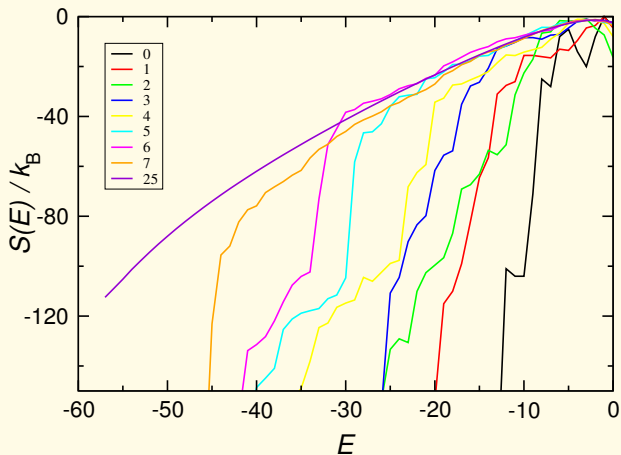
- 1 Set all $\mathbb{W}(E) = 1$, set factor $f = e = 2.71828$.
- 2 Set all $h(E) = 0$.
- 3 Conduct MC moves using $\mathbb{W}(E)$. Suppose after each move the new state is t , then
 - $\mathbb{W}(E_t) \rightarrow f \times \mathbb{W}(E_t)$, $S(E_t) \rightarrow S(E_t) + k_B \ln f$
 - $h(E_t) \rightarrow h(E_t) + 1$
- 4 Repeat from step 3 until $h(E)$ is **sufficiently flat**
- 5 $f \rightarrow \sqrt{f}$, $\ln f \rightarrow \frac{1}{2} \ln f$
- 6 Repeat from step 2 until f is **sufficiently small**.
- 7 $\mathbb{W}(E)$ has converged to the correct density of states.



FG Wang, DP Landau, *Phys. Rev. E*, **64**, 056101 (2001).

Example: 103-atom Lattice Polymer

Wang-Landau Density of States



Density of states at successive iterations of f .

Optimizing Wang-Landau

Is it best to make f change exponentially?

- At each stage of Wang-Landau $f \rightarrow \sqrt{f}$.
- It may be better to make $\ln f \propto 1/t$

 RE Berardinelli, VD Pereyra, *JCP*, **127**, 184105 (2007).

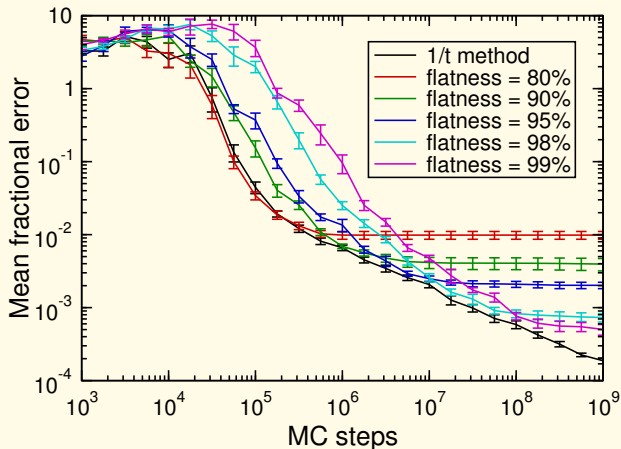
 C Zhou, J Su, *Phys. Rev. E*, **78**, 046705 (2008).

- To test properly requires exactly soluble model.
- Exact enumeration, isolated 18-bead homopolymer.
- Fractional error = $\epsilon_{\text{rms}} = \sqrt{\epsilon(E)^2}$ where

$$\epsilon(E) = \frac{\ln W(E) - \ln W_{\text{exact}}(E)}{\ln W_{\text{exact}}(E)} = \frac{S(E) - S_{\text{exact}}(E)}{S_{\text{exact}}(E)}$$

Optimizing Wang-Landau

Results for 18-bead Homopolymer



AD Swetnam, MP Allen, *J. Comp. Chem.*, **32**, 816 (2011).

Dynamical Density of States Sampling

- How to determine $S(U) = k_B \ln \mathbb{W}(U)$ using dynamics?
- Introduce momenta \mathbf{p} , kinetic energy $K = |\mathbf{p}|^2/2m$
- Formal hamiltonian $H = T_0 S(U(\mathbf{r})) + K(\mathbf{p})$
 - arbitrary temperature T_0 ; $S(U)$ to be determined.
- Use thermostatted MD or Hybrid MC with T_0

Equations of Motion

$$\dot{\mathbf{r}} = \frac{\mathbf{p}}{m}, \quad \dot{\mathbf{p}} = -\nabla(T_0 S(U)) = -T_0 \left(\frac{\partial S}{\partial U} \right) \nabla U(\mathbf{r}) = \frac{\beta(U)}{\beta_0} \mathbf{f}$$

$$P_{NVT}(\mathbf{r}) \propto \exp\{-S(U(\mathbf{r}))/k_B\} = \mathbb{W}(U)^{-1} \Rightarrow \mathcal{P}(U) = \text{const}$$



UHE Hansmann, Y Okamoto, F Eisenmenger, *Chem. Phys. Lett.*, **259**, 321 (1996).

Statistical Temperature MD/MC

- Use velocity Verlet algorithm or similar.
- To avoid errors, also apply Metropolis criterion

$$P_{\text{acc}}(\mathbf{r}' \leftarrow \mathbf{r}) = \min(1, e^{-\Delta K/k_B T_0} e^{-\Delta S/k_B})$$

- Use a Wang-Landau procedure to determine $S(U)$.
- Determine $\beta(U)$ by numerical differentiation.



J Kim et al., *Phys. Rev. Lett.*, **97**, 050601 (2006).



J Kim et al., *J. Chem. Phys.*, **126**, 135101 (2007).



E Darve et al., *J. Chem. Phys.*, **128** (2008).

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Free Energy Differences

- Suppose a parameter λ in our potential switches from $U_A(\mathbf{r}) = U(\mathbf{r}; \lambda_A)$ to $U_B(\mathbf{r}) = U(\mathbf{r}; \lambda_B)$.
- Set $\Delta U(\mathbf{r}) = U_B(\mathbf{r}) - U_A(\mathbf{r})$.

Free Energy Perturbation Equation

$$Q_A = \int d\mathbf{r} e^{-U_A(\mathbf{r})/k_B T}, \quad Q_B = \int d\mathbf{r} e^{-U_B(\mathbf{r})/k_B T}$$

$$Q_B = Q_A \frac{\int d\mathbf{r} e^{-U_A(\mathbf{r})/k_B T} e^{-\Delta U/k_B T}}{\int d\mathbf{r} e^{-U_A(\mathbf{r})/k_B T}} = Q_A \langle e^{-\Delta U/k_B T} \rangle_A$$

$$F_B = F_A - k_B T \ln \langle e^{-\Delta U/k_B T} \rangle_A.$$

where $\langle \dots \rangle_A$ denotes an average in system A.

Free Energy Derivatives

Thermodynamic Integration

$$\frac{\partial F_\lambda}{\partial \lambda} = -k_B T \frac{\partial \ln Q_\lambda}{\partial \lambda} = -k_B T \frac{1}{Q_\lambda} \left(\frac{\partial Q_\lambda}{\partial \lambda} \right) = \left\langle \frac{\partial U_\lambda}{\partial \lambda} \right\rangle_\lambda$$

$$F_B - F_A = \int_{\lambda_A}^{\lambda_B} d\lambda \left\langle \frac{\partial U_\lambda}{\partial \lambda} \right\rangle_\lambda$$

- The free energy difference formula requires the two systems to be reasonably similar.
- The thermodynamic integration approach typically requires a succession of closely spaced states.
- Using overlapping distributions $\mathcal{P}(U)$ usually improves the situation in either case.

Irreversible Work

Suppose $\lambda = \lambda(t)$, changing from λ_A to λ_B over a finite time interval $t = 0 \dots \tau$.

Work Done

$$W = \int_0^\tau dt \left(\frac{\partial H(\mathbf{r}_t, \mathbf{p}_t; \lambda_t)}{\partial \lambda_t} \right) \dot{\lambda}_t = H_B(\mathbf{r}_\tau, \mathbf{p}_\tau) - H_A(\mathbf{r}_0, \mathbf{p}_0)$$

- Initial $(\mathbf{r}_0, \mathbf{p}_0)$ averaged over NVT ensemble.
- System evolves over a path $(\mathbf{r}_t, \mathbf{p}_t)$, $t = 0 \dots \tau$.
- Average work over initial distribution:
 - $\langle W \rangle_+$ for forward $A \rightarrow B$ process.
 - $\langle W \rangle_-$ for reverse $B \rightarrow A$ process.

Second Law of Thermodynamics

$$\langle W \rangle_+ \geq \Delta F, \text{ and } \langle W \rangle_- \geq -\Delta F, \text{ where } \Delta F = F_B - F_A$$





Crooks and Jarzynski Equations

Jarzynski Equation

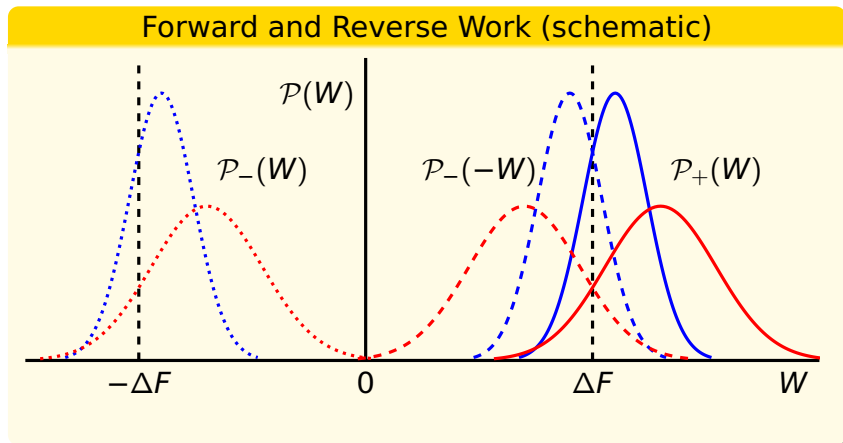
$$e^{-\beta\Delta F} = \langle e^{-\beta W} \rangle_+$$

Crooks Fluctuation Theorem

$$\frac{\mathcal{P}_+(W)}{\mathcal{P}_-(-W)} = \exp\left(\frac{W - \Delta F}{k_B T}\right)$$

-  DJ Evans, DJ Searles, *Phys. Rev. E*, **50**, 1645 (1994).
-  C Jarzynski, *Phys. Rev. Lett.*, **78**, 2690 (1997).
-  GE Crooks, *Phys. Rev. E*, **60**, 2721 (1999).
-  G Hummer, A Szabo, *Proc. Nat. Acad. Sci.*, **98**, 3658 (2001); *Acc. Chem. Res.*, **38**, 504 (2005).

Work Distributions



Jarzynski Equation: Comments

- Initial states (in either direction) are assumed to be at equilibrium.
- Final states will not be at equilibrium.
- For very slow changes we recover the thermodynamic integration formula.
- For very fast changes we recover the free energy perturbation formula.
- The Jarzynski formula allows anything in between.
- Still not clear which is the most efficient.
- The formula is used *experimentally* to estimate free energy changes at the single molecule level.

Conclusions

- This is just an introductory talk.
- So I don't really have any conclusions.
- Thanks for listening!