Introduction into computer simulation methods - classical techniques

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Literature:


• Advanced techniques: Christophe Chipot (Editor), Andrew Pohorille (Editor), *Free Energy Calculations: Theory and Applications in Chemistry and Biology* (Springer Series in Chemical Physics) (2007)

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Part I
Introduction

1 General considerations on simulations

Simulations

What are simulations?

- simulations are numerical procedures, motivated mathematically or physically
- applications in many fields: condensed matter physics, chemistry, biochemistry, materials science, geoscience, planetary science, etc.
- we focus here on equilibrium simulations using off-lattice models (continuous degrees of freedom) of solids and liquids

What do we get from simulations?

- Numbers: calculation of equilibrium thermodynamic quantities (averages, fluctuations, correlation functions), calculation of phase diagrams
- Insight gained by direct observation of dynamical processes (chemical reactions, phase transitions)
- Prediction of new phases and structures

Experiment, Theory, Model, Simulations

Why do we perform simulations?

- to understand experiments, we build models
- from model we calculate theoretical predictions
- unfortunately, very few non-trivial models are exactly solvable
- in theory we often use approximations, more or less under control
• if experiment and theory do not agree, we don’t know whether the problem is in the model or in the approximations involved

• *simulations can provide (in principle) exact results for models*

• *simulations vs. experiment:* test of model

• *simulations vs. approximations:* test of approximations

• the most fascinating use of simulations is to perform experiments in “*virtual laboratory*”: once we believe that our model is good, we can even use simulations to make *predictions* for real experiments

• e.g., we can simulate matter at extreme conditions (temperature, pressure) where we cannot perform real experiments

**Limitations of simulations**

• *WARNING:* also simulations have limitations

• higher model accuracy requires higher computational load and more resources

• often we use stochastic procedures - *statistical errors*

• GAP BETWEEN *TIME SCALES* AND *LENGTH SCALES* IN EXPERIMENT AND IN SIMULATIONS (will be discussed later in detail)

• in experiment often ms or s, in simulation at best µs, typically ns or even few tens of ps (ab-initio)

• in experiment macroscopic length scales, in simulation typically few nm

• in experiment $10^{23}$ particles, in simulation typically few hundreds or thousands, rarely few millions

• one of main directions in simulations is *bridging the gap between time and length scales*

• intrinsic limitations of specific simulation methods
2 Born-Oppenheimer approximation

Born-Oppenheimer approximation

Hamiltonian for a general condensed matter system consisting of interacting nuclei (ions) and electrons

\[
\hat{H} = \hat{T}_N(\{\vec{R}\}) + \hat{T}_e(\{\vec{r}\}) + \hat{V}_{ee}(\{\vec{r}\}) + \hat{V}_{NN}(\{\vec{R}\}) + \hat{V}_{eN}(\{\vec{r}\}, \{\vec{R}\})
\]

Born-Oppenheimer approximation continued

- the full Schrödinger equation

\[
\hat{H}\phi_T(\{\vec{r}\}, \{\vec{R}\}) = E_{tot}\phi_T(\{\vec{r}\}, \{\vec{R}\})
\]

represents an extremely complicated many-body problem

- the ions and electrons are coupled by the interaction term \(\hat{V}_{eN}(\{\vec{r}\}, \{\vec{R}\})\) which prevents the separation of variables \(\{\vec{r}\}\) and \(\{\vec{R}\}\)

- we are forced to use some physically motivated approximation method

- the mass of nuclei is 3 - 4 orders of magnitude larger than that of electron

- the electrons feel only the instantaneous positions of the ions (and not their velocities), ions feel an average position of the electrons

- we introduce \(\hat{H}_e = \hat{T}_e(\{\vec{r}\}) + \hat{V}_{eN}(\{\vec{r}\}, \{\vec{R}\}) + \hat{V}_{ee}(\{\vec{r}\}), \{\vec{R}\}\) is external field (parameter)
we consider a new Schrödinger equation only for electrons

\[ \hat{H}_e \phi_e(\{\vec{r}\}, \{\vec{R}\}) = E_e(\{\vec{R}\}) \phi_e(\{\vec{r}\}, \{\vec{R}\}) \]

with eigenvalues \( E_e(\{\vec{R}\}) \) and eigenfunctions \( \phi_e(\{\vec{r}\}, \{\vec{R}\}) \)

**Born-Oppenheimer approximation continued**

we write the solution of the full problem as

\[ \phi_T(\{\vec{r}\}, \{\vec{R}\}) = \phi_e(\{\vec{r}\}, \{\vec{R}\}) \phi_N(\{\vec{R}\}) \]

and substitute this to the original Schrödinger equation

\[ \hat{T}_e(\{\vec{r}\}) \phi_e(\{\vec{r}\}, \{\vec{R}\}) \phi_N(\{\vec{R}\}) = \phi_N(\{\vec{R}\}) \hat{T}_e(\{\vec{r}\}) \phi_e(\{\vec{r}\}, \{\vec{R}\}) \]

\[ \nabla_{\vec{R}_I}^2 \phi_e(\{\vec{r}\}, \{\vec{R}\}) \phi_N(\{\vec{R}\}) = \phi_e(\{\vec{r}\}, \{\vec{R}\}) \nabla_{\vec{R}_I}^2 \phi_N(\{\vec{R}\}) \]

\[ + 2 \nabla_{\vec{R}_I} \phi_e(\{\vec{r}\}, \{\vec{R}\}) \nabla_{\vec{R}_I} \phi_N(\{\vec{R}\}) + \phi_N(\{\vec{R}\}) \nabla_{\vec{R}_I}^2 \phi_e(\{\vec{r}\}, \{\vec{R}\}) \]

\[ = E_{\text{tot}} \phi_e(\{\vec{r}\}, \{\vec{R}\}) \phi_N(\{\vec{R}\}) \]

**Born-Oppenheimer approximation continued**

- the term in \( \{ \} \) can be estimated to be \( \approx \frac{\mu}{M} E_e(\{\vec{r}\}, \{\vec{R}\}) \phi_N(\{\vec{R}\}) \) and can be neglected, since \( \frac{\mu}{M} \ll 1 \)

- we get an equation for the ionic variables \( \{\vec{R}\} \)

\[ \left\{ \hat{T}_N(\{\vec{R}\}) + E_e(\{\vec{R}\}) + \hat{V}_{NN}(\{\vec{R}\}) \right\} \phi_N(\{\vec{R}\}) = E_{\text{tot}} \phi_N(\{\vec{R}\}) \]

- we obtained a separation of ionic and electronic variables

- we solve the electronic Schrödinger equation for each position of the ions and find the spectrum \( E_{ek}(\{\vec{R}\}) \)

- we assume that the electrons are always in the ground state, \( k = 0 \)
• the energy $E_{e0}(\{\vec{R}\}) + \hat{V}_{NN}(\{\vec{R}\}) = V_{\text{eff}}(\{\vec{R}\})$ represents an effective interaction between the ions

• conceptually, we achieved an enormous simplification - 2 separate equations for ions and electrons, respectively, instead of one coupled

• on the technical level, both problems are still extremely difficult, further approximations are needed

**How to get the electronic ground state $E_{e0}(\{\vec{R}\})$ ?**

• by solving the electronic Schrödinger equation in some approximation (to be discussed in the later part of the course)

• examples: tight-binding approach, *density functional theory*, quantum Monte Carlo methods etc.

• more accurate but computationally expensive, does not allow simulation of large systems but *chemical reactions can be simulated*

• by assuming some physically motivated form for the interaction $V_{\text{eff}}(\{\vec{R}\}) = E_{e0}(\{\vec{R}\}) + \hat{V}_{NN}(\{\vec{R}\})$ - classical potential or force field, depending on some number of parameters

• the parameters can be determined e.g. by fitting to experimental results, results of quantum mechanical calculations for small systems, combination of both approaches

• less accurate but computationally cheap, large systems can be treated

• crucial limitation: *chemical reactions are essentially thrown away*

• also combination of both approaches can be used - QM/MM scheme, important small part of the system is treated accurately and the rest less accurately

**How to represent the interaction $V(\{\vec{R}\})$ between the ions**

• we have to find a suitable form to parametrize the function of all coordinates $\{\vec{R}_i\}$

• we write the function as sum over single particles, pairs of particles (2-body force), triples (3-body force), quadruples (4-body force), etc.

\[
V(\{\vec{R}_i\}) = \sum_i V_1(\vec{R}_i) + \sum_i \sum_{j>i} V_2(\vec{R}_i, \vec{R}_j) + \sum_i \sum_{j>i} \sum_{k>j>i} V_3(\vec{R}_i, \vec{R}_j, \vec{R}_k) + \ldots
\]
• $V_1(\vec{R}_i)$ external field

• $V_2(\vec{R}_i, \vec{R}_j) = V_2(|\vec{R}_i - \vec{R}_j|) = V_2(R_{ij})$ pair potential, gives rise to central force, typically the most important term

• $V_3(\vec{R}_i, \vec{R}_j, \vec{R}_k) = V_3(\vec{R}_i - \vec{R}_j, \vec{R}_i - \vec{R}_k)$ 3-body forces, often used for bond angles

• $V_4(\vec{R}_i, \vec{R}_j, \vec{R}_k, \vec{R}_l)$ 4-body forces, often used for torsions

Some simple examples

Example 1.  
• Lennard-Jones potential $V(R) = 4\epsilon \left( \left( \frac{\sigma}{R} \right)^{12} - \left( \frac{\sigma}{R} \right)^6 \right)$
  
  • pair potential with repulsive and attractive component
  
  • well suited for noble gases, e.g. Ar, Ne
  
  • often used in various systems

![Lennard-Jones potential for Ar](image)

Figure 1: Lennard-Jones potential for Ar

Example 2.  
• 3-body angular potential $V(\theta_{ijk}) = \frac{1}{2}k (\theta_{ijk} - \theta_0)^2$
  
  • often used in systems with directional bonds
How to solve the ionic problem?

- in principle, we have to do quantum statistical mechanics for the Hamiltonian
  \[ H = T + V(\{\vec{R}\}) = -\sum_i \frac{\hbar^2}{2M_i} \nabla_i^2 + V(\{\vec{R}\}) \]

- density matrix, partition function, observables
  \[ \rho = \frac{1}{Z} \exp(-\beta H) \]
  \[ Z = \text{Tr} \exp(-\beta H) = \sum_k \langle \Phi_k | \exp(-\beta H) | \Phi_k \rangle = \sum_k \exp(-\beta E_k) \]
  \[ \langle A \rangle = \text{Tr}[\rho A] = \frac{1}{Z} \sum_k \langle \Phi_k | A | \Phi_k \rangle \exp(-\beta E_k) \]

- matrix elements of T are easily calculated in the momentum eigenstates \(|\{\vec{P}\}\rangle\), matrix elements of V are easily calculated in the position eigenstates \(|\{\vec{R}\}\rangle\)

- since \([T, V] \neq 0\), we cannot replace \(\exp(-\beta H)\) by \(\exp(-\beta T) \exp(-\beta V)\)

3 Classical Statistical Mechanics

Classical Statistical Mechanics Approximation to the quantum case

- \(\exp(-\beta K) \exp(-\beta V) = \exp(-\beta (K + V + O([K, V])))\)
- \(\beta O([K, V]) \sim \frac{\hbar^2}{k_B T 2M_i}\)
• classical limit corresponds to $\hbar \to 0$

• we approach the same limit if the ionic masses $M_i$ and the temperature $T$ are large enough (or at least not too low)

• if $\exp(-\beta H) \approx \exp(-\beta K) \exp(-\beta V)$, we can simplify considerably

$$\text{Tr} \exp[-\beta (K + V)] \approx \sum_{\{\vec{R}\}} \langle \{\vec{R}\} | \exp(-\beta K) \sum_{\{\vec{P}\}} |\{\vec{P}\}\rangle \langle \{\vec{P}\}| \exp(-\beta V) \{\vec{R}\}\rangle$$

$$= \sum_{\{\vec{R}\}} \sum_{\{\vec{P}\}} \langle \{\vec{R}\}|\{\vec{P}\}\rangle \langle \{\vec{P}\}|\{\vec{R}\}\rangle \exp(-\beta \sum_i \frac{\vec{P}_i^2}{2M_i}) \exp(-\beta V(\{\vec{R}\}))$$

• $\langle \{\vec{R}\}|\{\vec{P}\}\rangle \langle \{\vec{P}\}|\{\vec{R}\}\rangle = \frac{1}{V_N}$ and for a large system we replace the summation by integration over $\{\vec{R}\}$ and $\{\vec{P}\}$

### Classical Statistical Mechanics continued

$$\text{Tr} \exp[-\beta (K + V)] \approx \frac{1}{\hbar^{3N} N!} \int \int d\{\vec{P}\} d\{\vec{R}\} \exp \left\{ -\beta \left( \sum_i \frac{\vec{P}_i^2}{2M_i} + V(\{\vec{R}\}) \right) \right\} = Z_{cl}$$

• we obtained classical statistical mechanics

$$\langle \mathcal{A} \rangle_{cl} = \frac{\int \int d\{\vec{P}\} d\{\vec{R}\} \mathcal{A}(\{\vec{P}\}, \{\vec{R}\}) \exp \left\{ -\beta \left( \sum_i \frac{\vec{P}_i^2}{2M_i} + V(\{\vec{R}\}) \right) \right\}}{\int \int d\{\vec{P}\} d\{\vec{R}\} \exp \left\{ -\beta \left( \sum_i \frac{\vec{P}_i^2}{2M_i} + V(\{\vec{R}\}) \right) \right\}}$$

• the above equations are starting point of all classical simulations

• in this course we will consider only the classical case (in most cases qualitatively and even quantitatively very good approximation)

• if necessary, quantum static properties can be calculated relatively simply (Path Integral techniques), but quantum dynamical properties are extremely difficult
How to proceed with simulations

1. choose a model for your system of interest
   - classical force field
   - quantum (ab-initio, semiempirical ...)

2. choose system size - the larger the system, the more information we get, but at a larger computational cost

3. choose the proper ensemble for the process/conditions of interest (NVT, NpT, ...)

4. choose the simulation method (MD, MC, Langevin, etc.)

5. choose the simulation length (the longer, the better)

6. perform the simulation (generate a trajectory)

7. process the raw information (extract the desired quantities), estimate the errors

8. visualize the dynamical processes of interest (movie is often the most spectacular outcome of a simulational study)

Part II
Molecular Dynamics (MD)

4 The ergodic hypothesis

Intuitive idea

- technique to compute equilibrium and dynamical (e.g. transport) properties of classical systems
- the main idea is simple and related to the experiment
- we prepare the sample in conditions of interest and let it evolve for sufficiently long time so that the measurable quantities do not anymore depend on time (equilibration)
• then we start measurement and measure for sufficiently long time to reach a required statistical accuracy

• if we can follow the time evolution of the system in computer, we may apply a similar procedure in simulation

• a great advantage over Monte Carlo (MC) is that MD gives access to physical dynamics of the system, while the MC dynamics is artificial (on the other hand, in MC one can construct non-physical moves which can speed-up the simulation)

• some formal justification of the MD procedure has to be provided

**The ergodic hypothesis (formal justification of the MD procedure)**

• we measure a quantity $A(\{\vec{P}\}, \{\vec{R}\})$ over a time interval $t$

• the average

$$\bar{A} = \frac{1}{t} \int_0^t d\tau A(\{\vec{P}(\tau)\}, \{\vec{R}(\tau)\})$$

depends also on the initial condition $(\{\vec{P}(0)\}, \{\vec{R}(0)\})$

• time average over a long trajectory with energy $E$ does not depend on the initial condition and is equivalent to a corresponding ensemble average

$$\bar{A} = \lim_{t \to \infty} \frac{1}{t} \int_0^t d\tau A(\{\vec{P}(\tau)\}, \{\vec{R}(\tau)\}) = \frac{\int_E d\{\vec{P}\} d\{\vec{R}\} A(\{\vec{P}\}, \{\vec{R}\})}{\int_E d\vec{P} d\vec{R}} = \langle A \rangle_{NVE}$$

• it is plausible but it cannot be proved for a general case

• in practice we usually just assume it is true

• e.g. in glasses it is not true and things become more complicated, even a long trajectory is not enough (ergodicity breakdown)

**Equivalence of ensembles**

• we want to calculate the properties in the canonical ensemble (NVT)

• MD procedure conserves energy and linear momentum and thus represents the microcanonical (NVEP) ensemble
• it can be shown that both ensembles provide the same averages in the thermodynamic limit \( N \to \infty \)

• for finite systems they differ by \( O(N^{-1}) \)

• fluctuations in different ensembles are essentially different but can be related

• replacing extensive quantities by intensive ones, e.g. volume \( V \) by pressure \( P \) or number of particles \( N \) by chemical potential \( \mu \), many other ensembles can be constructed, (NVT, NPT, \( \mu \)VT, etc.)

• defining an ensemble, at least one extensive variable has to be included, usually the number of particles \( N \) or the volume \( V \), so that the system size becomes well defined

5 The Verlet integrator

The Newton’s equations of motion

• potential energy of system consisting of N particles \( V(\{\vec{R}\}) \)

• force acting at particle \( i \) is \( \vec{F}_i = -\frac{\partial V(\{\vec{R}\})}{\partial \vec{R}_i} \)

• equation of motion \( M_i \ddot{\vec{R}}_i = \vec{F}_i \)

• assume (for simplicity) a pair potential \( \sum_i \sum_{j>i} V_2(R_{ij}) = \frac{1}{2} \sum_i \sum_{j\neq i} V_2(R_{ij}) \)

• the force at each particle becomes a sum of central forces

\[
\vec{F}_i = -\frac{\partial V(\{\vec{R}\})}{\partial \vec{R}_i} = -\sum_{j \neq i} \frac{\partial V_2(R_{ij})}{\partial \vec{R}_i} \frac{\partial R_{ij}}{\partial \vec{R}_i} = -\sum_{j \neq i} \left( \frac{\partial V_2(R_{ij})}{\partial R_{ij}} \frac{\vec{R}_{ij}}{R_{ij}} \right) \vec{F}_{ij}
\]

The Verlet integrator Verlet (1967)

• initial condition at time \( t = 0 \): coordinates \( \{\vec{R}(0)\} \), velocities \( \{\vec{V}(0)\} \)

• the initial condition defines a trajectory \( \{\vec{R}(t)\}, \{\vec{V}(t)\} \)
• we want to **numerically integrate** the Newton’s equations of motion step by step, with a time step $\delta t$

• discrete time evolution of the system

$$
\ldots, \{\vec{R}(t_{n-1})\} = \{\vec{R}(t_n - \delta t)\}, \{\vec{R}(t_n)\}, \{\vec{R}(t_{n+1})\} = \{\vec{R}(t_n + \delta t)\}, \ldots
$$

$$
\ldots, \{\vec{V}(t_{n-1})\} = \{\vec{V}(t_n - \delta t)\}, \{\vec{V}(t_n)\}, \{\vec{V}(t_{n+1})\} = \{\vec{V}(t_n + \delta t)\}, \ldots
$$

• we expand the positions $\{\vec{R}(t)\}$ to third order both forward and backward in time and use the equations of motion

$$
\vec{R}_i(t + \delta t) = \vec{R}_i(t) + \delta t\vec{V}_i(t) + \frac{\delta t^2}{2M_i}\vec{F}_i(t) + \frac{\delta t^3}{6}\vec{b}_i(t) + \mathcal{O}(\delta t^4)
$$

$$
\vec{R}_i(t - \delta t) = \vec{R}_i(t) - \delta t\vec{V}_i(t) + \frac{\delta t^2}{2M_i}\vec{F}_i(t) - \frac{\delta t^3}{6}\vec{b}_i(t) + \mathcal{O}(\delta t^4)
$$

**The Verlet integrator continued**

• summing the 2 equations together we eliminate the odd order terms

$$
\vec{R}_i(t + \delta t) = 2\vec{R}_i(t) - \vec{R}_i(t - \delta t) + \frac{\delta t^2}{M_i}\vec{F}_i(t) + \mathcal{O}(\delta t^4)
$$

• the equation is exact up to $\delta t^3$ and can be used to propagate the positions

• the velocities can be calculated

$$
\vec{V}_i(t) = \frac{1}{2\delta t} \left[ \vec{R}_i(t + \delta t) - \vec{R}_i(t - \delta t) + \mathcal{O}(\delta t^3) \right]
$$

• *but they lag one step $\delta t$ behind the positions* $\vec{R}_i(t + \delta t)$

• this might be inconvenient in some cases, we want to have both quantities at the same time

**The velocity Verlet scheme Swope, Andersen, Berens, Wilson 1982 [1]**

• reformulation of the original Verlet scheme (completely equivalent)
• $\vec{R}_i(t), \vec{V}_i(t), \vec{F}_i(t)$ are known

$$\vec{R}_i(t + \delta t) = \vec{R}_i(t) + \delta t\vec{V}_i(t) + \frac{\delta t^2}{2M_i} \vec{F}_i(t)$$

$$\vec{V}_i(t + \delta t) = \vec{V}_i(t) + \frac{1}{2}\delta t \left( \vec{A}_i(t) + \vec{A}_i(t + \delta t) \right)$$

• we first propagate positions by $\delta t$ and velocities by $\delta t/2$

$$\vec{R}_i(t + \delta t) = \vec{R}_i(t) + \delta t\vec{V}_i(t) + \frac{\delta t^2}{2M_i} \vec{F}_i(t)$$

$$\vec{V}_i(t + \frac{1}{2}\delta t) = \vec{V}_i(t) + \frac{1}{2}\delta t\vec{A}_i(t)$$

• in the middle we calculate the forces $\vec{F}_i(t + \delta t)$

• we complete the velocity move in the second step

$$\vec{V}_i(t + \delta t) = \vec{V}_i(t) + \frac{1}{2}\delta t\vec{A}_i(t + \delta t)$$

Basic molecular dynamics loop with velocity Verlet (Example of a Fortran code)

```fortran
main_md_loop: DO istep=1,nstep
  DO i = 1,n
    rx(i) = rx(i) + dt * vx(i) + dt**2 * fx(i) / (2*mass(i))
    ry(i) = ry(i) + dt * vy(i) + dt**2 * fy(i) / (2*mass(i))
    rz(i) = rz(i) + dt * vz(i) + dt**2 * fz(i) / (2*mass(i))
    vx(i) = vx(i) + dt * fx(i) / (2*mass(i))
    vy(i) = vy(i) + dt * fy(i) / (2*mass(i))
    vz(i) = vz(i) + dt * fz(i) / (2*mass(i))
  ENDDO
  CALL force(rx, ry, rz, fx, fy, fz, epot)
  DO i = 1,n
    vx(i) = vx(i) + dt * fx(i) / (2*mass(i))
    vy(i) = vy(i) + dt * fy(i) / (2*mass(i))
    vz(i) = vz(i) + dt * fz(i) / (2*mass(i))
  ENDDO
  CALL ek(vx, vy, vz, ekin)
  econs = epot + ekin
  PRINT istep, epot, ekin, econs
ENDDO main_md_loop
```
Conservation of energy

- the most important quantity is the Hamiltonian \( \mathcal{H} = \mathcal{K} + \mathcal{V} = \frac{\vec{P}^2}{2M} + V(\{\vec{R}\}) \)
- in Cartesian coordinates \( \vec{P}_i = M_i \vec{V}_i \)
- total energy \( \mathcal{E} = H = \frac{1}{2} M_i \vec{V}_i^2 + V(\{\vec{R}\}) \)

\[
\frac{d\mathcal{E}}{dt} = \frac{d\mathcal{K}}{dt} + \frac{d\mathcal{V}}{dt} = \sum_i M_i \vec{\dot{R}}_i \cdot \vec{\ddot{R}}_i - \sum_i \vec{\ddot{R}}_i \cdot \vec{\dot{R}}_i = 0
\]
- total energy is a constant of motion, thus has to be conserved (more later)
- fluctuation (typically of the order of \( 10^{-4} \)) is fine, but there should not be a systematic drift
- energy conservation is crucially dependent on the time step \( \Delta t \)
- typically \( \Delta t \approx 0.5 - 2 \text{ fs} \), but it depends on the typical frequencies in the system, particle masses and interparticle interactions

\[
\Delta t \ll f^{-1}_{\text{max}}
\]
- all approximations used have impact on the energy conservation

Integration algorithms general considerations

- to choose an appropriate algorithm, various criteria can be applied
- Lyapunov instability: even a small perturbation \( \vec{\epsilon} \) causes the trajectories to diverge extremely fast

\[
\begin{align*}
\vec{R}_i(t) &= f[\{\vec{R}(0)\}, \{\vec{\dot{P}}(0)\}; t] \\
\vec{R}'_i(t) &= f[\{\vec{R}(0)\}, \{\vec{\dot{P}}(0) + \vec{\epsilon}\}; t] \\
|\vec{R}'_i(t) - \vec{R}_i(t)| &= |\Delta \vec{R}_i(t)| \sim \epsilon \exp(\lambda t)
\end{align*}
\]
- no algorithm can provide exact trajectories for a long time, but here we are doing statistical mechanics, so we don’t need them (fortunately)
- energy conservation is extremely important
- one would like to use a long time step to reduce the number of force calculations
- algorithm should be time reversible, as the Newton’s equations are
• algorithms that preserve volume in phase space are likely to have good energy conservation

• Verlet-type algorithms are simple, time reversible, area-preserving and have a little long-time energy drift

6 Some technical issues

Periodic boundary conditions

often we want to calculate the bulk properties (thermodynamic limit)

• in a 3D system in a cubic box, a fraction of $\sim 6N^{-\frac{1}{3}}$ particles are on the surface

• e.g. for 1000 particles about 50 %, for $10^6$ particles still about 6 %

• surface contribution is too large even for big systems

• we apply periodic boundary conditions (PBC)

$$V(\{\vec{R}\}) = \frac{1}{2} \sum_{i,j,\vec{n}} v(|\vec{r}_{ij} + \vec{n}L|)$$

$\vec{n} = (k, l, m)$ is a vector of integers

• in the sum $\sum_{i,j,\vec{n}}$ the term with $i = j$ is excluded when $\vec{n} = 0$

Periodic boundary conditions continued

• cubic box is the simplest one, but it can be a general parallelepiped, or even truncated octahedron, rhombic dodecahedron, etc.

• PBC eliminate surface, but introduce other artefacts:
  – effectively a topology of a torus is imposed, particle leaves the box on one side and enters on the other
  – fluctuations with wavelength $\lambda > L$ are suppressed

• close to critical points, where the long wavelengths fluctuations are important, strong finite size effects are present and special techniques (finite size scaling) have to be applied to correct for that

• the boundary of the simulation box has no physical meaning
• instead, the shape and orientation of the periodic cell is fixed and determines the correlations between particles

• Fortran implementation for a cubic box of size \( L \): 
  \[
  R = R - L \times \text{ANINT}(R/L)
  \]

• with PBC the system is not rotationally invariant and angular momentum is not conserved

**Truncation of pair interactions (Cutoff)**

• we introduced an effectively infinite system but we don’t want to sum over infinite number of particles

• *minimum image convention* for short-range interactions: only the nearest image of each particle is considered

• finite number of interactions, but still \( \sim N(N - 1) \) operations

Further approximation: *spherical cutoff*

• *pair interactions* typically decay fast, e.g., van der Waals \( V(r) \sim R^{-6} \)

• *we count only neighbours with* \( R_{ij} \leq r_c \) and approximate the interaction with more distant particles by mean field (we assume \( g(r) = 1 \))
\[
V(\{\vec{R}\}) = \sum_{j>i, R_{ij} < r_c} V_2(R_{ij}) + V_{LR}
\]
\[
V_{LR} \text{ is the long range correction}
\]

Figure 4: Cutoff sphere with radius \(r_c\)

**Truncation of pair interactions (Cutoff) continued**

- for consistency with the minimum image convention, we must have \(r_c < L/2\) (for a cubic box) so that all particles within \(r_c\) are also within the box
- it is also possible to use \(r_c > L/2\) but one has to generate the images in neighbouring boxes (no minimum image convention)
- long-range correction \(V_{LR} = \frac{N_p}{2} \int_{r_c}^{\infty} dr 4\pi r^2 V_2(r)\)
- also for pressure there is a long-range correction
- Note: this can only be done if the potential decays more rapidly than \(r^{-3}\), so it cannot be used for Coulomb
- because of discontinuity of the potential at \(r_c\), energy is no longer conserved
- shifted potential: \(V_2^s(R_{ij}) = V_2(R_{ij}) - V_2(r_c)\) for \(R_{ij} \leq r_c\), \(V_2^s(R_{ij}) = 0\) for \(R_{ij} > r_c\)
• still, discontinuity in the forces remains (may cause a problem in MD)

• shifted-force potential: $V_{s}^{2}(R_{ij}) = V_{2}(R_{ij}) - V_{2}(r_{c}) - \left. \frac{dV_{2}(R_{ij})}{dR_{ij}} \right|_{R_{ij}=r_{c}} (R_{ij} - r_{c})$ for $R_{ij} \leq r_{c}$, $V_{s}^{2}(R_{ij}) = 0$ for $R_{ij} > r_{c}$

The force loop for a pair potential

! ** ZERO FORCES, POTENTIAL, VIRIAL **
DO  I = 1, N
   FX(I) = 0.0
   FY(I) = 0.0
   FZ(I) = 0.0
END DO
V = 0.0
W = 0.0
! ** OUTER LOOP BEGINS **
DO 200 I = 1, N - 1
   RXI = RX(I)
   RYI = RY(I)
   RZI = RZ(I)
   FXI = FX(I)
   FYI = FY(I)
   FZI = FZ(I)
   ! ** INNER LOOP BEGINS **
DO 199 J = I + 1, N
   RXIJ = RXI - RX(J)
   RYIJ = RYI - RY(J)
   RZIJ = RZI - RZ(J)
   RXIJ = RXIJ - ANINT (RXIJ/BOX)*BOX
   RYIJ = RYIJ - ANINT (RYIJ/BOX)*BOX
   RZIJ = RZIJ - ANINT (RZIJ/BOX)*BOX
   RIJSQ = RXIJ**2 + RYIJ**2 + RZIJ**2
   IF ( RIJSQ < RCUTSQ ) THEN
      SR2 = SIGSQ / RIJSQ
      SR6 = SR2 * SR2 * SR2
      SR12 = SR6 ** 2
      VIJ = SR12 - SR6
      V = V + VIJ
      WIJ = VIJ + SR12
      W = W + WIJ
   END IF
20
FIJ = WIJ / RIJSQ
FXIJ = FIJ * RXIJ
FYIJ = FIJ * RYIJ
FZIJ = FIJ * RZIJ
FXI = FXI + FXIJ
FYI = FYI + FYIJ
FZI = FZI + FZIJ
FX(J) = FX(J) - FXIJ
FY(J) = FY(J) - FYIJ
FZ(J) = FZ(J) - FZIJ
ENDIF

199  CONTINUE
! ** INNER LOOP ENDS **
FX(I) = FXI
FY(I) = FYI
FZ(I) = FZI

200  CONTINUE

Verlet list (useful trick how to save time)

- if we check all the particles in the box to find those with $r_{ij} < r_c$, we would evaluate $\frac{1}{2}N(N - 1)$ pair distances

- order $N^2$ algorithm would be too slow for a large system

- we define another radius $r_v = r_c + \Delta$

- for each particle we store a list of all particles within $r_v$

- to find particles within $r_c$, we search only within the list (order $N$ operation)

- particles move at finite speed so for a while the list remains up to date

- when a particle moved over distance $> \Delta$, we update the list (order $N^2$ operation)

- the optimal “skin” $\Delta$ has to found for each case
Cell lists (useful trick how to save time)

- we want to eliminate the order $N^2$ operation completely
- we split the system into cells with size slightly larger than $r_c$
- each particle in a given cell interacts only with 26 neighbouring cells (in 3D)
- algorithm is order $N$
- Verlet list and cell list can be combined
- different algorithms are optimal, depending on the conditions and system size $N$

Temperature in Molecular Dynamics

- generalized equipartition theorem for generalized coordinates $q_k$ and momenta $p_k$

\[ \langle p_k \frac{\partial \mathcal{H}}{\partial p_k} \rangle = k_B T, \quad \langle q_k \frac{\partial \mathcal{H}}{\partial q_k} \rangle = k_B T \]
• we assume Cartesian coordinates
• for momenta we get \( \langle \sum_{i=1}^{N} \frac{\vec{P}^2_i}{m_i} \rangle = 2\langle K \rangle = 3Nk_B T \)
• but not all degrees of freedom are independent
• with PBC, total linear momentum is conserved (3 global constraints), without PBC also angular momentum is conserved (6 global constraints)
• for rigid molecular models, we have a number of constraints on bond lengths and angles
• if the total number of constraints in the system is \( N_c \), we define an “instantaneous temperature”

\[
\mathcal{T} = \frac{1}{(3N - N_c)k_B} \sum_{i=1}^{N} \left| \frac{\vec{P}_i^2}{m_i} \right| \\
\langle \mathcal{T} \rangle = T
\]

**Temperature in Molecular Dynamics continued**

**Example 3.**
• Rigid \( H_2O \) molecule (SPC, TIP4P, \ldots)

• 3 atoms per molecule, 9 degrees of freedom - 3 internal constraints = 6
• PBC: 3 components of linear momentum conserved
• total number of independent degrees of freedom is \( 6N_{mol} - 3 \)
• in case of isolated cluster without PBC, we get \( 6N_{mol} - 6 \)
• for a system of rigid molecules, it is useful to check separately the translational temperature \( T_{tr} \) and rotational temperature \( T_{rot} \).

• in equilibrium we should have \( \langle T_{tr} \rangle = \langle T_{rot} \rangle = T \)

The Ewald summation method (How to treat the long-range Coulomb forces)

• we have a system consisting of point charges in a cubic box with PBC, charge neutrality \( \sum_i q_i = 0 \)

• Coulomb interaction \( V_{\text{Coul}} = \frac{1}{2} \sum_i q_i \phi(\vec{R}_i) \)

• potential \( \phi(\vec{R}_i) = \sum'_{j,\vec{n}} \frac{q_j}{|\vec{r}_{ij} + \vec{n}L|} \) (\( i = j \) is excluded when \( \vec{n} = 0 \), particle interacts with all its periodic images but not with itself)

• problem is that the charge density is a sum of \( \delta \) functions, \( \frac{1}{r} \) potential converges very slowly

• we artificially manipulate the charge density so that we can make use of screening

• we surround each charge \( q_i \) by a diffuse charge distribution of opposite sign such that total charge of the cloud exactly cancels \( q_i \)

• at each distance from the charge, the potential is only due to the unscreened part

• choosing the screening charge as Gaussian distribution, the potential rapidly decays to zero

The Ewald summation method (continued)

we want to calculate the energy of the original point charge distribution so we have to compensate for the screening charge

• \( \rho_G(r) = -q_i \left( \frac{\alpha}{\pi} \right)^{\frac{3}{2}} \exp(-\alpha r^2) \), for the moment \( \alpha \) is arbitrary

• the energy of screened charges is easily calculated in real space

• the energy of compensating charges is easily calculated in reciprocal (Fourier) space

• Poisson’s equation in real space \( -\nabla^2 \phi_p(r) = 4\pi \rho_p(r) \)

• in Fourier form \( k^2 \phi_p(\vec{k}) = 4\pi \rho_p(\vec{k}) \)

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The Ewald summation method (Real space part)

- we calculate potential from a single Gaussian distribution of charge
- we use Poisson’s equation and make use of the spherical symmetry

\[
-\nabla^2 \phi(r) = 4\pi \rho(r) \\
\frac{1}{r} \frac{\partial^2 r \phi_G(r)}{\partial r^2} = 4\pi \rho_G(r) \\
\phi_G(r) = -\frac{q_i}{r} \text{erf} \left( \sqrt{\alpha r} \right) \\
\text{erf}(x) \equiv \frac{2}{\sqrt{\pi}} \int_0^x \exp(-u^2) du \\
\phi_{\text{short-range}}(r) = \frac{q_i}{r} - \frac{q_i}{r} \text{erf} \left( \sqrt{\alpha r} \right) = \frac{q_i}{r} \text{erfc} \left( \sqrt{\alpha r} \right) \\
V_{\text{short-range}} = \frac{1}{2} \sum_{i \neq j}^N \frac{q_i q_j}{r_{ij}} \text{erfc} \left( \sqrt{\alpha r_{ij}} \right)
\]

- this can be summed with a relatively small cutoff

The Ewald summation method (Reciprocal space part)
we calculate potential \( \phi_p(\vec{r}) \) from a periodic sum \( \rho_p(\vec{r}) \) of Gaussian charge
distributions, the resulting potential energy is $V_p$

$$
\rho_p(\mathbf{r}) = \sum_{j=1}^{N} \sum_{n} q_j \left( \frac{\alpha}{\pi} \right)^{\frac{3}{2}} \exp \left[ -\alpha |\mathbf{r} - (\mathbf{r}_j + n\mathbf{L})|^2 \right]
$$

$$
\rho_p(\mathbf{k}) = \sum_{j=1}^{N} q_j \exp(-i\mathbf{k} \cdot \mathbf{r}_j) \exp\left(-\frac{k^2}{4\alpha}\right)
$$

$$
\phi_p(\mathbf{k}) = \frac{4\pi}{k^2} \sum_{j=1}^{N} q_j \exp(-i\mathbf{k} \cdot \mathbf{r}_j) \exp\left(-\frac{k^2}{4\alpha}\right) \text{ only for } \mathbf{k} \neq 0
$$

$$
\phi_p(\mathbf{r}) = \sum_{k \neq 0} \sum_{j=1}^{N} \frac{4\pi q_j}{k^2} \exp\left[i\mathbf{k} \cdot (\mathbf{r} - \mathbf{r}_j)\right] \exp(-\frac{k^2}{4\alpha})
$$

$$
V_p = \frac{1}{2} \sum_{i} q_i \phi_p(\mathbf{R}_i) = \frac{1}{2V} \sum_{k \neq 0} \sum_{i,j=1}^{N} \frac{4\pi q_i q_j}{k^2} \exp\left[i\mathbf{k} \cdot (\mathbf{r}_i - \mathbf{r}_j)\right] \exp(-\frac{k^2}{4\alpha})
$$

**The Ewald summation method (Correction term and final result)**

- we define $\rho(\mathbf{k}) \equiv \sum_{i=1}^{N} q_i \exp(i\mathbf{k} \cdot \mathbf{r}_i)$ and obtain

$$
V_p = \frac{1}{2V} \sum_{k \neq 0} \frac{4\pi}{k^2} |\rho(\mathbf{k})|^2 \exp\left(-\frac{k^2}{4\alpha}\right)
$$

- we assumed that the term corresponding to $\mathbf{k} = 0$ is zero which corresponds to *metallic boundary condition at infinity*

- the reciprocal space sum also converges fast and can be truncated

- we have to *subtract the interaction of charge $q_i$ with its own charge cloud*, potential in the center of the Gaussian is $\phi_G(r = 0) = 2q_i \left( \frac{\alpha}{\pi} \right)^{\frac{3}{2}}$

- total contribution of such interaction is a constant $\frac{1}{2} \sum_{i=1}^{N} q_i \phi_G(r = 0) = (\frac{\alpha}{\pi})^{\frac{3}{2}} \sum_{i=1}^{N} q_i^2$, independent on the particle positions

- final result is

$$
V_{Coul} = \frac{1}{2V} \sum_{k \neq 0} \frac{4\pi}{k^2} |\rho(\mathbf{k})|^2 \exp\left(-\frac{k^2}{4\alpha}\right) - \left( \frac{\alpha}{\pi} \right)^{\frac{3}{2}} \sum_{i=1}^{N} q_i^2 + \frac{1}{2} \sum_{i \neq j}^{N} \frac{q_i q_j}{r_{ij}} \text{erfc} \left( \sqrt{\alpha r_{ij}} \right)
$$

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Ewald summation and other methods for Coulomb interactions (algorithmic complexity)

- the parameter $\alpha$ can be optimized and then the desired accuracy $\epsilon$ fixes also the cutoffs $r_c$ and $k_c$ in real and reciprocal space
- the algorithmic complexity of Ewald summation is $\mathcal{O} \left( N^{3/2} \right)$
- typically we have apart from Coulomb also other short-range interactions and we want to use the same cutoff $r_c$ for both sums
- for a fixed cutoff $r_c$ one cannot use the optimal values of the parameters and Ewald summation scales as $\mathcal{O} \left( N^2 \right)$
- smooth particle-mesh Ewald technique (SPME) [2], uses Fast Fourier Transform (FFT) to deal with the reciprocal space part
- $SPME$ scales as $N \ln N$, typically used for large systems (proteins etc.)
- reaction-field method - kind of mean-field technique [3]
- fast multipole method
- none of the methods is perfect, some introduce spurious effects, detailed comparison of merits of various methods can be found in the literature

Initial conditions - positions and velocities

Initialization of particle positions

- in principle, we could start from any configuration, in thermodynamic equilibrium the history of the system has no influence
- in practice, metastability can be a problem and might require an excessively long equilibration time
- e.g. liquid is usually prepared by melting a crystal lattice at sufficiently high temperature
- we should avoid overlap of particles in the initial configuration
- when continuously changing conditions (e.g. $P, T$), we always use the final configuration of one run as an initial configuration for the next one

Initialization of particle velocities
• we extract the initial velocities from the Maxwell distribution

\[ P(v_{ia}) = \sqrt{\frac{m_i}{2\pi k_B T}} \exp \left( -\frac{m_i v_{ia}^2}{2k_B T} \right), \quad \alpha = x, y, z \]

• we correct the velocities to have \( \vec{P} = \sum_{i=1}^{N} m_i \vec{v}_i = 0 \)

• in case of isolated systems without PBC (e.g. clusters) we set also the total angular momentum to zero

**Equilibration**

• first, we need to set the temperature to the desired value

• generally, during equilibration we typically use rescaling of velocities to bring the system to the target temperature \( T \)

• every \( N_{\text{resc}} \) steps we check the temperature, if \( T > T \), we scale all the velocities by \( \alpha < 1 \), if \( T < T \), we use \( \alpha > 1 \)

• we wait until the properties become stable in time (no drift)

• *warning:* different quantities may have different equilibration times

**Measurement**

• after equilibration we start with accumulation of data for evaluation of averages - measurement

\[ \bar{A} = \frac{1}{\tau_{\text{tot}} - \tau_{eq}} \sum_{\tau > \tau_{eq}} \tau_{\text{tot}} A(\{\vec{P}(\tau)\}, \{\vec{R}(\tau)\}) \]

• for some quantities (e.g. pressure, stress tensor) the relation between the mechanical observable and its thermodynamic counterpart is not obvious - we have to find the estimator \( A(\{\vec{P}\}, \{\vec{R}\}) \) to be be averaged

• some quantities related to response functions are expressed in terms of fluctuations instead of averages

• some quantities are difficult to calculate and we do not evaluate them at every step - often every 10 steps or even more is sufficient
Figure 8: Typical equilibration of temperature in MD simulation

- the instantaneous values of the measured quantity fluctuate and the final average has a statistical error

- How large is the error?

- How long do we have to simulate to reach a given accuracy?

7 Averages and fluctuations

Pressure (mechanistic derivation)

- here we assume particles in a container (cubic) with walls (no PBC)

- generalized equipartition theorem for generalized coordinates $q_k$

$$\langle q_k \frac{\partial H}{\partial q_k} \rangle = k_B T$$

- we assume Cartesian coordinates

$$-\frac{1}{3} \left( \sum_{i=1}^{N} \vec{R}_i \cdot \nabla \vec{R}_i V(\{\vec{R}\}) \right) = \frac{1}{3} \left( \sum_{i=1}^{N} \vec{R}_i \cdot \vec{F}_{i}^{\text{tot}} \right) = -Nk_B T$$
\[ \vec{F}_{i}^{\text{tot}} = \vec{F}_{i}^{\text{ext}} + \vec{F}_{i}^{\text{int}} \]

- Internal virial \( W = \frac{1}{3} \sum_{i=1}^{N} \vec{R}_{i} \cdot \vec{F}_{i}^{\text{int}} \)

- The force \( \vec{F}_{i}^{\text{ext}} \) arises from the walls, can be assumed to be short-ranged and its contribution can be represented as pressure effect

\[ \frac{1}{3} \left( \sum_{i=1}^{N} \vec{R}_{i} \cdot \vec{F}_{i}^{\text{ext}} \right) = -\frac{1}{3} \int_{S} \vec{R} \cdot (Pd\vec{S}) = -\frac{1}{3} P \int_{V} \text{div}\vec{R}dV = -PV \]

**Pressure continued**

- \( P = V^{-1}(Nk_{B}T + \langle W \rangle) \) ideal gas contribution + excess contribution

- For pair interactions, we get a *translationally invariant form* \( W = \frac{1}{3} \sum_{i<j} \vec{R}_{ij} \cdot \vec{F}_{ij} = -\frac{1}{3} \sum_{i<j} w(R_{ij}) \), where \( w(R) = R \frac{dV_{2}(R)}{dR} \)

- With PBC it is crucial to use the translationally invariant form

- Homework: show that even with PBC one obtains the same result for the pressure

- *Hint:* use the thermodynamic identity \( P = -\frac{\partial F}{\partial V} \) and introduce a scaling factor \( L = V^{\frac{1}{3}} \), writing the coordinates as \( \vec{R} = L\vec{s} \)

- Stress tensor is defined as \( \sigma_{\alpha\beta} = \frac{\partial F}{\partial u_{\alpha\beta}} \), where \( u_{\alpha\beta} \) is the strain tensor

- \( -\sigma_{\alpha\beta} = V^{-1}(Nk_{B}T + \langle W_{\alpha\beta} \rangle) \), \( W_{\alpha\beta} \) is the virial tensor

- For pair potential \( W_{\alpha\beta} = \sum_{i<j} R_{ij} \alpha F_{ij} \beta = - \sum_{i<j} \frac{dV_{2}(R)}{dR} \frac{R_{ij} \alpha R_{ij} \beta}{R_{ij}} \) is symmetric

- In a simulation, *pressure has typically large fluctuations*, especially when covalent bonds are present

**Fluctuations (related to response functions)**

- *Specific heat*

- Canonical ensemble (NVT or NPT)
• NVT ($\mathcal{H}$ is Hamiltonian)

$$c_V = \left(\frac{\partial E}{\partial T}\right)_V, \quad \langle (\delta \mathcal{H})^2 \rangle = k_B T^2 c_V$$

• NPT ($H = E + PV$ is enthalpy)

$$c_P = \left(\frac{\partial H}{\partial T}\right)_P = \left(\frac{\partial(\mathcal{H} + PV)}{\partial T}\right)_P, \quad \langle (\delta \mathcal{H} + PV)^2 \rangle = k_B T^2 c_P$$

• in the microcanonical ensemble (NVE) $c_V$ is related to fluctuations of the potential energy $\mathcal{V}$ or kinetic energy $\mathcal{K}$

$$\langle (\delta \mathcal{V})^2 \rangle_{NVE} = \frac{3}{2} N(k_B T)^2 \left(1 - \frac{3Nk_B}{2c_V}\right)$$

**Fluctuations continued**

• isothermal compressibility $\beta_T = -V^{-1} \left(\frac{\partial V}{\partial P}\right)_T, \quad \langle (\delta V)^2 \rangle_{NPT} = V k_B T \beta_T$

• thermal expansion coefficient $\alpha_P = V^{-1} \left(\frac{\partial V}{\partial T}\right)_P, \quad \langle (\delta V)(H + PV) \rangle_{NPT} = V k_B T^2 \alpha_P$

• Parrinello-Rahman fluctuation formula for elastic constants (will be discussed later)

**Structural quantities - radial distribution function** $g(r)$

• provides basic insight into the microscopic structure of the system

• useful in liquids and solids

• reduced configurational distribution function

$$g^{(2)}(\vec{R}_1, \vec{R}_2) = \frac{N(N-1)}{\rho^2 Z} \int d\vec{R}_3 \int d\vec{R}_4 \ldots \int d\vec{R}_N \exp(-\beta V(\{\vec{R}\}))$$

• for $|\vec{R}| \to \infty, \quad g^{(2)}(\vec{R}_1, \vec{R}_2) \to 1$

• can be calculated as a histogram $g(\vec{R}) = \frac{V}{N^2} \langle \sum_i \sum_{j \neq i} \delta(\vec{R} - \vec{R}_i) \rangle$

• in isotropic liquids, $g^{(2)}(\vec{R}_1, \vec{R}_2) = g(|\vec{R}_1 - \vec{R}_2|) = g(R)$ - radial distribution function (RDF)

• in liquids, $g(R)$ typically has a pronounced first neighbour peak (first coordination shell) and a broader second neighbour peak

• in systems consisting of several kinds of atoms, we have several kinds of $g(R)$

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Radial distribution function - coordination number

- the position of the first minimum $R_{\text{min}}$ is used as a common criterion to define the first coordination shell

- coordination number is defined as $N_c = 4\pi \rho \int_0^{R_{\text{min}}} dR R^2 g(R)$

Example 4. Evolution of the oxygen-oxygen RDF in amorphous ice with increasing pressure

- at low pressure, the first and second shell are clearly separated (LDA)
- with increasing pressure the second peak gradually disappears (HDA)
- the interstitial peak around 3.3 Å becomes strong (VHDA)

![Radial distribution functions of various amorphous ices](image)

Figure 9: Radial distribution functions of various amorphous ices [4]

Radial distribution function continued

- in a simulation using PBC, we can calculate $g(R)$ only up to $r_{\text{max}} = \frac{L}{2}$ (in a cubic box)
• in a system with pair potentials, important quantities can be expressed through $g(R)$, e.g. potential energy $V$ and pressure $P$

$$V = \frac{1}{2} N \rho \int_0^\infty V_2(R) g(R) 4\pi R^2 dR$$

$$P = \rho k_B T - \frac{1}{6} \rho^2 \int_0^\infty w(R) g(R) 4\pi R^2 dR$$

• can be experimentally measured by X-ray or neutron scattering (related to structure factor $S(k)$)

$$S(k) = 1 + 4\pi \rho \int \frac{\sin(kR)}{kR} g(R) R^2 dR$$

• in simulation, we can in principle calculate almost any kind of structural quantity, but only few can be measured experimentally

**Spatial distribution function** $g(R)$ *(molecular systems)*

• $g(R)$ provides only information averaged over angular orientation

• for **molecular systems**, the orientation is important and in simulation we can study also **spatial distribution functions** $g(\vec{R}) = g(R,\vec{\Omega})$

**Time correlation functions - dynamical properties from MD trajectory**

• Fourier transform of various time correlation functions are related to spectroscopic quantities

$$C(\tau)_{AB} = \langle A(t + \tau) B(t) \rangle = \langle A(\tau) B(0) \rangle$$

• for $\tau \to \infty$, $C(\tau)_{AB} \to \langle A \rangle \langle B \rangle$

• normalized time autocorrelation function $c(\tau)_{AA} = \langle (\delta A)^2 \rangle^{-1} \langle \delta A(\tau) \delta A(0) \rangle$

• for $\tau \to 0$, $c(\tau)_{AA} \to 1$, for $\tau \to \infty$, $c(\tau)_{AA} \to 0$

• from MD trajectory of total length $\Delta t = M \delta t$ we calculate

$$\bar{C}(m\delta t)_{AB} = \frac{1}{M - m} \sum_{n=1}^{M-m} A(t_{n+m}) B(t_n)$$

• as $m$ increases, the accuracy decreases, a long trajectory is needed

• there are special algorithms to calculate the autocorrelation functions in efficient way

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Figure 10: Oxygen-oxygen spatial distribution function $g_{OO}(\vec{R})$ in high-density amorphous ice, $|\vec{R}| \approx 2.8$ Å

Figure 11: First coordination shell, regions of acceptor and donor water molecules are well visible
Velocity autocorrelation function (relation to transport properties)

- diffusion equation \( \frac{\partial c(r,t)}{\partial t} = D \nabla^2 c(r, t) \), \( c(r, t) \) is concentration
- diffusion constant \( D \) is a macroscopic transport coefficient
- *Einstein relation* for \( t \to \infty \)
  \[
  \frac{\partial \langle r^2(t) \rangle}{\partial t} = 6D
  \]
- mean square displacement is a microscopic property and can be calculated from MD \( \langle r^2(t) \rangle = \frac{1}{N} \sum_{i=1}^{N} \Delta \vec{R}_i(t)^2 \)
- for long times \( t \to \infty \), in liquid \( \langle r^2(t) \rangle \) grows linearly with \( t \), while in a solid it saturates (no diffusion)
- using \( \Delta \vec{R}_i(t) = \int_0^t d\tau \vec{V}_i(\tau) \) we get the Green-Kubo relation
  \[
  D = \frac{1}{3} \int_0^\infty \langle \vec{V}_i(\tau) \cdot \vec{V}_i(0) \rangle
  \]
- calculating the mean square displacement, we have to follow the true motion of the particles and not apply the PBC

Mean square displacement in crystal and in liquid

*Example 6.* SiO\(_2\): crystalline form (\( \alpha \)-quartz) vs. liquid

Classical force field

BKS potential for silica (van Beest, Kramer, van Santen (1990) [5])

\[
V_{ij} = \frac{q_i q_j e^2}{r_{ij}} + A_{ij} \exp(-b_{ij} r_{ij}) - c_{ij} r_{ij}^6
\]

<table>
<thead>
<tr>
<th>i-j</th>
<th>( A_{ij} ) [eV]</th>
<th>( b_{ij} ) [( \text{Å}^{-1} )]</th>
<th>( c_{ij} ) [eV ( \text{Å}^{-6} )]</th>
<th>Atomic charge</th>
</tr>
</thead>
<tbody>
<tr>
<td>O-O</td>
<td>1388.773</td>
<td>2.76</td>
<td>175.</td>
<td>-1.2</td>
</tr>
<tr>
<td>Si-O</td>
<td>18003.7572</td>
<td>4.87318</td>
<td>133.5381</td>
<td>2.4</td>
</tr>
</tbody>
</table>
Figure 12: Crystal at $T = 5000$ K

Figure 13: Melting at $T = 6000$ K
Velocity autocorrelation function (relation to vibrational spectra)

- in a harmonic system with spectrum \( \{\omega_j\} \)

\[
2\beta \int_{-\infty}^{\infty} dt \ e^{-i\omega t} \sum_{i=1}^{N} m_i \langle \vec{V}_i(t) \cdot \vec{V}_i(0) \rangle = 2\pi \sum_{j=1}^{3N} \left[ \delta(\omega + \omega_j) + \delta(\omega - \omega_j) \right]
\]

- density of vibrational states \( g(\omega) \) is related to the Fourier transform of the mass-weighted velocity autocorrelation function

- also useful to calculate the free energy in the quasiharmonic approximation, quantum effects can be approximately taken into account

- density of vibrational states can be measured by inelastic neutron scattering

- in a neutron scattering experiment not all kind of atoms are equally seen (different scattering cross section)

**Example 7. Velocity autocorrelation function of amorphous ice**

Force field - TIP4P model for water (Jorgensen, Chandrasekhar, Madura, Impey, Klein (1983) [6]) – rigid molecule, a dummy atom \( M \) with zero mass

\[
V_{ij} = \frac{q_i q_j e^2}{r_{ij}} + \frac{A_{ij}}{r_{ij}^{12}} - \frac{C_{ij}}{r_{ij}^6}
\]

\[
\begin{align*}
    r_{OH} & = 0.9572 \text{ Å} \\
    \theta_{HOH} & = 104.52^\circ \\
    r_{OM} & = 0.15 \text{ Å} \\
    q(O) & = 0 \\
    q(H) & = 0.52 \\
    q(M) & = -1.04 \\
    A_{OO} & = 6. \times 10^5 \text{ kcal Å}^{12}/\text{mol} \\
    C_{OO} & = 610 \text{ kcal Å}^6/\text{mol}
\end{align*}
\]

**Amorphous ice**

- classical TIP4P model (rigid molecules)

- different forms of amorphous ice at \( T = 80 \text{ K} \)

- different vibrational spectra reflect different structure and density
Figure 14: TIP4P model of water [6]

Figure 15: Velocity autocorrelation function of LDA ice
8 Estimation of statistical errors

Statistical error of correlated data

- we follow a (in principle) continuous evolution of the system and obtain a time series of $\tau_{\text{run}}$ instantaneous values for the observable $A$
- the average is $\langle A \rangle_{\text{run}} = \frac{1}{\tau_{\text{run}}} \sum_{\tau=1}^{\tau_{\text{run}}} A(\tau)$
- we would like to know the statistical error $\sigma(\langle A \rangle_{\text{run}})$ of $\langle A \rangle_{\text{run}}$
- if the data were uncorrelated, the error of $\langle A \rangle_{\text{run}}$ would be

$$\sigma^2(\langle A \rangle_{\text{run}}) = \frac{1}{\tau_{\text{run}}} \sigma^2(A)$$

$$\sigma^2(A) = \frac{1}{\tau_{\text{run}}} \sum_{\tau=1}^{\tau_{\text{run}}} (A(\tau) - \langle A \rangle_{\text{run}})^2$$

- subsequent data are typically (strongly) correlated, the autocorrelation time is unknown

---

Example 8.

Figure 16: Vibrational density of states for hydrogen atoms for various amorphous ices [4]
Estimation of statistical errors (block analysis)

- **block analysis** (Friedberg, Cameron (1970) [7])
  
  - we group the data in blocks of length $\tau_b$ and calculate all $N_b = \frac{\tau_{run}}{\tau_b}$ block averages $\langle A \rangle_b = \frac{1}{\tau_b} \sum_{\tau=1}^{\tau_b} A(\tau)$
  
  - we estimate the variance of the block averages $\sigma^2(\langle A \rangle_b) = \frac{1}{N_b} \sum_{b=1}^{N_b} (\langle A \rangle_b - \langle A \rangle_{run})^2$
  
  - for large $\tau_b$ the blocks become uncorrelated $\sigma^2(\langle A \rangle_b) = \sigma^2(A) \frac{s}{\tau_b}$
  
  - we define “statistical inefficiency”
    
    $$s = \lim_{\tau_b \to \infty} \frac{\tau_b \sigma^2(\langle A \rangle_b)}{\sigma^2(A)}$$
  
  - once we know $s$, we take the whole run as one block $\sigma(\langle A \rangle_{run}) = \sigma(A) \sqrt{\frac{s}{\tau_{run}}}$
  
  - long runs are needed to get a good estimate of $s$, $\tau_{run} \gg \tau_b \gg s$
  
  - in MC, one can use more efficient techniques to decrease the autocorrelation time

Estimation of statistical errors continued

**Example 9.** Volume from *NPT* simulation of $\alpha$-quartz at $T = 3500$ K, $p = 0$ run of 55 ps, value written every 10 steps

- $\sigma(V) = 30.8$
- $\tau_{run} = 5500$
- $s \approx 16$
- $\sigma(\langle V \rangle_{run}) = 30.8 \times \frac{16}{5500} = 1.66$
- $\langle V \rangle_{run} = 4287.93 \pm 1.66$
9 Liouville formulation of integration algorithms

Liouville formulation of time-reversible integrators - systematic way to derive integrators (Tuckerman, Berne, Martyna) (1992) [8]

- phase space point $\Gamma = (q_1, \ldots, q_N, p_1, \ldots, p_N)$

- Hamilton equations $\dot{q}_j = \frac{\partial H}{\partial p_j}, \dot{p}_j = -\frac{\partial H}{\partial q_j}$

- consider time evolution of a function $A(\{\bar{p}\}, \{\bar{q}\})$

$$\frac{dA}{dt} = \frac{d}{dt} A(\Gamma(t)) = \sum_{j=1}^{N} \left[ \dot{q}_j \frac{\partial A}{\partial q_j} + \dot{p}_j \frac{\partial A}{\partial p_j} \right]$$

- we define a linear operator

$$iL = \sum_{j=1}^{N} \left[ \frac{\partial H}{\partial p_j} \frac{\partial}{\partial q_j} - \frac{\partial H}{\partial q_j} \frac{\partial}{\partial p_j} \right]$$

$$-\frac{i}{\hbar} \frac{dA}{dt} = L.A$$
• formal solution of equations of motion is \( A(\Gamma, t) = U(t)A(\Gamma, 0) \) where 
\( U(t) = \exp(iLt) \)

**Liouville formulation of time-reversible integrators**

• \( iL = iL_1 + iL_2 \), where (in Cartesian coordinates)

\[
iL_1 = \sum_{j=1}^{N} \vec{F}_j \frac{\partial}{\partial \vec{P}_j}, \quad iL_2 = \sum_{j=1}^{N} \dot{\vec{R}}_j \frac{\partial}{\partial \vec{R}_j}
\]

• the two operators \( iL_1 \) and \( iL_2 \) do not commute, \([iL_1, iL_2] \neq 0\)

• Trotter factorization

\[
\exp((iL_1+iL_2)t) = \left[ \exp((iL_1+iL_2)\frac{t}{P}) \right]^P = \left[ \exp(\frac{iL_1\delta t}{2}) \exp(iL_2\delta t) \exp(\frac{iL_1\delta t}{2}) \right]^P + \mathcal{O}(P(\delta t)^3), \quad \delta t = \frac{t}{P}
\]

• time evolution can be thought of as iterative approximation of short-time propagator

\[
G(\delta t) = U_1(\frac{\delta t}{2})U_2(\delta t)U_1(\frac{\delta t}{2}) = \exp(\frac{iL_1\delta t}{2}) \exp(iL_2\delta t) \exp(\frac{iL_1\delta t}{2})
\]

• operators acting on different particles commute, \( G(\delta t) = \prod_{i=1}^{N} G_j(\delta t) \)

• \( G_j(\delta t) = \exp[\frac{\delta t}{2} \vec{F}_j \cdot \frac{\partial}{\partial \vec{P}_j}] \exp[\partial \dot{\vec{R}}_j \cdot \frac{\partial}{\partial \vec{R}_j}] \exp[\frac{\delta t}{2} \vec{F}_j \cdot \frac{\partial}{\partial \vec{P}_j}] \)

• we apply the propagator \( \exp[\frac{\delta t}{2} \vec{F}_j \cdot \frac{\partial}{\partial \vec{P}_j}] \exp[\partial \dot{\vec{R}}_j \cdot \frac{\partial}{\partial \vec{R}_j}] \exp[\frac{\delta t}{2} \vec{F}_j \cdot \frac{\partial}{\partial \vec{P}_j}] \) to the

state of the system \( \left( \vec{R}_j, \vec{P}_j \right) = \left( \vec{R}_j(t), \vec{P}_j(t) \right) \)

• \( \exp(c \frac{\partial}{\partial q}) f(q) = f(q + c) \) translation in phase space

\[
\begin{align*}
\exp\left[\frac{\delta t}{2} \vec{F}_j \cdot \frac{\partial}{\partial \vec{P}_j}\right] \left( \vec{R}_j, \vec{P}_j \right) &= \left( \vec{R}_j, \vec{P}_j + \frac{\delta t}{2} \vec{F}_j(\vec{R}_j) \right) = \left( \vec{R}_j, \vec{P}_j \right) \\
\exp\left[\partial \dot{\vec{R}}_j \cdot \frac{\partial}{\partial \vec{R}_j}\right] \left( \vec{R}_j, \vec{P}_j \right) &= \left( \vec{R}_j + \partial t \vec{R}_j, \vec{P}_j \right) = \left( \vec{R}_j, \vec{P}_j \right) \\
\exp\left[\frac{\delta t}{2} \vec{F}_j \cdot \frac{\partial}{\partial \vec{P}_j}\right] \left( \vec{R}_j, \vec{P}_j \right) &= \left( \vec{R}_j, \vec{P}_j + \frac{\delta t}{2} \vec{F}_j(\vec{R}_j) \right) = \left( \vec{R}_j, \vec{P}_j \right)
\end{align*}
\]
we have $\vec{F}_j(\vec{R}) = \vec{F}_j(t)$, $\vec{F}_j''(\vec{R}) = \vec{F}_j(t + \delta t)$

the advanced state is

$$\begin{pmatrix} \vec{R}_j(t + \delta t) \\ \vec{P}_j(t + \delta t) \end{pmatrix} = \begin{pmatrix} \vec{R}_j'' \\ \vec{P}_j'' \end{pmatrix} = \begin{pmatrix} \vec{R}_j + \delta t \dot{\vec{R}}_j + \frac{(\delta t)^2}{2M_j} \vec{F}_j(\vec{R}) \\ \vec{P}_j + \frac{\delta t}{2} \left[ \vec{F}_j(\vec{R}) + \vec{F}_j(t + \delta t) \right] \end{pmatrix}$$

Liouville formulation of time-reversible integrators (continued)

- we found the velocity Verlet algorithm

- the operator $L$ is Hermitian and therefore $U(t) = \exp(iLt)$ is a unitary operator $U^\dagger = U^{-1}(t) = U(-t)$

- unitarity implies time reversibility and phase-space volume conservation

- this is exactly true also for the approximate short-time propagator $G(\delta t) = U_1(\frac{\delta t}{2})U_2(\delta t)U_1(\frac{\delta t}{2}) = \exp\left(\frac{iL_2\delta t}{2}\right) \exp(iL_2\delta t) \exp\left(\frac{iL_1\delta t}{2}\right)$

- Jacobian of each of the 3 elementary transformations is 1 so the Verlet integration conserves phase-space volume (symplectic property)

- if the computer did not introduce numerical errors, Verlet integrator would exactly conserve the phase space volume and be perfectly time reversible even for a finite time step $\delta t$

- it can be shown that a quantity exists (pseudo-Hamiltonian) that is exactly conserved by the Verlet integrator and is close to the true Hamiltonian

- higher-order Trotter factorizations can be used to generate higher-order integration algorithms

More advanced MD methods

- methods described so far can be used for simple $NVE$ simulation of atomic systems, often we need better control over the thermodynamic state of the system

- in particular, in study of phase transitions it is useful to have control over intensive variables

- e.g., different phases can coexist at given $P, T$ but not at constant $V$ (phase separation)
• if a transition to a more stable phase with lower potential energy occurs (chemical reaction, phase transition), in NVE the temperature would increase in an unrealistic way

• we need a thermostat to dissipate the extra energy

• in Monte Carlo, temperature $T$ enters naturally, but in MD it can be also introduced

• all ensembles other than NVE introduce some artificial effects on the dynamics

• if proper dynamical properties are important, the NVE simulation is the most reliable one

10 Molecular Dynamics at constant temperature

Temperature, kinetic energy and ensembles

• temperature is related to kinetic energy

\[ T = \langle T \rangle = \frac{1}{(3N - N_c)k_B} \sum_{i=1}^{N} \left\langle \frac{\vec{p}_i^2}{m_i} \right\rangle \]

• but constant $T$ does not mean constant kinetic energy, in a finite system the instantaneous kinetic temperature $T$ fluctuates

• Ad-hoc schemes guarantee the constant average $T$ but do not generate any known ensemble
  – Velocity rescaling
  – Berendsen thermostat

• more sophisticated schemes sample the correct canonical ensemble
  – Andersen thermostat
  – Nosé-Hoover thermostat
  – Nosé-Hoover chain

• during equilibration, any method is good, but during measurement it’s better to sample a well-defined ensemble

• the choice of the suitable scheme depends on the system and conditions of interest

- mimics weak coupling to a heat bath with first-order kinetics
  \[ \frac{dT}{dt} = -\frac{T - T}{\tau} \]
- simple to implement, at each step the velocities are rescaled by a time-dependent scaling factor \( \lambda \)
  \[ \lambda = \left[ 1 + \frac{\delta t}{\tau_T} \left( \frac{T}{T} - 1 \right) \right]^{1/2} \]
- redistribution of energy between \( K \) and \( V \) causes \( \tau > \tau_T, \tau = \frac{2cV\tau}{kB}, f \) is the number of degrees of freedom
- the time constant \( \tau_T \) is typically chosen about \( 0.2 - 0.5 \) ps, \( \tau_T \gg \delta t \)
- it is useful to restrict \( \lambda \), e.g. \( 0.8 < \lambda < 1.25 \) to avoid instabilities
- very convenient in equilibration, especially when the initial configuration is far away from the target temperature \( T \)
- Berendsen thermostat does not generate any known ensemble, provides good averages but wrong fluctuations and does not conserve energy

Berendsen thermostat (continued)

- interpretation in terms of friction coefficient \( \zeta \):
  \[ \dot{P}_i = \vec{F}_i - \zeta \vec{P}_i \]
  \[ \zeta = \frac{1}{2\tau_T T}(T - \bar{T}) \]

**Warning:** the flying ice cube phenomenon (Harvey, Tan, Cheatham (1998)) [10]

- periodic rescaling of velocities can lead to severe violation of equipartition of energy
- gradual drain of kinetic energy from high-frequency to low-frequency modes
- after a simulation time of several 100 ps, the whole kinetic energy is transferred to global translation and rotation, causing large drop of temperature (freezing - flying ice cube)
- to avoid the effect, one has to periodically subtract the center-of-mass momentum of the system

- coupling to a heat bath via stochastic impulsive forces
- “stochastic collisions” - occasional re-assignment of velocities to a (randomly chosen) subset of particles
- velocities are drawn from the Maxwell-Boltzmann distribution at temperature $T$
- between the collisions, normal Newtonian MD is performed
- strength of the coupling is given by the frequency $\nu$
- distribution of the Poisson form

\[ P(t, \nu) = \nu \exp(\nu t) \]

of the intervals between the successive collisions

- the method generates canonical ensemble, static properties are well reproduced
- collisions disturb the dynamics in an unrealistic way so dynamical properties, e.g. the diffusion, are not reproduced correctly
- the method is rarely used

The Nosé-Hoover thermostat original idea (Nosé 1984) [12]

- an undisturbed deterministic dynamics would be preferred
- temperature is related to kinetic energy and thus to velocities
- time scaling factor $s$ is introduced to control temperature
- extended Lagrangian (Andersen (1980))

\[ L_{Nose} = \sum_{i=1}^{N} \frac{m_i}{2} s^2 \dot{\vec{R}}_i^2 - V(\{\vec{R}\}) + \frac{Q}{2} s^2 - \frac{f}{\beta} \ln s \]

- $Q$ is an effective mass associated with $s$, $p_s = Q\dot{s}$
- $f$ is the number of degrees of freedom
• the extended system dynamics has a conserved Hamiltonian

\[ H_{\text{Nose}} = \sum_{i=1}^{N} \frac{\dot{P}_{i}^2}{2m_{i}s^2} + V(\{\vec{R}\}) + \frac{p_{s}^2}{2Q} + \frac{f + 1}{\beta} \ln s \]

• microcanonical density \( \rho_{NVE,s}(\{\vec{R}\}, \{\vec{P}\}, s, p_{s}) \sim \delta(H_{\text{Nose}} - E_{s}) \)

• integrating out \( s, p_{s} \) one finds a proper canonical distribution for the variables \( \{\vec{R}\}, \{\vec{P}'\} = \{\vec{P}/s\} \)

The Nosé-Hoover thermostat reformulation of the Nosé scheme by Hoover (1985) [13]

• instead of \( s \) a friction coefficient \( \zeta \) was introduced

\[ \begin{align*}
\dot{\vec{R}}_{i} &= \frac{1}{m_{i}} \vec{P}_{i} \\
\dot{\vec{P}}_{i} &= \vec{F}_{i} - \zeta \vec{P}_{i} \\
\dot{\zeta} &= \frac{1}{Q} \left[ \sum_{i=1}^{N} \frac{\vec{P}_{i}^2}{m_{i}} - fk_{B}T \right] = \frac{fk_{B}}{Q}(T - T) \\
\dot{s} &= \frac{d\ln s}{dt} = \zeta
\end{align*} \]

• \( \dot{\zeta} \sim (T - T) \), unlike \( \zeta \sim (T - T) \) (Berendsen)

• conserved quantity is

\[ H_{\text{Nose}} = \sum_{i=1}^{N} \frac{\dot{P}_{i}^2}{2m_{i}} + V(\{\vec{R}\}) + \frac{\zeta^2Q}{2} + fk_{B}T \ln s = \mathcal{H} + \frac{\zeta^2Q}{2} + fk_{B}T \int \zeta dt \]

• friction: \( \mathcal{H}(t_2) - \mathcal{H}(t_1) \approx -fk_{B}T \int_{t_1}^{t_2} \zeta dt, \zeta > 0 \) cooling, \( \zeta < 0 \) heating

The Nosé-Hoover thermostat continued

• via equations of motion it can be demonstrated that the canonical ensemble is generated

• very different relaxation from Berendsen: second order (oscillatory) vs. first order (damped)
- not suitable for equilibration, if started from an off-equilibrium configuration, generates strong oscillations of temperature

- the “mass” \( Q \) is typically chosen in terms of the time constant \( \tau_T, Q = \frac{\tau_T^2}{4\pi^2} \), \( \tau_T^{-1} \) should not be larger than highest vibration frequency in the system

- non-Hamiltonian dynamics due to the frictional (velocity-dependent) forces, Liouville formalism allows to find explicitly time-reversible integrators

- still some effect on diffusion, though much smaller that in case of the Andersen thermostat

- Nosé-Poincaré thermostat (yet another formulation) recovers the Hamiltonian structure

**Nosé-Hoover chains**

- for small or stiff systems, Nosé-Hoover thermostat may have problems with ergodicity

- solution is a chain of thermostats (Martyna, Klein, Tuckerman (1992) [14])

\[
\begin{align*}
\dot{\vec{R}}_i &= \frac{\vec{P}_i}{m_i} \\
\dot{\vec{P}}_i &= \vec{F}_i - \frac{p_{\xi_1}}{Q_1} \vec{P}_i \\
\dot{\xi}_k &= \frac{p_{\xi_k}}{Q_k} \quad k = 1, \ldots, M \\
\dot{p}_{\xi_1} &= \left( \sum_{i=1}^{N} \frac{\vec{F}_i^2}{m_i} - f k_B T \right) - \frac{p_{\xi_2}}{Q_2} p_{\xi_1} \\
\dot{p}_{\xi_k} &= \left( \frac{p_{\xi_{k-1}}^2}{Q_{k-1}} - k_B T \right) - \frac{p_{\xi_{k+1}}}{Q_{k+1}} p_{\xi_k} \\
\dot{p}_{\xi_M} &= \left( \frac{p_{\xi_{M-1}}^2}{Q_{M-1}} - k_B T \right)
\end{align*}
\]

- Nosé-Hoover chain is able to generate canonical distribution even for a harmonic oscillator
11 Molecular Dynamics at constant pressure

NPT ensemble in simulations bulk systems

- classical partition function of the \( NPT \)-ensemble, where \( P \) is isotropic (hydrostatic) pressure reads

\[
Q(N, P, T) = \int dV e^{-\beta PV} Z(N, V, T)
\]

where

\[
Z(N, V, T) = \frac{1}{\Lambda^{3N} N!} \int d\mathbf{r}_1 \ldots d\mathbf{r}_N e^{-\beta U(\mathbf{r}_1, \ldots, \mathbf{r}_N)}
\]

- \( \Lambda = \left( \frac{2\pi \hbar^2}{mk_B T} \right)^{\frac{1}{2}} \) is the thermal wavelength

- general box with edges \( \vec{a}, \vec{b}, \vec{c} \), PBC

- \( 3 \times 3 \) matrix \( \mathbf{h} = (a, b, c) \)

- volume of the periodic box is \( V = \text{det} \mathbf{h} \)

- to eliminate rotations, we take \( \mathbf{h} \) symmetric or upper triangular

- 6 degrees of freedom remain

NPT ensemble in simulations (bulk systems)

- temperature is related to time scaling, pressure is related to space scaling

- rescaled particle vectors \( \mathbf{s} \) are defined via relation \( \mathbf{r} = \mathbf{h} \mathbf{s} \)

\[
Q(N, P, T) = \frac{1}{\Lambda^{3N} N!} \int d\mathbf{h} e^{-\beta P \text{det} \mathbf{h}} \left( \text{det} \mathbf{h} \right)^N \int d\mathbf{s}_1 \ldots d\mathbf{s}_N e^{-\beta U(\mathbf{hs}_1, \ldots, \mathbf{hs}_N)}
\]

- the integration over rescaled positions \( \mathbf{s}_1, \ldots, \mathbf{s}_N \) is performed over a cubic box of unit size

- important difference between liquids and solids: shape of the volume

- liquids have zero restoring force against shape fluctuations

- full sampling of \( \mathbf{h} \) would lead to large (and undesired) fluctuations
• in this case one restricts the box shape to cubic $h = L^1$ and allows only the volume to fluctuate

• solids (both crystalline and amorphous) do not flow under shear stress

• the box shape can be allowed to fluctuate and one can sample all 6 independent components of $h$

• the general formulation is valid both for MC and MD


• similar to Berendsen thermostat, first order relaxation to prescribed external pressure $P$

$$\frac{dp}{dt} = -\frac{p - P}{\tau_P}$$

• convenient for equilibration, when starting from initial configuration with pressure far from the target pressure $P$

• at every step coordinates and cell vectors are scaled by matrix $\mu$, $\vec{R}_i' = \mu \vec{R}_i$, $h' = \mu h$
• isotropic version (liquids):

\[
\mu = \left( 1 - \frac{\delta t \beta}{3 \tau_P} (P - p) \right) 1
\]

• \(\beta\) is the isothermal compressibility

• anisotropic version (crystals):

\[
\mu = 1 - \frac{\delta t \beta}{3 \tau_P} (P 1 - \pi)
\]

• does not generate a proper ensemble


• useful for liquids

• introduced an extended Lagrangian (extremely powerful idea)

• cubic simulation box with linear size \(L\) and scaled variables \(s = r/L\)

• the volume of the system \(V = L^3\) is considered as additional dynamical variable, a \(PV\) term is added to the Lagrangian

• the following Lagrangian is assumed:

\[
\mathcal{L} = \frac{1}{2} m V^2 \sum_{i=1}^{N} \dot{s}_i s_i - \sum_{i<j} u \left( V^\frac{3}{2} s_{ij} \right) + \frac{1}{2} M \dot{V}^2 - PV
\]

• we assume a pairwise-additive potential energy \(U = \sum_{i<j} u(r_{ij})\)

• the distance \(r_{ij}\) between particles is calculated within the PBC minimum image convention

• from the Langrangian the equations of motion for the scaled variables can be derived
The Andersen barostat

- equations of motion for the original variables
  \[
  \frac{dr_i}{dt} = \frac{p_i}{m} + \frac{1}{3} r_i \frac{d \ln V}{dt}
  \]
  \[
  \frac{dp_i}{dt} = -\sum_{j \neq i} \hat{r}_{ij} u'(r_{ij}) - \frac{1}{3} p_i \frac{d \ln V}{dt}
  \]
  \[
  M \frac{d^2 V}{dt^2} = -P + \frac{1}{V} \left( \frac{2}{3} \sum_i p_i \cdot p_i - \frac{1}{3} \sum_{i<j} r_{ij} u'(r_{ij}) \right),
  \]
  where \( \hat{r}_{ij} \) denotes a unit vector in the direction of \( r_{ij} \)

- volume fluctuations are driven by the difference between the externally applied pressure \( P \) and internal pressure of the system

- dynamics generates the isoenthalpic-isobaric \((N, P, H)\) ensemble

- second order dynamics - oscillatory character

- choice of the artificial barostat mass \( M \): time scale \( \tau_V \) of the volume fluctuations \( \tau_V \approx L/c, c \) is the sound velocity in the bulk system

The Parrinello-Rahman barostat (Parrinello and Rahman (1980) [15])

- crystals are anisotropic and resist also shear deformations

- Andersen method not suitable

- as function of pressure, crystals may undergo structural transitions

- if the final phase in unknown, simulation may provide a prediction

- in small systems, defects are too costly

- the box matrix \( h \) has to be commensurate to the crystal unit cell \( u \)

- \( h = um \), where \( m \) is an integer matrix

- if a structural phase transition has to be simulated, the box has to be commensurate with the initial as well as with the final unit cell

- in the Parrinello-Rahman algorithm the box can adapt to the structure
The Parrinello-Rahman barostat

- all elements of the general box matrix $h$ are treated as dynamical variables
- scaled particle vectors $s_i$ defined as $r_i = hs_i$
- the distance between particles $i$ and $j$ is given by $r_{ij}^2 = (s_i - s_j)^T G (s_i - s_j)$ where $G = h^T h$ is the metric tensor
- $\sigma = V h^T h$ where $V = \text{det} h$ is the volume of the box
- extended Lagrangian with a $PV$ term

$$\mathcal{L} = \frac{1}{2} \sum_i m_i \dot{s}_i^T G \dot{s}_i - \sum_{i<j} u(r_{ij}) + \frac{1}{2} W \text{Tr} \dot{h}^T \dot{h} - PV$$

- $W$ is a fictitious mass, in equilibrium its value is in principle irrelevant
- choice of the artificial barostat mass $W$: time scale $\tau_V$ of the volume fluctuations $\tau_V \approx L/c$, $c$ is the sound velocity in the bulk system
- $W$ affects the dynamics and in case of structural transitions, the final structure may be dependent on $W$
The Parrinello-Rahman barostat

- equations of motion for $s_i$ and box $h$

$$m_i \ddot{s}_i = - \sum_{j \neq i} \frac{u'(r_{ij})}{r_{ij}} (s_i - s_j) - m_i G^{-1} \ddot{G} s_i$$

$$W \ddot{h} = (\pi - P) \sigma,$$

where

$$\pi = \frac{1}{V} \left( \sum_i m_i v_i v_i - \sum_{i<j} \frac{u'(r_{ij})}{r_{ij}} r_{ij} r_{ij} \right)$$

is the internal pressure tensor of the system and $v_i = h \dot{s}_i$

- the scheme generates the isoenthalpic-isobaric $(N, P, H)$ ensemble

- second order dynamics - oscillatory character

- can be generalized from hydrostatic pressure $P$ to the case of general anisotropic constant stress $S$

- simulation under conditions of e.g., uniaxial tension or compression, shear load, etc. is possible

- following the evolution of the box at different temperatures, thermal expansion can be studied

Parrinello-Rahman fluctuation formula calculation of elastic constants

- $h_0$ is the reference box (equilibrium average)

- the strain tensor $\epsilon = \frac{1}{2} (h_0^{-1} h^T h h_0^{-1} - 1)$

- the tensor of isothermal elastic moduli is defined as $C_{kl,ij} = (\partial S_{kl} / \partial \epsilon_{ij})_T$

where $S_{kl}$ is the stress tensor in the system

- the tensor $C_{kl,ij}$ can be evaluated from correlations of fluctuations of different components of $\epsilon$

- the Parrinello-Rahman fluctuation formula (1982)

$$\langle \Delta \epsilon_{ij} \Delta \epsilon_{kl} \rangle_{NPT} = \frac{k_B T}{(V)} (C)^{-1}_{ij,kl}$$

- typically, a long run is needed to converge well

- alternative is to simulate at different pressures and calculate elastic constants from finite differences of strain or vice versa
Simulation of structural transitions in solids

- main application of the Parrinello-Rahman technique
- applied to many systems, with classical potentials and ab-initio
- structural transitions often 1st order (no group-subgroup relation)
- PBC suppress nucleation
- collective transition mechanism - large barrier \( \Delta G \)
- if \( \Delta G \gg k_B T \), barrier crossing will take too long time
- overpressurization of the system to the point of mechanical instability \( \dot{p} > p_{eq} \), hysteresis
- some phases may be skipped
- time scale gap

First order transition at equilibrium

\[ p = p_{eq} \]

\[ \Delta G \]

Figure 20: Structural transition at equilibrium pressure

**Constant-pressure simulation of finite objects**

- finite objects under pressure, no PBC
- clusters, nanocrystals, big molecules, fullerenes, onion structures, nanotubes, etc.
- *pressure-transmitting liquid* method (real physical pressure-bath)
- methods based on *PV term*, requiring estimation of volume \( V = V(\{\mathbf{R}_i\}) \)
Figure 22: The E-V curves for silicon from the tight-binding model [16]

Figure 23: The time evolution of the temperature
Si, 512 atoms, P=45 GPa, T=600 K

Figure 24: The time evolution of the box lengths and angles

Figure 25: Si$_{35}$H$_{36}$ cluster at 25 GPa (a), 35 GPa (b), and 5 GPa (c). From Ref.[17]


- Lagrangian of the extended system cluster + liquid
  \[ \mathcal{L} = \frac{1}{2} \sum_i m_i \dot{R}_i^2 - \phi(\{R_i\}) \]
  \[ + \frac{1}{2} \sum_i m \dot{X}_i^2 - \sum_{I<i,J} V_{L-L}(|X_I - X_J|) - \sum_{i,J} V_{C-L}(|R_i - X_J|) \]

- if $V_{\text{liq}} \gg V_{\text{cluster}}$, liquid acts as pressure reservoir
- the whole system is simulated in a large box with PBC (constant volume)
- interaction potential for the artificial liquid has to be chosen
- simple choice - purely repulsive soft-sphere potential $V_{L-L} = \epsilon \left( \frac{\sigma_{L-L}}{r} \right)^{12}$
- pressure $P$ depends on density $\frac{N_{\text{liq}}}{V_{\text{liq}}}$, $\sigma_{L-L}$ and temperature $T$
- $\sigma_{L-L}$ can be tuned to obtain the desired pressure
- to transmit hydrostatic pressure the liquid has to flow sufficiently fast
- the liquid must be away from crystallization region
- typically a large number of liquid particles is needed
Pressure-transmitting liquid method (continued)

- *liquid-cluster interaction* can be chosen in the same form \( V_{C-L} = \epsilon \left( \frac{\sigma_{C-L}}{r} \right)^{12} \)
- \( \sigma_{C-L} \) has to be strong enough to prevent possible penetration of liquid particles inside the cluster
- the interface tension cluster-liquid gives contribution to pressure for curved surfaces
- \( \sigma_{C-L} \) should not be too large
- liquid particle mass \( m \) - not too large (fast liquid), not too small (reasonably large time step)
- for \( V_{L-L} \) very short cutoff can be used, small computational load

![Figure 26: Carbon nanotube in a pressure-transmitting liquid](image-url)
Methods based on estimation of volume

- Lagrangian with the $PV$ term

$$\mathcal{L} = \sum_{i} \frac{\vec{R}_i^2}{2m_i} - \Phi(\{\vec{R}_i\}) - P_{ext}V(\{\vec{R}_i\})$$

- volume is not equal to that of the simulation cell, but a function of coordinates $V(\{\vec{R}_i\})$

- generalized equipartition theorem $\langle q_k \frac{\partial H}{\partial q_k} \rangle = k_B T$

$$3Nk_B T = \langle \sum_{i=1}^{N} \vec{R}_i \cdot \left\{ \nabla_{\vec{R}_i} \Phi(\{\vec{R}\}) + P_{ext} \nabla_{\vec{R}_i} V(\{\vec{R}\}) \right\} \rangle$$

- $V(\{\vec{R}_i\})$ is a homogeneous function of degree 3

- Euler’s theorem $\sum_{i}^{N} \vec{R}_i \cdot \nabla_{\vec{R}_i} V(\{\vec{R}_i\}) = 3V$

- virial theorem

$$P_{ext} = \frac{1}{\langle V \rangle} \left( Nk_B T + \frac{1}{3} \langle \sum_{i} \vec{R}_i \cdot \vec{F}_i \rangle \right) = P_{int}$$

Methods based on estimation of volume (continued)

Problem - no unique definition of volume $V(\{\vec{R}_i\})$

- various ways to estimate $V(\{\vec{R}_i\})$

- partitioning of volume (I)

- average interparticle distance (II)

- radius of gyration (III) from moment of inertia - approximation by ellipsoid

- forces from external pressure act on all atoms (should act only on the surface atoms)

Methods based on triangulation of surface (IV)

- force $d\vec{F} = -P_{ext}d\vec{S}$ can be directly applied to surface atoms

- triangulation also allows to estimate the volume

$$\frac{1}{3} \int_{S} \vec{R} \cdot d\vec{S} = \frac{1}{3} \int_{V} \text{div} \vec{R} \, dV = \frac{1}{V}$$

- for review, see Ref.[18]
12 Molecular Dynamics of molecular systems

Molecular systems

- molecules have *hard internal degrees of freedom*, related to vibrations
- vibrational frequencies for light atoms reach above 3000 cm\(^{-1}\)
- in principle, one can integrate but very small time step would be required
- still, the internal degrees of freedom would require *quantum* treatment
- intramolecular forces are typically an order of magnitude larger than the intermolecular ones
- the amplitude of vibration is small compared to molecular dimensions
- a practical solution is to *freeze* the hard degrees of freedom completely by imposing constraints
- for example, diatomic molecule \(\sigma(\vec{R}_1, \vec{R}_2) = \vec{R}_{12} \cdot \vec{R}_{12} - d_0^2 = 0\)
- bond constraints, angle constraints
- *completely rigid or partially flexible* models
- in MC, implementation of constraints is complicated
- in MD it is fairly simple

Rigid molecules Quaternions (Evans (1977) [19])

- translational motion of center of mass \(\vec{p}_i = \sum_j \vec{f}_{ji}\)
- rotation around the center of mass \(\vec{L} = \tau_i = \sum_a (\vec{r}_{ia} - \vec{r}_i) \times \vec{f}_{ia} = \sum_a \vec{a}_{ia} \times \vec{f}_{ia}\)
- the local body frame is chosen such that rotational inertia tensor \(I_{\alpha\beta} = \frac{1}{2} \sum_a m_a r_{aa} r_{a\beta}\) is diagonal
- \(\vec{e}_l = R\vec{e}_s\), unitary rotational matrix \(R\) transform from the space frame to the local frame
- \(R\) can be expressed in terms of the Euler angles, but *singularities* arise
- *quaternions* (4D unit vectors) are a practical alternative
\( q = [q_0, q_1, q_2, q_3]^T, q_0^2 + q_1^2 + q_2^2 + q_3^2 = 1 \)

\[
\mathbf{R} = \begin{pmatrix}
q_0^2 + q_1^2 - q_2^2 - q_3^2 & 2(q_1q_2 + q_0q_3) & 2(q_1q_3 - q_0q_2) \\
2(q_1q_2 - q_0q_3) & q_0^2 - q_1^2 + q_2^2 - q_3^2 & 2(q_2q_3 + q_0q_1) \\
2(q_1q_3 + q_0q_2) & 2(q_2q_3 - q_0q_1) & q_0^2 - q_1^2 - q_2^2 + q_3^2
\end{pmatrix}
\]

- The Verlet integrator can be written for the quaternions, no singularities

**Constraints**

- Often we constrain only the hardest degrees of freedom, the bond lengths, and let angles and torsional angles fluctuate
- The method of constraints can be used for completely rigid as well as for partially flexible molecules
- In general, \( M \) constraint relations \( \sigma_\alpha(\{\vec{R}_i\}) = 0, \ \alpha = 1, \ldots, M \)
- Lagrangian \( L' = L - \sum_\alpha \lambda_\alpha \sigma_\alpha(\{\vec{R}_i\}) \) with undetermined Lagrange multipliers \( \lambda_\alpha \) is introduced
- Equations of motion

\[
\vec{g}_i = \sum_\alpha \lambda_\alpha \nabla_{\vec{R}_i} \sigma_\alpha \\
m_i \ddot{\vec{R}}_i = \vec{f}_i + \vec{g}_i
\]

- \( \lambda_\alpha \) have to be determined for each time \( t \) so that the constraints are obeyed
- Even with exact values of \( \lambda_\alpha \), the discrete time integration will satisfy the constraints only approximately and the evolution will be unstable
- Constraints are part of the model and should be satisfied rigorously

**Constraints (practical scheme)** Ryckaert, Ciccotti, Berendsen (1977) [20]

- Constraints are imposed exactly at each time step
- Direct propagation with the Verlet integrator violates the constraints

\[
\vec{R}_i^n(t + \delta t) = 2\vec{R}_i(t) - \vec{R}_i(t - \delta t) + \frac{\delta t^2}{M_i} \vec{F}_i(t) \\
\vec{R}_c^n(t + \delta t) = \vec{R}_c^n(t + \delta t) + \frac{\delta t^2}{M_i} \sum_\alpha \lambda_\alpha \nabla_{\vec{R}_c} \sigma_\alpha(t)
\]
• the “corrected” positions $\vec{R}_c(t + \delta t)$ are substituted into the constraint equations $\sigma_\alpha(\{\vec{R}_c(t + \delta t)\}) = 0$

• solution is found by linearizing and iteration

$$\sigma_c^\alpha(t + \delta t) = \sigma_u^\alpha(t + \delta t) + \sum_{i=1}^{N} \nabla_{\vec{R}_i} \sigma_u^\alpha(t + \delta t) \cdot [\vec{R}_c(t + \delta t) - \vec{R}_u^\alpha(t + \delta t)] = 0$$

$$\sigma_u^\alpha(t + \delta t) = -\sum_{\beta=1}^{M} \sum_{i=1}^{N} \frac{\delta t^2}{M_i} \nabla_{\vec{R}_i} \sigma_u^\alpha(t + \delta t) \cdot \nabla_{\vec{R}_i} \sigma_\beta(t) \lambda_\beta$$

Constraints (practical scheme) The SHAKE algorithm

• the system of linear equations $A\lambda = b$ can be solved for $\lambda_\alpha$

• new estimate of $\vec{R}_u^\alpha(t + \delta t)$ is computed and iterated until convergence

$$\sigma_k^\alpha(t + \delta t) = -\sum_{\beta=1}^{M} \sum_{i=1}^{N} \frac{\delta t^2}{M_i} \nabla_{\vec{R}_i} \sigma_k^\alpha(t + \delta t) \cdot \nabla_{\vec{R}_i} \sigma_\beta(t) \lambda_\beta^{(k+1)}$$

• solving linear system by matrix inversion is expensive

• SHAKE algorithm avoids matrix inversion by updating one constraint at a time

$$\sigma_k^\alpha(t + \delta t) = -\sum_{i=1}^{N} \frac{\delta t^2}{M_i} \nabla_{\vec{R}_i} \sigma_k^\alpha(t + \delta t) \cdot \nabla_{\vec{R}_i} \sigma_\alpha(t) \lambda_\alpha^{(k+1)}$$

• after all constraints are updated, a new iteration cycle is started until the prescribed accuracy is reached

• RATTLE (Andersen 1983) - similar algorithm for velocity Verlet integrator [21]

• idea of constrained dynamics is useful in many other situations

Multiple time steps Martyna, Tuckerman, Tobias, Klein (1996) [22]

• there are subtle questions related to averages calculated with constraints (different distribution functions)
\[ \vec{F} = \vec{F}_{\text{intra}} + \vec{F}_{\text{inter}}, \quad \vec{F}_{\text{intra}} \text{ is large but cheap to calculate, } \vec{F}_{\text{inter}} \text{ is smaller but more expensive to calculate} \]

\[ \vec{F}_{\text{inter}} \text{ hardly change on the time scale of the intramolecular vibrations} \]

\[ \text{intuitively, one could use different time step for } \vec{F}_{\text{inter}} \text{ and } \vec{F}_{\text{intra}} \]

\[ \text{NVE ensemble, Liouville formalism: } iL = iL_r + iL_p = \hat{V} \frac{\partial}{\partial \vec{R}} + \frac{\vec{F}}{m} \frac{\partial}{\partial \vec{V}} \]

\[ \text{we split } iL_p \text{ into two parts: } iL_{\text{intra}} = \frac{\vec{F}_{\text{intra}}}{m} \frac{\partial}{\partial \vec{V}}, \quad iL_{\text{inter}} = \frac{\vec{F}_{\text{inter}}}{m} \frac{\partial}{\partial \vec{V}} \]

\[ \text{Trotter expansion with two time steps: long } \Delta t \text{ and short } \delta t = \frac{\Delta t}{n} \]

\[ \exp(iL\Delta t) = \exp\left(i\left(L_{\text{intra}} + L_{\text{inter}} + L_r\right)\Delta t\right) \]

\[ \approx \exp\left(iL_{\text{inter}}\frac{\Delta t}{2}\right) \exp\left(i\left(L_{\text{intra}} + L_r\right)\Delta t\right) \exp\left(iL_{\text{inter}}\frac{\Delta t}{2}\right) \]

\[ \approx \exp\left(iL_{\text{inter}}\frac{\Delta t}{2}\right) \left[ \exp\left(i\left(L_{\text{intra}} + L_r\right)\frac{\Delta t}{n}\right) \right]^n \exp\left(iL_{\text{inter}}\frac{\Delta t}{2}\right) \]

**Multiple time steps (continued)**

\[ \exp(iL\Delta t) \approx \]

\[ \exp\left(iL_{\text{inter}}\frac{\Delta t}{2}\right) \left[ \exp\left(iL_{\text{intra}}\frac{\delta t}{2}\right) \exp\left(iL_r\delta t\right) \exp\left(iL_{\text{intra}}\frac{\delta t}{2}\right) \right]^n \exp\left(iL_{\text{inter}}\frac{\Delta t}{2}\right) \]

\[ \text{we first propagate the velocities by } \frac{\Delta t}{2} \text{ with } \vec{F}_{\text{inter}} \text{ only} \]

\[ \text{we follow by } n \text{ steps propagation by ordinary velocity Verlet integrator, using only } \vec{F}_{\text{intra}} \text{ and time step } \delta t \]

\[ \text{at the end we again propagate the velocities by } \frac{\Delta t}{2} \text{ with } \vec{F}_{\text{inter}} \text{ only} \]

\[ \text{the expensive force } \vec{F}_{\text{inter}} \text{ is calculated only at intervals of } \Delta t \]

\[ \text{scheme is by construction time-reversible} \]

\[ \text{provides an alternative to the use of constraints} \]

\[ \text{computational efficiency is comparable} \]

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13 Other schemes

Hybrid Monte Carlo Duane, Kennedy, Pendleton, Roweth (1987) [23]

- in MC it is hard to use collective moves, because of low acceptance ratio
- NVE MD generates naturally configurations with the same energy
- MD propagation can be used to generate trial moves which are accepted or rejected by Metropolis algorithm - *hybrid Monte Carlo*
- long time step (non-conservation of energy) can be used, provided the algorithm is time reversible, it is still a valid trial move
- useful for models with expensive potential calculation (e.g. ab-initio simulations)
- MD with *cheap approximate potential* is used to generate trial move
- Metropolis criterion with the *true potential* is used to decide the acceptance

Part III

Free energy calculations and phase diagram calculations

Free energy calculations

- free energy $F$ is a *very important quantity* in physics and chemistry

$$F(N,V,T) = -\frac{1}{\beta}\ln Z(N,V,T)$$

$$Z(N,V,T) = \frac{1}{\Lambda^{3N}N!} \int d\mathbf{r}_1 \ldots d\mathbf{r}_N e^{-\beta U(\mathbf{r}_1, \ldots, \mathbf{r}_N)}, \quad \Lambda = \left( \frac{2\pi \hbar^2}{mk_B T} \right)^{\frac{1}{2}}$$

- determines the *relative stability* of the phases
- calculation of *phase diagrams* (first-order transitions)
- understanding of *activated events*, phase transitions, reaction mechanisms, barriers, reaction rates, etc.
- difficult quantity, because it is not an average over phase space
- $F$ is related to the available phase volume
- $F$ includes the entropy, cannot be directly measured in experiment and cannot be directly calculated from simulation
- great need to develop methods for free energy calculations

14 The method of thermodynamic integration

The method of thermodynamic integration

- motivation comes from the experiment
- derivatives of $F$ represent observable quantities and can be measured as well as calculated, e.g.
  \[ P = -\frac{\partial F}{\partial V}, \quad E = \frac{\partial \beta F}{\partial \beta} \]

- if a suitable reversible path between the two states $A, B$ (not crossing a phase transition) exists, derivatives along the path can be calculated and integrated to get free energy difference $\Delta F = F_A - F_B$

- in simulation we can use also paths which are not physically realizable

- if we can refer the given state to a state of known free energy, we can calculate absolute free energies (important for phase equilibria where the states themselves cannot be connected via a reversible path)

- we know the free energy of harmonic oscillator and ideal gas

Coupling parameter method Kirkwood (1935)

- we change the Hamiltonian of the system (can be an unphysical change)
  \[ U(\lambda) = (1 - \lambda)U_I + \lambda U_{II} = U_I + \lambda(U_{II} - U_I) \]
  \[ F(\lambda) = -\frac{1}{\beta} \ln \frac{1}{\Lambda^{3N}N!} \int dr_1 \ldots dr_N e^{-\beta U(\lambda, r_1, \ldots, r_N)} \]

- we assume we know the free energy $F_I = F(\lambda = 0)$ for the system with $U_I = U(\lambda = 0)$
\[ \frac{\partial F(\lambda)}{\partial \lambda} \text{ is an ensemble average} \]

\[ \frac{\partial F(\lambda)}{\partial \lambda} = \frac{\int d\mathbf{r}_1 \ldots d\mathbf{r}_N \frac{\partial U(\lambda)}{\partial \lambda} e^{-\beta U(\lambda, \mathbf{r}_1, \ldots, \mathbf{r}_N)}}{\int d\mathbf{r}_1 \ldots d\mathbf{r}_N e^{-\beta U(\lambda, \mathbf{r}_1, \ldots, \mathbf{r}_N)}} = \left\langle \frac{\partial U(\lambda)}{\partial \lambda} \right\rangle_{N,V,T,\lambda} \]

\[ \Delta F = F_{II} - F_I = F(\lambda = 1) - F(\lambda = 0) = \int_{\lambda=0}^{\lambda=1} d\lambda \left\langle \frac{\partial U(\lambda)}{\partial \lambda} \right\rangle_{N,V,T,\lambda} \]

**Coupling parameter method continued**

- the integration is performed numerically
- Gibbs-Bogoliubov inequality can be used to check the accuracy

\[ \frac{\partial^2 F(\lambda)}{\partial \lambda^2} = -\beta \left\{ \langle (U_{II} - U_I)^2 \rangle_{\lambda} - \langle U_{II} - U_I \rangle^2_{\lambda} \right\} \leq 0 \]

- method is often used to calculate the \( \Delta F \) of similar molecules which differ in some atom or functional group (biochemistry)
- also useful for liquids and solids (examples will be shown later)
- the intermediate states are artificial, only the endpoints are relevant

**Order parameter method**

- the same Hamiltonian, different states \( A \) (reactant) and \( B \) (product) of the system
- typically \( A \) is metastable (local minimum) and \( B \) is stable (global minimum of the free energy, separated by a barrier)
- reduction of complexity by use of collective variable \( s = s(\{\mathbf{r}\}) \) (in phase transitions called order parameter, in chemistry reaction coordinate)
- \( s \) is chosen such that it clearly distinguishes the \( A \) and \( B \) states
- \( s \) can be also a multicomponent (low-dimensional) vector \( s = (s_1, \ldots, s_M) \)
- we define a restricted partition function

\[ Z(s) = \frac{1}{A^{3N} N!} \int d\mathbf{r}_1 \ldots d\mathbf{r}_N e^{-\beta U(\mathbf{r}_1, \ldots, \mathbf{r}_N)} \delta(s - s(\{\mathbf{r}\})) \]

\[ Z = \int ds Z(s) \]
• probabilistic interpretation

\[ \frac{Z(s)}{Z} = \langle \delta(s - s(\{r\})) \rangle = P(s) \]

**Order parameter method**

• we define \( F(s) \) (Landau (1958))

\[
F(s) = -\frac{1}{\beta} \ln Z(s) = F - \frac{1}{\beta} \ln P(s) \\
P(s) = \exp \left( -\beta (F(s) - F) \right)
\]

• the whole dependence \( F(s) \) is of interest, in particular the location of the maximum between A and B (transition state) and the barrier

• we want to calculate \( f(s) = -\frac{\partial F(s)}{\partial s} = k_B T \frac{\partial}{\partial s} \ln P(s) \)

• *thermodynamic integration* \( F(s) - F(s_0) = -\int_{s_0}^{s} f(s') ds' \)

• choice of good order parameter for a given problem is non-trivial (requires intuition and/or insight)

• in *phase transitions* we often choose some quantity that is clearly different in the two phases, typically a *function of coordinates of all particles*

• in *chemical reaction* we choose some *local geometric property* which substantially changes across the reaction

*How to calculate \( -\frac{\partial F(s)}{\partial s} \)?*

**Example of particle distance [25] - The reversible work theorem**

• in chemistry particle distance is often a good reaction coordinate

• we consider a simple chemical equilibrium between *two atoms A and B in a solution*

• the atoms form bond if they approach \( A + B \rightleftharpoons AB \)

• reaction coordinate \( r_{12} = |r_1 - r_2| = |r_{12}| \)

• free energy difference is equal to the *reversible work* needed to bring the system from one state to another \( w(r) = F(r_f) - F(r_i) = -k_B T (\ln P(r_f) - \ln P(r_i)) \)
\[ P(r) = \langle \delta(r_{12} - r) \rangle = \frac{1}{V} g(r) \]

- \( w(r) = -k_B T \ln \left( \frac{g(r_f)}{g(r_i)} \right) \)
- We assume that initially \( r \to \infty \) so \( g(r_i) = 1 \)
- The reversible work theorem
  \[ g(r) = e^{-\beta w(r)} \]
- \( w(r) \) is called potential of mean force (Kirkwood (1935))

**Example of particle distance - activated process**

- The bound state and the dissociated state are separated by a high free energy barrier \( \Delta G \)
- In principle, it is enough to calculate the radial distribution function \( g(r) \) and we get the activation energy
- Practically, this is impossible in normal simulation if \( \Delta G \gg k_B T \) - time scale gap
- We have to force the system to sample improbable regions of \( r \) and cross the barrier

**Example of particle distance (Statistical mechanics)**

- For the 2 atoms A,B, we introduce center of mass \( \mathbf{R} \) and relative coordinate \( r_{12} \) in spherical coordinates

\[
Z(r) = \int dr_1 \, dr_2 \, dr_3 \ldots dr_N e^{-\beta U} \delta(r_{12} - r) \\
= \int dr_{12} \, r_{12}^2 \, d\Omega \, d\mathbf{R} \, dr_3 \ldots dr_N e^{-\beta U} \delta(r_{12} - r) \\
f(r) = -\frac{\partial F(r)}{\partial r} = \frac{k_B T}{Z(r)} \int dr_{12} \, r_{12}^2 \, d\Omega \, d\mathbf{R} \, dr_3 \ldots dr_N e^{-\beta U} \frac{\partial}{\partial r} \delta(r_{12} - r) \\
= -\frac{1}{Z(r)} \int dr_{12} \, r_{12}^2 \, d\Omega \, d\mathbf{R} \, dr_3 \ldots dr_N e^{-\beta U} \delta(r_{12} - r) \left[ \frac{\partial U}{\partial r_{12}} - \frac{2k_B T}{r_{12}} \right] \\
= -\left\langle \frac{\partial U}{\partial r_{12}} \right\rangle_{r_{12} = r} + 2k_B T \frac{r}{r_{12}}
\]
Figure 27: Free energy and radial distribution function for dissociating pair of atoms. Adapted from Ref. [25]
• force \( \langle \frac{\partial U}{\partial \mathbf{r}_{12}} \rangle_{r_{12}=r} \) includes the effect of the solvent

• it can be calculated by MC or MD, but MD provides a simpler way

Example of particle distance - connection to dynamics

• kinetic energy of the atoms A and B
\[
K = \frac{\mu}{2} \mathbf{r}_{12}^2 = \frac{\mu}{2} (\dot{r}_{12}^2 + r_{12}^2 \dot{\theta}^2 + r_{12}^2 \sin^2 \theta \dot{\phi}^2)
\]

• equation of motion for the radial coordinate
\[
\mu \ddot{r}_{12} = -\frac{\partial U}{\partial r_{12}} + \mu r_{12} \dot{\theta}^2 + \mu r_{12} \sin^2 \theta \dot{\phi}^2 = f_r
\]

• potential force + centrifugal force

• for fixed \( r_{12} \) we have a linear rotor with angular kinetic energy
\[
\frac{\mu}{2} \langle r_{12}^2 \dot{\theta}^2 + r_{12}^2 \sin^2 \theta \dot{\phi}^2 \rangle_{r_{12}=r} = k_B T
\]

\[
\langle f_r \rangle_{r_{12}=r} = -\left< \frac{\partial U}{\partial r_{12}} \right>_{r_{12}=r} + \frac{2k_B T}{r} = f(r)
\]

• we found a connection between thermodynamic force and average radial force in the dynamics

Example of particle distance - connection to dynamics

• we impose the condition \( r_{12} = r \) by a constraint \( \sigma(r_{12}) = r_{12} - r = 0 \) and a Lagrange multiplier \( \lambda \)

• the constraint force must exactly compensate the total force \( f_r = \left( \lambda \frac{d\sigma}{dr_{12}} \right)_{r_{12}=r} = \lambda \)

• Lagrange multiplier \( \lambda \) is an estimator for the mean force \( f(r) \)
\[
\langle \lambda \rangle_{r_{12}=r} = f(r) = -\frac{\partial F(r)}{\partial r}
\]

• we can use thermodynamic integration \( F(r) - F(r_0) = -\int_{r_0}^{r} dr' \langle \lambda \rangle_{r_{12}=r'} \)

• this was a particularly simple case

• the general case is more complicated and a correction is needed
The blue-moon ensemble Carter, Ciccotti, Hynes, Kapral (1989) [24]

- reaction coordinates are dynamical variables, not parameters
- we want to calculate the conditional average $\langle \ldots \rangle^{\text{cond.}}_{s'}$

$$\langle A(\{r\}) \rangle^{\text{cond.}}_{s'} = \frac{\langle A(\{r\}) \delta(s(\{r\}) - s') \rangle}{\langle \delta(s(\{r\}) - s') \rangle}$$

- imposing a constraint $s(\{r\}) = s$ in MD imposes also a kinetic constraint $\dot{s}(\{r\}) = 0$ and introduces a bias
- MD calculates a constrained average $\langle \ldots \rangle_{s'}$

$$\langle A(\{r\}) \rangle^{\text{cond.}}_{s'} = \frac{\langle Z^{-\frac{1}{2}} A(\{r\}) \rangle_{s'}}{\langle Z^{-\frac{1}{2}} \rangle_{s'}}$$

$$Z = \sum_i \frac{1}{m_i} \left( \frac{\partial s}{\partial r_i} \right)^2$$

The blue-moon ensemble

- equation of motion for the reaction coordinate $\dot{p}^s = -\frac{\partial H}{\partial s} - \lambda$

$$\frac{dF(s)}{ds'} = \frac{\langle Z^{-\frac{1}{2}}[-\lambda + k_B T \rho] \rangle_{s'}}{\langle Z^{-\frac{1}{2}} \rangle_{s'}}$$

$$\rho = \frac{1}{Z^2} \sum_{i,j} \frac{1}{m_i m_j} \frac{\partial s}{\partial r_i} \frac{\partial^2 s}{\partial r_i \partial r_j}$$

- in the special case of particle distance $r_{12} = |r_1 - r_2| = |r_{12}|$ no correction is needed, since $Z = \text{const}$ and $\rho = 0$

Example of coordination number Sprik (1998) [26]

- coordination number is a useful quantity in physics and chemistry
- can be used as order parameter to enforce chemical reaction
- can be defined e.g. using a Fermi function

$$n_0 = \sum_{i \neq 0} S(|r_i - r_0|) = \sum_{i \neq 0} S(r_{i0})$$

$$S(r) = \frac{1}{\exp(\kappa(r - r_c)) + 1}$$

$$g_i = -\lambda \frac{\partial n_0}{\partial r_i} = \frac{\lambda \kappa}{2 \cosh[\kappa(r_{i0} - r_c)] + 1} r_{i0}$$

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the constraint force acts only in a narrow shell (of width $\kappa^{-1}$) around $r_c$
particles are either pulled into the coordination sphere or pushed out
$\kappa$ cannot be too large
here the Lagrange multiplier $\lambda$ is not an exact estimator for the mean force $f(r)$ but can provide a good approximation

**Example 12.** Liquid argon at $T = 150$ K (M. Sprik 1998) [26]

- Lennard-Jones potential
- the unconstrained coordination number is $\langle n_0 \rangle = 11.1$

## 15 The particle insertion method

The particle insertion method Widom (1963)

- method for measuring the chemical potential of fluids
- in the NVT ensemble $\mu = \frac{\partial F}{\partial N}$
- in the NPT ensemble, $\mu(P, T) = \frac{\partial G(P, T)}{\partial N} = \frac{G(P, T)}{N}$
- we introduce scaled coordinates $s_i = r_i / L$

\[
Z(N, V, T) = \frac{V^N}{A^3 N!} \int ds_1 \ldots ds_N e^{-\beta U(s_1, \ldots, s_N; L)}
\]

\[
F(N, V, T) = -\frac{1}{\beta} \ln \left( \frac{V^N}{A^3 N!} \right) - \frac{1}{\beta} \ln \int ds_1 \ldots ds_N e^{-\beta U(s_1, \ldots, s_N; L)}
= F_{id}(N, V, T) + F_{ex}(N, V, T)
\]

- for large $N$, $\mu = -\frac{1}{\beta} \ln \frac{Z(N + 1, V, T)}{Z(N, V, T)}$

\[
\mu = -\frac{1}{\beta} \ln \left( \frac{V}{A^3 (N + 1)} \right) - \frac{1}{\beta} \ln \frac{\int ds_1 \ldots ds_{N+1} e^{-\beta U(s_1, \ldots, s_{N+1}; L)}}{\int ds_1 \ldots ds_N e^{-\beta U(s_1, \ldots, s_N; L)}} = \mu_{id} + \mu_{ex}
\]

- we write $\Delta U = U(s_1, \ldots, s_{N+1}; L) - U(s_1, \ldots, s_N; L)$
The particle insertion method

\[ \mu_{ex} = -\frac{1}{\beta} \ln \frac{\int ds_{N+1} \ldots ds_{N} e^{-\beta U(s_1, \ldots, s_N; L)} e^{-\beta \Delta U}}{\int ds_{1} \ldots ds_{N} e^{-\beta U(s_1, \ldots, s_N; L)}} = -\frac{1}{\beta} \ln \int ds_{N+1} \langle e^{-\beta \Delta U} \rangle \]

- \( \mu_{ex} \) is expressed as ensemble average of an integral over the position of the extra particle \( s_{N+1} \)
- we run a normal simulation and periodically insert a “test particle” \( s_{N+1} \) at a random position within the unit cube
- for this position of the particle we average the Boltzmann factor \( e^{-\beta \Delta U} \)
- method works for not too dense liquids, in dense systems the insertion almost always leads to strong repulsion
- for use in NPT and NVE ensembles the method requires some modifications

16 Overlapping distribution method

Overlapping distribution method Bennett (1976) [27]

- two N-particle systems with (not too different) potentials \( U_1(\{R\}) \) and \( U_0(\{R\}) \)
- \( p_1(\Delta U) \) is a histogram of the energy difference \( \Delta U = U_1(\{R\}) - U_0(\{R\}) \) accumulated during sampling the system 1

\[ p_1(\Delta U) = \langle \delta(U_1(\{R\}) - U_0(\{R\}) - \Delta U) \rangle_1 = \frac{1}{Z_1} \int d\{R\} \exp[-\beta(U_1(\{R\}) - U_0(\{R\}) - \Delta U)] \delta(U_1(\{R\}) - U_0(\{R\}) - \Delta U) \]

\[ = \frac{1}{Z_1} \int d\{R\} \exp[-\beta(U_0(\{R\}) + \Delta U)] \delta(U_1(\{R\}) - U_0(\{R\}) - \Delta U) \]

\[ = \frac{Z_0}{Z_1} \exp(-\beta \Delta U) \frac{1}{Z_0} \int d\{R\} \exp[-\beta U_0(\{R\})] \delta(U_1(\{R\}) - U_0(\{R\}) - \Delta U) \]

\[ = \frac{Z_0}{Z_1} \exp(-\beta \Delta U) \langle \delta(U_1(\{R\}) - U_0(\{R\}) - \Delta U) \rangle_0 \]

\[ = \frac{Z_0}{Z_1} \exp(-\beta \Delta U) p_0(\Delta U) \]

- \( p_0(\Delta U) \) is a histogram of the energy difference \( \Delta U \) accumulated during sampling the system 0
Overlapping distribution method

we calculate the histograms $p_1(\Delta U)$ and $p_0(\Delta U)$ sampling from both distributions

\[
\ln p_1(\Delta U) = \beta(F_1 - F_0 - \Delta U) + \ln p_0(\Delta U)
\]
\[
f_0(\Delta U) = \ln(p_0(\Delta U)) - \frac{\beta}{2} \Delta U
\]
\[
f_1(\Delta U) = \ln(p_1(\Delta U)) + \frac{\beta}{2} \Delta U
\]
\[
\beta \Delta F = \beta(F_1 - F_0) = f_1(\Delta U) - f_0(\Delta U)
\]

• we fit the data for $f_1(\Delta U)$ and $f_0(\Delta U)$ and determine their offset

• in principle the two distributions do not need to overlap

• accuracy is good only if the two distributions overlap

Figure 28: Determination of the free energy difference from two histograms. Adapted from Ref.[27]
17 The method of umbrella sampling

Need for non-Boltzmann sampling Why one histogram is not sufficient?

\[ p_1(\Delta U) = p_0(\Delta U) \exp[\beta(\Delta F - \Delta U)] \]

\[ \int_{-\infty}^{\infty} d\Delta U \, p_1(\Delta U) = \exp(\beta \Delta F) \int_{-\infty}^{\infty} d\Delta U \, p_0(\Delta U) \exp(-\beta \Delta U) \]

\[ \exp(-\beta \Delta F) = \langle \exp[-\beta \Delta U] \rangle_0 \]

- seems to be a very simple way to calculate \( \Delta F \)
- problem is that the large contribution to the integral may come from the region where \( \exp[-\beta \Delta U] \) is large but \( p_0(\Delta U) \) is small and poorly sampled

Figure 29: Illustration of difficulty in calculating free energy difference. Adapted from M. P. Allen, D. J. Tildesley, Computer Simulation of Liquids, Clarendon Press - Oxford (1996)
The method of umbrella sampling Torrie, Valleeau (1977) [28]

\[
\langle \exp[-\beta \Delta U] \rangle_0 = \frac{\int d\{R\} \exp[-\beta U_1(\{R\})]}{\int d\{R\} \exp[-\beta U_0(\{R\})]}
\]

\[
= \frac{\int d\{R\} w(\{R\}) \exp[-\beta U_1(\{R\})] / w(\{R\})}{\int d\{R\} w(\{R\}) \exp[-\beta U_0(\{R\})] / w(\{R\})} = \langle \exp[-\beta \Delta U_1] / w(\{R\}) \rangle_w / \langle \exp[-\beta \Delta U_0] / w(\{R\}) \rangle_w
\]

- Boltzmann factor is replaced by a positive weight function \(w(\{R\})\)
- \(w\) acts as an umbrella, bridging the two distributions
- it enables a good sampling of both distributions by forcing the system to visit improbable states
- weight factor \(w(\{R\})\) can be introduced via a biasing potential, averages \(\langle \ldots \rangle_w\) can be calculated by MC or MD
- bias is introduced in the sampling and compensated for in the averaging
- problem is that \(w\) is not known a priori

The method of umbrella sampling

- the idea of sampling with biasing potential is used in a broader sense
- in case of activated processes we have two isolated regions of configuration space, separated by a high barrier
- we want to reconstruct the potential of mean force \(F(s)\) corresponding to the order parameter \(s\)

\[
F(s) = -\frac{1}{\beta} \ln P(s) + \text{const}
\]

\[
P(s) = \frac{1}{Z} \int d\{R\} \exp[-\beta U(\{R\})] \delta(s - s(\{r\}))
\]

- we introduce a biasing potential \(W(s(\{r\}))\)

\[
P_w(s') = \frac{1}{Z_w} \int d\{R\} \exp[-\beta(U(\{R\}) + W(s(\{r\})))] \delta(s' - s(\{r\}))
\]

\[
= \frac{1}{Z_w} \exp[-\beta W(s')] \int d\{R\} \exp[-\beta U(\{R\})] \delta(s' - s(\{r\}))
\]

\[
= \frac{Z}{Z_w} \exp[-\beta W(s')] \langle \delta(s' - s(\{r\})) \rangle = \frac{Z}{Z_w} \exp[-\beta W(s')] P(s')
\]
The method of umbrella sampling

\[ P(s) = \frac{Z_w}{Z} \exp[\beta W(s)] P_w(s) \]
\[ F(s) = -\frac{1}{\beta} \ln P(s) + \text{const} = -W(s) - \frac{1}{\beta} \ln P_w(s) + \text{const} \]

- removing the bias potential \( W(s) \) we reconstruct the original \( F(s) \) up to a constant
- it is convenient to split the interval of interest \( \Delta s \) into \( n \) narrow intervals
- assume a diffusion constant \( D_s \) for the order parameter \( s \)
- sampling a subinterval \( \frac{\Delta s}{n} \) takes time \( \tau_n = \frac{(\Delta s/n)^2}{D_s} \)
- total time to sample \( n \) windows is \( \tau_{\text{tot}} = \frac{\Delta s^2}{nD_s} \)
- one has to equilibrate also degrees of freedom orthogonal to \( s \) which takes time \( \tau_\perp \)
- optimal choice of \( n \) is such that \( \tau_n \approx \tau_\perp \)

The method of umbrella sampling

- window potential - simple and useful form is a harmonic restraint
  \[ W(s) = \frac{1}{2} K (s(|\{r}\}) - s_0)^2 \]
- for each window we get a piece of \( F(s) \) curve in an interval around \( s_0 \)
- we can sample accurately a width \( \delta F \approx k_B T \), so the number of windows should be \( n \approx \frac{\Delta F_{AB}}{k_B T} \)
- choice of the spring constant \( K \) - the distributions in the neighbouring intervals should overlap
- the pieces have to be assembled together to reconstruct the whole curve (by hand or by an automatic procedure)
Figure 30: Assembling the free energy curve from pieces
The weighted histogram analysis method (WHAM) Ferrenberg, Swendsen (1989) [29]; Kumar et al. (1992) [30]

- N windows, \( W_i(s) = \frac{1}{2} K(s\{r\}) - s_i^2 \)
- in each window we accumulate \( M_i \) data points for the histogram \( P_{wi}(s) \)
- we define
  \[
  \exp(-\beta F_i) = \langle \exp[-\beta W_i(s)] \rangle = \frac{Z_{W_i}}{Z} = \int ds \exp[-\beta W_i(s)] P(s)
  \]
- in principle, \( P(s) \) can be reconstructed from each window \( P_{wi}(s) \)
  \[
  P(s) = \frac{Z_{W_i}}{Z} \exp[\beta W_i(s)] P_{wi}(s) = \exp(-\beta F_i) \exp[\beta W_i(s)] P_{wi}(s)
  \]
  but the accuracy would be very poor
- we construct \( P(s) \) as a linear combination of the estimates from different windows with a weight function \( C_i(s), \sum_{i=1}^{N} C_i(s) = 1 \)
  \[
  P(s) = \sum_{i=1}^{N} C_i(s) \exp(-\beta F_i) \exp[\beta W_i(s)] P_{wi}(s)
  \]

The weighted histogram analysis method (WHAM)

- the weigths \( C_i(s) \) can be chosen in such way that the total statistical error is minimized
- the result is
  \[
  P(s) = \frac{\sum_{i=1}^{N} M_i P_{wi}(s)}{\sum_{i=1}^{N} M_i \exp[-\beta (W_i(s) - F_i)]}
  \]
  where the constants \( F_i \) are determined from
  \[
  \exp(-\beta F_i) = \int ds \exp[-\beta W_i(s)] P(s)
  \]
- the system of equations must be solved self-consistently
- in practice, an iteration procedure is used
- the method provides an automatic procedure
- extension to the multidimensional case is straightforward (mainly 2D, more is not practical)
The method of \textit{umbrella sampling} (Analogy to blue-moon ensemble and thermodynamic integration)

\[
\langle s \rangle = \frac{\int d\{r\} s(\{r\}) \exp \left[ -\beta (U(\{r\}) + \frac{1}{2} K (s(\{r\}) - s_0)^2) \right] \int ds \delta(s(\{r\}) - s)}{\int d\{r\} \exp \left[ -\beta (U(\{r\}) + \frac{1}{2} K (s(\{r\}) - s_0)^2) \right] \int ds \delta(s(\{r\}) - s)}
\]

\[
= \frac{\int ds \exp \left[ -\beta \frac{1}{2} K (s - s_0)^2 \right] \int d\{r\} \exp \left[ -\beta U(\{r\}) \right] \delta(s(\{r\}) - s)}{\int ds \exp \left[ -\beta U(\{r\}) \right] \delta(s(\{r\}) - s)}
\]

\[
= \frac{\int ds \exp \left[ -\beta (F(s) + \frac{1}{2} K (s - s_0)^2) \right]}{\int ds \exp \left[ -\beta (F(s) + \frac{1}{2} K (s - s_0)^2) \right]}
\]

The method of \textit{umbrella sampling}

- we expand \(F(s)\) around \(s_0\)

\[
F(s) = F(s_0) + \frac{\partial F}{\partial s} \bigg|_{s_0} (s - s_0) + \frac{1}{2} \frac{\partial^2 F}{\partial s^2} \bigg|_{s_0} (s - s_0)^2
\]

- we assume that \(K \gg \left. \frac{\partial^2 F}{\partial s^2} \right|_{s_0}\)

\[
\langle s \rangle = \frac{\int ds \exp \left[ -\beta \left( F(s_0) + \left. \frac{\partial F}{\partial s} \right|_{s_0} (s - s_0) + \frac{1}{2} K (s - s_0)^2 \right) \right]}{\int ds \exp \left[ -\beta \left( F(s_0) + \left. \frac{\partial F}{\partial s} \right|_{s_0} (s - s_0) + \frac{1}{2} K (s - s_0)^2 \right) \right]}
\]

\[
= s_0 - \frac{1}{K} \left. \frac{\partial F}{\partial s} \right|_{s_0}
\]

- we found the derivative \(\left. \frac{\partial F}{\partial s} \right|_{s_0} = K (s_0 - \langle s \rangle)\)

- analogy to blue-moon ensemble and thermodynamic integration

- instead of a \textit{hard constraint} we impose the value of the order parameter by a \textit{harmonic restraint}

\textbf{Study of crystal nucleation by umbrella sampling van Duijneveldt and Frenkel (1992) [31]}

- liquid and crystalline state are separated by a barrier, freezing does not occur spontaneously
- order parameter should distinguish between liquid and generic solid, but not prefer a particular structure

- for each particle we define bonds $r$ connecting particle to its nearest neighbours

- order parameter characterizing local coordination (Steinhardt et al. (1983))

$$Q_{lm}(r) = Y_{lm}(\theta(r), \phi(r))$$

- we sum over all bonds in the system to get a global order parameter $\bar{Q}_{lm} = \frac{1}{N_b} \sum Q_{lm}(r)$

$$Q_l = \left( \frac{4\pi}{2l+1} \sum_{m=-l}^{m=l} |\bar{Q}_{lm}|^2 \right)^{\frac{1}{2}}$$ is rotationally invariant

- best choice to study crystallization is $l = 6$, $Q_6 \approx 0.5$ for crystalline structures, $Q_6 = 0$ for a liquid

- free energy $F(Q_6)$ is studied by umbrella sampling


- a strong finite size effect is seen, large system needed

- apart from the free energy profile, we get also information about the mechanism of formation and structure of the critical nucleus

- study of kinetics of crystallization is highly important e.g. for pharmaceutical industry

18 Calculation of phase diagrams

Phase diagrams general considerations

- prediction of phase behaviour of a given substance is one of most important aims of computer simulations

- techniques used to study first order and second order transitions are very different

- we focus here on first order transitions
finite size effects are of order $O(N^{-1})$
thermodynamic coexistence conditions for two phases $\alpha$ and $\beta$: $T_\alpha = T_\beta$, $P_\alpha = P_\beta$, $\mu_\alpha = \mu_\beta$
first order transitions are abrupt, without precursors
proceed via nucleation, to go from one phase to another an interface has to be created
interfacial energy creates a free energy barrier - metastability, hysteresis

Phase diagrams continued

many methods for locating the transition point exist
direct observation of phase changes by crossing phase boundaries (most problematic method)
direct observation of phase changes in a system prepared in a state with both phases present - better
free energy calculations, $\mu_\alpha(P, T) = \mu_\beta(P, T)$
direct observation of phase separation without interface (Gibbs ensemble)
direct study of phase boundary (Clausius-Clapeyron integration)

Calculation of free energies of liquids

melting - prototypical first order transition
for phase equilibria the states themselves cannot be connected via a reversible path (hysteresis)
direct thermodynamic integration can’t be used
we have to calculate absolute free energies, referring the given state to a state of known free energy
liquid can be connected to ideal gas

\[
\begin{align*}
P &= -\frac{\partial F}{\partial V} = \frac{1}{N} \rho^2 \frac{\partial F}{\partial \rho} \\
F(\rho) &= F_{id}(\rho) + N \int_0^\rho d\rho' \frac{(P(\rho') - \rho' k_B T)}{\rho'^2} \end{align*}
\]
• one has to avoid crossing the vapour-liquid boundary

• typically, one starts at high temperature and integrates along isotherm to the desired density

• in the second step one integrates at constant density down to the desired temperature (using relation \( E = \frac{\partial \beta F}{\partial \beta} \))

**Calculation of free energies of solids**

• we know free energy of *harmonic oscillator*

• thermodynamic integration starting from a low temperature where the solid behaves as *harmonic crystal* (collection of harmonic oscillators)

• problem: between melting temperature and low temperature many crystals undergo *structural phase transitions*

• more general solution is thermodynamic integration to *Einstein crystal* structurally identical to the real one

• simple for atomic solids with continuous potentials

\[
U(\lambda) = U(\{r_0\}) + (1 - \lambda) [U(\{r\}) - U(\{r_0\})] + \lambda \sum_{i=1}^{N} \alpha_i (r_i - r_{0i})^2
\]

\[
F = F_{Ein} + \int_{\lambda=0}^{\lambda=1} d\lambda \left( \frac{\partial U(\lambda)}{\partial \lambda} \right)_\lambda
\]

\[
= F_{Ein} + \int_{\lambda=0}^{\lambda=1} d\lambda \left( \sum_{i=1}^{N} \alpha_i (r_i - r_{0i})^2 - [U(\{r\}) - U(\{r_0\})] \right)_\lambda
\]

**Calculation of free energies of solids (continued)**

\[
F_{Ein} = U(\{r_0\}) - \frac{3}{2\beta} \sum_{i=1}^{N} \ln \frac{\pi}{\alpha_i \beta}
\]

• the spring constants \( \alpha_i \) can be optimized for accuracy of the numerical integration
• the mean square displacements of the atoms in both systems are chosen to be equal

\[ \langle \sum_{i=1}^{N} (r_i - r_{0i})^2 \rangle_{\lambda=0} = \langle \sum_{i=1}^{N} (r_i - r_{0i})^2 \rangle_{\lambda=1} \]

\[ \frac{3}{2\beta} \alpha_i = \langle \sum_{i=1}^{N} (r_i - r_{0i})^2 \rangle_{\lambda=0} \]

• possible also for molecular crystals (but more complicated)

• feasible even for hard spheres

The Gibbs-Duhem (Clausius-Clapeyron) integration Kofke (1993) [33]

• two phases, \( \alpha, \beta \)

\[ d(\mu_\alpha - \mu_\beta) = -(s_\alpha - s_\beta)dT + (v_\alpha - v_\beta)dP \]

• \( s \) and \( v \) are molar entropy and volume, respectively

• along the coexistence curve \( \mu_\alpha = \mu_\beta \)

\[ \frac{dP}{dT} = \frac{s_\alpha - s_\beta}{v_\alpha - v_\beta} \]

• at coexistence \( \Delta \mu = \Delta e + P \Delta v - T \Delta s = \Delta h - T \Delta s = 0 \)

• Clausius-Clapeyron equation \( \frac{dP}{dT} = \frac{\Delta h}{T \Delta v} \)

• the slope \( \frac{dP}{dT} \) is expressed in terms of measurable quantities \( \Delta h = \Delta e + P \Delta v \)

• if one transition point is known (initial condition), the phase boundary can be determined by direct integration

• powerful method, computationally less intensive than free energy calculations but it is good to fix more than one transition point

Example 14. Phase diagram of water (Sanz, Vega, Abascal and MacDowell (2004) [34])

• liquid free energy calculated by switching off the Coulomb interaction and transforming to Lennard-Jones liquid
• solid free energy calculated with the Einstein crystal method
• phase boundary integrated according to the Kofke method
• TIP4P reproduces qualitatively well the phase diagram of water, correct topology, SPC does not provide the right topology
• calculation of phase diagrams is very stringent test on the quality of potential

19 Non-equilibrium free energy methods

Non-equilibrium free energy methods Jarzynski (1997) [35]

• $H_0(\Gamma), H_1(\Gamma)$ two Hamiltonians
• time-dependent switching parameter $\lambda(t)$, $H_{\lambda=0} = H_0, H_{\lambda=1} = H_1$
• work done on the system during the switching is

$$W(t_s) = \int_0^{t_s} dt \lambda \frac{\partial H_\lambda[\Gamma(t)]}{\partial \lambda} = H_1(\Gamma(t_s)) - H_0(\Gamma(0))$$

• for infinitely slow switching $t_s \to \infty, W = \Delta F$ (reversible work)
• for finite $t_s$ we have $W(t_s) \geq \Delta F$ (some work is dissipated)
• $W(t_s, \Gamma(0))$ depends on the path through the phase space which depends on initial condition $\Gamma(0)$
• at the beginning we assume the system to be in equilibrium

$$P_0[\Gamma(0)] = \frac{1}{Z_0} \exp\{-\beta H_0[\Gamma(0)]\}$$

Non-equilibrium free energy methods

• we calculate the average

$$\exp[-\beta W(t_s)] = \int d\Gamma(0) P_0[\Gamma(0)] \exp[-\beta W(t_s, \Gamma(0))]$$

$$= \int d\Gamma(0) \frac{1}{Z_0} \exp\{-\beta H_0[\Gamma(0)]\} \exp\{-\beta (H_1[\Gamma(t_s)] - H_0[\Gamma(0)])\}$$

$$= \int d\Gamma(0) \frac{1}{Z_0} \exp\{-\beta H_1[\Gamma(t_s)]\}$$
• Hamiltonian evolution preserves area \( d\Gamma(0) = d\Gamma(t_s) \)

\[
\exp[-\beta W(t_s)] = \int d\Gamma(t_s) \frac{1}{Z_0} \exp\{-\beta H_1[\Gamma(t_s)]\} = \frac{Z_1}{Z_0} = \exp(-\beta \Delta F)
\]

• equilibrium quantity \( \exp(-\beta \Delta F) \) equals average over a non-equilibrium process \( \exp[-\beta W(t_s)] \)

• the thermodynamic inequality \( W(t_s) \geq \Delta F \) follows from \( \exp x \geq \exp \bar{x} \)

• elegant result, but in simulations the accuracy in case of strongly non-equilibrium transitions is not good

Part IV
Simulation of Rare Events

20 Introduction to rare events

Limits of MD - time scale problem for activated processes

• MD simulations follow atomic motion on the time scale of atomic vibrations - can be stretched to time intervals of order 10 - 100 ns

• many processes occur on much longer time scale - glassy systems, critical phenomena, activated processes, protein folding

• activated processes - the problem is not that the dynamics is slow, but that rare (and important) events are involved

• atomic scale transitions in condensed matter - chemical reactions, nucleation, diffusion, transport processes

• importance for study of chemical and physical transformations, 1st order phase transitions, biochemistry, materials science, technology

• the dynamical bottleneck might be either a classical barrier-crossing, or quantum tunelling through the barrier

• at normal conditions, thermal energy \( k_B T \approx 0.025 \text{ eV} \), barriers are often of order of \( \Delta F \approx 0.5 \text{ eV} \) or more

• in the classical case, probability is suppressed by \( \exp\left(-\frac{\Delta E}{k_B T}\right) \leq \exp(-20) \)
• arbitrarily increasing temperature accelerates the processes, but might lead to crossover to a different transition mechanism

From A to B problem

• most of the time is just waiting for the unlikely fluctuation
• once the fluctuation occurs, the barrier crossing process is fast and can be followed by MD simulations
• separation of time scales
• activated processes - from A to B
• the dividing surface (separatrix) in the phase space dividing reactants and products is of central importance - transition state
• all reactive trajectories pass through the transition state
• transition state is the dynamical bottleneck (can be of energetic or entropic character)
• different situations depending on what we know and what we look for
• we know B but don’t know how to get there (search for transition state and energy or free energy barrier)
• we know B but want the exact reaction mechanism (dynamical trajectory) and reaction rate (how fast does it go)
• we know only A and want to find B

Transition state theory (TST) Kramers (1940)

• we assume that we know the product B
• unimolecular reaction $A \rightleftharpoons B$
• concentration of the species $c_A$ and $c_B$, rate constants $k_{A \rightarrow B}$ and $k_{B \rightarrow A}$

\[
\frac{dc_A}{dt} = -k_{A \rightarrow B}c_A(t) + k_{B \rightarrow A}c_B(t)
\]

\[
\frac{dc_B}{dt} = +k_{A \rightarrow B}c_A(t) - k_{B \rightarrow A}c_B(t)
\]
• phenomenological Arrhenius law $k = \nu \exp(-\beta E_b)$ (Arrhenius 1889)

• TST allows to find $k$ if the transition state is known

• *reaction rate* (dynamical quantity) is proportional to the *equilibrium density at the transition state* (static quantity)

• assumption of no recrossing of the transition state (not obvious)

### 21 Searching for saddle points

![Two-state potential with a barrier. Adapted from Ref. [36]](image)

**Figure 31:** Two-state potential with a barrier. Adapted from Ref. [36]

**Harmonic approximation to TST (hTST)**

• approximation valid when the free energy barrier is *energy dominated*

• simplest case is in 1D

$$k_{hTST}^+ = \nu_0 \exp(-\beta E_b^+), \quad \nu_0 = \frac{1}{2\pi} \sqrt{\frac{U''(q_0)}{M}}$$

• $\omega_0$ is the frequency at the bottom of the initial well

• generalization to more dimensions

90
• saddle point \((\neq)\) on the potential energy surface has to be found, corresponding to the maximum along a minimum energy path (MEP) from one state to another

\[
k_{hTST}^+ = \frac{\prod_{i=1}^{3N} \nu_i^{\text{init}}}{\prod_{i=1}^{3N-1} \nu_i^\neq} \exp \left[ -\beta (E^\neq - E^{\text{init}}) \right]
\]

• entropic contribution is taken into account in the harmonic approximation

• the reaction coordinate at the saddle point is the direction of the unstable mode

• when all relevant saddle points are identified, the prefactors can be calculated from the hTST and the long-time activated dynamics of the system can be simulated e.g. by kinetic Monte Carlo

Nudged elastic band (NEB) (Mills, Jonsson, Schenter (1995) [37])

• How to find (efficiently) the minimum energy path and the saddle points in high-dimensional space?

• minimum energy path is stationary with respect to any perpendicular degrees of freedom

• the force acts only along the path

• for any direction \(p_s\) perpendicular to the path \(\Gamma_s\), \(p_s \cdot \frac{d}{ds} \Gamma_s = 0\), potential energy is at minimum \(p_s \cdot \nabla V(\Gamma_s) = 0\)

• the nudged elastic band method finds the MEP variationally

• set of replicas is used to define the discretized transition path \([\{R_0\}, \ldots, \{R_P\}]\)

• we define the function to be minimized (elastic band)

\[
A[\{R_1\}, \ldots, \{R_{P-1}\}] = \sum_{i=1}^{P-1} V(\{R_i\}) + \sum_{i=1}^{P} \frac{k_P}{2} (\{R_i\} - \{R_{i-1}\})^2
\]

• the harmonic springs guarantee the continuity of the path
Nudged elastic band (NEB)

- Spring forces tend to deviate the path from the curves MEP ("corner-cutting")
- Gradient forces tend to avoid the region of high energy ("sliding down"), reducing the density of replicas in the region of interest
- We define the tangent vector to the path by

\[ \tau = \frac{\{R_i\} - \{R_{i-1}\}}{|\{R_i\} - \{R_{i-1}\}|} + \frac{\{R_i\} - \{R_{i+1}\}}{|\{R_i\} - \{R_{i+1}\}|} \]

and normalize \( \hat{\tau} = \frac{\tau}{|\tau|} \)
- "nudging" - projection of the forces
- We set to zero the perpendicular component of the spring force

\[ F_s^\perp = k [(\{R_{i+1}\} - \{R_i\}) + (\{R_i\} - \{R_{i-1}\})] \cdot \hat{\tau}, \hat{\tau} \]

- Spring forces only control the spacing of the images along the path
- We set to zero the parallel component of the gradient force

\[ \nabla V(\{R_i\}) \perp = \nabla V(\{R_i\}) - \nabla V(\{R_i\}) \cdot \hat{\tau} \]

- Gradient forces only control the convergence of the band to the MEP

Nudged elastic band (NEB)

- We optimize the band under the action of the force (minimization of the forces)

\[ F_i = F_i^\perp - \nabla V(\{R_i\}) \perp \]

- As a starting band we use a linear interpolation from the reactant \( \{R_0\} \) to the product \( \{R_P\} \)
- The method requires only first derivatives (forces)
- NEB is not very efficient to get a precise location of the saddle points
- MEP found by NEB can be refined
- The dimer method (Henkelman and Jonsson (1999) [38])
Example 15. Application to the problem of crystal growth Pt(111) Jonsson (2000) [39]

- understanding of crystal growth is very important in basic science as well as in technology
- growth simulated on the experimental time scale, rich phenomena found

22 Transition Path Sampling

Problems with the saddle points

Methods of the previous sections are applicable to relatively simple systems, where the transition state surface usually intersects saddle points in the potential energy surface

- high-dimensional surfaces are very complex, rough and contain many saddle points
- at finite temperature all details on the energy scale smaller than $k_B T$ are irrelevant
- only few saddle points are dynamically relevant
- explicit enumeration of all saddle points is impossible
- often there is a competition between many different pathways
- re-crossings of the transition state may be important

Transition Path Sampling Dellago, Bolhuis, Chandler (1998) [40]

- Throwing Ropes Over Rough Mountain Passes, in the Dark
- generalization of importance sampling (MC) from configuration space to space of dynamical trajectories
- true dynamical trajectories are sampled, no bias or constraint
- requires only order parameter and is able to find the microscopic dynamical mechanism
- can be used in two manners: heuristic (search for mechanism) and quantitative (calculation of reaction rates)
Transition path ensemble

- order parameter defined as characteristic function of the states A,B
  \[ h_{A,B} = \begin{cases} 1, & \text{if } x \in A, B \\ 0, & \text{if } x \notin A, B \end{cases} \]

- we consider an ensemble of reactive trajectories which start in point \( x_0 \) in region A and reach region B within time \( t \)

- time \( t \) should be long enough to allow the process of interest to occur

- we assume deterministic dynamics, \( x_{\tau} = x_{\tau}(x_0) \)

- \( \rho(x) \) is the distribution of phase state points

- distribution function for the ensemble probability
  \[ f_{AB}(x_0) = \frac{1}{Q_{AB}} \rho(x_0) h_A(x_0) H_B(x_0) \]
  \[ Q_{AB} = \int dx_0 \rho(x_0) h_A(x_0) H_B(x_0) \]

  where \( H_B(x_0) = \begin{cases} 1, & \text{if there is a } \tau \in [0, t] \text{ such that } h_B(x_\tau) = 1 \\ 0, & \text{otherwise} \end{cases} \)

Sampling of the path ensemble - shooting moves

- sampling is performed by Monte Carlo procedure

- the new path is accepted according to the detailed balance
  \[ f_{AB}(x_0^o) P_{gen}^{o \rightarrow n} P_{acc}^{o \rightarrow n} = f_{AB}(x_0^n) P_{gen}^{n \rightarrow o} P_{acc}^{n \rightarrow o} \]

- shooting - new path is created by modifying an old one

- point is selected at random on an existing path and particle momenta are slightly modified

- equations of motion are integrated forward and backward
Sampling of the path ensemble

- because of the Lyapunov instability, the change of momenta must be very small to have a reasonable acceptance ratio

- Metropolis criterion is used to accept the new path

\[ P_{acc}^{n \rightarrow o} = \min \left[ 1, \frac{f_{AB}(x_0^n) P_{gen}^{n \rightarrow o}}{f_{AB}(x_0^o) P_{gen}^{o \rightarrow n}} \right] \]

- to improve the statistics, shifting moves (reptation) can also be used

- we delete a piece at the beginning or at the end of an existing path and grow a new piece forward or backward in time

How to recognize a good order parameter? (reaction coordinate vs. order parameter)

- order parameter characterizes basins of attraction, has to distinguish the initial and final state
• *reaction coordinate* characterizes dynamical mechanism(s) (has to represent the progress of the process)

• *committor* \( P_A \) represents the probability of finishing in the stable state A starting from a given point with random velocities

• if the maximum of \( F(s) \) at \( s^* \) is a *true transition state*, committor distributions when starting from a point compatible with \( s^* \) will be peaked at \( \frac{1}{2} \)

**How to get the initial path?**

Generally this is a *difficult* procedure

• in principle, a proper path can be always obtained by gradual *shrinking* of the characteristic function \( h_B \) of the region B

• initially all paths start and finish in A

• at certain point the boundary crosses the transition state and the path finishes in B

• the initial path does not have to be representative of the typical transition path at given conditions

• upon “annealing” of an improbable path a good one will be found

• one can start e.g. from a path obtained at higher temperature, temperature can be also lowered gradually

*Example 16. Lennard-Jones clusters in 2D studied by transition path sampling* [40]

• heptamers at low temperature \( k_B T = 0.1 \epsilon \)

• isomerizations (central particle escapes to the surface) are rare events

• several different mechanisms are possible

### 23 Methods based on biasing potential

**Escaping from A - search for B (methods based on biasing potential)**

• no knowledge of the final product is assumed - *predictive power*
• auxiliary biasing potential is added to the system in a controlled way
• aim is to reduce the barrier height and accelerate the escape
• forcing the system to escape from A, we find the product B as well as the reactive trajectory
• the auxiliary potential can be constructed in different ways

Conformational flooding (Grubmüller (1995) [41])

Figure 33: Free energy well with a biasing potential. Adapted from Grubmüller (1995) [41]

• auxiliary biasing potential is constructed in one step in the configurational space
• simplified model for the system close to equilibrium

\[ A^{-1} = C = \langle (x - \bar{x})(x - \bar{x})^T \rangle \]

\[ \rho(x) \propto \exp \left[ -\frac{1}{2} (x - \bar{x})^T A(x - \bar{x}) \right] \]
A is calculated from fluctuations around equilibrium and diagonalized $A = Q^T \Lambda Q$ with an orthonormal matrix $Q$.

new collective coordinates $q = Q(x - \bar{x})$

$$\bar{\rho}(x) \propto \exp\left[-\frac{1}{2} q^T \Lambda q\right]$$

collective motion is typically slow

for a coarse-grained description we choose a subset $c = (q_1, \ldots, q_m)^T$ of $q$ corresponding to $m$ smallest eigenvalues of $\Lambda$, $\Lambda_c = (\delta_{ij} \lambda_i), i = 1, \ldots, m$

Conformational flooding

harmonic effective Hamiltonian for the metastable state

$$H_{eff}(c) = \frac{1}{2} \beta^{-1} c^T \Lambda_c c$$

we define a local and uniform “flooding” potential $V_{fl}$ to be included in the simulation

we choose $V_{fl}$ in Gaussian form

$$V_{fl}(c) = E_{fl} \exp\left[-\frac{1}{2} c^T \Lambda_{fl} c\right], \quad \Lambda_{fl} = \frac{1}{\gamma^2} \Lambda_c$$

we require

$$\frac{\partial^2 (H_{eff} + V_{fl})}{\partial c_i \partial c_j} = 0, \quad i, j = 1, \ldots, m$$

we get $\gamma = \sqrt{\beta E_{fl}}$, flooding parameter $E_{fl}$ is increased until a transition occurs

similar approach - hyperdynamics (Voter (1997) [42])
24 Metadynamics

Coarse-grained dynamics (Gear, Kevrekidis, Theodoropoulos (2002) [43])

- multilevel approach
- *direct microscopic simulation* (analogue of experiment) and *computer-assisted analysis*
- two levels of description - microscopic and coarse-grained
- use of order parameter to reduce the dimensionality
- coarse-grained dynamics in the space of the order parameter using information gained from microscopic dynamics

Metadynamics (Laio and Parrinello (2002) [44])

- *unified approach* to calculate the free energy, accelerating rare events and constructing reactive trajectories
- use of history-dependent potential (local elevation, Huber, Torda, van Gunsteren (1994) [45])
- biasing potential is constructed *iteratively in the space of the order parameter* \(s(r)\)
- ideally, \(s(r)\) should include *all slow variables* in the system
- discrete dynamics in the order parameter space (steepest-descent-like)

\[
\begin{align*}
s^{t+1} &= s^t + \delta h \frac{\phi^t}{|\phi^t|} \\
\phi^t &= -\frac{\partial F^t}{\partial s}
\end{align*}
\]

- the force \(\phi^t\) is derived from a modified free energy \(F^t(s)\)

\[
F^t(s) = F(s) + \sum_{t'<t} W e^{-\frac{|s - s^{t'}|^2}{2s^2}}
\]
Metadynamics

- for each point already visited we add a Gaussian to discourage the system from visiting the same point again
- history-dependent potential *iteratively compensates the free energy*
- the initial minimum is filled up to the lowest energy transition state and then the system enters into another minimum
- *low-energy reactive* paths are constructed
- the derivatives $-\frac{\partial F}{\partial s}$ can be calculated e.g. by MD
- we add constraints $\lambda \cdot (s(r) - s^t)$ and average the Lagrange multipliers
  $\langle \lambda \rangle = -\frac{\partial F}{\partial s} \bigg|_{s=s^t}$ (plus the blue-moon corrections)

Two different ways of using metadynamics

- escaping free energy minima
- reconstruction of the free energy

Examples of collective variables (order parameters)

- distances between particles or groups of particles
- angles, torsional angles
- coordination numbers
- local electric fields
- lattice vectors
- ring statistics (number of $n$-membered rings)
- energy
- …
Reconstruction of the free energy profile

- for long time \( t \) the function \( F^t(s) \) become more or less flat (up to roughness of order of \( W \))

\[
\lim_{t \to \infty} F^t(s) = F(s) + \sum_{t' < t} We^{-\frac{|s-s'|^2}{2\delta s^2}} \approx const
\]

\[
F(s) \to - \sum_{t' < t} We^{-\frac{|s-s'|^2}{2\delta s^2}} + const
\]

- the evolution has to be \emph{reversible} all the time
- the filling has to be performed in a \emph{restricted} region of the \( s \) space
- evolution has to become diffusive (several recrossings of the transition state)

Figure 34: Modified free energy at different times showing the filling of the well by Gaussians. Adapted from Ref.[44]
Escaping free energy minima

How to detect passing through the transition state? [46]

- thermodynamic force \( \phi_c = -\frac{\partial F}{\partial s} \)
- Gaussian force \( \phi_g = -\frac{\partial}{\partial s} \sum_{t} W e^{-\frac{|s-s'_t|^2}{2\sigma^2}} \)
- during filling of the well, \( \phi_c + \phi_g \approx 0, \phi_c \approx -\phi_g \) (opposite orientation)
- after passing the transition state, \( \phi_c \) and \( \phi_g \) become parallel, both oriented along the unstable eigenvector of the Hessian matrix at the transition state
- indicator \( I = \frac{\phi_c \cdot \phi_g}{|\phi_c||\phi_g|} \) develops sharp positive spikes at transitions

![Figure 35: Evolution of the indicator I during metadynamics simulation](image)

Parameters

- Gaussian height \( W \) determines the free energy resolution
• Gaussian width $\delta_s$ determines the resolution of the order parameter $s$
• the number of Gaussians needed to fill the well is $\propto (\delta s)^{-D}$, $D$ is the dimensionality of the order parameter $s$
• Gaussians should not be too sharp, no artificial minima should be created

**Continuous metadynamics (Laio and Parrinello (2006) [47])**

• in equilibrium, system is always in a local minimum of the free energy
• continuous evolution, normal MD is performed, Gaussians are added at every step
• extra force from the Gaussians act directly on the particles

\[
f^G(t) = -\frac{\partial}{\partial r} \frac{w}{\tau_G} \int_0^t dt' \exp \left( -\frac{(s(r) - s(r(t')))^2}{2\delta s^2} \right),
\]

$r(t')$ is the trajectory of the system
• the parameter $\frac{w}{\tau_G}$ controls the rate of deposition of the Gaussians
• non-equilibrium dynamics, because it is perturbed at every step
• technically easy to implement in any MD code

\[
f_i \rightarrow f_i - \frac{wdt}{\tau_G} \sum_{\nu < \ell} \sum_{j=1}^d \left( \frac{s^\nu_j - s^\ell_j}{\delta s^2} \right) \exp \left( -\frac{|s^\nu_j - s^\ell_j|^2}{2\delta s^2} \right) \frac{\partial s_j(r)}{\partial r_i} \bigg|_{r=r(t)}
\]

**Application of metadynamics to structural phase transitions in solids (Martonak, Laio, Parrinello (2003) [46])**

• **box matrix** $\mathbf{h} = (\mathbf{a}, \mathbf{b}, \mathbf{c})$ (Parrinello and Rahman (1980) [15]) is used as order parameter
• crystal structures correspond to minima of the Gibbs free energy $G(\mathbf{h}) = F(\mathbf{h}) + PV = F(\mathbf{h}) + P \det \mathbf{h}$
• we perform *exploration* of $G(\mathbf{h})$ instead of constant-pressure simulation
• restricting the matrix $\mathbf{h}$ to upper triangular form *freezes box rotations*
• 6-dimensional order parameter $\mathbf{h} = (h_{11}, h_{22}, h_{33}, h_{12}, h_{13}, h_{23})^T$
derivatives are easily calculated from the pressure tensor

\[-\frac{\partial G}{\partial h_{ij}} = V [h^{-1}(p - P)]_{ji}\]

metadynamics is performed in the 6D space of \(\tilde{h}\)

after the box is modified \(\tilde{h}^t \rightarrow \tilde{h}^{t+1}\) the particle positions are rescaled in order to fit into the new box \(r' = h' h^{-1} r\)

Application of metadynamics to structural phase transitions in solids

the loop is repeated until a transition is observed

when a new structure is found, a steepest descent relaxation to the new structure is performed

few ps of MD simulation at each step are sufficient

only pressure tensor is needed

Application of metadynamics to structural phase transitions - preconditioning (Martoňák, Donadio, Oganov, Parrinello (2006) [49])

a crystal is much more resistant to deformations that change the volume than to other types of strain, \(G(h)\) is strongly anisotropic function

close to an equilibrium crystal structure \(\tilde{h}^0\) the Gibbs free energy reads

\[G(\tilde{h}) \approx G(\tilde{h}^0) + \frac{1}{2}(\tilde{h} - \tilde{h}^0)^T A (\tilde{h} - \tilde{h}^0)\]

we calculate the positive definite Hessian matrix \(A_{ij} = \frac{\partial^2 G(h)}{\partial h_i \partial h_j} |_{h_0}\)

\(A_{ij}\) is diagonalized by orthogonal matrix \(O\) and has positive real eigenvalues \(\{\lambda^i\}\)

new collective coordinates \(s_i = \sqrt{\lambda^i} \sum_j O_{ij} (\tilde{h}_j - \tilde{h}_j^0)\) for metadynamics

in the coordinates \(s_i\) the free energy well becomes spherical \(G(s) \approx G(\tilde{h}^0) + \frac{1}{2} \sum_i s_i^2\)
Figure 36: Flowchart diagram for metadynamics simulations of structural phase transitions. Adapted from Ref. [48]
• the derivatives are
\[ \frac{\partial G}{\partial s_i} = \sum_j \frac{\partial G}{\partial \tilde{h}_j} O_{ji} \frac{1}{\sqrt{\lambda_i}} \]

• all degrees of freedom are treated on equal footing which results in better sampling of the order parameter space

• the technique has been applied to many systems - see review papers [50, 51]

Part V
Optimization methods for complex problems

Literature:

25 Optimization problems in science and in everyday life

• optimization problems are very often encountered in science and in everyday life

• many other problems do not look like optimization problems but can be represented in this form

• Examples: the Traveling Salesman Problem, study of physical systems such as clusters, crystals, proteins etc.

• we search for a minimum of a function (called cost function) or a maximum of a function (called fitness function)

• the cost function depends on variables which can be discrete or continuous

• the cost function typically depends on a large number of variables - Combinatorial Optimization
The Traveling Salesman Problem (TSP)

- N cities and their mutual distances are given
- one searches for the shortest closed path which visits each city exactly once
- the TSP is a paradigm in combinatorial optimisation
- many methods are known
- many applications of the problem exist - traffic problems, hole drilling, optimization of circuits in computers

Figure 37: Problem pr1002 from the TSPLIB library [52]

Optimization problems and cost function landscapes

- cost function landscapes is the evaluation of the cost function for all solution candidates
- it is hard to imagine because of large number of variables (high dimensional space)
• we think in terms of mountains (most ways lead down) and valleys (most ways lead up)

• the difficulty of the optimization problem depends mainly on the structure of the landscape

• simple case - a single minimum, local and at the same time global minimum

• steepest-descent (gradient) methods are effective

![Figure 38: Approach to a simple minimum](image)

**Complex landscapes**

• in real-life problems there is often competition between different interactions that cannot be satisfied at the same time - frustration

• complex landscapes - high mountains separated by deep valleys

• non-convex cost functions - many local minima

• to leave a local minimum one has to move uphill

• more complicated procedures needed to find the global minimum
• large number of almost degenerate solutions
• many local minima, one global minimum

Figure 39: Complex energy landscape

26 Solution of optimization problems by computer - algorithms

• looks easy but actually is not always so
• for complex problems, unless the size of the problem is very small, it is often extremely difficult to find an exact solution (global minimum)

How do resources (time, memory) needed to find the solution depend on the size of the problem?

• polynomial problems $t \propto N^m$, $m > 0$
• non-polynomial problems $t \propto e^{\alpha N}$, $\alpha > 0$
Computational Complexity Theory

- developed by S.A. Cook (1972)

- NP-complete problems - class of non-polynomial problems which are in some sense "equally difficult" - if one is solved, all others are solved, too

- no algorithm is known which solves such problems in polynomial time and we believe that is actually does not exist (but there is no proof)

- Example: problem requiring $2^N$ operations, $N = 100$

- computer performing $10^{10}$ operations (10 gigaoperations)/s

- time needed is $2^{100}/10^{10} \approx 10^{20} \approx 4 \times 10^{12}$ years

- astronomical time (longer than the age of universe) is needed

- brute computer force not sufficient, only small problems can be solved exactly

- intractable problems - solvable in theory but not in practice

- Examples of intractable problems: SAT (Logic), Traveling Salesman Problem, Protein Folding, and many others

- *is the situation hopeless?*

Heuristic Optimization Methods

- often it is enough to find an approximate solution if it can be obtained fast enough

- heuristic algorithms find acceptable solutions in relatively short time

- how to find such algorithms?

- optimization problems are very different, is it possible to find a generic algorithm which works well for many problems?

From Nature to Algorithms

- Nature often solves extremely complicated optimization problems in very efficient way

- Examples: Biology, Physics

- Goal: development of universal algorithms

- it is always important to find a suitable mathematical representation
27 Nature inspired heuristic algorithms

- natural selection optimizes fitness of living organisms
- an ant colony searches an optimal way from food to the nest
- neural networks (brain) solve difficult computational problems
- atoms and molecules approach a minimum of potential energy upon decrease of temperature (crystallization)

Evolutionary and genetic algorithms

- genetic algorithms (GA) try to mimic the biological evolution (J.H. Holland (1975) [53])
- Initialisation: a population of individuals (solution candidates) is created
- Evaluation: the fitness-function is computed for all solution candidates
- Selection: choice of best solution candidates
- Crossover: the properties of different individuals are combined in order to produce a new generation of individuals
- Mutation: random change of properties of individuals of the new generation
- for the TSP problem GA are very efficient
- generally GA belong to the strongest heuristic algorithms
Examples of application of a genetic algorithm in physics

Figure 41: Finding the ground state of 60 carbon atoms - C$_{60}$ fullerene [54]

- no information on gradients (derivatives) is necessary
- application of GA to the Crystal structure prediction problem (Oganov and Glass (2006) [55]) was extremely successful - USPEX algorithm

**Ant colony optimization (ACO)**

- ants walk randomly and when they find food they return back to the colony
- while walking they leave a pheromone trail which attracts other ants which preferentially follow the same one
- over time pheromone evaporates so the trail disappears
- if the path is long, it takes more time to travel and the pheromone evaporates more
- if the path is short, the pheromone accumulates faster
- if one ant finds a short path, the others will follow
- the ACO algorithm (Dorigo (1991,1992) [56, 57]) simulates this behaviour with simulated ants

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• the algorithm can be used for TSP
• can be run continuously and has the ability to adapt in real time to changes in the situation
• can be used in traffic problems

**Annealing in physical systems**
• metallurgy studies crystallisation of metals from a melt upon cooling
• slower cooling produces better crystals with less defects
• less defects means lower energy, perfect crystal is a global minimum of energy
• how does the physical system manage to approach the minimum?
• Boltzmann distribution: \[ P(E) = C e^{-E/T} \]

Figure 42: Basic idea of simulated annealing - slow cooling drives the system towards the ground state

**Simulated Annealing (SA)**
• Kirkpatrick et al. (1983) [58], V. Černý (1985) [59]
• simulation of the cooling process on the computer
• deep analogy between statistical mechanics and optimization process
• fictitious temperature T controls which parts of the landscape can be visited
• at the beginning T is high
• slow cooling down to T=0
• at the end the system is likely to be in a low-energy state close to the global minimum

28 Simulated annealing of the Traveling Salesman Problem

How to implement the "cooling of path" on a computer ?

• control of temperature is key to steering the optimization process towards the minimum
• we need two ingredients
• generate a new path by transforming one path into another (tour construction)
• mimic the temperature effect
• there are various ways how to implement the SA algorithm
• Monte Carlo (MC) is a general stochastic simulation technique based on generating random numbers
• stochastic optimization

How can we transform one path into another ?

• so-called 2-opt move is simple and efficient (Fig.43)
• we pick at random 4 cities, cut the path at 2 points and reconnect the other possible way
• the new path has a length different from that of the old one
• another similar possibility is 3-opt move
How to generate paths with probability $\sim \exp(-E/T)$?

Metropolis algorithm (Metropolis, Rosenbluth, Rosenbluth, Teller and Teller (1953) [60])

- the new configurations are accepted or rejected in particular way so that every configuration is visited with the probability given by the Boltzmann factor
- downhill moves are accepted always
- uphill moves are accepted with a certain transition probability $P_{\text{old} \rightarrow \text{new}}$
  \[ P_{\text{old} \rightarrow \text{new}} = \exp\left[-\frac{(E_{\text{new}} - E_{\text{old}})}{T}\right] \quad \text{when} \quad E_{\text{new}} > E_{\text{old}} \]
  \[ P_{\text{old} \rightarrow \text{new}} = 1 \quad \text{when} \quad E_{\text{new}} < E_{\text{old}} \]
- if the new configuration is rejected, the old one is considered to be the new one

Stochastic optimization: Simulated Annealing by Monte Carlo technique

- annealing schedule defines how the temperature is reduced
- at the end of the allocated time budget temperature $T$ must be close to zero
- often one uses an exponential schedule:
  \[ T_{n+1} = \alpha T_n, \alpha < 1 \quad \text{(for example } \alpha = 0.99) \]
- at every temperature one performs some number of moves
one keeps track of the best solution found
the algorithm stops when no moves are accepted

**Pseudo-code for simulated annealing**
we take the length L of the path as cost function or energy E

1. generate a random starting path
2. set temperature \( T_0 = T_{\text{init}} \)
3. perform M times the steps 4 - 7
4. pick 4 cities for the 2-opt move
5. perform the 2-opt move
6. calculate the change of the path length \( \Delta L = L_{\text{new}} - L_{\text{old}} \)
7. accept or reject the move according to the Metropolis algorithm
8. take a new temperature \( T_{\text{new}} = \alpha T_{\text{old}} \) and repeat the steps 3 - 8
9. stop when no moves are accepted (or at a prescribed final temperature \( T_{\text{final}} \))
10. take as result either the final value of L or the best one found

**Results of SA for the TSP**
- problem pr1002 with 1002 cities using the 2-opt moves [52]
- temperature T was linearly decreased
- it is relatively easy to get to within 1% of the optimal solution, but further improvement is very difficult (Figs.44, 45)
- SA is a very general method that is easy to implement for various systems
- no information on gradients (derivatives) is necessary

**Why does SA work?**
- allowing for uphill moves in controlled manner provides a way to get out of a local minimum
- a kind of divide-and-conquer strategy is present
- at higher temperatures only gross features of the landscape are seen and the algorithm induces major changes to the path
- at lower temperatures fine details emerge and the algorithm accordingly performs minor corrections to the path
Figure 44: Simulated annealing of the pr1002 problem - excess length vs. total annealing time

29 Summary

- optimization is a ubiquitous and important problem
- there is no completely universal method but generic heuristic algorithms often work well
- heuristic algorithms motivated by Nature are powerful
- not modeling of Nature but transfer of ideas
- it is possible to combine different optimization methods
- lot of space for improvement
Figure 45: Comparison of the best result found by SA with the optimal solution
References


[52] http://comopt.ifi.uni-heidelberg.de/software/TSPLIB95/


