

Statistical Physics and Computer Simulation

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A summary of the course “Statistical Physics and Computer Simulation”

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1. Overview of Physics

1.1. Energy

- Energy is **conserved** for **isolated** systems, it can only undergo **interconversion** between different forms.
 - “wasting energy” in a system means to take work, heat and/or molecules from an isolated system
 - Prevent the unnecessary conversion of high-quality energy (**work or chemical**) into low-quality one (**heat**)
- Noether’s theorem: Every differentiable **symmetry** of the action of a physical system with conservative forces has a corresponding **conservation law**
 - Translation in space \leftrightarrow Linear momentum conservation
 - Rotation in space \leftrightarrow Angular momentum conservation
 - Translation in time \leftrightarrow Energy conservation

At the classical level

$$E = \mathcal{V}(\mathbf{r}^N) + \mathcal{K}(\mathbf{v}^N) \quad (1)$$

- $\mathbf{r}^N \leftrightarrow$ 3N-dimensional coordinate vector
- $\mathbf{v}^N \leftrightarrow$ 3N-dimensional velocity vector
- $\mathcal{V}(\mathbf{r}^N) \leftrightarrow$ potential energy (interactions)
- $\mathcal{K}(\mathbf{v}^N) = \sum_i^N \left(\frac{m_i v_i^2}{2} \right) \leftrightarrow$ kinetic energy (motion)

At the quantum mechanical level

$$\hat{\mathcal{H}}\Psi(\mathbf{r}^N) = E\Psi(\mathbf{r}^N) \quad (2)$$

- $\hat{\mathcal{H}} = \hat{\mathcal{K}} + \mathcal{V} \leftrightarrow$ Hamiltonian operator
- $\Psi \leftrightarrow$ System wave function

$$\hat{\mathcal{K}} = -\sum_i^N \frac{\hbar^2}{2m_i} \frac{\partial^2}{\partial r_i^2} \quad (3)$$

1.2. Pressure

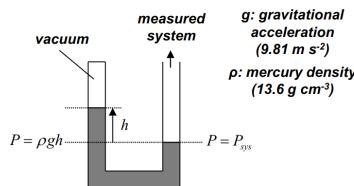
Mechanical Definition

Pressure P equals to the magnitude of the force F exerted on a surface, divided by the area Σ .

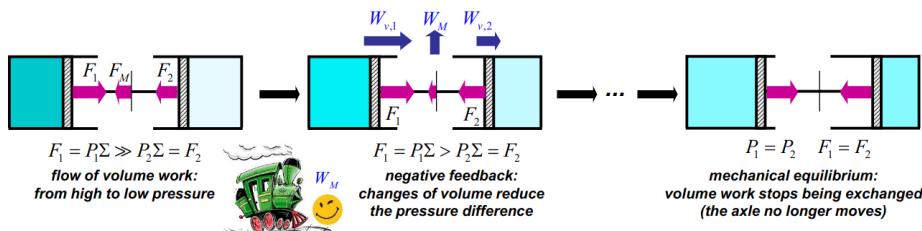
$$P = \frac{F}{\Sigma} \quad (4)$$

Example: Mercury barometer at mechanical equilibrium

$$P_{\text{sys}} = \rho gh \quad (5)$$



Thermodynamic Definition



Pressure is the thermodynamic potential controlling the flow of volume work (mechanical work).

- an **intensive** quantity, it is **local** in space and **not additive** over space
- Pressure units:

$1 \text{ [Pa]} = 1 \text{ [N} \cdot \text{m}^{-2}\text{]} = 1 \text{ [J} \cdot \text{m}^{-3}\text{]}$	SI UNIT
$1 \text{ [bar]} = 10^5 \text{ [Pa]} = 10^5 \text{ [J} \cdot \text{m}^{-3}\text{]}$	Unit most common in thermodynamics
$1 \text{ [atm]} = 1.013 \text{ [bar]}$	Average atmospheric pressure at sea level
$1 \text{ [torr]} = 1 \text{ [mm Hg]} = \frac{1}{760} \text{ [atm]}$	

Microscopic Interpretation

The pressure in a **confined** system results from the **collisions** of the molecules with the walls of the container

For **one particle** over a given **time interval**

$$k_i(t; \Delta t) = \begin{cases} v_{\perp}(t) & \text{if a collision occurs between } t \text{ and } t + \Delta t \\ 0 & \text{otherwise} \end{cases} \quad (6)$$

Overall pressure in the container

Note: the generalized definition is not restricted to an integral over walls

- one can define an arbitrary infinitesimal surface element in the system and consider the rate of momentum transfer through this element
- can also be generalized to an anisotropic pressure tensor

$$\begin{cases} k_{\text{tot}}(t; \Delta t) = \sum_i^N k_i(t; \Delta t) & \leftrightarrow \text{total 'kick' of all N particles} \\ P(t) = \frac{2m k_{\text{tot}}(t; \Delta t)}{\Delta t \Sigma} & \leftrightarrow \text{instantaneous pressure} \\ P = \lim_{t \rightarrow \infty} \frac{1}{t} \int_0^t dt' P(t') & \leftrightarrow \text{average pressure} \end{cases} \quad (7)$$

1.3. Temperature

Mechanical Definition

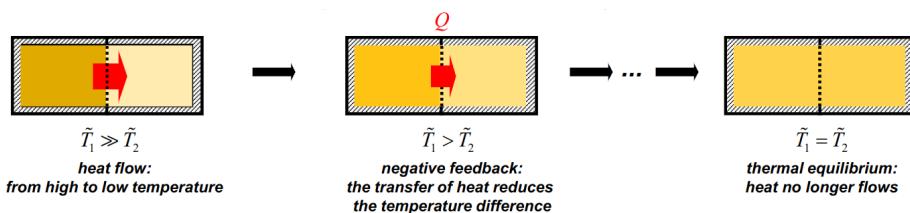
The temperature measures the average kinetic energy per degree of freedom in units of the half Boltzmann constant $\frac{k_B}{2}$

$$T = \frac{2K}{k_B N_{\text{dof}}} \quad (8)$$

- Boltzmann constant: $k_B = 1.381 \times 10^{-23} \text{ J} \cdot \text{K}^{-1}$

Thermodynamic Definition

Temperature is the thermodynamic potential controlling the flow of heat



Temperature is a measure for the thermal energy (extent of jiggling and wiggling [translation, rotation, vibration] of the molecules)

- an intensive quantity like pressure, i.e. it is local in space and not additive over space
- At the absolute zero (zero Kelvin) thermal motion ceases (except for the quantum-mechanical zero-point energy)

Unit conversions

1 [K]	SI UNIT
$T \text{ [K]} = \tilde{T} \text{ [}^{\circ}\text{C} \text{]} + 273.15 \text{ [}^{\circ}\text{C}]$	Unit most common in thermodynamics
$\tilde{T} \text{ [}^{\circ}\text{C}] = (\tilde{T}' \text{ [}^{\circ}\text{F}] - 32 \text{ [}^{\circ}\text{F}]) \times \frac{5}{9}$	used in the US

$$\left\{ \begin{array}{ll} 0^\circ F \rightarrow -17.8^\circ C & 0^\circ C \rightarrow 32^\circ F \\ 32^\circ F \rightarrow 0^\circ C & 25^\circ C \rightarrow 77^\circ F \\ 100^\circ F \rightarrow 37.8^\circ C & 50^\circ C \rightarrow 122^\circ F \end{array} \right\}$$

1.4. Ideal Gas

$$PV = nRT \quad (9)$$

With gas constant $\leftrightarrow R = 9.134 J \cdot mol^{-1} \cdot K^{-1}$

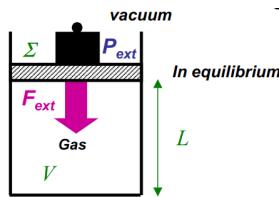
Per-mole variant of the Boltzmann constant

$$R = N_A k_B \quad (10)$$

- $k_B = 1.380649 \times 10^{-23} J \cdot K^{-1}$ \leftrightarrow Boltzmann constant
- $N_A = 6.02214076 \times 10^{23} mol^{-1}$ \leftrightarrow Avogadro constant

1.4.1. Temperature - macroscopic view

Derived from the ideal gas law for gas in a container



$$T = \frac{PV}{nR} = \frac{P_{ext}V}{nR} = \frac{F_{ext}V}{n\Sigma R} = \frac{mg}{n\Sigma R} L = C \cdot L \quad (11)$$

- $C = \frac{mg}{nR}$ is constant

1.4.2. Temperature - microscopic view

Equipartition principle: In a molecular system at equilibrium and in the classical limit, the average kinetic energy “stored” in each degree of freedom amounts to $\frac{1}{2}k_b T$

- holds only in the classical limit, quantum effects reduce this capacity especially at low temperature

Special Case: Monoatomic substance (irrespective gas, liquid or solid)

$$T = \frac{2K}{k_B N_{dof}} \begin{cases} K = \frac{1}{2} \sum_{i=1}^N m_i v_i^2 & \text{if a collision occurs between } t \text{ and } t + \Delta t \\ \text{with} \\ N_{dof} = 3N \end{cases} \quad (12)$$

Thermodynamic beta

$$\beta = \frac{1}{k_B T} \quad (13)$$

1.4.3. Kinetic Theory of the Ideal Gas

- For derivations of the **Ideal Gas Equation** and the **Maxwell-Boltzmann velocity distribution**
- hard-sphere collision model for understanding the macroscopic properties of the **ideal gas**, assuming gas molecules as *hard spheres* of **mass** m and **radius** $r \rightarrow 0$

Calculation of pressure

- Instantaneous pressure

$$P = \frac{F}{\Sigma} = \frac{\overbrace{\Delta p}^{\text{momentum transferred}}}{\Sigma \cdot \Delta t} = \frac{1}{2} \cdot \frac{\overbrace{\rho \sum |v_x| \Delta t \cdot 2m |v_x|}^{\text{no. atoms}}}{\Sigma \cdot \Delta t} = \rho m v_x^2 \quad (14)$$

- Pressure as mean-square velocity

$$P = \langle P \rangle = \rho m \langle v_x^2 \rangle = \langle \frac{\rho m}{3} \rangle \quad (15)$$

- Relation to kinetic energy

$$K = \langle \mathcal{K} \rangle = \frac{Nm}{2} \langle v^2 \rangle = \frac{\rho mV}{2} \langle v^2 \rangle \quad (16)$$

Thus, when combining:

$$PV = \frac{2}{3}K \quad (17)$$

Comparing with the ideal gas law

$$PV = Nk_B T \quad (18)$$

The right-hand-side gives the following relation

$$K = \frac{3}{2}Nk_B T = \frac{Nm}{2} \langle v^2 \rangle \quad (19)$$

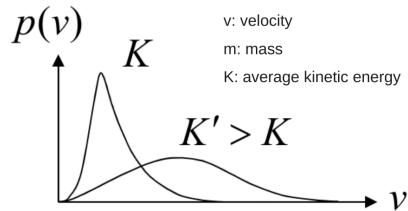
This gives

$$\langle v^2 \rangle = \frac{3k_B T}{m} \quad (20)$$

1.4.4. Maxwell-Boltzmann velocity distribution

Let $p(v)dv$ be the probability that the velocity (norm) of a gas particle is between v and $v + dv$, such that $\int_0^\infty p(v)dv = 1$.

$$p(v) = 4\pi \left(\frac{3m}{4\pi K} \right)^{\frac{3}{2}} v^2 \exp\left(-\frac{3mv^2}{4K}\right) \quad (21)$$



1.5. Real Gas

Modified ideal gas equation can be modified to account for **non-ideality**

Ideal gas:

$$P = \frac{nRT}{V} \quad (22)$$

Real gas:

$$P = \underbrace{\frac{nRT}{V - nb}}_{\text{effective volume for particles}} - \overbrace{a \left(\frac{n}{V} \right)^2}^{\substack{\text{attractive forces} \\ \text{reduce the effective pressure}}} \quad (23)$$

Excluded volume of a gas particle:

$$N_A^{-1} b \quad (24)$$

Assuming spherical particles of radius r , we would have:

$$b = \frac{1}{2} \cdot \frac{4\pi}{3} \cdot (2r)^3 \cdot N_A = \frac{16}{3} N_A r^3 \quad (25)$$

1.6. Entropy

In an isolated system, when processes are relaxing to equilibrium (e.g. after a change in boundary conditions), the **spontaneity** is governed by the **entropy** of processes.

$$S = k_B \ln(\Omega) \quad (26)$$

This definition by Boltzmann refers to a projection from **high-dimensional** space of **microstates** to a **lower-dimensional** space of **macro-states**. It drastically reduce the dimensionality by projection.

$$\Omega(\mathcal{Q}') = \underbrace{C}_{\text{normalization constant}} \cdot \int d\mathbf{x} \delta\left(\underbrace{\mathcal{Q}(\mathbf{x})}_{\text{projection}} - \mathcal{Q}'\right) \quad (27)$$

Here, Ω is the **weight** of a macro-state, defined as the hyper-volume of micro-state space that projects onto this point in macro-state space. δ is the Dirac Delta function for selecting all vectors \mathbf{x} for which $\mathcal{Q}(\mathbf{x}) = \mathcal{Q}'$.

Entropy is Logarithmic

Entropy is logarithmic and thus extensive, i.e. additive over subsystems. The contribution of correlations between the two subsystems is negligible, provided that the systems are sufficiently large.

$$\begin{cases} \Omega_{1+2} = \Omega_1 \cdot \Omega_2 \\ S_{1+2} = S_1 + S_2 \end{cases} \quad (28)$$

Human biases in understanding entropy

Entropy is a macro-state and given configurations of micro-states, humans often implicitly define a projection from given micro-state configurations into macro-states.

1.6.1. Micro-canonical Entropy

Consider a molecular system at constant N, T as microstates of high-dimensionality, the total energy of a configuration is a one-dimensional macro-state(projection).

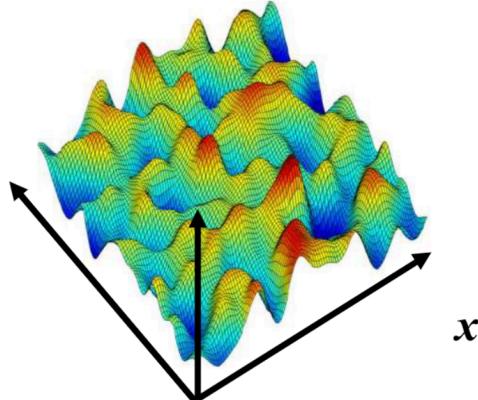
$$S(E) = k_B \ln(\Omega(E)) \quad (29)$$

where $\Omega(E)$ represents number of states at energy E ,

$$\Omega(E') = \int d\mathbf{x} \delta(E - E') \quad (30)$$

Moreover,

$$\frac{dS}{dE} = \frac{1}{T} \quad (31)$$



1.6.2. Probability distribution as a special type of projection

$$S(p) = k_B \underbrace{- \ln \sum p_m \ln(p_m)}_{\sim \Omega(p) \text{ at large } N} \quad (32)$$

Principle of *a priori* equiprobability

All microstates compatible with the specified macroscopic constraints (fixed N, V, P, E or T) are equally probable.

Principle of ergodicity

Given sufficient time, a system will visit all the microstates compatible with the specified macroscopic constraints.

Größe, Bezeichnung	F, L, T, ϑ	M, L, T, ϑ	Einheiten
Länge	L	L	Meter, m
Kraft	F	MLT^{-2}	Newton, N
Masse	$FL^{-1}T^2$	M	Kilogramm, kg
Zeit	T	T	Sekunde, s
Temperatur	ϑ	ϑ	Kelvin, K
Geschwindigkeit	LT^{-1}	LT^{-1}	m/s
Beschleunigung	LT^{-2}	LT^{-2}	m/s^2
Druck, Spannung	FL^{-2}	$ML^{-1}T^{-2}$	Pascal, $Pa = N/m^2$
Moment, Arbeit, Energie	FL	ML^2T^{-2}	Joule, $J = Ws = Nm$
Leistung, Energiestrom	FLT^{-1}	ML^2T^{-3}	Watt, $W = Nm/s$
Dichte	$FL^{-4}T^2$	ML^{-3}	kg/m^3
Massenstrom	$FL^{-1}T^1$	MT^{-1}	kg/s
dynamische Viskosität	$FL^{-2}T$	$ML^{-1}T^{-1}$	$Pa\ s = Ns/m^2$
kinematische Viskosität	L^2T^{-1}	L^2T^{-1}	m^2/s
Oberflächenspannung	FL^{-1}	MT^{-2}	$N/m = kg/s^2$
spezifische Wärmekapazität	$L^2T^{-2}\vartheta^{-1}$	$L^2T^{-2}\vartheta^{-1}$	$J/(kg\ K)$
Wärmeleitfähigkeit	$FT^{-1}\vartheta^{-1}$	$MLT^{-3}\vartheta^{-1}$	$W/(m\ K)$
spezielle Gaskonstante R	$L^2T^{-2}\vartheta^{-1}$	$L^2T^{-2}\vartheta^{-1}$	$J/(kg\ K)$

2. Classical Mechanics

2.1. Newtonian Formulation

Newtonian formulation of classical mechanics is **only valid** in a Cartesian coordinate system. Consider a system of N particles involving $3N$ Cartesian degrees of freedom, changing as a function of time t .

- The Cartesian coordinate vector $\mathbf{r}^N = \mathbf{r}^N(t)$,

$$\mathbf{r}^N = \{\mathbf{r}_1, \mathbf{r}_2, \dots, \mathbf{r}_N\} \quad (33)$$

- The Cartesian momentum vector $\mathbf{p}^N = \mathbf{p}^N(t)$,

$$\mathbf{p}^N = \{\mathbf{p}_1, \mathbf{p}_2, \dots, \mathbf{p}_N\} \quad (34)$$

where for each particle:

$$\mathbf{p}_i = m_i \dot{\mathbf{r}}_i \quad (35)$$

2.1.1. Newtonian Equation of Motion (Newton's second law)

The rate of change of the momentum of a particle is equal to the force acting on the particle.

$$m_i \ddot{\mathbf{r}}_i = \dot{\mathbf{p}}_i = \mathbf{F}_i, \text{ where } i = 1, 2, \dots, N \quad (36)$$

Consider the Cartesian force vector of the N -particle system,

$$\mathbf{F}^N = \{\mathbf{F}_1, \mathbf{F}_2, \dots, \mathbf{F}_N\} \quad (37)$$

Then at any time t , with \underline{M} being the $3N \times 3N$ mass matrix that is diagonal,

$$\underline{M} \ddot{\mathbf{r}}^N = \dot{\mathbf{p}}^N = \mathbf{F}^N \quad (38)$$

2.1.2. The Law of Action and Reaction (Newton's Third Law)

The forces between two objects always arise by *pairs of forces* with *equal magnitudes* and *opposite directions*. Between two point masses i and j .

$$\begin{array}{c} \text{force exerted} \\ \text{by i onto j} \\ \widehat{\mathbf{F}}_{ji} \end{array} = \underbrace{-\mathbf{F}_{ij}}_{\substack{\text{force exerted} \\ \text{by j onto i}}} \quad (39)$$

In most cases, these two forces are also **central**, obeying the strong law; in some cases such as magnetic forces the weak law is obeyed.

ISOLATED SYSTEM (ALL FORCE PAIRS WITHIN THE SYSTEM)	OPEN SYSTEM
$\mathbf{p}_{\text{tot}} = \sum_i \mathbf{p}_i \quad (40)$	$\dot{\mathbf{p}}_{\text{tot}} = \mathbf{F}_{\text{ext, tot}} \quad (41)$
$\mathbf{L}_{\text{tot}} = \sum_i \mathbf{r}_i \times \mathbf{p}_i \quad (42)$	$\dot{\mathbf{L}}_{\text{tot}} = \mathbf{M}_{\text{ext, tot}} \quad (43)$

2.1.3. Force Expression of a System

$$\mathbf{F}^N = \mathbf{F}^N(\mathbf{r}^N, \mathbf{p}^N, t) \quad (44)$$

NEWTON (GRAVITATION)	COULOMB FOR POINT CHARGES
$\mathbf{F}_1 = \frac{Gm_1 m_2}{r^2} \mathbf{e}_x$ (45)	$ \mathbf{F} = k_e \frac{ q_1 q_2 }{r^2}$ (46)
Archimedes (buoyancy)	Lorentz (electromagnetism)
$\mathbf{F} = -\rho g V \mathbf{e}_x$ (47)	$\mathbf{F} = q(\mathbf{E} + \dot{\mathbf{r}} \times \mathbf{B})$
Lenard-Jones (closed-shell interactions)	Friction (resistance to motion)
$\mathbf{F}_1 = 4\varepsilon \left(-12 \left(\frac{\sigma}{r} \right)^{12} + f \left(\frac{\sigma}{r} \right)^6 \right) \frac{\mathbf{r}}{r^2}$ (48)	$\mathbf{F} = -k\dot{\mathbf{r}}$
Hooke (harmonic spring)	
$\mathbf{F} = -k(x - x_o)\mathbf{e}_x$ (49)	

2.1.4. Deterministic Nature of Classical Mechanics

Given the *equation of motion* and a *force expression*, classical mechanics is deterministic.

From Newton's second law, where $\dot{\mathbf{p}}^N = \mathbf{F}^N$ holds:

$$\begin{aligned} \underline{\mathbf{M}} \ddot{\mathbf{r}}^N &= \dot{\mathbf{p}}^N \\ \ddot{\mathbf{r}}^N &= \underline{\mathbf{M}}^{-1} \dot{\mathbf{p}}^N \end{aligned} \quad (50)$$

At final state at $t = t_{\text{fin}}$, $\mathbf{r}^N(t_{\text{fin}})$ and $\mathbf{p}^N(t_{\text{fin}})$ are predictable.

2.1.5. Conservative Field in Newtonian Formulations

A force corresponds to a field if it only depends on the coordinate vector

$$\mathbf{F}^N = \mathbf{F}^N(\mathbf{r}) \quad (51)$$

The field is conservative if the forces do not work over a closed path.

$$\oint d\mathbf{r}^N \cdot \mathbf{F}^N(\mathbf{r}^N) = \sum_i^N \oint d\mathbf{r}_i \cdot \mathbf{F}_i(\mathbf{r}^N) = 0 \quad (52)$$

It means bringing particles back to the same position, the forces have done a total work of zero.

Stokes Theorem Sufficient condition to be a conservative field, if the force is curl-free for all particles.

$$\frac{\partial}{\partial \mathbf{r}_i} \times \mathbf{F}_i(\mathbf{r}^N) = 0, \forall i \quad (53)$$

Application: Potential energy of a conservative field

$$\mathbf{F}_i(\mathbf{r}^N) = -\frac{\partial}{\partial \mathbf{r}_i} \mathcal{V}(\mathbf{r}^N) \quad (54)$$

- minus sign means the force drives a particle towards a lower potential energy.
- time-dependent potential energy function:** more generalized, it can be time-dependent but conservative at any instant

$$\mathbf{F}_i(\mathbf{r}^N, t) = -\frac{\partial}{\partial \mathbf{r}_i} \mathcal{V}(\mathbf{r}^N, t) \quad (55)$$

2.1.6. Total Energy of Conservative Fields

For a conservative field, the total energy is a constant of the motion. For a conservative N-particle system it holds:

$$\mathcal{V}(\mathbf{r}^N) + \mathcal{K}(\dot{\mathbf{r}}^N) = E = \text{const} \quad (56)$$

with the **kinetic energy** defined as follows, with $\mathbf{p}_i = m_i \dot{\mathbf{r}}_i$

$$\begin{aligned} \mathcal{K}(\dot{\mathbf{r}}^N) &= \sum_i^N \frac{m_i \dot{\mathbf{r}}_i^2}{2} \\ &= \sum_i^N \frac{m_i^2 \dot{\mathbf{r}}_i^2}{2m_i} \\ &= \sum_i^N \frac{\mathbf{p}_i^2}{2m_i} \end{aligned} \quad (57)$$

If the system has a time-dependent potential energy function $\mathcal{V}(\mathbf{r}^N, t)$, then it holds $\mathcal{V}(\mathbf{r}^N, t) + \mathcal{K}(\dot{\mathbf{r}}^N) = E(t)$.

2.2. Lagrangian Formulation

- Valid in any **generalized** coordinate system.

Practical Usage:

- Enforcing **constraints** in the dynamics
- Adding **artificial degrees of freedom** to the dynamics
- **Generalizing** mechanics to entities other than point particles

Generalized coordinate system A generalized coordinate system is any set of M scalars (eg. positions, angles, dihedrals...) sufficient to specify the coordinates of all particles in the system

- Generalized coordinates

$$\mathbf{q}^M = \{q_1, q_2, \dots, q_M\}, \text{ where for } N \text{ particles } M = 3N \quad (58)$$

such that the position is well-defined using the scalar quantities, and there is an invertible mapping to express \mathbf{q}_i using \mathbf{r}_i .

$$\begin{cases} \mathbf{r}^N = \mathbf{r}^N(\mathbf{q}^M) \\ \mathbf{q}^M = \mathbf{q}^M(\mathbf{r}^N) \end{cases} \quad (59)$$

- Generalized velocities

$$\dot{\mathbf{q}}^M = \{\dot{q}_1, \dot{q}_2, \dots, \dot{q}_M\} \quad (60)$$

such that $\dot{\mathbf{r}}^N = \dot{\mathbf{r}}^N(\mathbf{q}^M, \dot{\mathbf{q}}^M)$

2.2.1. Energy in Conservative Fields with Lagrangian Function

Recall from Newtonian formulation of energy conservation of a conservative field

$$\mathcal{V}(\mathbf{r}^N) + \mathcal{K}(\dot{\mathbf{r}}^N) = E = \text{const} \quad (61)$$

with

$$\mathcal{K}(\dot{\mathbf{r}}^N) = \sum_i^N \frac{m_i \dot{\mathbf{r}}_i^2}{2} \quad (62)$$

For a conservative field, one can define the Lagrangian function as

$$\mathcal{L}(\mathbf{q}^M, \dot{\mathbf{q}}^M) = \mathcal{K}(\mathbf{q}^M, \dot{\mathbf{q}}^M) - \mathcal{V}(\mathbf{q}^M) \quad (63)$$

- In case the potential energy is **time-dependent**, we have

$$\mathcal{L}(\mathbf{q}^M, \dot{\mathbf{q}}^M, t) = \mathcal{K}(\mathbf{q}^M, \dot{\mathbf{q}}^M) - \mathcal{V}(\mathbf{q}^M, t) \quad (64)$$

with

$$\frac{\partial \mathcal{L}}{\partial t} = -\frac{\partial \mathcal{V}}{\partial t} \quad (65)$$

The kinetic energy is a quadratic expression, that depends not only on generalized velocities, but also on the generalized coordinates.

$$\mathcal{K}(\mathbf{q}^M, \dot{\mathbf{q}}^M) = \frac{1}{2} (\dot{\mathbf{q}}^M)^T \underline{\mathbf{M}}(\mathbf{q}^M) \dot{\mathbf{q}}^M \quad (66)$$

Mass-metric tensor A symmetric but not necessarily diagonal, \mathbf{q} -dependent mass-metric tensor.

$$\underline{\mathbf{M}}_{kl} = \sum_i^N m_i \frac{\partial \mathbf{r}_i}{\partial q_k} \frac{\partial \mathbf{r}_i}{\partial q_l} \quad (67)$$

2.2.2. Lagrangian Equation of Motion

- Euler-Lagrange equation.
- Derivable from the **principle of least action**
 - *The physical trajectory between the system configurations at two time points is the one that minimizes the action.*

$$\frac{d}{dt} \left(\frac{\partial \mathcal{L}(\mathbf{q}^M, \dot{\mathbf{q}}^M)}{\partial \dot{q}_m} \right) = \frac{\partial \mathcal{L}(\mathbf{q}^M, \dot{\mathbf{q}}^M)}{\partial q_m}, \text{ with } m = 1, 2, \dots, M \quad (68)$$

Example: Polar coordinates

$$\begin{cases} \frac{d}{dt} \left(\frac{\partial \mathcal{L}}{\partial \theta} \right) = \frac{\partial \mathcal{L}}{\partial \dot{\theta}} \\ \frac{d}{dt} \left(\frac{\partial \mathcal{L}}{\partial r} \right) = \frac{\partial \mathcal{L}}{\partial \dot{r}} \end{cases} \quad (69)$$

Example: Lagrangian Equations of Motion in Cartesian Coordinates

In Cartesian coordinates, we have the general form as follows. Replacing generalized coordinates \mathbf{q}^M by Cartesian coordinate vectors \mathbf{r}^N .

$$\begin{aligned} \mathcal{L}(\mathbf{r}^N, \dot{\mathbf{r}}^N) &= \mathcal{K}(\dot{\mathbf{r}}^N) - \mathcal{V}(\mathbf{r}^N) \\ &= \sum_i^N \frac{m_i \dot{\mathbf{r}}_i^2}{2} - \mathcal{V}(\mathbf{r}^N) \end{aligned} \quad (70)$$

For the left-hand side, note that the $\frac{\partial}{\partial r_i}$ is derivative with respect to only one coordinate, thus all other entries in the summation disappear.

$$\begin{aligned} \frac{d}{dt} \left(\frac{\partial \mathcal{L}(\mathbf{r}^N, \dot{\mathbf{r}}^N)}{\partial \dot{r}_i} \right) &= \frac{d}{dt} \left(\frac{\partial}{\partial \dot{r}_i} \left(\sum_i^N \frac{m_i \dot{\mathbf{r}}_i^2}{2} - \mathcal{V}(\mathbf{r}^N) \right) \right) \\ &= m_i \ddot{\mathbf{r}}_i \end{aligned} \quad (71)$$

For the right-hand side:

$$\begin{aligned} \frac{\partial \mathcal{L}(\mathbf{r}^N, \dot{\mathbf{r}}^N)}{\partial r_i} &= \frac{\partial}{\partial r_i} \left(\sum_i^N \frac{m_i \dot{\mathbf{r}}_i^2}{2} - \mathcal{V}(\mathbf{r}^N) \right) \\ &= -\frac{\partial}{\partial r_i} \mathcal{V}(\mathbf{r}^N) \\ &= \mathbf{F}_i(\mathbf{r}^N) \end{aligned} \quad (72)$$

Combining both sides, we have the equivalent formulation to the Newtonian one $m_i \ddot{\mathbf{r}}_i = \mathbf{F}_i(\mathbf{r}^N)$.

2.3. Hamiltonian Formulation

- Also **Valid** in any **generalized** coordinate system.
- *Connecting quantum to classical mechanics*, with Hamiltonian function as an operator
- *Formulation of statistical mechanics*, where total energy is a central quantity

Conjugate momenta

$$\mathbf{p}^M = \{p_1, p_2, \dots, p_M\} \quad (73)$$

defined as

$$p_m := \frac{\partial \mathcal{L}(\mathbf{q}^M, \dot{\mathbf{q}}^M)}{\partial \dot{q}_m} \quad (74)$$

2.3.1. Hamiltonian as Total Energy in Conservative Fields

$$\mathcal{H}(\mathbf{q}^M, \mathbf{p}^M) = \underbrace{\mathcal{K}(\mathbf{q}^M, \mathbf{p}^M)}_{\text{kinetic energy}} + \underbrace{\mathcal{V}(\mathbf{q}^M)}_{\text{potential energy}} = E = \text{const} \quad (75)$$

Hamiltonian Function

$$\mathcal{H} = \mathbf{p} \cdot \dot{\mathbf{q}} - \mathcal{L} \quad (76)$$

$$\mathcal{H}(\mathbf{q}^M, \mathbf{p}^M, [\dot{\mathbf{q}}^M]) = \mathbf{p}^M \cdot \dot{\mathbf{q}}^M - \mathcal{L}(\mathbf{q}^M, \dot{\mathbf{q}}^M) \quad (77)$$

Differential of Hamiltonian

$$\begin{aligned}
d\mathcal{H} &= d(\mathbf{p}^M \cdot \dot{\mathbf{q}}^M) - d(\mathcal{L}(\mathbf{q}^M, \dot{\mathbf{q}}^M)) \\
&= (\mathbf{p}^M \cdot d\dot{\mathbf{q}}^M + d\mathbf{p}^M \cdot \dot{\mathbf{q}}^M) - \left(\underbrace{\frac{\partial \mathcal{L}(\mathbf{q}^M, \dot{\mathbf{q}}^M)}{\partial \mathbf{q}^M} \cdot d\mathbf{q}^M}_{\text{Lagrange p}} + \underbrace{\frac{\partial \mathcal{L}(\mathbf{q}^M, \dot{\mathbf{q}}^M)}{\partial \dot{\mathbf{q}}^M} \cdot d\dot{\mathbf{q}}^M}_{\text{Definition of p}} \right) \\
&= \cancel{\mathbf{p}^M \cdot d\dot{\mathbf{q}}^M} + d\mathbf{p}^M \cdot \dot{\mathbf{q}}^M - \cancel{\dot{\mathbf{p}}^M \cdot d\mathbf{q}^M} - \cancel{\mathbf{p}^M \cdot d\dot{\mathbf{q}}^M} \\
&= d\mathbf{p}^M \cdot \dot{\mathbf{q}}^M - \dot{\mathbf{p}}^M \cdot d\mathbf{q}^M \\
&= \underbrace{\frac{\partial \mathcal{H}}{\partial \mathbf{p}^M} \cdot d\mathbf{p}^M}_{\dot{\mathbf{q}}} + \underbrace{\frac{\partial \mathcal{H}}{\partial \mathbf{q}^M} \cdot d\mathbf{q}^M}_{-\dot{\mathbf{p}}}
\end{aligned} \tag{78}$$

Hamiltonian formulation for time-dependent potential energies

$$\mathcal{H}(\mathbf{q}^M, \mathbf{p}^M, t) = \mathcal{K}(\mathbf{q}^M, \mathbf{p}^M) + \mathcal{V}(\mathbf{q}^M, t) = E(t) \tag{79}$$

2.3.2. Hamiltonian Equations of Motion

For $m = 1, 2, \dots, M$, $2M = 6N$ equations of first order.

$$\begin{cases} \dot{q}_m := \frac{\partial \mathcal{H}(\mathbf{q}^M, \mathbf{p}^M)}{\partial p_m} \\ \dot{p}_m := -\frac{\partial \mathcal{H}(\mathbf{q}^M, \mathbf{p}^M)}{\partial q_m} \end{cases} \tag{80}$$

Example: Hamiltonian Equations of Motion in Cartesian Coordinates

First, we express the kinetic energy in terms of Cartesian momenta.

$$\begin{aligned} \mathcal{H}(\mathbf{r}^N, \mathbf{p}^N) &= \mathcal{K}(\mathbf{r}^N, \mathbf{p}^N) + \mathcal{V}(\mathbf{r}^N) \\ &= \sum_i^N \frac{\mathbf{p}_i^2}{2m_i} + \mathcal{V}(\mathbf{r}^N) \end{aligned} \tag{81}$$

Then we apply the operators for equations of motion

$$\frac{\partial \mathcal{H}(\mathbf{r}^N, \mathbf{p}^N)}{\partial p_i} = \underbrace{\frac{\mathbf{p}_i}{m_i}}_{\substack{\stackrel{!}{=} \dot{r}_m \\ \text{definition of} \\ \text{Cartesian momentum}}} \tag{82}$$

$$\frac{\partial \mathcal{H}(\mathbf{r}^N, \mathbf{p}^N)}{\partial r_i} = \frac{\partial \mathcal{V}(\mathbf{r}^N)}{\partial r_i} = \underbrace{-\mathbf{F}_i}_{\substack{\stackrel{!}{=} -\dot{\mathbf{p}}_i \\ \text{Newtonian equation} \\ \text{of motion}}} \tag{83}$$

2.4. Example: Newtonian Formulation in Polar Coordinates

We consider a single particle in two dimensions with a central attractive potential energy in $\frac{1}{r}$. We relate the coordinates between Cartesian and polar coordinate systems, and compute the derivatives $x = r \cos(\theta)$, $y = r \sin(\theta)$ by chain rule:

$$\begin{cases} \dot{x} = \dot{r} \cos(\theta) - r\dot{\theta} \sin(\theta) \\ \dot{y} = \dot{r} \sin(\theta) + r\dot{\theta} \cos(\theta) \end{cases} \quad (84)$$

Second derivatives

$$\begin{aligned} \ddot{x} &= \ddot{r} \cos(\theta) - \dot{r}\dot{\theta} \sin(\theta) - \dot{r}\dot{\theta} \sin(\theta) - r\ddot{\theta} \sin(\theta) - r\dot{\theta}^2 \cos(\theta) \\ &= \cos(\theta) [\ddot{r} - r\dot{\theta}^2] - \sin(\theta) [2\dot{r}\dot{\theta} + r\ddot{\theta}] \end{aligned} \quad (85)$$

$$\begin{aligned} \ddot{y} &= \ddot{r} \sin(\theta) + \dot{r}\dot{\theta} \cos(\theta) + \dot{r}\dot{\theta} \cos(\theta) + r\ddot{\theta} \cos(\theta) - r\dot{\theta}^2 \sin(\theta) \\ &= \sin(\theta) [\ddot{r} - r\dot{\theta}^2] + \cos(\theta) [2\dot{r}\dot{\theta} + r\ddot{\theta}] \end{aligned} \quad (86)$$

In polar coordinate system, we can compute the force field by

$$\mathbf{F}(r) = -\frac{\partial \mathcal{V}(r)}{\partial r} = -\frac{k}{r^2} \mathbf{r} = \begin{cases} F_x = -\frac{k}{r^2} \cos(\theta) \\ F_y = -\frac{k}{r^2} \sin(\theta) \end{cases} \quad (87)$$

where the derivative $\frac{\partial r}{\partial r}$ can be computed as

$$\frac{\partial r}{\partial r} := \begin{pmatrix} \frac{\partial r}{x} \\ \frac{\partial r}{y} \end{pmatrix} \text{ in polar coord. } \frac{1}{r} \mathbf{r} \quad (88)$$

Applying Newton's equation of motion

$$\begin{aligned} m\ddot{r} &= \mathbf{F} \\ m\ddot{r} - \mathbf{F} &= 0 \end{aligned} \quad (89)$$

Expressing using x and y in the 2D Cartesian coordinates

$$\begin{cases} m\ddot{x} - F_x = \cos(\theta) [m(\ddot{r} - r\dot{\theta}^2) + \frac{k}{r^2}] - m\sin(\theta) [2\dot{r}\dot{\theta} + r\ddot{\theta}] \stackrel{!}{=} 0 \\ m\ddot{y} - F_y = \sin(\theta) [m(\ddot{r} - r\dot{\theta}^2) + \frac{k}{r^2}] + m\cos(\theta) [2\dot{r}\dot{\theta} + r\ddot{\theta}] \stackrel{!}{=} 0 \end{cases} \quad (90)$$

→ Substituting into the Cartesian equations of motion and collecting the $\sin \theta$ and $\cos \theta$ terms gives

$$\begin{aligned} \left[m(\ddot{r} - r\dot{\theta}^2) + \frac{k}{r^2} \right] \cos \theta - m(r\ddot{\theta} + 2\dot{r}\dot{\theta}) \sin \theta &= 0 && \times \sin \theta && \times \cos \theta \\ \left[m(\ddot{r} - r\dot{\theta}^2) + \frac{k}{r^2} \right] \sin \theta + m(r\ddot{\theta} + 2\dot{r}\dot{\theta}) \cos \theta &= 0 && \times (-\cos \theta) && \times \sin \theta \end{aligned}$$

➡ $m(r\ddot{\theta} + 2\dot{r}\dot{\theta}) = \frac{d}{dt}(mr^2\dot{\theta}) = 0$ *that* $L = 0$ *where* $L \triangleq mr^2\dot{\theta}$ *the angular momentum is conserved*
➡ $m(\ddot{r} - r\dot{\theta}^2) + \frac{k}{r^2} = 0$ *that* $m\ddot{r} = -\frac{k}{r^2} + \frac{L^2}{mr^3}$ *presence of a centrifugal force*

→ Contrary to possible “naive” expectations

$$m\dot{r} \neq -\frac{\partial \mathcal{V}}{\partial r} \quad m\dot{\theta} \neq -\frac{\partial \mathcal{V}}{\partial \theta} \quad \begin{array}{l} \text{i.e. we don't have a “Newtonian”} \\ \text{form for the equations of motion} \\ \text{in terms of the polar coordinates} \\ \text{(only for the Cartesian ones)} \end{array}$$

2.5. Example: Lagrangian Formulation in Polar Coordinates

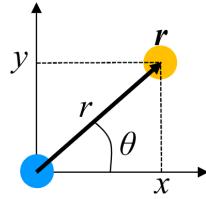
Using the Lagrangian function $\mathcal{L}(\mathbf{q}^M, \dot{\mathbf{q}}^M) = \mathcal{K}(\mathbf{q}^M, \dot{\mathbf{q}}^M) - \mathcal{V}(\mathbf{q}^M)$ for conservative fields on polar coordinates, where it holds $\mathbf{q} = \begin{pmatrix} r \\ \theta \end{pmatrix}$ and $\dot{\mathbf{q}} = \begin{pmatrix} \dot{r} \\ \dot{\theta} \end{pmatrix}$.

$$\begin{aligned} \mathcal{L}(r, \theta, \dot{r}, \dot{\theta}) &= \mathcal{K}(r, \theta, \dot{r}, \dot{\theta}) - \mathcal{V}(r, \theta) \\ &= \frac{1}{2}m[\dot{r}^2 + (r\dot{\theta})^2] + \frac{k}{r} \end{aligned} \quad (91)$$

Applying the equation of motion $\frac{d}{dt}\left(\frac{\partial \mathcal{L}(\mathbf{q}^M, \dot{\mathbf{q}}^M)}{\partial \dot{q}_m}\right) = \frac{\partial \mathcal{L}(\mathbf{q}^M, \dot{\mathbf{q}}^M)}{\partial q_m}$, with $m = 1, 2, \dots, M$ in polar coordinates, this results in the following system of equations:

$$\begin{cases} \frac{d}{dt}\left(\frac{\partial \mathcal{L}}{\partial \dot{\theta}}\right) = \frac{\partial \mathcal{L}}{\partial \theta} \\ \frac{d}{dt}\left(\frac{\partial \mathcal{L}}{\partial \dot{r}}\right) = \frac{\partial \mathcal{L}}{\partial r} \end{cases} \rightarrow \begin{cases} \frac{d}{dt}(mr^2\dot{\theta}) = 0 \\ \frac{d}{dt}(m\dot{r}) = m\ddot{r} = -\frac{k}{r^2} + mr\dot{\theta}^2 \end{cases} \quad (92)$$

Using the angular momentum $L = mr^2\dot{\theta}$, it holds $\dot{L} = 0$ and $m\ddot{r} = -\frac{k}{r^2} + \frac{L^2}{mr^3}$



2.6. Example: Hamiltonian Formulation in Polar Coordinates

Formulate the Lagrangian,

$$\begin{aligned} \mathcal{L}(r, \theta, \dot{r}, \dot{\theta}) &= \mathcal{K}(r, \theta, \dot{r}, \dot{\theta}) - \mathcal{V}(r, \theta) \\ &= \frac{1}{2}m[\dot{r}^2 + (r\dot{\theta})^2] + \frac{k}{r} \end{aligned} \quad (93)$$

Compute conjugate momenta in polar coordinates,

$$\begin{cases} p_\theta \stackrel{!}{=} \frac{\partial \mathcal{L}}{\partial \dot{\theta}} = \underbrace{mr^2\dot{\theta}}_{\text{angular momentum}} \\ p_r \stackrel{!}{=} \frac{\partial \mathcal{L}}{\partial \dot{r}} = m\dot{r} \end{cases} \quad (94)$$

The Hamiltonian $\mathcal{H}(\mathbf{r}^N, \mathbf{p}^N) = \mathcal{K}(\mathbf{r}^N, \mathbf{p}^N) + \mathcal{V}(\mathbf{r}^N)$ can also be computed using the Lagrangian $\mathcal{H} = \mathbf{p} \cdot \dot{\mathbf{q}} - \mathcal{L}(\mathbf{q}, \dot{\mathbf{q}})$, where $\mathbf{q} = \begin{pmatrix} r \\ \theta \end{pmatrix}$ and $\mathbf{p} = \begin{pmatrix} p_r \\ p_\theta \end{pmatrix}$

$$\begin{aligned} \mathcal{H}(r, \theta, p_r, p_\theta) &= \overbrace{p_r \cdot \dot{r} + p_\theta \dot{\theta}}^{\text{dot product}} - \mathcal{L}(r, \theta, p_r, p_\theta) \\ &= m\dot{r}^2 + mr^2\dot{\theta}^2 - \mathcal{L}(r, \theta, p_r, p_\theta) \\ &= m\dot{r}^2 + mr^2\dot{\theta}^2 - \frac{1}{2}m[\dot{r}^2 + (r\dot{\theta})^2] - \mathcal{L}(r, \theta, p_r, p_\theta) \\ &= \frac{1}{2m}[2(m\dot{r})^2 + 2(mr\dot{\theta})^2 - (m\dot{r})^2 - (mr\dot{\theta})^2] - \mathcal{L}(r, \theta, p_r, p_\theta) \\ &= \frac{1}{2m}[(m\dot{r})^2 + (mr\dot{\theta})^2] - \mathcal{L}(r, \theta, p_r, p_\theta) \\ &= \frac{1}{2m}\left[p_r^2 + \frac{p_\theta^2}{r^2}\right] - \mathcal{L}(r, \theta, p_r, p_\theta) \\ &= \frac{1}{2m}\left[p_r^2 + \frac{p_\theta^2}{r^2}\right] - \frac{k}{r} \end{aligned} \quad (95)$$

Applying the Hamilton equations of motion, we obtain expressions for respective coordinates, and express $\dot{\theta}$ and \dot{r} using conjugate momenta computed at the beginning:

$$\begin{cases} \dot{q}_m := \frac{\partial \mathcal{H}(\mathbf{q}^M, \mathbf{p}^M)}{\partial p_m} \\ \dot{p}_m := -\frac{\partial \mathcal{H}(\mathbf{q}^M, \mathbf{p}^M)}{\partial q_m} \end{cases} \rightarrow \begin{cases} \dot{\theta} := \frac{\partial \mathcal{H}}{\partial p_\theta} \rightarrow \dot{\theta} = \frac{p_\theta}{mr^2} \\ \dot{r} := \frac{\partial \mathcal{H}}{\partial p_r} \rightarrow \dot{r} = \frac{p_r}{m} \end{cases} \quad (96)$$

We arrive at the results by applying derivatives with respect to r and θ for the Hamiltonian

$$\begin{aligned}\dot{p}_\theta &:= \frac{\partial \mathcal{H}}{\partial \theta} = 0 \\ \dot{p}_r &:= -\frac{\partial \mathcal{H}}{\partial r} = -kr^{-2} + \frac{p_\theta^2}{r^3}\end{aligned}\tag{97}$$

Thus we arrive at identical results with $\dot{L} = 0$ and $m\ddot{r} = -\frac{k}{r^2} + \frac{L^2}{mr^3}$.

2.7. Application of Constraints

A constraint implies the existence of some force for which the force law is **not known explicitly**, but only **known implicitly** via its effect on the trajectory.

- active force: with explicitly known force law, **free**
- reactive force: enforces the **constraint**

Holonomic constraint

$$C(\mathbf{q}^M, t) \equiv 0 \quad (98)$$

A constraint is called holonomic if it depends only on coordinates and time, but not on velocities

Static holonomic constraint No dependence in time \rightarrow static

$$C(\mathbf{q}^M) \equiv 0 \quad (99)$$

Example: Roller coaster

- active force \mathbf{F} , gravitation

$$\begin{aligned} \mathcal{V}(\mathbf{r}) &= -gmz \\ \mathbf{F}(\mathbf{r}) &= -gm \frac{\mathbf{z}}{z} \end{aligned} \quad (100)$$

- reactive force \mathbf{r} , from track to carriage
 - constraint known but not the force law

$$\begin{aligned} z(\mathbf{r}) - z_{\text{track}}(\mathbf{r}) &= 0 \\ \mathbf{R}(\mathbf{r}, \dot{\mathbf{r}}) &= \text{unknown force law} \end{aligned} \quad (101)$$

Treatment 1: Generalized Coordinates

Replacement for the equation of motion of the constrained M-th coordinate, in which we have $K = M - 1$ free coordinates.

$$\begin{aligned} q_M &= Q \\ \dot{q}_M &= 0 \end{aligned} \quad (102)$$

We formulate Lagrangian for the K free coordinates.

$$\mathcal{L}(\mathbf{q}^K, \dot{\mathbf{q}}^K; Q) = \mathcal{K}(\mathbf{q}^K, \dot{\mathbf{q}}^K; Q) - \mathcal{V}(\mathbf{q}^K; Q) \quad (103)$$

Formulate K Lagrangian equations of motion for the free coordinates:

$$\frac{d}{dt} \left(\frac{\partial \mathcal{L}(\mathbf{q}^K, \dot{\mathbf{q}}^K; Q)}{\partial \dot{q}_m} \right) = \frac{\partial \mathcal{L}(\mathbf{q}^K, \dot{\mathbf{q}}^K; Q)}{\partial q_m}, \text{ with } m = 0, 1, \dots, K \quad (104)$$

Treatment 2: Lagrange Multipliers

Add the **constraint equation** *explicitly* to the **Cartesian Lagrangian** via a Lagrange multiplier.

$$C(\mathbf{r}^N) \equiv 0 \rightarrow \overbrace{\tilde{\mathcal{L}}(\mathbf{r}^N, \dot{\mathbf{r}}^N, \lambda)}^{\text{constraint Lagrangian}} = \mathcal{L}(\mathbf{r}^N, \dot{\mathbf{r}}^N) + \underbrace{\lambda \cdot C(\mathbf{r}^N)}_{\substack{\text{does not change Lagrangian} \\ \text{value, contribute to only derivatives}}} \quad (105)$$

with $\lambda = \lambda(t)$ as a function of time which modulates the magnitude of the reactive force.

Determining value of λ

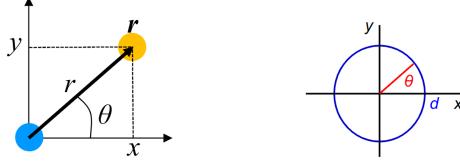
$$\frac{d^2}{dt^2} C(\mathbf{r}^N) \stackrel{!}{=} 0 \quad (106)$$

Treatment 3: Gauss' Principle of Least Constraint

- more general than previous two approaches
- equivalent with the virtual-work principle of D'Alembert

2.7.1. Example: Apply Constraints with Generalized Coordinates

SINGLE PARTICLE IN 2D HOLONOMIC AND STATIC CONSTRAINTS WITH AN ATTRACTIVE POTENTIAL TO MOVE ON A CIRCULAR PATH OF RADIUS d .



We identify the **active force**,

$$\mathcal{V}(r) = -\frac{k}{r} \quad (107)$$

and the **reactive force** with constraint $r = d$.

$$\mathbf{R}(r, \dot{r}) = \text{unknown} \quad (108)$$

We compute the Lagrangian

$$\begin{aligned} \mathcal{L}(r, \theta, \dot{r}, \dot{\theta}) &= \mathcal{K}(r, \theta, \dot{r}, \dot{\theta}) - \mathcal{V}(r, \theta) \\ &= \frac{1}{2}m[\dot{r}^2 + (r\dot{\theta})^2] + \frac{k}{r} \end{aligned} \quad (109)$$

and replace one dimension r with the constraint

$$\mathcal{L}(\theta, \dot{\theta}; d) = \frac{1}{2}m(d\dot{\theta})^2 + \frac{k}{r} \quad (110)$$

Accordingly, only the equation of motion for θ is remaining

$$\begin{cases} \frac{d}{dt}\left(\frac{\partial \mathcal{L}}{\partial \dot{\theta}}\right) = \frac{\partial \mathcal{L}}{\partial \theta} \\ \frac{d}{dt}\left(\frac{\partial \mathcal{L}}{\partial r}\right) = \frac{\partial \mathcal{L}}{\partial r} \end{cases} \rightarrow \begin{cases} \frac{d}{dt}(mr^2\dot{\theta}) = 0 \\ \frac{d}{dt}(m\dot{r}) = m\ddot{r} = -\frac{k}{r^2} + mr\theta^2 \end{cases} \quad (111)$$

We replace again $r = d$,

$$\frac{d}{dt}\left(\frac{\partial \mathcal{L}}{\partial \dot{\theta}}\right) = \frac{\partial \mathcal{L}}{\partial \theta} \rightarrow \frac{d}{dt}\underbrace{(md^2\dot{\theta})}_{:= \text{angular momentum } L} = 0 \quad (112)$$

This constraints means the angular velocity $\dot{\theta}$ must stay constant.

Reducing reactive force

Recall from expression obtained from Newtonian formulation,

$$m\ddot{r} = -\frac{k}{r^2} + mr\dot{\theta}^2 \quad (113)$$

Additionally, we account for the reactive force \mathbf{R} , considering its scalar R

$$m\ddot{r} = R - \frac{k}{r^2} + mr\dot{\theta}^2 \quad (114)$$

we replace r by d

$$\begin{aligned} m\ddot{d} &= R - \frac{k}{d^2} + md\dot{\theta}^2 \\ 0 &= R - \frac{k}{d^2} + md\dot{\theta}^2 \\ R &= \frac{k}{d^2} - md\dot{\theta}^2 \end{aligned} \quad (115)$$

Thus, the unconstrained equation of motion for r would be:

- compensates for the attraction and includes a centripetal force

$$\mathbf{R}(\theta, \dot{\theta}; d) = \left(\frac{k}{d^2} - md\dot{\theta}^2 \right) \frac{\mathbf{r}}{d} \quad (116)$$

2.7.2. Example: Apply Constraints with Lagrange Multiplier

- We consider Cartesian coordinates, but add the constraint to the Lagrangian

We first consider the constraint equation,

$$\begin{aligned} C(\mathbf{r}^N) &\equiv 0 \\ \rightarrow C(x, y) &= \frac{1}{2}(x^2 + y^2 - d^2) = 0 \end{aligned} \quad (117)$$

We formulate the Lagrangian in Cartesian coordinates

$$\begin{aligned} \mathcal{L}(x, y, \dot{x}, \dot{y}) &= \mathcal{K}(x, y, \dot{x}, \dot{y}) - \mathcal{V}(x, y) \\ &= \frac{1}{2}m\dot{\mathbf{v}}^T \dot{\mathbf{v}} + \frac{k}{|\mathbf{r}|} \\ &= \frac{1}{2}m(\dot{x}^2 + \dot{y}^2) + \frac{k}{\sqrt{x^2 + y^2}} \end{aligned} \quad (118)$$

Reformulate the Lagrangian with the constraint,

$$\begin{aligned} \tilde{\mathcal{L}}(\mathbf{r}^N, \dot{\mathbf{r}}^N, \lambda) &= \mathcal{L}(\mathbf{r}^N, \dot{\mathbf{r}}^N) + \lambda \cdot C(\mathbf{r}^N) \\ &= \underbrace{\frac{1}{2}m(\dot{x}^2 + \dot{y}^2)}_{\mathcal{L}} + \frac{k}{\sqrt{x^2 + y^2}} + \frac{\lambda}{2}(x^2 + y^2 - d^2) \end{aligned} \quad (119)$$

Now we use the Lagrangian equations of motion for the constrained Lagrangian

$$\frac{d}{dt} \left(\frac{\partial \mathcal{L}(\mathbf{q}^M, \dot{\mathbf{q}}^M)}{\partial \dot{q}_m} \right) = \frac{\partial \mathcal{L}(\mathbf{q}^M, \dot{\mathbf{q}}^M)}{\partial q_m}, \text{ with } m = 1, 2, \dots, M \quad (120)$$

For the left-hand side,

$$\begin{cases} \frac{d}{dt} \left(\frac{\partial \tilde{\mathcal{L}}}{\partial \dot{x}} \right) = \frac{d}{dt}(m\dot{x}) = m\ddot{x} \\ \frac{d}{dt} \left(\frac{\partial \tilde{\mathcal{L}}}{\partial \dot{y}} \right) = \frac{d}{dt}(m\dot{y}) = m\ddot{y} \end{cases} \quad (121)$$

We compute the right-hand side

$$\begin{cases} \frac{\partial \tilde{\mathcal{L}}}{\partial x} = -k(x^2 + y^2)^{-\frac{2}{3}}x + \lambda x \\ \frac{\partial \tilde{\mathcal{L}}}{\partial y} = -k(x^2 + y^2)^{-\frac{2}{3}}y + \lambda y \end{cases} \quad (122)$$

Thus we have

$$\begin{cases} m\ddot{x} = -k(x^2 + y^2)^{-\frac{2}{3}}x + \lambda x \\ m\ddot{y} = -k(x^2 + y^2)^{-\frac{2}{3}}y + \lambda y \end{cases} \quad (123)$$

To find the value for the multiplier λ , compute the second time-derivative $\frac{d^2}{dt^2} C(\mathbf{r}^N) \stackrel{!}{=} 0$

$$\begin{aligned} \frac{d^2}{dt^2} C(x, y) &= \frac{d^2}{dt^2} \left[\frac{1}{2}(x^2 + y^2 - d^2) \right] \\ &= \frac{d}{dt}[x\dot{x} + y\dot{y}] \\ &= \dot{x}\dot{x} + x\ddot{x} + \dot{y}\dot{y} + y\ddot{y} \\ &= \dot{x}^2 + \dot{y}^2 + x\ddot{x} + y\ddot{y} \stackrel{!}{=} 0 \\ &= (\dot{r}^2 + (r\dot{\theta})^2) + x\ddot{x} + y\ddot{y} \stackrel{!}{=} 0 \end{aligned} \quad (124)$$

2.8. Configuration and Phase Spaces

Configuration space

The space corresponding to the **coordinates** of a system. (i.e. coordinate/conformational space)

Trajectory

$$\mathbf{q}^{M(t)} \quad (125)$$

The **time-dependent** evolution of a system in a configuration space.

Phase space

The space corresponding to the **coordinates** and **momenta** of a system.

$$\mathbf{x}^{2M} = \{\mathbf{q}^M, \mathbf{p}^M\} \quad (126)$$

Example: Phase space in Cartesian coordinates

$$\mathbf{x}^{2N} = \{\mathbf{r}^N, \mathbf{p}^N\} \quad (127)$$

Orbit

$$\mathbf{x}^{2M}(t) \quad (128)$$

The **time-dependent** evolution of a system in phase space.

- Example: orbit of a one-dimensional harmonic oscillator, like a periodic pendulum.

2.9. Hamiltonian Equations of Motion in Phase Space

$$\dot{\mathbf{x}}^{2M}(\mathbf{x}^{2M}) = \underline{\mathbf{J}} \frac{d\mathcal{H}(\mathbf{x}^{2M})}{d\mathbf{x}^{2M}}, \text{ with Hamiltonian matrix } \underline{\mathbf{J}} = \begin{pmatrix} 0 & \underline{\mathbf{I}}^M \\ -\underline{\mathbf{I}}^M & 0 \end{pmatrix} \quad (129)$$

where the $\mathcal{H}(\mathbf{x}^{2M})$ is the Hamiltonian function with some initial condition $\mathbf{x}^{2M}(t_o)$

3. Quantum Mechanics

Classical mechanics fails to provide an accurate description of the physics at the **sub-atomic** scale.

- at actions (*quantum of action*) that become close to the **Planck's constant**,

$$h = 6.6 \cdot 10^{-34} J \cdot s \quad (130)$$

- conveniently,

$$\hbar = \frac{h}{2\pi} \quad (131)$$

3.1. Wave-Particle Duality

1. Particles behave as waves

- with wave vector \mathbf{k} associated to a particle
- with \mathbf{p} the momentum vector

$$\mathbf{p} = \hbar \mathbf{k} \quad (132)$$

Example: 1D relation

$$k = \frac{2\pi}{\lambda} \quad (133)$$

Through two-slit experiment, one can show particles behave as waves. They show interference patterns in their distributions.

2. Waves also behave as particles

- Typical phenomena are *blackbody radiation* and *photoelectric effect*.
- the energy packaged in a photon is linked to its angular frequency ω .

$$E = \hbar \omega \quad (134)$$

using frequency $\nu = \frac{\omega}{2\pi}$, one can also rewrite

$$E = h\nu \quad (135)$$

3.2. Wavefunction

$$\Psi(\mathbf{r}^N, t) \in \mathbb{C} \quad (136)$$

- wave function is a complex function of position and time, also dependent of momentum $\mathbf{p}^N = f(\mathbf{r}^N)$
- **phase-space orbit** or a particle is more precisely a **wave function**, due to the wave-particle duality.

3.2.1. Probabilistic Interpretation

The probability of finding the particles in infinitesimal volumes specified by $d\mathbf{r}^N$ around \mathbf{r}^N at time t .

$$d\mathbf{r}^N |\Psi(\mathbf{r}^N, t)|^2 \quad (137)$$

with probability density defined as:

$$|\Psi(\mathbf{r}^N, t)|^2 = \Psi^*(\mathbf{r}^N, t) \cdot \Psi(\mathbf{r}^N, t) \quad (138)$$

Normalization

The wave function is normalized

$$\int d\mathbf{r}^N |\Psi(\mathbf{r}^N, t)|^2 \stackrel{!}{=} 1, \forall t \quad (139)$$

Superposition

The wave function can be expanded as a superposition of plane waves

$$\Psi(\mathbf{r}^N, t) = \int d\mathbf{k}^N \int d\omega G(\mathbf{k}^N, \omega) \cdot e^{i(\mathbf{k}^N \cdot \mathbf{r}^N - \omega t)} \quad (140)$$

Position & Momentum Representation

- Position representation

$$\Psi(\mathbf{r}^N, t) = (2\pi)^{-\frac{3}{2}} \int d\mathbf{k}^N \varphi(\mathbf{k}^N, t) \cdot e^{i\mathbf{k}^N \cdot \mathbf{r}^N} \quad (141)$$

- Momentum representation

$$\varphi(\mathbf{k}^N, t) = (2\pi)^{-\frac{3}{2}} \int d\mathbf{r}^N \Psi(\mathbf{r}^N, t) \cdot e^{-i\mathbf{k}^N \cdot \mathbf{r}^N} \quad (142)$$

also normalized where

$$\int d\mathbf{k}^N |\varphi(\mathbf{k}^N, t)|^2 = 1 \quad (143)$$

3.3. Correspondence Principle & Operators and Observables

Operator An operator acts on a wave function and returns another wave function.

Hermitian Operator

with real expectation values.

$$\int d\mathbf{r} \Psi_1^* \hat{\mathcal{A}} \Psi_2 = \left(\int d\mathbf{r} \Psi_2^* \hat{\mathcal{A}} \Psi_1 \right)^* \quad (144)$$

Correspondence Principle The classical mechanics is a limiting case of quantum mechanics corresponding to $\hbar \rightarrow 0$.
Classical observables can be mapped to **Hermitian operators**.

Expectation Value of Observable \mathcal{A} at time t

$$\langle \mathcal{A} \rangle := \int d\mathbf{r}^N \Psi^*(\mathbf{r}^N, t) \hat{\mathcal{A}}(t) \Psi(\mathbf{r}^N, t) \quad (145)$$

Mapping of Key Observables

- In the position representaion

	classical	quantum-mechanical	operation
position of particle i	\mathbf{r}_i	\mathbf{r}_i	multiplication
momentum of particle i	\mathbf{p}_i	$-i\hbar \frac{\partial}{\partial \mathbf{r}_i}$	position-gradient
squared	\mathbf{p}_i^2	$-\hbar^2 \frac{\partial^2}{\partial \mathbf{r}_i^2}$	position-Laplacian
energy	E	$i\hbar \frac{\partial}{\partial t}$	time-derivative

Example: Plane wave

PARTICLES AS WAVES	WAVE AS PARTICLES
$\mathbf{p} = \hbar \mathbf{k} \quad (146)$	$E = \hbar \omega \quad (147)$
take position-gradient	take time derivative
$\rightarrow -i\hbar \frac{\partial}{\partial \mathbf{r}} e^{i(\mathbf{k} \cdot \mathbf{r} - \omega t)}$	$\rightarrow i\hbar \frac{\partial}{\partial t} e^{i(\mathbf{k} \cdot \mathbf{r} - \omega t)}$
$= -i\hbar(i\mathbf{k}) e^{i(\mathbf{k} \cdot \mathbf{r} - \omega t)} \quad (148)$	$= -i\hbar(-i\omega) e^{i(\mathbf{k} \cdot \mathbf{r} - \omega t)} \quad (149)$
$= \mathbf{p} e^{i(\mathbf{k} \cdot \mathbf{r} - \omega t)}$	$= E e^{i(\mathbf{k} \cdot \mathbf{r} - \omega t)}$

3.4. Time dependent Schrödinger Equation (TDSE)

The equation is associated with the classical equivalence of Hamiltonian and total energy via the correspondence principle.

CLASSICAL EXPRESSION
$\mathcal{H}(\mathbf{r}^N, \mathbf{p}^N, t) = \underbrace{\sum_i^N \frac{\mathbf{p}_i^2}{2m_i}}_{E(t)} + \mathcal{V}(\mathbf{r}^N, t)$ (150)
Hamiltonian operator of a N-particle system
$\widehat{\mathcal{H}}(\mathbf{r}^N, \mathbf{p}^N, t) = -\sum_i^N \frac{\hbar^2}{2m_i} \underbrace{\frac{\partial^2}{\partial \mathbf{r}_i^2}}_{\text{Laplacian } \Delta_i} + \mathcal{V}(\mathbf{r}^N, t)$ (151)
TDSE, equation of motion for wave function Ψ
$\widehat{\mathcal{H}}(t)\Psi(\mathbf{r}^N, t) = i\hbar \frac{\partial \Psi(\mathbf{r}^N, t)}{\partial t}$ (152)

3.4.1. Time Independent Schrödinger Equation

If the Hamiltonian does not depend explicitly on **time**, $\widehat{\mathcal{H}}(t) \rightarrow \widehat{\mathcal{H}}$, then the wave function becomes separable in the coordinate and time variables,

$$\Psi(\mathbf{r}^N, t) = \Psi(\mathbf{r}^N)T(t) \quad (153)$$

where $T(t) := e^{-i\omega t}$ with $\omega = \frac{E}{\hbar}$ is a “pulsation” by rotation in the complex plane, the higher the energy, the faster the “beat”.

We can rewrite the time-dependent Schrödinger equation as:

$$\begin{aligned} \widehat{\mathcal{H}}\Psi(\mathbf{r}^N)T(t) &= i\hbar \frac{d}{dt}[\Psi(\mathbf{r}^N)T(t)] \\ \widehat{\mathcal{H}}\Psi(\mathbf{r}^N)T(t) &= i\hbar\Psi(\mathbf{r}^N) \frac{dT(t)}{dt} \\ \widehat{\mathcal{H}}\Psi(\mathbf{r}^N)T(t) &= i\hbar\Psi(\mathbf{r}^N) \frac{E}{i\hbar} T(t) \\ \widehat{\mathcal{H}}\Psi(\mathbf{r}^N) &= E\Psi(\mathbf{r}^N) \end{aligned} \quad (154)$$

use the mapping $E = i\hbar \frac{\partial}{\partial t}$, we know

$$\frac{dT(t)}{dt} = \frac{E}{i\hbar} T(t) = -i\omega T(t) \quad (155)$$

3.4.2. Solution of the Time-Independent Schrödinger Equation

Assuming the Hamiltonian does not depend on time, one has the time-independent Schrödinger equation.

$$\widehat{\mathcal{H}}\Psi_k(\mathbf{r}^N) = E\Psi_k(\mathbf{r}^N) \quad (156)$$

with $\int d\mathbf{r}^N |\Psi(\mathbf{r}^N)|^2 \stackrel{!}{=} 1$

General Solution

The TISE can be solved analytically or numerically for a given potential energy function $\mathcal{V}(\mathbf{r}^N)$. The solutions can be chosen to define a **real orthonormal basis set**.

$$\Psi(\mathbf{r}^N, t) = \sum_k c_k \Psi_k(\mathbf{r}^N) \cdot e^{-i\omega_k t} \quad (157)$$

with $\int d\mathbf{r}^N |\Psi(\mathbf{r}^N, t)|^2 \stackrel{!}{=} 1, \forall t$

- value pairs $\{E_k, \Psi_k\}$
 - E_k : TISE eigenvalue
 - Ψ_k : associated eigenfunction
- complex coefficients c_k

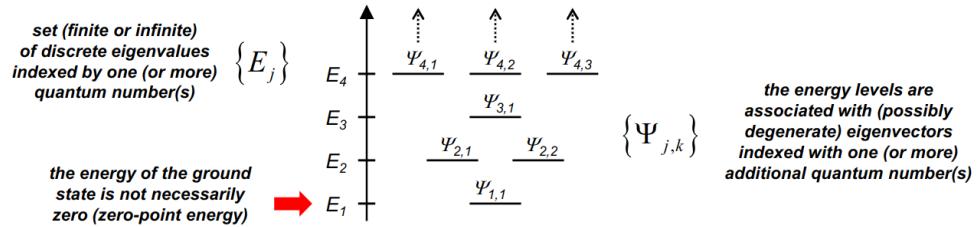
- $\omega_k = \frac{E_k}{\hbar}$

Special Case: Discrete Set of Solutions

When potential energy or boundary conditions effectively **confine the system** in space, the set of solutions is discrete (**quantized**).

- **counter-example:** free particle would have continuum of states.

The allowed states that consists of **Hamiltonian eigenvalues** and **wave functions** can be indexed using one or more integer **quantum number(s)**.



Copenhagen Interpretation of Quantum Mechanics

The system is in all the possible energy states at the same time, weighted by the probability of each state. (**superposition of states**)

At measurement the system collapses into a single state randomly (**collapse of the wave function**).

Examples:

$$|\Psi\rangle = \sqrt{0.6} \cdot |1\rangle + \sqrt{0.3} \cdot |2\rangle + \sqrt{0.1} \cdot |3\rangle \quad (158)$$

3.5. Bracket Notation

- a bra $\langle \cdot |$
- a ket $|\cdot \rangle$

EXPLICIT NOTATION	BRAKET NOTATION	WITH JUST QUANTUM NUMBERS
$\Psi_m^*(\mathbf{r}^N)$ (159)	$\langle \Psi $ (160)	$\langle m $ (161)
$\Psi_n(\mathbf{r}^N)$ (162)	$ \Psi\rangle$ (163)	$ n\rangle$ (164)
$\int d\mathbf{r}^N \Psi_m^*(\mathbf{r}^N) \Psi_n(\mathbf{r}^N)$ (165)	$\langle \Psi_m \Psi_n \rangle$ (166)	$\langle m n \rangle$ (167)
$\int d\mathbf{r}^N \Psi_m^*(\mathbf{r}^N) \hat{\mathcal{A}} \Psi_n(\mathbf{r}^N)$ (168)	$\langle \Psi_m \hat{\mathcal{A}} \Psi_n \rangle$ (169)	$\langle m \hat{\mathcal{A}} n \rangle$ (170)

3.6. Quantum Chemistry

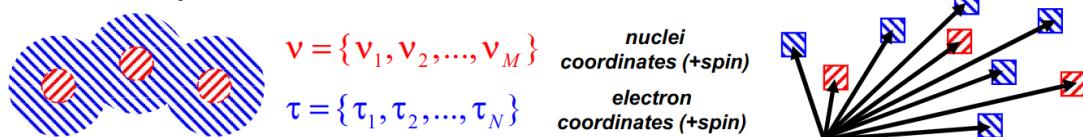
An atom or a molecule is a many-particle system, consisting of nuclei + electrons.

- for atoms and molecules (polyelectronic systems)

3.6.1. System Description

System wave function

→ The system **wavefunction**



The probability of finding the nuclei and electrons in the $4(M + N)$ -dimensional coordinate/spin volume at time t .

$$|\Psi(\tau, v, t)|^2 d\tau dv \quad (171)$$

System Hamiltonian operator

$$\begin{aligned}
\hat{\mathcal{H}} &= \hat{\mathcal{K}} + \hat{\mathcal{V}} \\
&= \sum_i^N \hat{k}_i + \sum_{i<j}^N \hat{v}_{ij} \\
&= - \sum_i^N \frac{\hbar^2}{2m_i} \frac{\partial^2}{\partial \mathbf{r}_i^2} + \sum_{i<j}^N \frac{1}{4\pi\epsilon_0} \frac{q_i q_j}{|\mathbf{r}_j - \mathbf{r}_i|}
\end{aligned} \tag{172}$$

with one-particle operator,

$$\hat{k}_i = - \frac{\hbar^2}{2m_i} \frac{\partial^2}{\partial \mathbf{r}_i^2} \tag{173}$$

and two-particle operator, where q are charges

$$\hat{v}_{ij} = \frac{1}{4\pi\epsilon_0} \frac{q_i q_j}{|\mathbf{r}_j - \mathbf{r}_i|} \tag{174}$$

System Hamiltonian operator for one particle

$$\hat{\mathcal{H}} = \hat{\mathcal{K}} = - \sum_i^N \frac{\hbar^2}{2m_i} \frac{\partial^2}{\partial \mathbf{r}_i^2} \tag{175}$$

Example: for a particle of mass m in 1D

$$\hat{\mathcal{H}} = \hat{\mathcal{K}} = - \sum_i^N \frac{\hbar^2}{2m_i} \frac{\partial^2}{\partial x^2} \tag{176}$$

3.6.2. Numerical Solution

Difficulties

- high computational cost (trade-off between accuracy and performance)
- calculations limited to few configurations
 - not enough for using statistical mechanics
- limited to isolated molecules in vacuum or continuum/cluster solvation
 - no bulk solvation

Approximations

- time-independence
 - no quantum dynamics, assuming only isolated molecules
- Born-Oppenheimer approximation
 - decoupling the electronic from the nuclear problem
 - e.g. nuclei is assumed to be way heavier than electrons and assumed the nuclei to be **motionless**
- neglect of electron correlation
 - Bad approximation!
 - Assuming electrons are not interacting with each other dynamically, see electrons as probability distributions and average out interactions between distributions
 - and partial correction for this neglect
- basic set projection
 - to enable a solution using linear algebra on a computer

3.7. Solutions of Some Standard Problems

3.7.1. Quantum Mechanics of the Free Particle

We consider a particle of mass m in one-dimension that is free in space, we can establish its:

1. Time-independent Schrödinger Equation

$$\hat{\mathcal{H}}\Psi(\mathbf{r}^N) = E\Psi(\mathbf{r}^N) \quad (177)$$

2. Hamiltonian Operator

$$\hat{\mathcal{H}} = \hat{\mathcal{K}} = \frac{-\hbar^2}{2m} \frac{\partial^2}{\partial x^2} \quad (178)$$

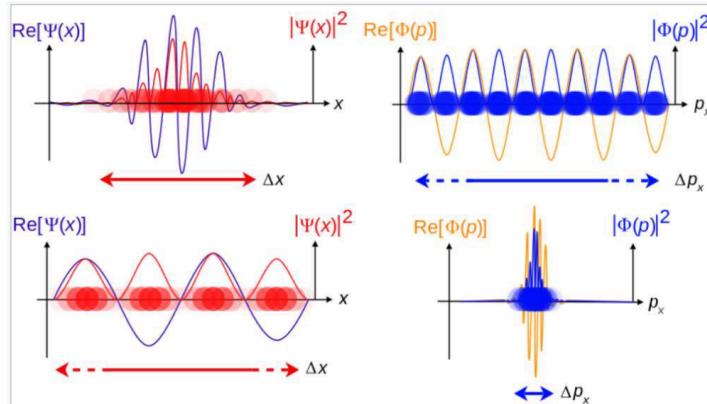
3. Boundary Conditions

- **no** additional boundary conditions!

The time-independent solution

- where $\Psi_k(x) = e^{ikx}$ indicates the general solution is a superposition (a continuum) of plane waves.
 - Fourier pairs: if one is broad, the other one is narrow

$$\begin{cases} \Psi(x) = (2\pi)^{-\frac{1}{2}} \int_{-\infty}^{\infty} dk \Phi(k) e^{ikx} \\ \Phi(k) = (2\pi)^{-\frac{1}{2}} \int_{-\infty}^{\infty} dx \Psi(x) e^{-ikx} \end{cases} \quad (179)$$



The time-dependent solution

$$\Psi(x, t) = (2\pi)^{-\frac{1}{2}} \int_{-\infty}^{\infty} dk \phi(k, 0) \cdot e^{i(kx - \frac{\hbar k^2}{2m}t)} \quad (180)$$

Example: the Gaussian wavepacket

$$\begin{aligned} \psi(x, 0) &= (\pi a)^{-1/4} e^{-a^{-1}x^2/2} \\ \Rightarrow \phi(k, 0) &= (\pi / a)^{-1/4} e^{-ak^2/2} \\ \text{the center moves at constant momentum} \\ &\text{(error on } p \text{ is constant) but it also} \\ &\text{broadens (error on } x \text{ increases).} \end{aligned}$$

Uncertainty Relationship

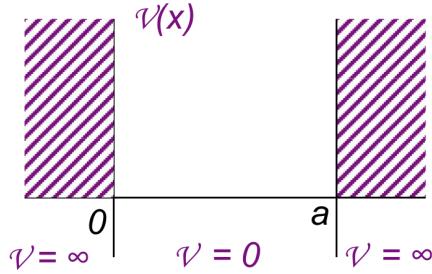
It holds that

$$\sigma_x \sigma_k \geq \frac{1}{2} \quad (181)$$

$$\begin{cases} \sigma_x^2 = \langle (x - \langle x \rangle)^2 \rangle \\ \sigma_k^2 = \langle (k - \langle k \rangle)^2 \rangle \end{cases} \quad (182)$$

3.7.2. Confined Translation (Particle in a Box)

We consider a particle of mass m in 1D, confined in a box of length a , surrounded by **infinitely hard walls**.



We again consider the

1. Time-independent Schrödinger Equation

$$\begin{aligned}\hat{\mathcal{H}}\Psi(\mathbf{r}^N) &= E\Psi(\mathbf{r}^N) \\ \hat{\mathcal{H}}\Psi(x) &= E\Psi(x) \text{ in 1D}\end{aligned}\tag{183}$$

2. Hamiltonian Operator

$$\hat{\mathcal{H}} = \hat{\mathcal{K}} = \frac{-\hbar^2}{2m} \frac{\partial^2}{\partial x^2}\tag{184}$$

3. Boundary Conditions

$$\Psi(0) = \Psi(a) = 0\tag{185}$$

The time-independent solution 1D

Given some quantum number n , the energy level is given by

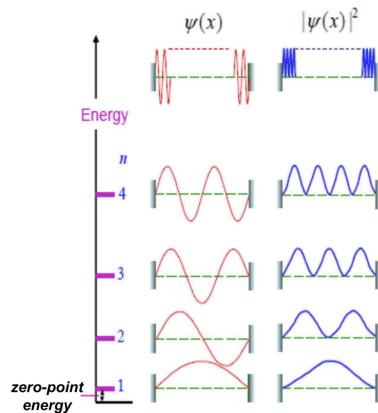
$$E_n = \underbrace{\frac{\hbar^2 \pi^2}{2ma^2}}_{\equiv \frac{\hbar^2}{8ma^2}} \cdot n^2, \quad n = 1, 2, \dots\tag{186}$$

We have

$$\Psi_n(x) = C \cdot \sin\left(\frac{n\pi}{a}x\right)\tag{187}$$

After normalization, enforcing

$$\begin{aligned}\int_0^a dx \cdot C^2 \sin^2\left(\frac{n\pi}{a}x\right) &\stackrel{!}{=} 1 \\ \rightarrow C &= \left(\frac{2}{a}\right)^{\frac{1}{2}}\end{aligned}\tag{188}$$

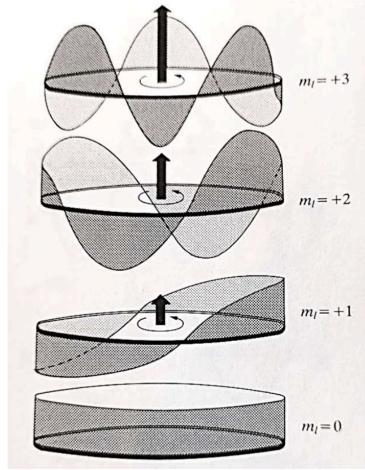


Exercise: 2D/3D cases

- consider three quantum numbers in 3D (n_x, n_y, n_z)

3.7.3. Rotational Motion (The Rigid Rotor)

We consider a particle of mass m undergoing a rotation in 2D at fixed distance r from a point in the plane.



Moment of Inertia

$$I := mr^2 \quad (189)$$

The time-independent solution 2D (without derivation)

- in **polar coordinates** (r, ϕ)

With $m_l \in \{0, \pm 1, \pm 2, \dots\}$ we can represent the energy levels E_l of the rigid rotor, associated with the quantum number m scale quadratically with m .

$$E_l = \frac{\hbar^2}{2I} m_l^2 \quad (190)$$

We have

$$\Psi_{m_l}(\phi) = C_{m_l} e^{im_l \phi} \quad (191)$$

Normalized with $C_{m_l} := \frac{1}{\sqrt{2\pi}}$

Angular Momentum

$$L_z = \hbar m_l \quad (192)$$

Note: two states per level beside $m_l = 0$, clockwise & counter-clockwise

The time-independent solution 3D

- in **polar coordinates** (r, θ, ϕ)

With $m_l \in \{0, \pm 1, \pm 2, \dots, \pm l\}$ we can represent the energy levels E_l of the rigid rotor, associated with the quantum number m scale quadratically with m .

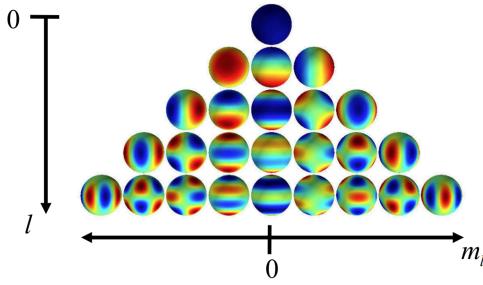
$$E_l = \frac{\hbar^2}{2I} l \cdot (l + 1) \quad (193)$$

With the spherical harmonics Y_{l,m_l} , we have

$$\begin{aligned} \Psi_{l,m_l}(\theta, \phi) &= Y_{l,m_l}(\theta, \phi) \\ &= \underbrace{C_{l,m_l}}_{\text{normalization}} \underbrace{\Theta_{l, |m_l|}(\theta)}_{\substack{\text{associated} \\ \text{Legendre function}}} \cdot e^{im_l \phi} \end{aligned} \quad (194)$$

Angular Momentum

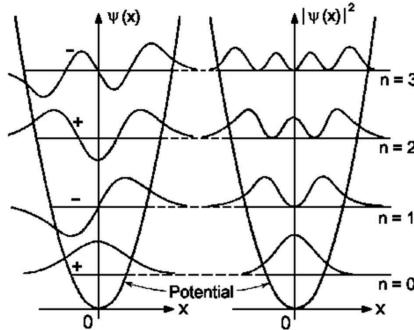
$$\begin{aligned} L &= \hbar [l \cdot (l + 1)]^{\frac{1}{2}} \\ L_z &= \hbar m_l \end{aligned} \quad (195)$$



3.7.4. Vibrational Motion (The Harmonic Oscillator)

We consider a particle of mass m in 1D within a **harmonic potential of force constant k** .

$$\mathcal{V}(x) = \frac{1}{2}kx^2 \quad (196)$$



For harmonic oscillator one can define:

Angular Frequency

$$\omega = \left(\frac{k}{m} \right)^{\frac{1}{2}} \quad (197)$$

Quantization Parameter

- unit: length

$$\alpha = \left(\frac{\hbar^2}{mk} \right)^{\frac{1}{4}} \quad (198)$$

The time-independent solution 1D (without derivation)

Given some quantum number n , the energy levels of the harmonic oscillator are **equidistant**.

$$E_n = \hbar\omega \left(n + \frac{1}{2} \right), \quad n = 1, 2, \dots \quad (199)$$

We have

$$\Psi_n(x) = C_n \underbrace{H_n}_{\substack{\text{Hermite polynomial} \\ \text{of order } n}} \frac{x}{\alpha} e^{-\frac{x^2}{2\alpha^2}} \quad (200)$$

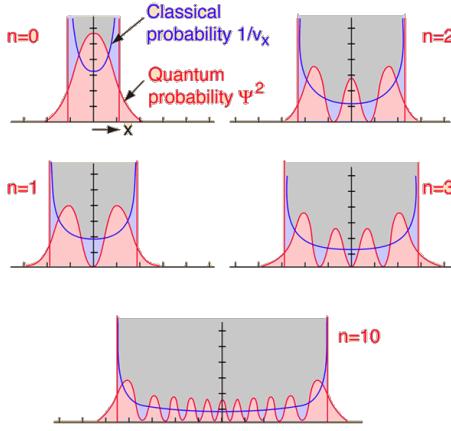
Normalized with $C_n = (\alpha\sqrt{\pi}2^n n!)^{-\frac{1}{2}}$

Zero-point energy is given by

$$E_0 = \frac{1}{2}\hbar\omega \quad (201)$$

Convergence to the classical limit

- At high n , it converges to the **classical limit**
 - however, bond vibrations in molecules are often **not** at the classical limit
- in quantum domain, it is more probable to find particle in the center; in classical world, it is the opposite with more density at turning points (slowest at turning points)



3.7.5. Two-Particle $\frac{1}{r}$ System (The Hydrogen Atom)

We consider a two-particle system in 2D

- e.g. H, He⁺, Li⁺

We represent some necessary properties with

- r : nucleus, electron vector in Bohr
- η : reduced mass of the system in atomic units
- r : nuclear charge in electron units

We consider the system as

- Time-independent Schrödinger Equation (**spherical coordinates**)

$$\begin{aligned}\widehat{\mathcal{H}}\Psi(\mathbf{r}^N) &= E\Psi(\mathbf{r}^N) \\ \widehat{\mathcal{H}}\Psi_{nlmS_eS_\alpha}(r, \theta, \varphi, \sigma_e, \sigma_a) &= E_n\Psi_{nlmS_eS_\alpha}(r, \theta, \varphi, \sigma_e, \sigma_a)\end{aligned}\quad (202)$$

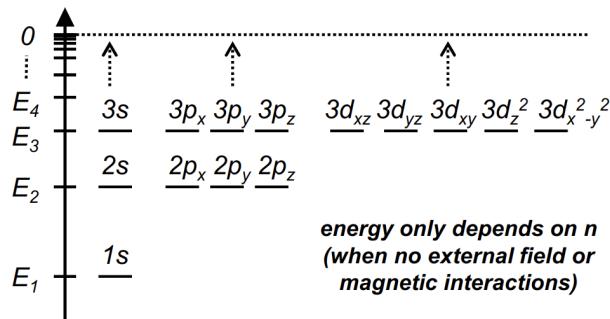
- Hamiltonian Operator

$$\begin{aligned}\widehat{\mathcal{H}} &= \widehat{\mathcal{K}} + \widehat{\mathcal{V}} \\ &= -\frac{1}{2\eta}\frac{\partial^2}{\partial r^2} - \frac{Z}{r}\end{aligned}\quad (203)$$

The time-independent solution 2D

With $n \in \{1, 2, \dots\}$, the energy levels are given by **eigenvalues**.

$$E_n = -\frac{\eta Z^2}{2n^2} \quad (204)$$



The associated eigenfunctions are orbitals.

$$\begin{aligned}\Psi_{nlmS_eS_\alpha}(r, \theta, \varphi, \sigma_e, \sigma_a) &= \underbrace{R_{nl}(r)}_{\text{radial functions}} \cdot \underbrace{Y_{lm}(\theta, \varphi)}_{\text{spherical harmonics}} \cdot \underbrace{S_{S_e}(\sigma_e) \cdot S_{S_\alpha}(\sigma_\alpha)}_{\text{2 spin functions}}\end{aligned}\quad (205)$$

The orbitals are labelled according to five quantum numbers.

- **Principal** $n = 1, 2, \dots$
- **Azimuthal** $l = 0, 1, 2, \dots, n-1$
- **Magnetic** $m = -l, -l+1, \dots, l-1, l$
- **Electronic spin** $s_e = -\frac{1}{2}, \frac{1}{2}$
- **Nuclear spin** $s_\alpha = -s_m, -s_m + 1, \dots, s_m - 1, s_m$
 $(s_m \in \mathbb{Z} \text{ or } \frac{1}{2} \mathbb{Z})$

Note:

- One can find analytical solution of TISE for two-particle systems
 - no analytical solution when more than 2 particles involved

3.7.6. Spin Functions

Example 1: Electron

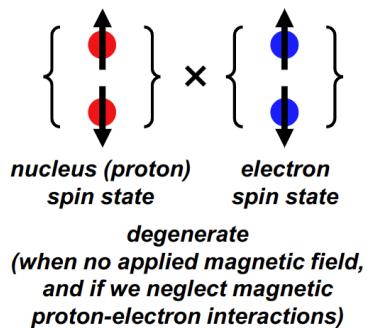
For an electron we have,

$$\begin{cases} \text{spin-up function: } S_{\frac{1}{2}}(\sigma) = \delta_{\delta, \frac{1}{2}} \\ \text{spin-down function: } S_{-\frac{1}{2}}(\sigma) = \delta_{\delta, -\frac{1}{2}} \end{cases} \quad (206)$$

where the spin-up function $S_{\frac{1}{2}}$ can only accommodate a **spin-up electron**, and the spin-down function $S_{-\frac{1}{2}}$ can only accommodate a **spin-down electron**.

Example 2: Hydrogen atom

- with 4 states



4. Phenomenological Thermodynamics

- physics concerned with the description of **macroscopic systems**, where *heat* and *temperature* play a role
- generalization to *chemical exchanges* and *reactions*
- the entire formulation is derived from three fundamental laws
 - only **justification** of these laws, **no violations** ever observed!
 - Statistical mechanics** is an interpretation of these laws based on a microscopic physical model

4.1. Definitions

Thermodynamic system A part of space of interest, separated by a **boundary** from its **environment**.

Thermodynamic state of a system A label that describes the system at a given time from a macroscopic point of view. States have no “memory” of how they were reached.

- macroscopically identical \leftrightarrow same state

Equilibrium state The system has properties that are **homogeneous in space** and **independent of time**.

Thermodynamic process An evolution of the system from a given **starting state** to a given **end state** along a specified **path**.

Exchanges The exchanges during a process correspond to what the system receives from or gives to its environment.

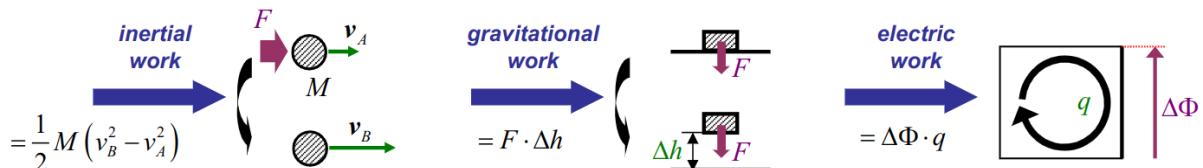
- work, heat, matter (atoms, molecules etc.)
- a closed system cannot have diffusive energy exchange (exchange of matter)

Thermodynamic machine (cyclic process) A process that comes back to the same state in a periodic fashion. The exchanges are measured over **one cycle**.

4.2. Quality of Work

- Work
 - work exchange forms

$$W = \underbrace{W_v}_{\text{volume work}} + \underbrace{W_n}_{\text{non-volume work}} \quad (207)$$



- Heat
 - heat exchange forms
 - conduction
 - radiation

Not all forms of microscopic work have the same quality, we distinguish

$$W_{\text{mic}} = \underbrace{W}_{\substack{\text{high-quality energy} \\ \text{collective motion} \\ \text{coherent macroscopic forces}}} + \underbrace{Q}_{\substack{\text{low-quality energy} \\ \text{random motion} \\ \text{incoherent microscopic forces}}} \quad (208)$$

With **coherent** motion we mean to have **aligned velocities**, while **incoherent** motion refers to **randomly distributed velocities**.

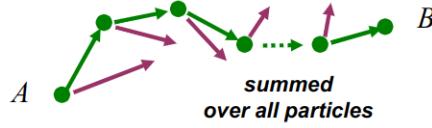
4.3. Exchange of Energy for a Closed System

Consider a closed system and take a **microscopic point of view**, energy exchanges occur when external forces perform on or abstract from the system.

$$dW_{\text{mic},i} = \mathbf{F}_{\text{mic,ext},i} \cdot d\mathbf{r}_i \quad (209)$$

Consider all N particles (of magnitude $\sim 10^{23}$ atoms) and a finite process between some states A and B.

$$\begin{aligned}
W_{\text{mic, AB}} &= \sum_i^N W_{\text{mic,i,AB}} \\
&= \sum_i^N \int_{r_A}^{r_B} \mathbf{F}_{\text{mic,ext,i}} \cdot d\mathbf{r}_i
\end{aligned} \tag{210}$$



4.4. Volume Work and Pressure

During an infinitesimal volume change, the volume work received can be expressed as:

$$\delta W_v := -P_{\text{ext}} \cdot dV \tag{211}$$

Derivation: Assuming a closed system, where the work goes from system to the environment, thus have the negative sign for work.

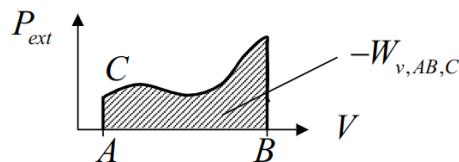
$$P_{\text{ext}} := \frac{F_{\text{ext}}}{\Sigma} \tag{212}$$

$$\begin{aligned}
-\delta W_v &= F_{\text{ext}} \cdot dl \\
-\delta W_v &= P_{\text{ext}} \cdot \underbrace{\Sigma \cdot dl}_{dV} \\
-\delta W_v &= P_{\text{ext}} \cdot dV
\end{aligned} \tag{213}$$

4.4.1. Volume Work Over a Finite Process

Volume work received during a finite process from state A to state B along path C.

$$W_{v,AB,C} = \int_{A,C}^B \delta W_v = - \int_{A,C}^B P_{\text{ext}} \cdot dV \tag{214}$$



Example: isothermal compression of an ideal gas

- Quantity of work depends on the path

PATH 1	PATH 2
Add all mass sheets dm at once	Add the mass sheets dm one by one
<ul style="list-style-type: none"> more work is done comparing to path 2 $ \begin{aligned} P &= P_B = \text{const} \\ \downarrow \\ W_{AB,1} &= -P_B \Delta V \\ &= -P_B (V_B - V_A) \\ &= P_B V_B \\ &= nRT \end{aligned} \tag{215} $	$ \begin{aligned} P &= \frac{nRT}{V} \\ \downarrow \\ W_{AB,2} &= - \int_{V_A}^{V_B} dV \frac{nRT}{V} \\ &= -nRT \ln\left(\frac{V_B}{V_A}\right) \\ &= nRT \ln(2) \\ &\approx 0.69nRT \end{aligned} \tag{216} $

4.5. Heat Transfer and Temperature

- Heat exchange over an infinitesimal process δQ .

4.5.1. Heat Transfer over a Finite Process

Heat received during a finite process from state A to state B along path C.

$$Q_{AB,C} = \int_{A,C}^B \delta Q \quad (217)$$

4.6. Mechanical Equilibrium

Assume we have two systems with different pressure. When two systems are brought into mechanical contact, they exchange volume work, flowing from high to low pressure, until the same pressure holds in both system, i.e. the **mechanical equilibrium** is reached.

- **Application:** Pressure measuring with barometer

4.7. Thermal Equilibrium

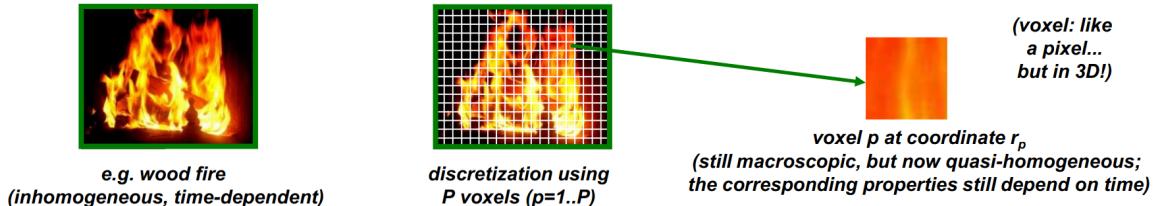
When two systems are brought into **thermal contact**, they exchange heat, flowing from high to low temperature, until they have the **same temperature**, i.e. reach **thermal equilibrium**.

- heat transfer Q and temperature T
- **Application:** Temperature measuring with thermometer

$$T = \frac{PV}{nR} \quad (218)$$

4.8. System State

- In general, physical properties of a system depend on space and **time**.
- Imagine a domain that is discretized in space into cells.

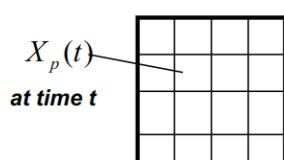


Extensive quantities

- e.g. volume, mass, no. molecules of a species i, internal energy U and entropy S.

$$X_{\text{sys}}(t) = \sum_{p=1}^P X_p(t) \quad (219)$$

- characterize the **content** of a cell and are **additive** over the cells.



- The **density** (volume density) of an extensive quantity is an intensive quantity
 - e.g. the mass density

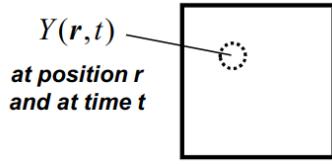
$$\rho_X(\mathbf{r}, t) := \frac{dX(\mathbf{r}, t)}{dV} \quad (220)$$

Intensive quantities

- e.g. pressure, temperature, chemical potential of a species i, densities

$$Y(\mathbf{r}, t) \quad (221)$$

- **quantifies** the state of a cell locally and are **not additive** over the cells.



4.8.1. Characterizing the State

The state of the system is characterized by a thermodynamic **state vector** \mathbf{z} , which contains a **minimal** set of **independent state variables**

- the set of state variables **unambiguously** characterize the system at a given time from a macroscopic point of view.
- choice of these variables is **not unique**, often one chooses
 1. no. moles n
 2. pressure P
 3. temperature T

In general, the state vector is **high-dimensional** and **time-dependent**.

At equilibrium, the properties of the system are **homogeneous** and **time-independent**. Only a few variables for the entire system required.

4.8.2. State Functions

When fixing independent state variables in a system, all other macroscopic properties can be expressed as dependent variables and are called **state functions**.

- e.g. one can express the volume as a state function, here we have on the LHS the **volume** and RHS the **molar volume**.

$$V = V(n, P, T) \xrightarrow{\times \frac{1}{n}} v = v(P, T) \quad (222)$$

Partial Derivatives of a State Function

Given a state function F , the partial derivatives are also state functions

$$\delta F_i := \left(\frac{\partial F}{\partial Z_i} \right)_{\{z_j \neq i\}} dZ_i \quad (223)$$

Total Derivatives of a State Function

In thermodynamics, the differential of any state function is always a total differential.

Example: total differentials of pressure

$$\begin{aligned} dV &= \left(\frac{\partial V}{\partial n} \right)_{P,T} dn + \left(\frac{\partial V}{\partial P} \right)_{n,T} dP + \left(\frac{\partial V}{\partial T} \right)_{n,P} dT \\ &= vdn - V\kappa_T dP + V\alpha_P dT \end{aligned} \quad (224)$$

One can also further compute the total differential for dv .

- Isothermal compressibility (intensive, always positive)

$$\kappa_T := -\frac{1}{V} \left(\frac{\partial V}{\partial P} \right)_{n,T} \quad (225)$$

- Isobaric expansivity (intensive, usually positive)
 - also called thermal expansion coefficient

$$\alpha_P := \frac{1}{V} \left(\frac{\partial V}{\partial T} \right)_{n,P} \quad (226)$$

Equation of state: An equation that connects state variables for a given type of system. If the equation of state can be solved for different variables, these can be expressed as state functions of other variables.

- e.g. for an single-component ideal gas with n, R, T as independent variables.

$$PV = nRT \text{ equation of state}$$

$$V = \frac{nRT}{P} \text{ V as a state function} \quad (227)$$

4.9. Thermodynamic Boundary Conditions

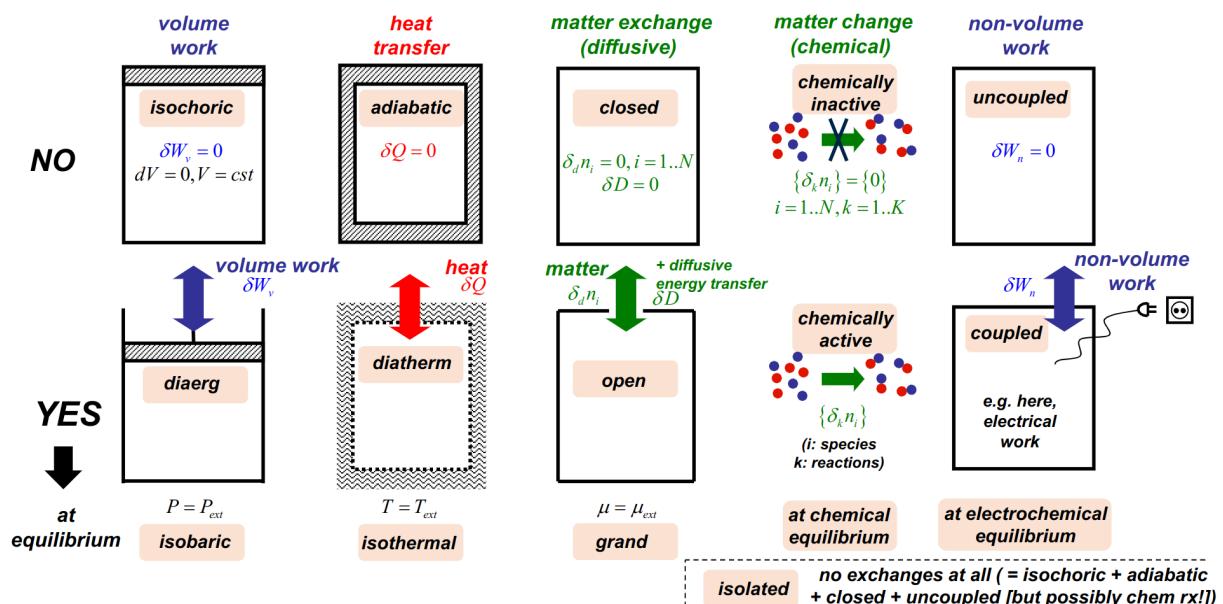
Corresponds to constraints concerning the allowed/forbidden exchanges during the process

- boundary conditions for a **system** apply to all processes in the system

Process path A “recipe” for the process in terms of (a sequence of) boundary conditions. Defining process paths is the **only influence** human can have on process.

- eg. Giving a system containing 1 mol of a gas volume 1 dm^3 , temperature 25°C . The final state is 1 mol of a gas volume 2 dm^3 , at 50°C .
 - the path is the recipe in which the volume may be expanded to 2 dm^3 against external pressure of 0.1 bar and got heat up.
- one can end up in same end states irrespective of path chosen
- but the **exchanges** between system and environment **depend** on the selected **path**

4.10. BC for Different Types of Exchanges



4.11. First Law of Thermodynamics

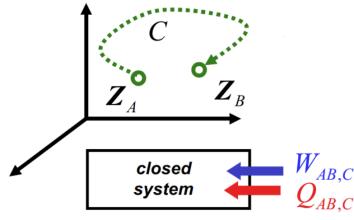
There exists an extensive state function called the internal energy U , with its total differential dU given in a closed system by the sum of the work δW and the supplied heat δQ .

$$\underbrace{dU}_{\text{independent of path}} = \underbrace{\delta W + \delta Q}_{\text{dependent on path}}$$

Recall from Newtonian formulation of energy conservation of a conservative field (previous section)

$$\mathcal{V}(\mathbf{r}^N) + \mathcal{K}(\dot{\mathbf{r}}^N) = E = \text{const} \quad (228)$$

4.11.1. Non-Cyclic Process



For a closed system & finite process

$$\begin{aligned}
 \Delta U_{AB} &= U(Z_B) - U(Z_A) \\
 &= \int_{Z_A}^{Z_B} dU \\
 &= \int_{Z_{A,C}}^{Z_B} \delta W + \int_{Z_{A,C}}^{Z_B} \delta Q \\
 &= \underbrace{W_{AB,C} + Q_{AB,C}}_{\text{path-dependent}}
 \end{aligned} \tag{229}$$

Compactly, for any process in a closed system it holds

$$W + Q = \Delta U \tag{230}$$

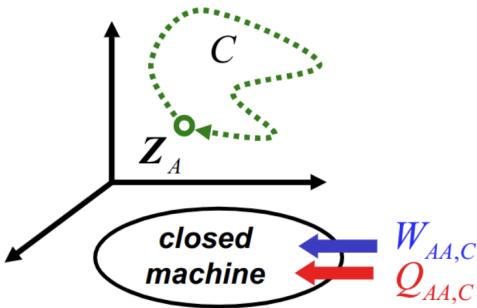
For an isolated system

$$\begin{aligned}
 dU &= 0 \\
 U &\stackrel{!}{=} \text{const}
 \end{aligned} \tag{231}$$

For the universe The energy of the universe is constant, if the energy of a system increases, that of its environment decreases by the same amount.

$$\begin{aligned}
 dU_{\text{env}} &= -dU_{\text{sys}} \\
 U := U_{\text{sys}} + U_{\text{env}} &\stackrel{!}{=} \text{const}
 \end{aligned} \tag{232}$$

4.11.2. Cyclic Process



For a closed system & finite process

$$\begin{aligned}
 \Delta U_{AA} &= U(Z_A) - U(Z_A) \\
 &= \oint_{Z_A} dU \\
 &= \oint_{Z_{A,C}} \delta W + \oint_{Z_{A,C}} \delta Q \\
 &= \underbrace{W_{AA,C} + Q_{AA,C}}_{\text{path-dependent}}
 \end{aligned} \tag{233}$$

Compactly, for any process in a closed system it holds

$$W_O + Q_O = \Delta U \stackrel{!}{=} 0 \tag{234}$$

4.11.3. Isochoric & Isobaric Processes

Given a closed and uncoupled system where no exchange of matter or non-volume (e.g. electrical) work takes place.

4.11.3.1. Isochoric process

The internal energy U is directly related to heat exchange in **isochoric process**. We assume $\delta W_n = 0$ and $dV = 0$, the **first law of thermodynamics** gives:

$$dU = \underbrace{\delta W}_{=0} + \delta Q = \delta Q \quad (235)$$

Thus for any isochoric process in a closed and uncoupled system it holds

$$dU = \delta Q \quad (236)$$

4.11.3.2. Isobaric process

- Enthalpy

For isobaric processes, one introduces the enthalpy

$$H := U + PV \quad (237)$$

and the *differential form* is

$$dH = dU + VdP + PdV \quad (238)$$

The **enthalpy** H is directly related to the **heat exchanged** in isobaric processes. By assuming $\delta W_n = 0$ and $dP = 0$, the *differential form* boils down to:

$$\begin{aligned} dH &= dU + VdP + PdV \\ &= dU + PdV \\ &= (\delta W_v + \delta Q) + PdV \\ &= (-PdV + \delta Q) + PdV \\ &= \delta Q \end{aligned} \quad (239)$$

In a step we uses the identity

$$\delta W_v = -P_{\text{ext}}dV = -PdV \quad (240)$$

Thus for any isobaric process in a closed and uncoupled system it holds

$$dH = \delta Q \quad (241)$$

4.11.3.3. Heat Capacity

The heat capacity is the **heat required** to raise the system temperature by **one degree**.

- **extensive** quantities, but can be made **intensive**

► e.g. molar heat-capacity $c_m := \frac{C}{n}$ (divides by no. moles in the system), specific heat $\frac{C}{m}$ (divides by mass of the system)

TYPE	HEAT CAPACITY	RELATION (FOR CLOSED, UNCOUPLED SYSTEM)
Isochoric	$C_V := \left(\frac{\partial U}{\partial T}\right)_{n,V}$ (242)	$dU = \delta Q = C_V dT$ (243)
Isobaric	$C_P := \left(\frac{\partial H}{\partial T}\right)_{n,P}$ (244)	$dH = \delta Q = C_P dT$ (245)

Note

- for all system it holds

$$C_p > C_V > 0 \quad (246)$$

- for an ideal gas it holds

$$C_p - C_V > nR \quad (247)$$

4.12. Second Law of Thermodynamics

There exists an extensive state function called the **entropy** $S = S(\mathbf{Z})$, and \mathbf{Z} are independent state variables.

Its **total differential** dS given in a **closed system** by the **quotient** $\frac{\delta Q}{T}$ of the supplied heat to the absolute temperature increased by an **internal entropy production** $\delta\Sigma$, where:

$$\begin{cases} \delta\Sigma > 0 & \text{spontaneous + irreversible} \\ \delta\Sigma = 0 & \text{reversible} \\ \delta\Sigma < 0 & \text{unnatural} \end{cases} \quad (248)$$

$$\underbrace{dS}_{\text{independent of path}} = \frac{\delta Q}{T} + \delta\Sigma \quad (249)$$

Reversible Process

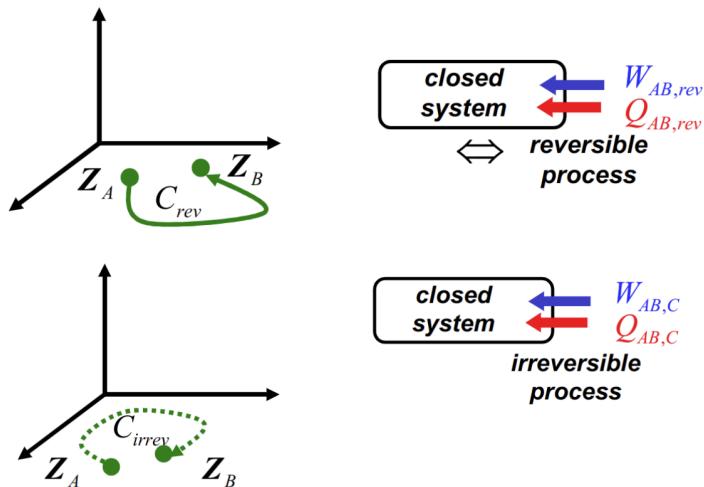
Assume the process is reversible ($\delta\Sigma = 0$), from the total differential of the entropy it holds

$$\begin{aligned} dS &= \frac{\delta Q}{T} \\ \delta Q &= TdS \end{aligned} \quad (250)$$

Example: A macroscopic process always goes **spontaneously** in **one direction** and never in the **opposite direction**.

- e.g. warm coffee gets cold but cold coffee never gets spontaneously warm

4.12.1. Non-Cyclic Process



Compactly, for any process in a closed system it holds

$$\Delta S = I_{\text{rev}} = I + \Sigma \quad (251)$$

For a closed system & **reversible finite process**

$$\begin{aligned} \overbrace{\Delta S_{AB}}^{\text{path independent}} &= S(Z_B) - S(Z_A) \\ &= \int_{Z_A}^{Z_B} dS \\ &= \int_{Z_A}^{Z_B} \frac{\delta Q_{\text{rev}}}{T} \\ &= \underbrace{I_{AB, \text{ rev}}}_{\text{independent of the choice of a reversible path}} \end{aligned} \quad (252)$$

For a closed system & **irreversible finite process**

$$\begin{aligned}
\overbrace{\Delta S_{AB}}^{\text{path independent}} &= S(\mathbf{Z}_B) - S(\mathbf{Z}_A) \\
&= \int_{\mathbf{Z}_A}^{\mathbf{Z}_B} dS \\
&= \int_{\mathbf{Z}_A, C}^{\mathbf{Z}_B} \frac{\delta Q}{T} + \int_{\mathbf{Z}_A, C}^{\mathbf{Z}_B} \delta \Sigma \\
&= \underbrace{I_{AB,C} + \Sigma_{AB,C}}_{\text{path dependent}}
\end{aligned} \tag{253}$$

For an isolated system

$$dS = \delta \Sigma \geq 0 \tag{254}$$

For the universe

The entropy of the universe increases

$$dS_{\text{uni}} = \delta \Sigma_{\text{uni}} > 0$$

It is an extensive property

$$S_{\text{uni}} := S_{\text{sys}} + S_{\text{env}} \tag{255}$$

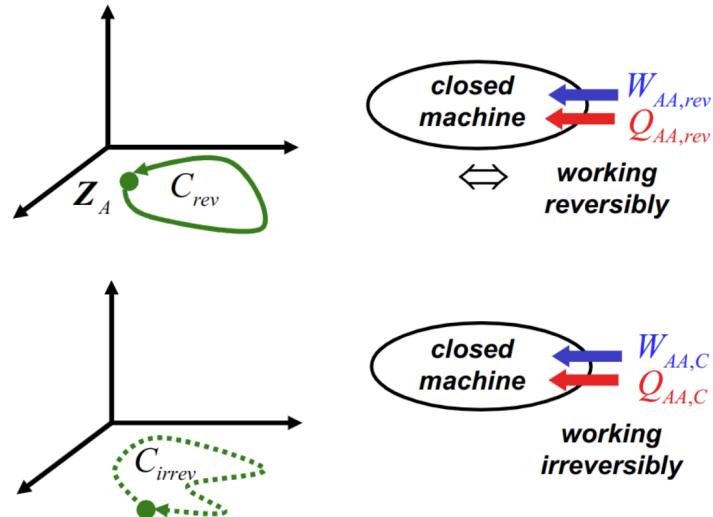
The differential

$$dS_{\text{env}} = dS_{\text{uni}} - dS_{\text{sys}} > -dS_{\text{sys}} \tag{256}$$

Note: The entropy of a system can decrease, but when it does there must be **at least** the same amount of **increase** in the **entropy of the environment**.

$$dS_{\text{sys}} \leq 0 \Rightarrow dS_{\text{env}} \geq -dS_{\text{sys}} \tag{257}$$

4.12.2. Cyclic Process



Compactly, for any cyclic process in a closed system it holds

$$I_O = -\Sigma_O (I_{O, \text{rev}} = 0) \quad (258)$$

with

$$\begin{aligned} I_O &= \oint \frac{\delta Q}{T} \\ \Sigma_O &\geq 0 \end{aligned} \quad (259)$$

For a closed system & reversible finite process

$$\begin{aligned} 0 &\stackrel{!}{=} \Delta S_{AA} = S(Z_A) - S(Z_A) \\ &= \oint_{Z_A} dS \\ &= \oint_{Z_A} \frac{\delta Q_{\text{rev}}}{T} \\ &= \underbrace{I_{AA, \text{rev}}}_{\text{independent of the choice of a reversible path}} \end{aligned} \quad (260)$$

For a closed system & irreversible finite process

$$\begin{aligned} 0 &\stackrel{!}{=} \Delta S_{AA} = S(Z_A) - S(Z_A) \\ &= \oint_{Z_A} dS \\ &= \oint_{Z_{A,C}} \frac{\delta Q}{T} + \oint_{Z_{A,C}} \delta \Sigma \\ &= \underbrace{I_{AA,C}}_{\text{path-dependent}} + \Sigma_{AA,C} \end{aligned} \quad (261)$$

4.13. Fundamental Equation of Thermodynamics

The fundamental equation connects state functions and holds for all processes, regardless of paths taken.

$$dU = -PdV + TdS + \sum_i^N \mu_i dn_i$$

where

$$\mu_i := \left(\frac{\partial U}{\partial n_i} \right)_{\{n_j\}, V, S} \quad (262)$$

Derivation

Given an uncoupled system where no exchange of matter takes place. (*same condition as for isobaric/isochoric processes*)

We consider a process that is

- closed

$$\begin{aligned} \delta_d n_i &= 0 \\ \delta D &= 0 \\ dn_i &= \delta_c n_i \end{aligned} \quad (263)$$

- isobaric

$$\delta W_v = -P_{\text{ext}} dV = -PdV \quad (264)$$

- reversible

$$\delta Q = TdS \quad (265)$$

- with non-volume (e.g. electrical) work

$$\delta W_n := \sum_i^N \mu_i \delta_c n_i \quad (266)$$

Thus by the first law of thermodynamics,

$$\begin{aligned} dU &= \delta W + \delta Q \\ dU &= (\delta W_n + \delta W_v) + TdS \\ dU &= \left(\sum_i^N \mu_i dn_i - PdV \right) + TdS \end{aligned} \quad (267)$$

Spontaneity Condition of Processes

The spontaneity condition that is valid for all processes is defined as:

$$\delta W + \delta D \geq -PdV + \sum_{i=1}^N \mu_i dn_i \quad (268)$$

Derivation

We take the first law of thermodynamics for an open system

$$\begin{aligned} dU &= \delta W + \delta Q + \delta D \\ dU &= \delta W + (TdS - T\delta\Sigma) + \delta D \\ dU &\leq \delta W + TdS + \delta D \\ -PdV + TdS + \sum_i^N \mu_i dn_i &\leq \delta W + TdS + \delta D \\ \delta W + \delta D &> -PdV + \sum_i^N \mu_i dn_i \end{aligned} \quad (269)$$

Note: in the derivation, we replaced the δQ with enthalpy in second law, as well as replacing dU using the fundamental law of thermodynamics.

$$dS = \frac{\delta Q}{T} + \delta\Sigma$$

$$\delta Q = TdS - \underbrace{T\delta\Sigma}_{>0} \leq TdS$$
(270)

4.14. Free Energy

4.14.1. Helmholtz free energy F

An extensive thermodynamic potential, defined as

$$F := U - TS \quad (271)$$

Differential

$$dF = -PdV - SdT + \sum_i^N \mu_i dn_i \quad (272)$$

Derivation

We calculate the differential

$$\begin{aligned} F &= U - TS \\ dF &= \underbrace{dU}_{\text{fundamental law}} - SdT - TdS \\ dF &= \left(-PdV + TdS + \sum_i^N \mu_i dn_i \right) - SdT - TdS \\ dF &= -P\underbrace{dV}_{dF} - S\underbrace{dT}_{dF} + \sum_i^N \mu_i \underbrace{dn_i}_{dF} \end{aligned} \quad (273)$$

Natural Variables

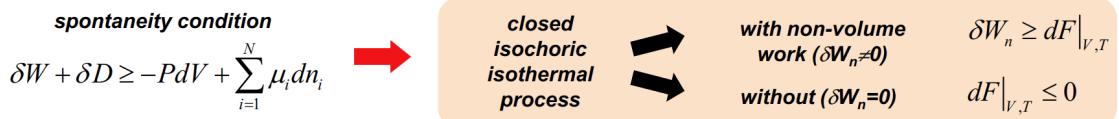
Thus naturally, one shall express Helmholtz free energy as

$$F := F(\{n_i\}, V, T) \quad (274)$$

where the chemical potential tells you the direction of spontaneous process, e.g. physical diffusion or chemical reaction from high to low potential until equilibrium.

$$\mu_i := \left(\frac{\partial F}{\partial n_i} \right)_{\{n_j\}, V, T} \quad (275)$$

- The **spontaneity condition** for closed, isochoric & isothermal processes becomes



- So, when **V** and **T** are constant (a common experimental situation)
 - the **maximal non-volume work** (e.g. electrical in a battery) you can get is $-dF$
 - if there is no non-volume work a process is only **spontaneous** if it **decreases F**

4.14.2. Gibbs free energy G

An extensive thermodynamic potential defined as

$$\begin{aligned} G &:= F + PV \\ G &= U - TS + PV \end{aligned} \quad (276)$$

Differential

$$dG = VdP - SdT + \sum_i^N \mu_i dn_i \quad (277)$$

Derivation

$$\begin{aligned} G &= U + PV - TS \\ dG &= dU + VdP + PdV - SdT - TdS \\ dG &= \left(-PdV + TdS + \sum_i^N \mu_i dn_i \right) + VdP + PdV - SdT - TdS \\ dG &= VdP - SdT + \sum_i^N \mu_i dn_i \end{aligned} \quad (278)$$

Natural Variables

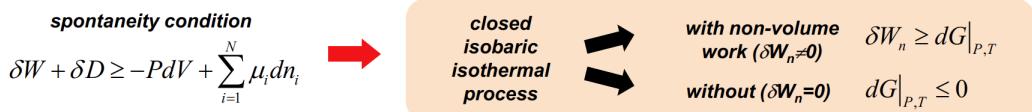
Thus naturally, one shall express Helmholtz free energy as

$$G := G(\{n_i\}, P, T) \quad (279)$$

where the chemical potential

$$\mu_i := \left(\frac{\partial G}{\partial n_i} \right)_{\{n_j\}, P, T} \quad (280)$$

- The **spontaneity condition** for closed, isobaric & isothermal processes becomes



- So, when **P and T are constant** (a common experimental situation; even more than V and T)
 - the **maximal non-volume work** (e.g. electrical in a battery) you can get is $-dG$
 - if there is no non-volume work a process is only **spontaneous** if it **decreases G**

4.15. Fundamental Equation (Integrated Form)

The integrated form of the fundamental equation is valid on all systems and given as follows

$$U = -PV + TS + \sum_{i=1}^N \mu_i n_i \quad (281)$$

Derivation

We start from the fundamental equation of thermodynamics

$$dU = -PdV + TdS + \sum_i^N \mu_i dn_i \quad (282)$$

Using Euler's homogeneous function theorem on an extensive state function F , where the extensive functions are U, V, S and $\{n_i\}$.

$$F(\{X_k\}, \{Y_k\}) = \sum_{k=1}^{N_X} \frac{\partial F(\{X_k\}, \{Y_k\})}{\partial X_k} \cdot X_k \quad (283)$$

Application

- one can derive the Gibbs-Duhem equation using the integrated form

$$-VdP + SdT + \sum_{i=1}^N n_i d\mu_i = 0 \quad (284)$$

4.16. Free Energy (Integrated Form)

4.16.1. Helmholtz free energy F

$$F := U - TS$$

$$\rightarrow F = -PV + \sum_{i=1}^N \mu_i n_i \quad (285)$$

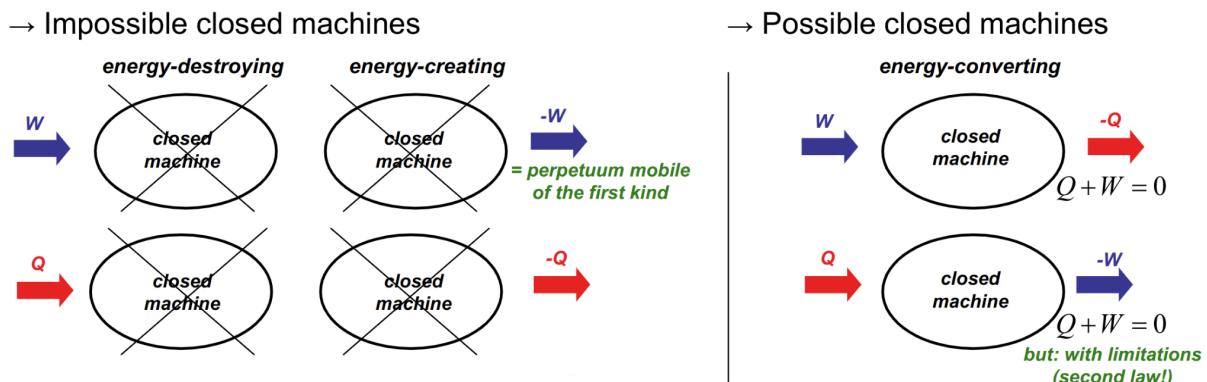
4.16.2. Gibbs free energy G

$$G := U + PV - TS$$

$$\rightarrow G = \sum_{i=1}^N \mu_i n_i \quad (286)$$

4.17. Energy cannot be destroyed nor created

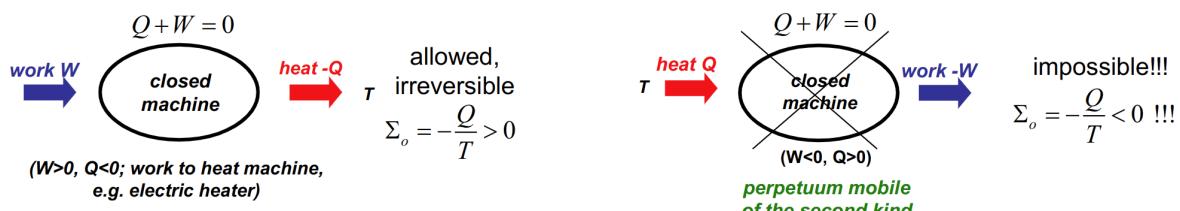
First law



Second law

The second law makes the second case of the closed machine in the first law impossible. As a **closed machine** cannot convert **heat** into **work**, if it is only in contact with a **single heat-reservoir**.

- Machines with one heat-reservoir



5. Free Energy Calculations

Recall from previous sections, one has

1. Helmholtz Free Energy

$$F = U - TS \quad (287)$$

2. Gibbs Free Energy

$$\begin{aligned} G &= F + PV \\ &= U - FS + PV \equiv U + PV - FS \\ &= H - FS \end{aligned} \quad (288)$$

The central challenge: The scheme must be able to

- sample all relevant parts of phase space irrespective of relative free energies
- sample sufficient no. transitions irrespective of barrier heights

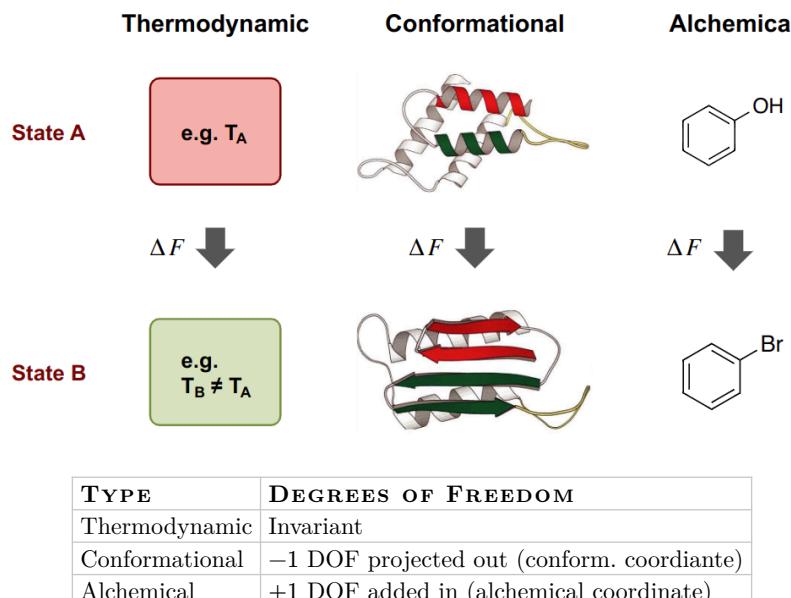
5.1. Methods for Free-Energy Calculation

Free energy is related to the partition function, and can be formally written based on an ensemble average.

Problem: Using MD simulations, the ensemble average will never converge.

Solution: Calculate free-energy differences

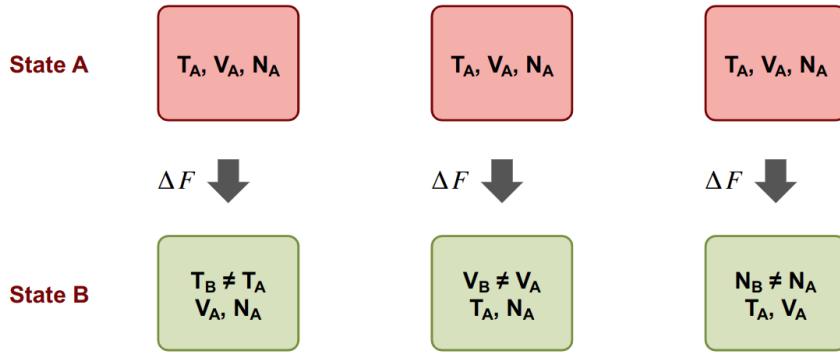
- different methods differ in DOF



1. Thermodynamic Methods

Free-energy change associated with a **thermodynamic state change**

- change is **physical** and **real**
- involves one of the parameters defining the **thermodynamic boundary conditions**
 - Temperature change ΔT
 - Volume change ΔV
 - No. particle change Δn



5.1.0.1. Temperature Integration

Equation

$$\begin{aligned} \frac{\partial(\frac{F}{T})}{\partial \frac{1}{T}} &= \langle H \rangle_T \\ \Rightarrow \frac{\int \cdot d\frac{1}{T} F(T_B)}{T_B} - \frac{F(T_A)}{T_A} &= \int_{T_A^{-1}}^{T_B^{-1}} \langle H \rangle_T d(T^{-1}) \end{aligned} \quad (289)$$

Procedure

- perform constant NVT simulations at **different temperatures T** and compute the **average energy**
- integrate numerically over **temperature T**

Derivation

$$\begin{aligned} \frac{\partial(\frac{F}{T})}{\partial \frac{1}{T}} &= \langle H \rangle_T \\ \Rightarrow \int_{\frac{1}{T_A}}^{\frac{1}{T_B}} \frac{d(\frac{F}{T})}{d\frac{1}{T}} \cdot d\frac{1}{T} &= \int_{\frac{1}{T_A}}^{\frac{1}{T_B}} \langle H \rangle_T d\frac{1}{T} \\ \left[\frac{F}{T} \right]_{\frac{1}{T_A}}^{\frac{1}{T_B}} &= \int_{\frac{1}{T_A}}^{\frac{1}{T_B}} \langle H \rangle_T d\frac{1}{T} \\ \frac{F(T_B)}{T_B} - \frac{F(T_A)}{T_A} &= \int_{T_A^{-1}}^{T_B^{-1}} \langle H \rangle_T d(T^{-1}) \end{aligned} \quad (290)$$

5.1.0.2. Pressure Integration

Equation

$$\begin{aligned} \frac{\partial F}{\partial V} &= -P \\ \Rightarrow F(V_B) - F(V_A) &= - \int_{V_A}^{V_B} P \cdot dV \end{aligned} \quad (291)$$

Procedure

- perform constant NVT simulations at **different volumes V** and compute the **average pressure**
- integrate numerically over the **volume V**

Derivation

$$\begin{aligned}
\frac{\partial F}{\partial V} &= -P \\
\Rightarrow \int_{V_A}^{V_B} \frac{dF}{dV} dV &= - \int_{V_A}^{V_B} P dV \\
[F]_{V_A}^{V_B} &= - \int_{V_A}^{V_B} P dV \\
F(V_B) - F(V_A) &= - \int_{V_A}^{V_B} P \cdot dV
\end{aligned} \tag{292}$$

5.1.0.3. Particle Insertion

The main goal is to estimate the **excess chemical potential** μ , two methods are commonly available.

1. Widom's particle insertion method
2. Switch off all intermolecular interactions (NVT)
 - turn the liquid into an ideal gas and estimate the work using the **thermodynamical integration**

Equation: Widom's particle insertion method

1. Add or remove 1 particle (VT or PT)

Denote the energy of the test particle with $\mathcal{V}(\mathbf{r}_{\text{test}})$.

$$\begin{aligned}
&F(N+1) - F(N) \\
&= -k_B T \ln \left[\int \langle \exp \left(-\frac{\mathcal{V}(\mathbf{r}_{\text{test}})}{k_B T} \right) \rangle_{\mathbf{r}_1, \dots, \mathbf{r}_N} d\mathbf{r}_{N+1} \right] \\
&= -k_B T \ln \left[\int \langle \exp \left(-\frac{\mathcal{V}(\mathbf{r}_1, \dots, \mathbf{r}_{N+1}) - \mathcal{V}(\mathbf{r}_1, \dots, \mathbf{r}_N)}{k_B T} \right) \rangle_{\mathbf{r}_1, \dots, \mathbf{r}_N} d\mathbf{r}_{N+1} \right]
\end{aligned} \tag{293}$$

2. Perturbation Formula

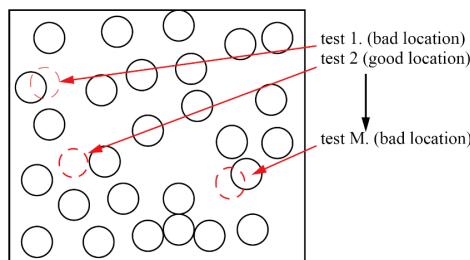
The excess (additional) chemical potential can be calculated with

$$\mu_{\text{excess}} = -k_B T \ln \langle \exp \left(-\frac{\mathcal{V}(\mathbf{r}_{\text{test}})}{k_B T} \right) \rangle_{\mathbf{r}_1, \dots, \mathbf{r}_N} \tag{294}$$

Procedure

For a series of equilibrium configurations of N particles

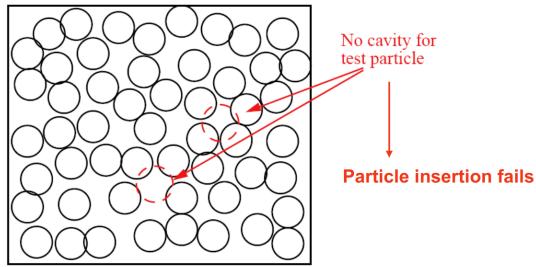
1. randomly add 1 additional particle in each single step
 - performs this M times
 - state A: N particles
 - state B: $N+1$ particles



2. estimate the free energy using the **perturbation formula**

Problem

- Not efficient for dense systems or large particles
 - Possible that **no spontaneously formed cavities** are large enough to give reasonably low energy of the inserted test particle



- low energy (=good) configurations are hardly sampled

Solution: slowly grow particles such that the system can adapt (e.g. thermodynamical integration)

- but much more time-consuming

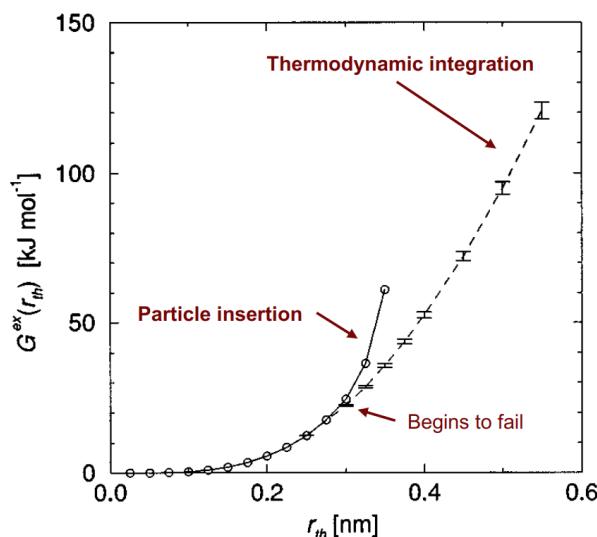
Example: creation of a purely repulsive cavity in water

- uses a simple point charge model
- considers 512 water molecules in a cubic box, 600 ps MD simulations

Cavity-water interaction: with only the repulsive part of the LJ interaction

$$\mathcal{V}(r_{ij}) = \frac{C_{12}}{r_{ij}^{12}} \quad (295)$$

Results



TYPE	ADVANTAGE	DISADVANTAGE
Particle Insertion	<ul style="list-style-type: none"> • works well if many appropriately sized cavities are sampled 	<ul style="list-style-type: none"> • fails if no appropriate cavities are present
Thermodynamical Integration	<ul style="list-style-type: none"> • larger cavities can be created because the environment can relax around (growing) particle 	

2. Conformational Methods

Free-energy change associated with a **conformational change**

- change is **physical** but **virtual**
- involves a **partition** of the **conformational space** of the system into **distinct conformational states**, where definition of states can be
 - Thermodynamic (Free energy minima)
 - Structural
 - Kinetic
 - Experimental (e.g. NMR)

5.1.0.4. Counting Configurations

- A priori the simplest method to calculate free-energy differences

Usable for conformational, alchemical and thermodynamic changes

Problem: Almost never converges within finite trajectories

- works only if both states of interest appeared in simulation
- if one state is **much higher in energy** than the other
 - **insufficient sampling** of high energy conformations
- if **barrier** between states is too high
 - **insufficient no. transitions**

Equation

- Free-energy difference: Given f the binary assignment function, we have

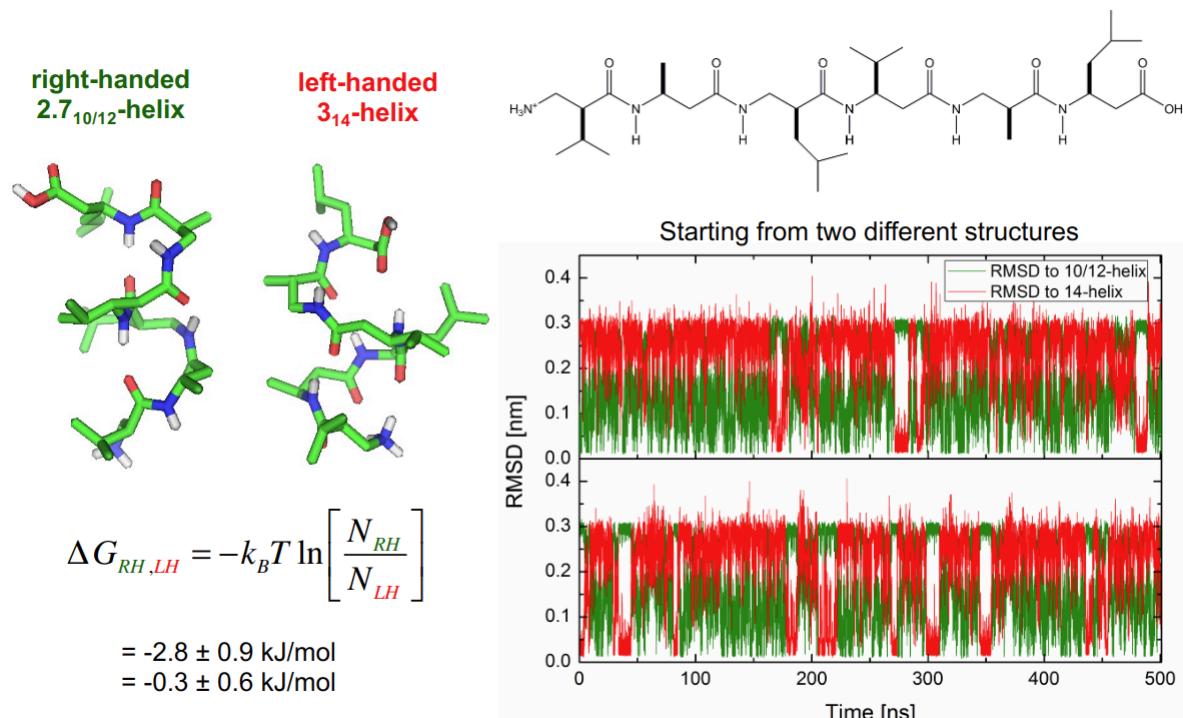
$$\begin{aligned}\Delta F_{BA} &= F_B - F_A \\ &= -k_B T \ln \left[\frac{\langle f_B(\mathbf{r}) \rangle}{\langle f_A(\mathbf{r}) \rangle} \right] \\ &= -k_B T \ln \left[\frac{N_B}{N_A} \right]\end{aligned}\quad (296)$$

Example: Folding equilibrium of β -hexapeptide

We calculate the Gibbs free energy with,

$$\Delta G_{RH,LH} = -k_B T \ln \left[\frac{N_{RH}}{N_{LH}} \right] \quad (297)$$

one needs to select a cutoff (e.g. 1 ns) and count the occurrences of *red* or *green*.



5.1.0.5. Umbrella Sampling

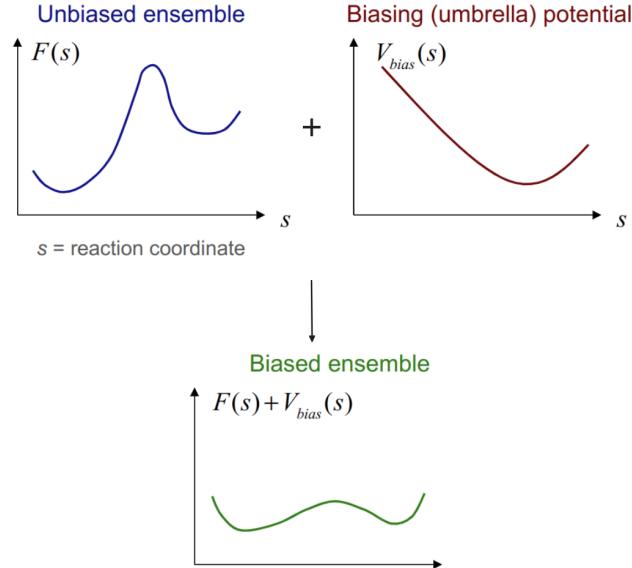
Perform MD simulation with a biased Hamiltonian

- biasing potential s.t. all relevant parts are sampled and sufficient transitions occur

Problem: Challenging to design

Equation

$$\mathcal{H}_{\text{bias}}(\mathbf{r}, \mathbf{p}) := \mathcal{H}(\mathbf{r}, \mathbf{p}) + \mathcal{V}_{\text{bias}}(\mathbf{r}) \quad (298)$$



We calculate the free energy difference

$$\begin{aligned} \Delta F_{BA} &= F_B - F_A \\ &= -k_B T \ln \left[\frac{\langle f_B(\mathbf{r}) \cdot \exp\left(+\frac{\mathcal{V}_{\text{bias}}(\mathbf{r})}{k_B T}\right) \rangle_{\text{bias}}}{\langle f_A(\mathbf{r}) \cdot \exp\left(+\frac{\mathcal{V}_{\text{bias}}(\mathbf{r})}{k_B T}\right) \rangle_{\text{bias}}} \right] \end{aligned} \quad (299)$$

Procedure

One modify the Hamiltonian to account for the $\mathcal{V}_{\text{bias}}$ term, and need to roll back to the unbiased version before one can then use direct counting.

Calculation of weight

$$w_i = \frac{\exp\left(+\frac{\mathcal{V}_{\text{bias}}(\mathbf{r}_i)}{k_B T}\right)}{\underbrace{\sum_{j=0}^N \exp\left(+\frac{\mathcal{V}_{\text{bias}}(\mathbf{r}_j)}{k_B T}\right)}_{\text{normalization}}} \quad (300)$$

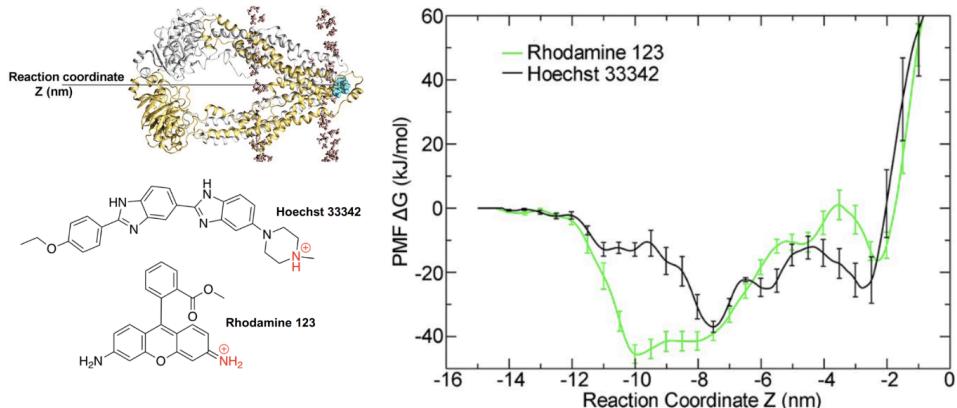
UNBIASED MD	BIASED MD
All configurations have same weight in the ensemble average	Configurations weighted by likelihood to be in unbiased ensemble
$w_i = \frac{1}{N}$	$\sum_{j=1}^N w_j = 1$

Diagram illustrating the distribution of configurations in the unbiased ensemble (blue bars) and the biased ensemble (green bars). The reaction coordinate is shown with positions 1, n, and N. In the biased ensemble, configurations are more likely to be at positions where $V_{\text{bias}}(\mathbf{r}) \ll 0$ (oversampled) and less likely to be at positions where $V_{\text{bias}}(\mathbf{r}) \gg 0$ (undersampled).

Example: Drug binding to P-gp efflux transporter

- biasing potential is a **position restraint**
 - making one or another configuration more/less **favorable**

$$\mathcal{V}_{\text{bias}}(s(\mathbf{r}); s_0) = \frac{1}{2} K_{\text{bias}} (s(\mathbf{r}) - s_0)^2 \quad (303)$$



3. Alchemical Methods

Free-energy change associated with an **alchemical state change**

- change is **unphysical** (no experimental counterpart, **only in computer simulations!**)
- involves a **change** in the form of the **potential energy function** via the associated molecular topology

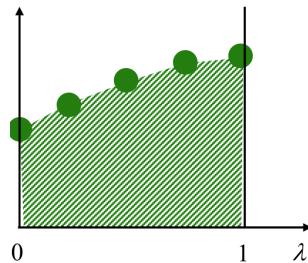
Considerations

- no. particles must be identical in two states, only atom mutations possible
- creation/deletion of an atom \Leftrightarrow mutation from/to a dummy atom
- calculated free-energy difference cannot be directly compared to experiment
 - use of **thermodynamic cycles**

5.1.0.6. Thermodynamic Integration

- can be used for alchemical, conformational and thermodynamic free-energy differences

Introduce a coupling parameter λ in the Hamiltonian



Equation

The coupling parameter is defined as

$$\lambda = \begin{cases} 0 & \text{state A} \\ 1 & \text{state B} \end{cases} \quad (304)$$

$$\mathcal{H}(\mathbf{r}, \mathbf{p}; \lambda) := (1 - \lambda)\mathcal{H}_A(\mathbf{r}, \mathbf{p}) + \lambda\mathcal{H}_B(\mathbf{r}, \mathbf{p}) \quad (305)$$

Derivative

$$\begin{aligned} F'(\lambda) &:= \frac{\partial F(\lambda)}{\partial \lambda} \\ &= \langle \frac{\partial \mathcal{H}(\mathbf{r}, \mathbf{p}; \lambda)}{\partial \lambda} \rangle_\lambda \end{aligned} \quad (306)$$

We calculate the free energy difference

$$\begin{aligned} \Delta F_{BA} &= F(\lambda_B) - F(\lambda_A) \\ &= \int_{\lambda_A}^{\lambda_B} \underbrace{F'(\lambda)}_{\text{derivative}} d\lambda \end{aligned} \quad (307)$$

Example: Introducing the coupling parameter

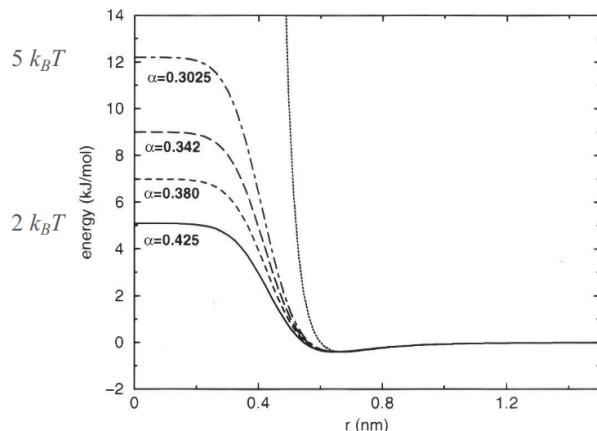
- By introducing the coupling parameter λ , one needs to also reformulate physical equations
- Reformulation
 - mass: $m_i(\lambda) = (1 - \lambda)m_i^A + \lambda m_i^B$
 - bonds: $\mathcal{V}(b; \lambda) = \frac{1}{2}(((1 - \lambda) \cdot K_b^A + \lambda K_b^B)(b - ((1 - \lambda) \cdot b_0^A + \lambda b_0^B)))^2$
 - bond angles, improper dihedrals, torsional dihedrals ...
 - **non-bonded interactions:**

$$\begin{aligned} \mathcal{V}_{LJ}(r_{ij}; \lambda) &= (1 - \lambda) \left[\frac{C_{12}^A}{(\alpha_{LJ}\lambda^2 + r_{ij}^6)^2} - \frac{C_6^A}{\alpha_{LJ}\lambda^2 + r_{ij}^6} \right] + \\ &\quad \lambda \left[\frac{C_{12}^B}{(\alpha_{LJ}(1 - \lambda)^2 + r_{ij}^6)^2} - \frac{C_6^B}{\alpha_{LJ}(1 - \lambda)^2 + r_{ij}^6} \right] \end{aligned} \quad (308)$$

We note that in **non-bonded interaction**, we introduced also the parameter α .

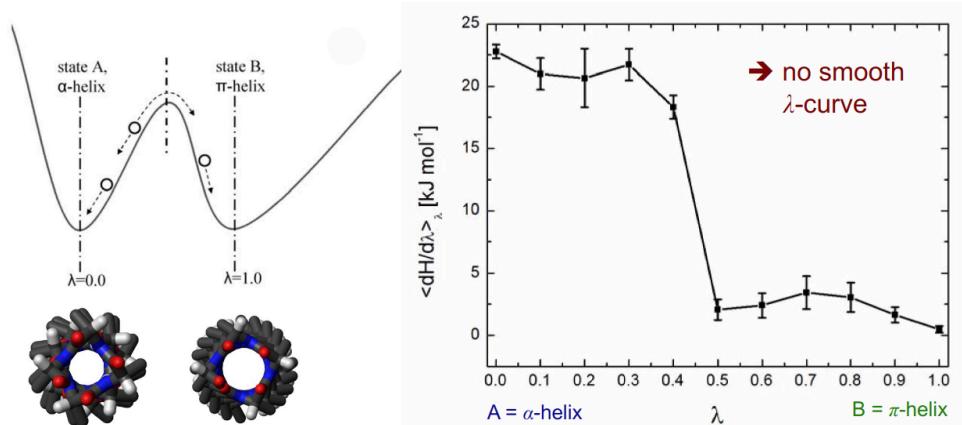
Soft-core nonbonded interaction

- in the particle insertion method, inserted dummy atom has mass, but **no charge** and **no LJ interactions**.
 - atoms can get very close at intermediate λ -points and induce **numerical instability**
 - thus the energy profile is softened for non-bonded interactions



Counter Example: different conformations of Alanine decapeptide

- **Barrier** along λ is **too high**
 - thermodynamical integration fails due to insufficient smoothness



5.1.1. Technique: Hamiltonian Replica Exchange for Smoother Sampling

Goal: Makes the curve for λ smoother.

Exchange configurations between neighbouring λ -points

- overcome orthogonal barriers as we had in the above counter example for thermodynamical integration

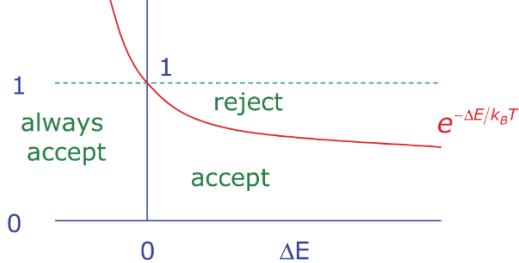
Equation

$$\Delta := \frac{(\mathcal{H}(\mathbf{r}_j ; \lambda_i) - \mathcal{H}(\mathbf{r}_i ; \lambda_j)) - (\mathcal{H}(\mathbf{r}_j ; \lambda_j) - \mathcal{H}(\mathbf{r}_i ; \lambda_i))}{k_B T} \quad (309)$$

Algorithm

1. Do a given number of simulation steps
2. Attempt Monte Carlo exchange between neighbouring replicas with exchange probability

$$p(\lambda_i \leftrightarrow \lambda_j) = \begin{cases} 1 & \text{for } \Delta \leq 0 \\ e^{-\Delta} & \text{for } \Delta > 0 \end{cases} \quad (310)$$



5.1.1.1. Free-Energy Perturbation

The basic idea lies in deriving information from adjacent λ -points

- Similar to thermal integration (TI), one also introduces the coupling parameter λ .

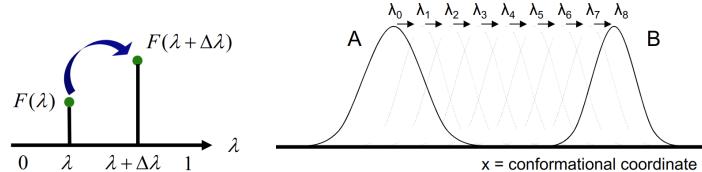
Challenge

Step size $\Delta\lambda$ must be small enough to have overlap between adjacent points

Equation

Uses the perturbation formula instead

$$\begin{aligned} \Delta F_{(\lambda+\Delta\lambda)-\lambda} &= F(\lambda + \Delta\lambda) - F(\lambda) \\ &= -k_B T \ln \left[\langle \exp \left(-\frac{\mathcal{H}(\mathbf{r}, \mathbf{p}; \lambda + \Delta\lambda) - \mathcal{H}(\mathbf{r}, \mathbf{p}; \lambda)}{k_B T} \right) \rangle_\lambda \right] \end{aligned} \quad (311)$$



6. Combinatorics & Statistics

6.1. Randomness and Patterns

Randomness: the quality of state **of lacking a pattern or principle of organization**, of being **unpredictable**.

6.2. Combinatorics

Branch of mathematics dealing with counting combinations of objects belonging to a **finite set** in accordance with certain **constraints**.

Binomial Coefficient

- read as “K choose N”
- related to Pascal’s triangle and the binomial theorem

$$\binom{K}{N} := \frac{K!}{N!(K-N)!} \quad (312)$$

Binomial Theorem

$$(p+q)^N = \sum_{n=1}^N \binom{N}{n} p^n q^{N-n} \quad (313)$$

Multinomial Coefficient

- read as “product of njs”

$$\binom{K}{n_1, n_2, \dots, n_M} := \frac{K!}{\prod_m n_m!} \quad (314)$$

6.2.1. Selection Problem

How many ways N_{sel} to select a subset of N elements from a set of K elements?

- elements are all **distinguishable** with **no duplicates**, and **the ordering is irrelevant**.
- a special case of the partition problem for $M = 2$ subsets, with subset 1 with $n_1 = N$ as “selected”, and subset 2 with $n_2 = K - N$ as “not selected”.

$$N_{\text{sel}} = \binom{K}{N} = \frac{K!}{N!(K-N)!} \quad (315)$$

Derivation

One consider possible choices for a sequence of objects

$$\begin{cases} K \text{ choices for 1st object} \\ K-1 \text{ choices for 2nd object} \\ \dots \\ K-N+1 \text{ choices for Nth object} \end{cases} \quad (316)$$

Taking into account the amount of equivalent permutations, which are identical (e.g. (apple, egg) vs. (egg, apple))

$$N! \quad (317)$$

6.2.2. Partition Problem

How many ways N_{par} to partition a **set of K elements** into **M subsets of n_1, \dots, n_M elements**

- elements are all distinguishable with no duplicates and the ordering is irrelevant.
- The subsets must be **non-overlapping** and **fully cover** the ensemble.

$$N_{\text{par}} = \binom{K}{n_1, n_2, \dots, n_M} \quad (318)$$

Example:

How many ways to partition $K = 6$ different fruits into $M = 3$ subsets of 1, 2 and 3 fruits?

$$N_{\text{par}} = \frac{6!}{1! \cdot 2! \cdot 3!} = 60 \quad (319)$$

Derivation

Consider a case where we have K objects to partition into M subsets. The first subset may require n_1 elements, then there would be $n_1!$ equivalent permutations of the n_1 objects.

$$\begin{cases} K & \text{choices for 1st object of subset 1} \\ K-1 & \text{choices for 2nd object of subset 1} \\ \dots & \\ K-n_1+1 & \text{choices for } n_1\text{-th object of subset 1} \end{cases} \quad (320)$$

Similarly it holds for other subset. We consider now the last subset M with n_M elements required in the partition, it also have $n_M!$ equivalent permutations of the n_M objects.

6.2.3. Assignment Problem

How many ways N_{ass} to assign K **distinguishable** objects to M sets?

The number of possible assignment of K different objects to M distinct sets:

$$N_{\text{ass}} = M^K \quad (321)$$

Assignment vector

$$\mathbf{m} := \{m_1, m_2, \dots, m_k\} \quad (322)$$

Example 1:

- possible combinations of bits
- one can see each set m_i as a digit/bit
 - K objects are values $\{0, 1\}$.

Example 2:

Assign $K = 6$ different fruits to $M = 3$ distinct persons A, B and C , for each object, one needs to decide if it is assigned to A, B or C .

$$N_{\text{ass}} = M^K = 3^6 = 729 \quad (323)$$

Example 3:

Assign K systems to M microstates

- systems numbered by $k \in \{1, 2, \dots, K\}$, each of them has a microstate assigned m_k that takes encoded indices of microstates chosen $m_k \in \{0, 1, \dots, M - 1\}$

6.2.4. Distribution Problem

How many ways N_{dis} to distribute K **indistinguishable objects** into M sets.

- **indistinguishable objects:** e.g. objects to be assigned are identical

Population Vector

A population of a set m refers to number of objects assigned to set m .

$$n_m \leftrightarrow \text{no. objects assigned to set } m \quad (324)$$

A population vector represents each possible distribution.

$$\begin{aligned} \mathbf{n} &:= \{n_1, n_2, \dots, n_M\} \\ \text{with } \sum_{m=1}^M n_m &= K \end{aligned} \quad (325)$$

Number of possible distributions of K indistinguishable objects into M distinct set

$$N_{\text{dis}} = \binom{K + M - 1}{K} \quad (326)$$

Example 1: Distribute $K = 6$ undistinguishable apples to $M = 3$ distinct persons.

$$\begin{aligned}
N_{\text{dis}} &= \binom{K+M-1}{K} \\
&= \frac{(K+M-1)!}{K!(M-1)!} \\
&= \frac{8!}{6!(3-1)!} \\
&= \frac{8!}{6!2!} = 28
\end{aligned} \tag{327}$$

One can also comprehend it as

$$N_{\text{dis}} = \underbrace{\frac{8!}{6!}}_{\substack{\text{how many ways} \\ \text{to put the delimiters}}} \cdot \underbrace{\frac{1}{2!}}_{\substack{\text{remove ordering} \\ \text{of delimiters}}} \tag{328}$$

The term $\frac{8!}{6!} = \frac{8 \cdot 7 \cdot 6 \dots \cdot 1}{6 \cdot 5 \dots \cdot 1} = 8 \cdot 7$ meaning there are 8 ways to put the first delimiter and 7 ways to put the second.

Example 2: Distribution of systems over microstates

Assume the mapping of systems to microstate is given by the assignment vector $\mathbf{m} = \{m_1, \dots, m_k\}$, one denote the number of systems in microstate m by

$$n_m = \sum_{k=1}^K \delta_{m_k, m}, \text{ with } m \in \{0, \dots, M-1\} \tag{329}$$

Accordingly, the population vector that fulfills $\sum_{m=0}^{M-1} n_m = K$ can be written compactly as:

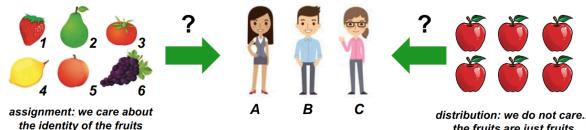
$$\mathbf{n} = \{n_0, n_1, \dots, n_{M-1}\} \tag{330}$$

The number of possible distinct distributions (i.e. of possible population vectors)

$$N_{\text{dis}} = \frac{(K+M-1)!}{K!(M-1)!} \tag{331}$$

6.2.5. Statistical Weight of a Distribution

- **main idea:** assignment and distribution problems for K objects and M sets have something in common
 - it boils down to if one considers distinguishable objects or not
 - “we wonder how many assignments contribute to one distribution”



Map many assignment vectors to the same population vector

Given assignment vectors $\mathbf{m} := \{m_1, m_2, \dots, m_k\}$ and population vectors $\mathbf{n} := \{n_1, n_2, \dots, n_m\}$ with $\sum_{m=1}^M n_m = K$.

One can have mapping that maps many assignment vectors to a given population (distribution) vector.

$$n_m(\mathbf{m}) := \sum_{k=1}^K \underbrace{\delta_{m_k, m}}_{\substack{\text{has the object } k \\ \text{been assigned to} \\ \text{subset } m?}}
\tag{332}$$

Essentially, by making objects “indistinguishable”, we map from $N_{\text{ass}} = M^K$ possibilities to $N_{\text{dis}} = \binom{K+M-1}{K}$ possibilities. We will always have

$$N_{\text{dis}} \leq N_{\text{ass}} \tag{333}$$

Moreover, for large K and M it holds that,

$$N_{\text{dis}} \ll N_{\text{ass}} \tag{334}$$

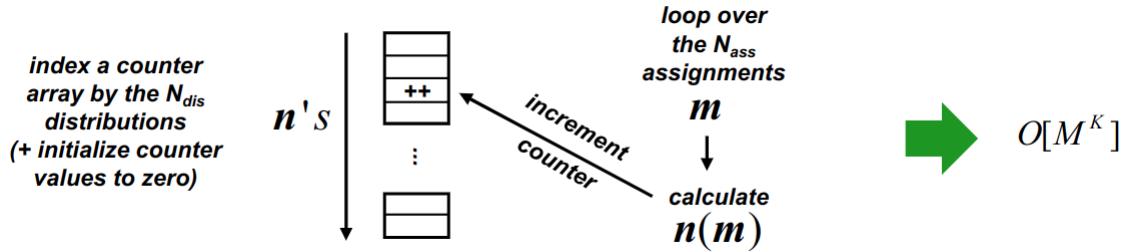
Note: the mapping above is essentially comparing the case with/without distinguishable objects.

Statistical Weight of a Distribution

The statistical weight of a population vector \mathbf{n} when distributing K objects into M bins is:

$$W_k(\mathbf{n}) := \sum_{\mathbf{m}}^{N_{\text{ass}}=M^K} \delta_{\mathbf{n}(\mathbf{m}), \mathbf{n}} \quad (335)$$

- The **statistical weight** of a distribution $W_k \leftrightarrow$ no. assignments compatible with the corresponding populations
- This formula gives us a way to categorize **assignments** into **populations**, with the following illustration of the algorithm



?Boils down to a partition problem

It boils down to a partition problem, and the resulting weight is given by N_{par} , that uses the multinomial coefficient to calculate:

$$W_k(\mathbf{n}) \equiv N_{\text{par}} = \binom{K}{n_1, n_2, \dots, n_M} = \frac{K!}{\prod_{m=1}^M n_m!} \quad (336)$$

In statistical mechanics, one often uses in combination of the Boltzmann distribution (see later). One often takes its logarithm to define the **entropy**.

6.2.6. Stirling Approximation

Factorials of very large numbers can be approximated using **Stirling approximation**.

$$\ln N! \approx N \cdot \ln N - N \quad (337)$$

Proof Using continuous integral on discrete case as approximation.

$$\begin{aligned} \ln N! &= \ln \left(\prod_{n=1}^N n \right) \\ &= \sum_{n=1}^N \ln(n) \\ &\approx \int_1^N dx \ln(x) \\ &= [x \cdot \ln(x) - x]_1^N \\ &= [N \cdot \ln(N) - N - 0 + 1] \\ &\approx N \cdot \ln(N) - N \end{aligned} \quad (338)$$

Equivalent Formulation

Equivalently, one can also write

$$N! \approx N^N \cdot e^{-N} \quad (339)$$

which is a simple result by taking both sides to exponential:

$$\begin{aligned} \ln N! &\approx N \cdot \ln N - N \\ e^{\ln(N!)} &\approx e^{N \cdot \ln N - N} \\ N! &\approx \frac{e^{\ln(N^N)}}{e^N} \\ N! &\approx N^N \cdot e^{-N} \end{aligned} \quad (340)$$

Error in Stirling Approximation

In the limit of large integers N , the error term is bounded by:

$$O(\ln N) \quad (341)$$

6.2.7. Dirac Delta Function

A generalized function that is **infinitely high** and **infinitely narrow**, but with **an integral of one**.

- the unit of δ is the inverse unit of x .

$$\begin{aligned} \delta(x) &= 0, \forall x \neq 0 \\ \int_{-\infty}^{\infty} dx \delta(x) &\stackrel{!}{=} 1 \end{aligned} \quad (342)$$

Key Property

$$\int_{-\infty}^{\infty} dx f(x) \delta(x - a) = f(a) \quad (343)$$

Different from Kronecker Delta Symbol

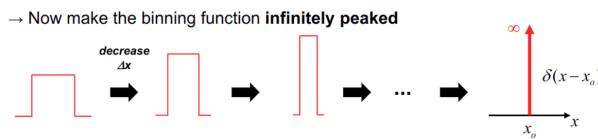
Kronecker Delta selects one value x , and is unitless and nor normalized.

$$\delta_{x,x_o} = \begin{cases} 1 & \text{if } x = x_o \\ 0 & \text{otherwise} \end{cases} \quad (344)$$

6.2.7.1. Alternative Definition

a normalized binning function (or using a normalized Gaussian) at limit $\Delta x \rightarrow 0$

$$\omega(x; \Delta x) = \begin{cases} \frac{1}{\Delta x} & \text{if } x \in [-\frac{\Delta x}{2}, \frac{\Delta x}{2}] \\ 0 & \text{otherwise} \end{cases} \quad (345)$$



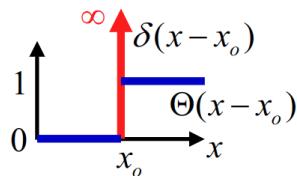
Heaviside Function

Also called the step-function

$$\Theta(x) := \begin{cases} 0 & \text{if } x \leq 0 \\ 1 & \text{if } x > 0 \end{cases} \quad (346)$$

As Derivative of Heaviside

$$\delta(x) = \frac{d\Theta(x)}{dx} \quad (347)$$



6.3. Probabilities

Probability theory is the branch of mathematics dealing with probabilities, i.e. a number between zero (impossible) and 1 (certain) that tells **likelihood** of **occurrence** of an **event**.

Frequency of the outcome

- the fraction of systems in the set of repetitions in which the outcome r occurs, the no. of the occurrence of outcome r is denoted by N_r . The total number of **repetitions** done is given by N .
 - repetitions are assumed **statistically independent**

$$f(r) = \frac{N_r}{N} \quad (348)$$

Probability of outcome r

$$p(r) = \lim_{N \rightarrow \infty} f(r) \quad (349)$$

Normalization of the probability distribution

- A probability distribution is normalized to unity.

$$\sum_r^{N_r} p_r \stackrel{!}{=} 1 \quad (350)$$

6.3.1. Discrete vs. Continuous Random Variables

DISCRETE		<i>cf quantum mechanics (sample space ~ energy levels)</i>	CONTINUOUS		<i>cf classical mechanics (sample space ~ phase-space points)</i>
sample space	$x \in S = \{x_k\}$			$S = [x_{min}, x_{max}]$	
probability function	$p(x_k) \triangleq P(X = x_k)$ <i>(unitless)</i>	probability mass function	probability distribution (or density) function	$p(x') \triangleq \delta(x - x')$ <i>(inverse of units of x)</i>	$p(x)dx$ is the probability that x lies in the interval from x to $x + dx$
normalization	$\sum_k p(x_k) = 1$			$\int_{x_{min}}^{x_{max}} dx p(x) = 1$	
expectation value (mean)	$E[X] = \sum_k p_k x_k$			$E[X] = \int_{x_{min}}^{x_{max}} dx p(x)x$	
variance	$\text{Var}(X) = \sum_k p_k (x_k - E[X])^2$			$\text{Var}(X) = \int_{x_{min}}^{x_{max}} dx p(x)(x - E[X])^2$	
standard deviation	$\sigma(X) = [\text{Var}(X)]^{1/2}$			$\sigma(X) = [\text{Var}(X)]^{1/2}$	

6.3.2. Distribution

TYPE	PROBABILITY FUNCTION	MEAN	VARIANCE
Binomial	$P_b(n; p) = \binom{N}{n} p^n (1-p)^{N-n}$ for $n \in [N]$	$E[X] = Np$ (352)	$\text{Var}[X] = Np(1-p)$ (353)
Uniform	$p_u(x) := \begin{cases} \frac{1}{b-a} & \text{if } x \in (a, b) \\ 0 & \text{else} \end{cases}$	$E[X] = \frac{a+b}{2}$ (355)	$\text{Var}[X] = \frac{(b-a)^2}{12}$ (356)
Exponential	Define $I := (0, +\infty)$ $p_e(x) := \begin{cases} \alpha \cdot e^{-\alpha x} & \text{if } x \in I \\ 0 & \text{else} \end{cases}$	$E[X] = \frac{1}{\alpha}$ (358)	$\text{Var}[X] = \frac{1}{\alpha^2}$ (359)
Normal	$p_n(x) := \frac{1}{\sqrt{2\pi}\sigma} e^{-\frac{(x-\mu)^2}{2\sigma^2}}$ for $x \in \mathbb{R}$	$E[X] = \mu$ (361)	$\text{Var}[X] = \sigma^2$ (362)

Note: some special properties for different distributions

6.3.2.1. Binomial Distribution

Normalization

$$\sum_{n=1}^N \binom{N}{n} p^n (1-p)^{N-n} = (p + (1-p))^N = 1 \quad (363)$$

Applications

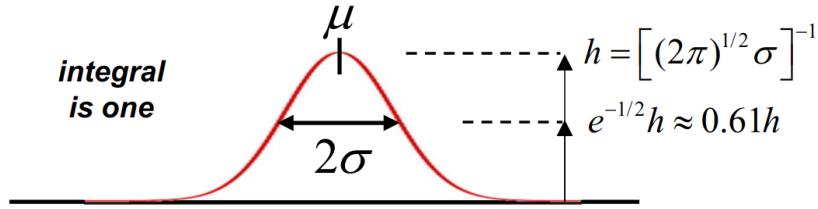
- At limit $N \rightarrow \infty$, the binomial distribution can be approximated by a normal Gaussian distribution.
 - central limit theorem
- Bernoulli process
- 1D random walk

6.3.2.2. Uniform Distribution

Applications

- pseudo-random number generator on computer

6.3.2.3. Normal Distribution



6.3.3. Central Limit Theorem

When N independent random variables X_n are drawn from arbitrary distribution $p(x)$ with average μ and variance σ^2 , in the limit of large N , their mean X distributes according to a normal Gaussian distribution with average μ and variance $\frac{\sigma^2}{N}$.

$$P(X) := \frac{1}{\sqrt{2\pi}\tilde{\sigma}} e^{-\frac{(X-\mu)^2}{2\tilde{\sigma}^2}}, \text{ for } x \in \mathbb{R} \quad (364)$$

De Moivre-Laplace Theorem

- For large N , the binomial distribution becomes close to a Gaussian.
- A special case of CLT

$$\binom{N}{k} p^k q^{N-k} \approx \frac{1}{\sqrt{2\pi N p q}} e^{-\frac{(k-Np)^2}{2Npq}} \quad (365)$$

with $p, q > 0$ and $p + q = 1$.

Consequence for Statistical Mechanics

- A macroscopic thermodynamic property represents the average of a microscopic (instantaneous) observable over a huge number of particles ($\sim 10^{23}$).
 - particles behave as independent random objects
- If the microscopic property distribution has mean μ and variance σ^2 , the macroscopic observable will be single-values at μ .
 - its distribution will be an infinitely sharp peak with negligible variance.

6.4. Stochastics

Branch of mathematics dealing with **processes**, **procedures** and **algorithms** involving **random numbers**.

Stochastic process

A process is called stochastic if it corresponds to a sequence of values

$$\begin{cases} \text{discrete-index process } X_N = \{x_i \mid i = 1, 2, \dots, N\} \\ \text{continuous-time process } X_t = \{x_t \mid t \in \mathbb{R}^+\} \end{cases} \quad (366)$$

and satisfies **two properties**:

- values in the sequence **occur randomly**
- values are **distributed deterministically**

e.g. Bernoulli process, random walk, Gaussian process, Gaussian white-noise process, Wiener process

Correlation probabilities along the sequence

The correlation probabilities connecting the x_i to previous or same x_j along the sequence are well-defined.

$$\begin{cases} \text{discrete-index process } p(x_{t+u}, x_t) \forall u \geq 0 \\ \text{continuous-time process } p(x_{i+j}, x_i) \forall j > 0 \end{cases} \quad (367)$$

6.4.1. Pseudo-Random Numbers

Most pseudo-random number generators aim to generate **non-correlated uniformly distributed** real numbers over the interval $[0, 1]$

- However, machine precision already involves non-uniformity
- one often converts results to
 - integers in range $[0, N]$ (`(int)(N*rand())`)
 - other distributions, e.g. Box-Müller for Gaussian
- Introduction of correlations with previous numbers is possible

Algorithms

- Multiplicative congruential generator (MCG)
- Mersenne Twister

6.4.1.1. Tests for Pseudo-Random Number Generators

There is no single *necessary* and *sufficient* test of randomness! One need to test for the occurrence of

1. Non-uniformity (Uniformity Test)
2. Correlation (Correlation Test)

- **Measure of non-uniformity**

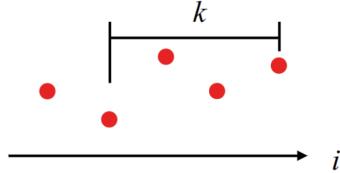
$$\chi^2 = \frac{1}{K} \sum_k^K \frac{[n_k - K^{-1}N]^2}{K^{-1}N} \quad (368)$$

One often repeats the χ^2 test multiple times and follows the *rule of thumb* (for $N > 10 K$)

$$1 - \chi^2 < \frac{2}{\sqrt{K}} \quad (369)$$

- **Correlation function $C(k)$**

Given K as the total number of points



$$C(k) = \frac{\langle x_i x_{i+k} \rangle_i - \langle x_i \rangle_i \langle x_{i+k} \rangle_i}{\langle x_i x_i \rangle_i - \langle x_i \rangle_i \langle x_i \rangle_i} \quad (370)$$

with

$$\langle x_i x_{i+k} \rangle_i := \frac{1}{K-k} \sum_{i=1}^{K-k} x_i x_{i+k} \quad (371)$$

If no correlation exists, it holds:

$$\begin{aligned} \langle x_i x_{i+k} \rangle_i - \langle x_i \rangle_i \langle x_{i+k} \rangle_i &\stackrel{!}{=} 0 \\ \rightarrow C(k) &= 0 \end{aligned} \quad (372)$$

6.4.2. Bernoulli Process

The Bernoulli process consists of N trials with **binary outcomes** $\{0, 1\}$. The success probability is always the same, where $p \in [0, 1]$ and

$$\begin{cases} \text{success} \rightarrow p \\ \text{failure} \rightarrow 1 - p \end{cases} \quad (373)$$

Successive trials are **independent** and thus have no correlation.

What is the probability of observing exactly n successes?

- recall binomial distribution, it gives the probability of observing n successes over N trials.

$$P_b(n; p) = \binom{N}{n} p^n (1-p)^{N-n} \text{ for } n \in [N] \quad (374)$$

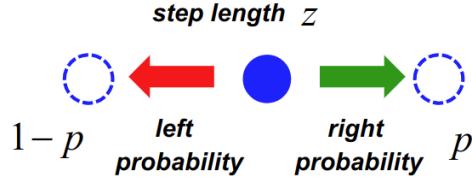
6.4.3. Random Walk

A stochastic process involving a sequence of steps taken in random directions.

- every direction taken is chosen according to a given **probability distribution**, and direction of different steps are **uncorrelated**.

Random Walk 1D

Each step is a Bernoulli process, with success defined as a step to right with the probability p .



Given such process, where we took in all N steps, with n steps to the right and $N - n$ steps to the left, it follows the binomial distribution. The probability of a given net move Z over such N steps is given by

$$P_b(n; p) = \binom{N}{n} p^n (1-p)^{N-n} \text{ for } n \in [N] \quad (375)$$

The **net displacement** to the **right** in units of z .

$$M(n) = \underbrace{n}_{\text{right}} - \underbrace{(N-n)}_{\text{left}} \quad (376)$$

we can calculate the **general net displacement** as

$$\begin{aligned} \tilde{P}(M) &:= \gamma_{M+N} \cdot P_b\left(\frac{m+n}{2}; p\right) \\ &:= \gamma_{M+N} \cdot \binom{N}{\frac{N+M}{2}} p^n (1-p)^{N-\frac{N+M}{2}} \end{aligned} \quad (377)$$

Statistical properties

- mean

$$E[Z] = N \cdot (2p - 1)z \quad (378)$$

- variance

$$\text{Var}[Z] = 4N \cdot p(1-p)z^2 \quad (379)$$

Note: In limit of very long walk

One can apply the de Moivre-Laplace theorem, for large N . The binomial distribution close to Gaussian.

$$\tilde{P}(M) := \gamma_{M+N} \cdot P_b\left(\frac{m+n}{2}; p\right) \quad (380)$$

becomes

$$\begin{aligned} \tilde{P}(M) &\approx \gamma_{M+N} \cdot \frac{1}{\sqrt{\frac{1}{2}\pi Np(1-p)}} e^{-\frac{(M+N-Np)^2}{2Np(1-p)}} \\ &\approx \gamma_{M+N} \cdot \frac{1}{\sqrt{\frac{1}{2}\pi Np(1-p)}} e^{-\frac{(M+N-(1-2p))^2}{8Np(1-p)}} \end{aligned} \quad (381)$$

Special Case: symmetric 1D random walk

- consider $p = \frac{1}{2}$

$$\tilde{P}(M) = \gamma_{M+N} \cdot \binom{N}{\frac{N+M}{2}} 2^{-N} \quad (382)$$

- mean effective displacement is zero
- standard deviation scales as $N^{\frac{1}{2}}$

$$\text{Var}^{\frac{1}{2}}[Z] = N^{\frac{1}{2}}z \quad (383)$$

Note: In limit of very long walk

$$\tilde{P}(M) \approx \gamma_{M+N} \cdot \frac{1}{\sqrt{\frac{1}{2}\pi N}} e^{-\frac{M^2}{2N}} \quad (384)$$

Random Walk 3D

In Cartesian coordinates, consider $\mathbf{r} := (x, y, z)^T$

- Approach 1: take $\Delta x, \Delta y, \Delta z$ from uncorrelated uniform random distributions
 - $(2*\text{rand}() - 1)/(2\Delta)$
 - However, this generates a walk of variable step-size that is affected by step anisotropy, one does not have a constant step-size (cube-corner effects)
- Approach 2: Generate random 3D coordinate for \mathbf{r} directly
 - approach 2.1: rescale vector to fixed length Δr
 - but this still generates a walk that is affected by step anisotropy
 - approach 2.2: discard attempts with length exceeding Δr
 - now we have fixed-length isotropic steps, but it comes with inefficiency by explicitly trashing points
- Approach 3: Generate normally-distributed Cartesian components and rescale to Δr
 - no rejection needed!

In polar coordinates, one can map with

$$\begin{pmatrix} \Delta x \\ \Delta y \\ \Delta z \end{pmatrix} = \begin{pmatrix} \Delta r \cdot \cos(\theta) \cos(\varphi) \\ \Delta r \cdot \cos(\theta) \sin(\varphi) \\ \Delta r \cdot \sin(\theta) \end{pmatrix} \quad (385)$$

where we generate the angles φ, θ such that

- φ is uniform random over $[0, 2\pi)$
- θ is computed by $\theta := \arccos(u)$
 - and u is uniform random over $[-1, 1]$
- no rejection needed!

6.4.4. Continuous-Time White-Noise (CTWN) Process

Recall a continuous time process is

$$X_t = \{x_t \mid t \in \mathbb{R}^+\} \quad (386)$$

For CTWN, the zero correlation between different times holds x_t and x_{t+u} are uncorrelated $\forall u$.

The distribution at any time is Gaussian with zero mean, and σ is a parameter that gives the amplitude (standard deviation) of the noise.

$$x_t \sim \mathcal{N}(0, \sigma^2), \quad \forall t \quad (387)$$

6.4.5. Wiener Process (Brownian Motion)

A generalization of the discrete-step 1D random walk to a continuous process (real numbers).

Consider N independent and i.i.d random variables with mean $\mu = 0$ and variance $\text{Var}[X] = 1$.

We consider $t \in [0, 1]$ without loss of generality and ξ_k , where $k \in [N]$ and define $W_t^{(N)}$ as

$$W_t^{(N)} := \frac{1}{\sqrt{N}} \sum_{k=1}^{\lfloor N_t \rfloor} \xi_k \quad (388)$$

By taking the limit, it holds that

$$W_t = \lim_{N \rightarrow \infty} W_t^{(N)} \quad (389)$$

Properties of W_t

UNIT	<ul style="list-style-type: none"> • UNIT: TAKES UNIT OF $\frac{1}{\sqrt{t}}$
Continuity & Differentiability	<p>It is continuous but not differentiable in t</p> <ul style="list-style-type: none"> • e.g. in Brownian motion one has $r(t) - r(0) \sim W_t$
Increments	<ul style="list-style-type: none"> • increments are Gaussian, $\forall t > 0, u \geq 0$ $W_{t+u} - W_t \sim \mathcal{N}(0, u) \quad (390)$ <p>but increments are independent, $\forall s < t$</p> $W_{t+u} - W_t \text{ independent of } W_s \quad (391)$
Scale Invariance	Given a Wiener process W_t , for any $\alpha \neq 0$, it holds that $\frac{1}{\alpha}W_{\alpha^2 t}$ is also a Wiener process

6.4.6. Monte Carlo Sampling

Monte Carlo methods are a class of algorithms where a **deterministic problem** is solved **numerically** using a **stochastic approach**.

Applications

One uses pseudo random numbers, where accuracy of algorithms heavily rely on quality of the random number generator

Classes of problems targeted by MC methods

- optimization
- numerical integration
- generating draws from a probability distribution
 - one desires to have an uniform distribution of statistically independent configurations.
 - e.g. Metropolis Monte Carlo

6.4.6.1. Example: MC sampling for ensemble of polymer conformations

- Consider a **polymer** in **vacuum** with **rigid bonds** that can form arbitrary angles and atoms that have no interactions through space with each other. Such chain can adopt a very large number of **configurations**.

Mean of end-to-end distance

Given a set of Ω virtual copies of the chain, each in a given configuration at random (statistical ensemble) with probability of distance d_i given by p_i , we can calculate the expected value:

$$E[d] = \sum_{i=1}^{\Omega} d_i p_i \quad (392)$$

Note: this is challenging to compute as all possible configurations would need to be known, technically if Ω is large enough, all possible configurations are encompassed by **ergodic hypothesis**.

→ one opts to use Monte Carlo method here by **approximating** the sum over all configurations by a sum over some **configurations**, taken as a **statistical sample**.

$$E[d] \approx \frac{1}{N} \sum_{i=1}^M d_i \quad (393)$$

```
// Pseudo-code
Begin sampling loop from i = 1 to i = M
Start site: x = 0, y = 0
  Begin stepping loop j = 1 to j = N
    Choose direction: Generate random integer n between [0,3]
    If n = 0: x = x+1
    If n = 1: x = x-1
    If n = 2: y = y+1
    If n = 3: y = y-1
  End stepping loop
End sampling loop
Compute mean end-to-end distance
and mean square radius
```

6.5. Misc

- (time-)correlations
- Gaussian process (general)
- Galton board & regression to the mean
- Bayesian statistics
- Gibbs sampling

7. Statistical Mechanics Part I

7.1. Microscopic & Macroscopic Descriptions of the World

Microscopic Point of View

- Classical Mechanics & Quantum Mechanics
- wave functions of particles

Statistical Mechanics as the Bridge

- Analytical or computational

Macroscopic Point of View

- Phenomenological Thermodynamics
- phases, composition, pressure, temperature, heat, work...
- n is no. moles, N is no. atoms/molecules

$$n = \frac{N}{N_A} \quad (394)$$

Avogadro Number: $N_A \approx 6.02214076 \times 10^{23} \text{ mol}^{-1}$

7.2. Microstate & Macrostate

For a system at **equilibrium** with a **time-independent Hamiltonian**, depending how a specific choice of values is made:

- **macrostate**: choice made for independent variables
 - eg. $Z = \{n, V, T\}$
- **microstate**: choice made for all variables
 - huge amount of variables involved

7.3. Statistical-Mechanical Ensemble

One **macrostate** can be seen as a **projection** of a huge number of **compatible microstates**.

Statistical Mechanical Ensemble: a hypothetical construct consisting of K **identical independent copies** of the system.

- the **Ensemble** is a time-independent object (Liouville Theorem)
 - ensemble itself is representative of one macrostate
- system **copies** can be in different microstates

Compatibility of microstates and macrostates

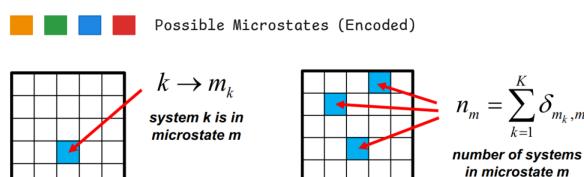
- constraints imposed
 1. System constraints: affect the systems individually
 2. Ensemble constraints: affect the systems collectively

7.3.1. Assignment & Population

Assume we have $k \in \{1, \dots, K\}$ systems and $m_k \in \{0, \dots, M-1\}$ microstates

There are $N_{\text{ass}} = M^K$ ways to assign each system into a set of microstates. Using the assignment vector $\mathbf{m} = \{m_1, m_2, \dots, m_K\}$ that encode the assigned microstate for each system.

Based on this, one defines the population vector $\mathbf{n} = \overbrace{\{n_0, n_1, \dots, n_{M-1}\}}^{\text{should sum up to } K}$. The number of possible distinct distributions is given by $N_{\text{dis}} = \frac{(K+M-1)!}{K!(M-1)!}$.



7.3.2. Statistical weight

Statistical weight of a population vector in an ensemble of K systems

$$W_K(\mathbf{n}) = \frac{K!}{\prod_{m=0}^{M-1} n_m!} \quad (395)$$

- no. microstates into a macrostate

There are N_{dis} choices for the vector \mathbf{n} and one has

$$\sum_n W_K(\mathbf{n}) = N_{\text{ass}} \quad (396)$$

Example: Given a system with three states $M = 3$ and an ensemble with six systems $K = 6$.

- How many possible distinct assignment vectors are there?

$$N_{\text{ass}} = M^K = 3^6 = 729 \quad (397)$$

- What is the number of possible distinct distributions (i.e. number of possible population vectors)?

$$N_{\text{dis}} = \frac{(K+M-1)!}{K!(M-1)!} = \frac{(6+3-1)!}{6!(3-1)!} = \frac{8!}{6!2!} = 28 \quad (398)$$

- What is the statistical weight of a population that consists of $\mathbf{n} = \{3, 2, 1\}$?

$$W_{K=6}(\mathbf{n} = \{3, 2, 1\}) = \frac{K!}{\prod_{m=0}^{M-1} n_m!} = \frac{6!}{3! \cdot 2! \cdot 1!} = \frac{6 \cdot 5 \cdot 4 \cdot 3 \cdot 2 \cdot 1}{3! \cdot 2! \cdot 1!} = 60 \quad (399)$$

7.4. Postulate of a priori Equiprobability

All the microstates of a system are in principle intrinsically equally probable, the only restriction on their probability arises from the imposed macroscopic constraints.

Implications

1. all possible **assignment vectors** in an ensemble are equiprobable in the absence of constraints
 - the **probability** of occurrence of a given **population vector** in a collection of random ensembles is proportional to its **statistical weight**

Fractional-Population Vector

Rewrite the population vector $\mathbf{n} = \{n_0, n_1, \dots, n_{M-1}\}$. Using the fact $\sum_{m=0}^{M-1} n_m = K$, we define the **fractional-population vector** $\mathbf{p} = \{p_0, \dots, p_{M-1}\}$

$$\begin{aligned} p_m &\stackrel{\text{def}}{=} K^{-1} n_m \\ \text{with } \sum_{m=0}^{M-1} p_m &= 1 \end{aligned} \quad (400)$$

Normalized probability of the distribution vectors

$$\begin{aligned} P_K(\mathbf{p}) &= \frac{K!}{M^K \prod_{m=0}^{M-1} (Kp_m)!} \\ \text{with } \sum_{\mathbf{p}} P_K(\mathbf{p}) &= 1 \end{aligned} \quad (401)$$

The corresponding weight

$$W_K(K\mathbf{p}) = M^K P_K(\mathbf{p}) \quad (402)$$

For the vector \mathbf{p} there are $N_{\text{dis}} = \frac{(K+M-1)!}{K!(M-1)!}$ choices.

Derivation:

From the statistical weight of a given population vector in an ensemble of K systems

$$W_K(\mathbf{n}) = \frac{K!}{\prod_{m=0}^{M-1} n_m!} \quad (403)$$

Examples: intrinsically equally probable microstates

- quantum states $m \in \{0, 1, \dots, M-1\}$
- phase-space volume elements $\mathbf{x}^{2N} d\mathbf{x}^{2N}$

7.4.1. Peaking of the Distribution Probability (Central-limit theorem)

The probability $P_K(\mathbf{p})$ of the distributions \mathbf{p} becomes increasingly peaked as the number K of systems in the ensemble increases.

In the limit $K \rightarrow \infty$ a single most-probable distribution will have such an overwhelming probability that the contribution of all the other distributions can be entirely disregarded.

Single Peaked Distribution

- it corresponds to $K \rightarrow \infty$ and is independent of K
- it is the **most probable** one, the **average** one and the **only relevant** one

Lemma. Central-Limit Theorem for Fractional Population Vector

The fractional population vector with the probability

$$P_K(\mathbf{p}) = \frac{K!}{M^K \prod_{m=0}^{M-1} (Kp_m)!} \quad (404)$$

with $\sum_{\mathbf{p}} P_K(\mathbf{p}) = 1$

converges to a single overwhelmingly most-probable distribution at limit $\lim_{K \rightarrow \infty}$

$$\rho = \{\rho_0, \rho_1, \dots, \rho_{M-1}\} \quad (405)$$

with $\sum_{m=0}^{M-1} \rho_m = 1$

Example: Two-state system

Given two states $M = 2$, K systems, and the fractional-population vector for some distribution $\mathbf{p} = \{p_1, p_2\}$, for which it holds $p_1 + p_2 = 1$.

$$\begin{aligned} P_K(\mathbf{p} = \{p_1, p_2\}) &= \frac{K!}{M^K \prod_{m=0}^{M-1} (Kp_m)!} \\ &= \frac{K!}{2^K (Kp_0)!(Kp_1)!} \\ &\stackrel{p_0=p}{=} \frac{K!}{2^K (Kp)!(K(1-p))!} \end{aligned} \quad (406)$$

with $\sum_{\mathbf{p}} P_K(\mathbf{p}) = 1$

where in intermediate step we parameterize with $\mathbf{p} = \{p, 1-p\}$, $p \in [0, 1]$

By defining $\Delta p := K^{-1}$ ($N_{\text{dis}} = K + 1$), one can further normalize

$$\tilde{P}_K(p) = \frac{P_K(p)}{\Delta p} \quad \text{with } \sum_{\mathbf{p}} \tilde{P}_K(p) \Delta p = 1 \quad (407)$$

7.5. Ensemble Average

The ensemble average of a **microscopic** (instantaneous) **observable** is the **expected value** of this quantity in a **macroscopic system at equilibrium**.

$$\underbrace{\langle A \rangle}_{\text{macro. value}} = \lim_{K \rightarrow \infty} \underbrace{\sum_{\substack{\mathbf{p} \\ \text{over} \\ \text{distributions}}} P_K(\mathbf{p})}_{\sum_{m=0}^{M-1} p_m} \underbrace{\mathcal{A}_m}_{\substack{\text{micro. value} \\ \text{in state m}}} \quad (408)$$

the number of distributions $N_{\text{dis}} = \frac{(K+M-1)!}{K!(M-1)!}$

7.5.1. Ensemble Average for Peaked Distribution

$$\langle A \rangle = \sum_{m=0}^{M-1} \rho_m \mathcal{A}_m \quad (409)$$

where ρ_m is the probability of state m in the overwhelmingly most probable distributions.

7.6. Boltzmann & Gibbs Entropies

Boltzmann postulate Entropy is a logarithmic measure of the **statistical weight** of a distribution.

Boltzmann Entropy

$$S_K(\mathbf{p}) = k_B K^{-1} \ln \underbrace{W_K(K\mathbf{p})}_{*} \quad (410)$$

with Boltzmann constant

$$k_B = \frac{R}{N_A} = 1.381 \times 10^{-23} J \cdot K^{-1} \quad (411)$$

Gibbs Entropy

- directly based on the distribution
- also called the Shanon entropy in information theory

$$S_K(\mathbf{p}) = -k_B \sum_{m=0}^{M-1} p_m \ln p_m \quad (412)$$

Derivation: from Boltzmann to Gibbs Entropy

$$\begin{aligned} \underbrace{W_K(K\mathbf{p})}_{*} &= M^K P_K(\mathbf{p}) \\ &= M^K \frac{K!}{\prod_{m=0}^{M-1} (Kp_m)!} \end{aligned} \quad (413)$$

the expression for Boltzmann entropy can be simplified

$$\begin{aligned}
S_K(\mathbf{p}) &= k_B K^{-1} \ln \underbrace{W_K(K\mathbf{p})}_{*} \\
&= k_B K^{-1} \ln \left[\frac{K!}{\prod_{m=0}^{M-1} (Kp_m)!} \right] \\
&= k_B K^{-1} \left[\ln K! - \ln \left(\prod_{m=0}^{M-1} (Kp_m)! \right) \right] \\
&= k_B K^{-1} \left[\ln K! - \sum_{m=0}^{M-1} \ln(Kp_m)! \right] \\
&= k_B K^{-1} \left[(K \ln K - K) - \sum_{m=0}^{M-1} ((Kp_m) \ln(Kp_m) - (Kp_m)) \right] \\
&= k_B K^{-1} \left[(\ln K - 1) - \sum_{m=0}^{M-1} (p_m \ln(Kp_m) - p_m) \right] \\
&= k_B \left[(\ln K - 1) - \sum_{m=0}^{M-1} (p_m [\ln(K) + \ln(p_m)] - p_m) \right] \\
&= k_B \left[(\ln K - 1) - \sum_{m=0}^{M-1} (p_m (\ln(K) - 1) + p_m \ln(p_m)) \right] \\
&= k_B \left[(\ln K - 1) - (\ln(K) - 1) \underbrace{\sum_{m=0}^{M-1} p_m}_{=1} - \sum_{m=0}^{M-1} p_m \ln(p_m) \right] \\
&= -k_B \sum_{m=0}^{M-1} p_m \ln(p_m)
\end{aligned} \tag{414}$$

Using Stirling's approximation

$$(Kp_m) \ln N! \approx N \ln N - N \tag{415}$$

In the limit of an infinite ensemble

In the limit $K \rightarrow \infty$, the entropy of a thermodynamic system is uniquely defined by the given macroscopic constraints $S := S(N, V, T)$.

$$\begin{aligned}
S_\infty(\mathbf{p}) &= \lim_{K \rightarrow \infty} S_K(\mathbf{p}) \stackrel{\text{Boltzmann}}{=} \lim_{K \rightarrow \infty} k_B K^{-1} \ln W_K(K\mathbf{p}) \\
&= k_B \lim_{K \rightarrow \infty} K^{-1} \ln W_K(K\mathbf{p}) \\
&\stackrel{\text{Gibbs}}{=} -k_B \sum_{m=0}^{M-1} \rho_m \ln(\rho_m)
\end{aligned} \tag{416}$$

- $S \triangleq S_\infty(\boldsymbol{\rho})$ thermodynamic entropy

To find the unique distribution $\boldsymbol{\rho}$

1. impose macroscopic constraints added in the form of Lagrange multipliers
2. Maximize S_∞ relative to \mathbf{p}

$$\begin{aligned}
&\text{Objective } S_\infty(\boldsymbol{\rho}) + \lambda C_{\text{mac}(\boldsymbol{\rho})} \\
&\text{s.t. } C_{\text{mac}(\boldsymbol{\rho})} = 0 \\
&\Rightarrow \frac{\partial S_\infty(\boldsymbol{\rho})}{\partial \rho_m} + \underbrace{\lambda}_{\substack{\text{selected} \\ \text{to enforce} \\ \text{constraints}}} \frac{\partial C_{\text{mac}(\boldsymbol{\rho})}}{\partial \rho_m} = 0
\end{aligned} \tag{417}$$

7.6.1. Classical Expressions

- not discrete but integrable

Phase-Space Probability Density

- units: $[\rho(\mathbf{x}^{2N})] = \frac{1}{\text{action}^{3N}}$

$$\rho(\mathbf{x}^{2N}) \text{ with } \int d\mathbf{x}^{2N} \rho(\mathbf{x}^{2N}) = 1 \quad (418)$$

Ensemble Average

- Given the microscopic (instantaneous observable) $\mathcal{A}(\mathbf{x}^{2N})$ and $\rho(\mathbf{x}^{2N})$

$$\langle A \rangle = \int d\mathbf{x}^{2N} \rho(\mathbf{x}^{2N}) \mathcal{A}(\mathbf{x}^{2N}) \quad (419)$$

Entropy

- of the most-probable phase-space probability density
- $\xi^{-1} = h^{3N} N!$
- units: $[\xi] = \frac{1}{\text{action}^{3N}}$

$$S = -k_B \int d\mathbf{x}^{2N} \rho(\mathbf{x}^{2N}) \ln[\xi^{-1} \rho(\mathbf{x}^{2N})] \quad (420)$$

7.7. Types of Ensembles

Statistical-Mechanical Ensembles

The four most important ensembles

- microcanonical (NVE)
- canonical (NVT)
- isothermal-isobaric (NPT)
- grand-canonical (μVT)

others

- isoenthalpic-isobaric
- grand-microcanonical
- grand-isoenthalpic-isobaric
- generalized

7.8. The Microcanonical Ensemble (NVE)

The microcanonical ensemble corresponds to the situation of an isolated system.

In MD simulations, one integrates by default the **classical Newtonian equations of motion** for an **isolated** and (ideally) **conservative** system.

- as a result, a microcanonical (NVE) ensemble is in principle sampled
- default behavior can be modified using a thermostat or barostat
- energy not strictly conserved in a classical MD due to numerical inaccuracies and approximation errors

In experiments, a rigorously isolated system is **not achievable in practice**. Noise exists and most experiments are performed at **constant pressure** or/and **temperature** instead of constant energy.

7.8.1. Constraints

$$\begin{cases} 1. \text{ Constant number of molecules } N \\ 2. \text{ Constant volume } V \\ 3. \text{ Constant energy } E \end{cases} \Rightarrow \text{are all system constraints} \quad (421)$$

- N, V define the accessible energy levels $j \in \{0, \dots, J-1\}$ of the system with their energies

$$E = E(N, V) = \left\{ \underbrace{E_0, \dots, E_{J-1}}_{=0} \right\} \quad (422)$$

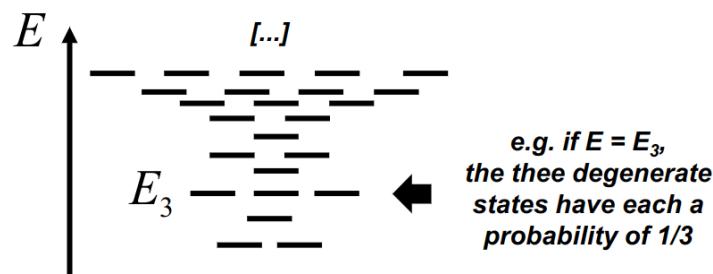
and degeneracies $g = \{g_0, \dots, g_{J-1}\}$.

- the value of E must match one of the E_j 's, one denote this level as $j(E)$

7.8.2. Most-Probable Distribution

The probabilities of the degenerate states at a given energy level are all the same, and equal to the inverse of its degeneracy.

$$\tilde{\rho}_m = g_{j(E)}^{-1} \delta_{j_m, j(E)} \quad (423)$$



Derivation

Starting from Gibbs entropy, we express it as the total probability

$$\begin{aligned} S_K(\mathbf{p}) &= -k_B \sum_{m=0}^{M-1} p_m \ln p_m \\ k_B^{-1} S_K(\mathbf{p}) &= - \underbrace{\sum_{m=0}^{M-1} p_m \ln p_m}_{\text{ensemble constraint}} \end{aligned} \tag{424}$$

we add constraints using the Lagrange multiplier α , also making sure $\sum_{m=0}^{M-1} p_m = 1$ holds

$$\text{objective: } - \sum_{m=0}^{M-1} p_m \ln p_m + \alpha \underbrace{\left(1 - \sum_{m=0}^{M-1} p_m\right)}_{\text{ensemble constraint}} \tag{425}$$

we maximize the $(-1) \cdot \text{objective}$

$$\begin{aligned} & \sum_{m=0}^{M-1} p_m \ln p_m - \alpha \left(1 - \sum_{m=0}^{M-1} p_m\right) \\ \Leftrightarrow & \left(\sum_{m=0}^{M-1} p_m \ln p_m\right) - \alpha + \alpha \left(\sum_{m=0}^{M-1} p_m\right) \\ \Leftrightarrow & \left(\sum_{m=0}^{M-1} p_m \ln p_m + \alpha p_m\right) - \alpha \\ \stackrel{\frac{\partial}{\partial p_m}}{\Leftrightarrow} & \left(\sum_{m=0}^{M-1} \frac{\partial}{\partial p_m} (p_m \ln p_m) + \alpha \frac{\partial}{\partial p_m} (p_m)\right) - \frac{\partial}{\partial p_m} (\alpha) \\ \Leftrightarrow & \left(\sum_{m=0}^{M-1} \frac{\partial}{\partial p_m} (p_m \ln p_m) + \alpha\right) \\ \Leftrightarrow & \left(\sum_{m=0}^{M-1} \underbrace{\ln p_m + 1 + \alpha}_{\stackrel{!}{=} 0}\right) \end{aligned} \tag{426}$$

To find stationary point

$$\begin{aligned} & \ln p_m + 1 + \alpha = 0 \\ \Leftrightarrow & \ln p_m = -1 - \alpha \\ \stackrel{\exp(\cdot)}{\Leftrightarrow} & \underbrace{p_m}_{\circ} = e^{-(\alpha+1)} \end{aligned} \tag{427}$$

In the microcanonical ensemble, only states that match the energy E are accessible, we account this using the Kronecker delta.

$$\begin{aligned} & \sum_{m=0}^{M-1} \delta_{j_m, j(E)} = g_{j(E)} \\ \Leftrightarrow & g_{j(E)}^{-1} \sum_{m=0}^{M-1} \delta_{j_m, j(E)} = 1 \end{aligned} \tag{428}$$

Also it must hold that $\sum_{m=0}^{M-1} p_m = 1$.

$$\begin{aligned} & \sum_{m=0}^{M-1} p_m = g_{j(E)}^{-1} \sum_{m=0}^{M-1} \delta_{j_m, j(E)} \\ \Leftrightarrow & \sum_{m=0}^{M-1} p_m = \sum_{m=0}^{M-1} g_{j(E)}^{-1} \delta_{j_m, j(E)} \\ \Leftrightarrow & p_m = g_{j(E)}^{-1} \delta_{j_m, j(E)} \end{aligned} \tag{429}$$

This leads to

$$\tilde{p}_m = g_{j(E)}^{-1} \delta_{j_m, j(E)} \tag{430}$$

7.8.3. Boltzmann Entropy

$$S = k_B \ln g_{j(E)} \tag{431}$$

7.8.4. Gibbs Entropy

$$S_K(\rho_m) = k_B \ln(g_{j(E)}) \quad (432)$$

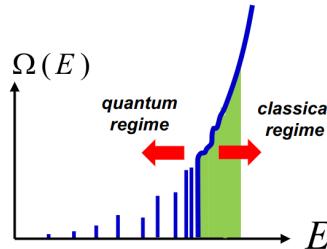
Derivation: using $\rho_m = \frac{1}{g_{j(E)}}$

$$\begin{aligned} S_K(\rho_m) &= -k_B \sum_{m=0}^{M-1} \rho_m \ln \rho_m \\ &= k_B \sum_{m=0}^{M-1} (g_{j(E)}^{-1} \delta_{j_m, j(E)}) \ln (g_{j(E)} \delta_{j_m, j(E)}) \\ &= k_B g_{j(E)}^{-1} \ln(g_{j(E)}) \underbrace{\sum_{m=0}^{M-1} (\delta_{j_m, j(E)})}_{g_{j(E)}} \\ &= k_B \ln(g_{j(E)}) \end{aligned} \quad (433)$$

7.8.5. Density of States

- quantum-mechanical density of states
 - units: $[\Omega] = \frac{1}{\text{energy}}$

$$\Omega(E) = \sum_{m=0}^{M-1} \delta(E - E_m) = \sum_{j=0}^{J-1} g_j \delta(E - E_j) \quad (434)$$

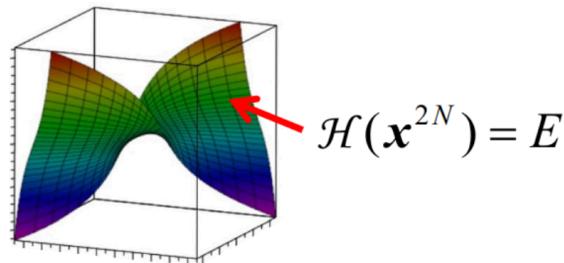


Alternative Formulations

DISCRETE	CONTINUOUS
$\tilde{\rho}_m = g_{j(E)}^{-1} \delta_{j_m, j(E)}$	$\rho_m = \Omega^{-1}(E) \delta(E - E_m)$
$S = k_B \ln g_{j(E)}$	$S = k_B \ln \Omega(E)$

7.8.6. Density of States (classical)

$$\Omega(E) = \xi \cdot \underbrace{\int dx^{2N} \delta(E - \mathcal{H}(x^{2N}))}_{\text{area of hypersurface } \mathcal{H} = E \text{ in the phase space}} \quad (439)$$



- units:
 - $[\Omega] = \frac{1}{\text{energy}}$
 - $[\xi] = \frac{1}{\text{action}^{3N}}$ value selected based on ideal gas at the quantum and classical levels
- Planck constant: $[\hbar] = \text{action}$
- $N!$ if consider indistinguishable particles, otherwise omit

$$\xi = \frac{1}{h^{3N} N!} \quad (440)$$

Mostly, not normalizable

$$\int_0^\infty dE \Omega(E) = \xi \underbrace{\int dx^{2N}}_{\infty - \text{entire volume of phase space}} \quad (441)$$

7.8.7. Most-probable Distribution (classical)

- normalized probability of a classical phase-space point in the NVE ensemble
- units: $[\rho] = \frac{1}{\text{action}^{3N}}$

$$\rho(x^{2N}) = \xi \Omega^{-1}(E) \delta(E - \mathcal{H}(x^{2N})) \quad (442)$$

7.8.8. Entropy (classical)

- logarithmic measures of the number of ways you can realize a given energy
 - units: $[S] = \frac{\text{energy}}{\text{temperature}}$

$$S = k_B \ln \Omega(E) \quad (443)$$

7.8.9. Kinetic-Energy Density of States (Classical Expression)

- classical density of states of the ideal gases
- units: $[\Omega] = \frac{1}{\text{energy}}$

$$\Omega(E) = \xi V^N \frac{R^{3N}}{2E} \cdot S_{3N-1}(1) \quad (444)$$

with $R = \sqrt{2mE}$

7.8.10. Kinetic-Energy Density of States (Quantum Expression)

- quantum-mechanical density of states of the ideal gas
- units: $[\Omega] = \frac{1}{\text{energy}}$

$$\Omega(E) = \frac{V^N}{h^{3N}} \frac{R^{3N}}{2E} \cdot S_{3N-1}(1) \quad (445)$$

with $R = \sqrt{2mE}$

7.8.11. Relation between Classical Phase-Space and QM

- Planck's constant h provides a bridge between these two descriptions
 - units: $[dx^{2N}] = \text{action}^{3N}$

$$dx^{2N} \stackrel{+h^{3N}}{\Rightarrow} \{\Psi_m\}(\text{unitless}) \quad (446)$$

⇒ quantizing the phase space and allowing the classical phase space volume to be expressed in terms of discrete quantum states.

7.9. The Canonical Ensemble (NVT)

7.9.1. Constraints

$$\begin{cases} 1. \text{ Constant number of molecules } N \\ 2. \text{ Constant volume } V \\ 3. \text{ Constant average energy } \bar{E} \end{cases} \Rightarrow \text{system constraints} \quad (447)$$

- system constraints N, V define the accessible energy ~~levels~~ states $j \in \{0, \dots, J - 1\}$ of the system with their energies

$$E = E(N, V) = \left\{ \underbrace{E_0, \dots, E_{M-1}}_{=0} \right\} \quad (448)$$

- ensemble constraint must be considered when determining the most probable distribution

7.9.2. (Boltzmann) Distribution

- normalized probability ρ_m a quantum state m in the NVT ensemble

$$\rho_m = Z^{-1} e^{-\beta E_m}$$

with $Z = \sum_{m=0}^{M-1} e^{-\beta E_m}$

(449)

- “Zustandssumme”: quantum partition function of the NVT ensemble
 - unitless
 - $\beta = \frac{1}{k_B T}$

Derivation There are two ensemble constraints, for the total probability and for the average energy

$$\left. \begin{array}{l} \sum_{m=0}^{M-1} p_m = 1 \\ \sum_{m=0}^{M-1} p_m E_m = \bar{E} \end{array} \right\} \xrightarrow{-\partial / \partial p_m} -\sum_{m=0}^{M-1} p_m \ln p_m + \alpha \left(1 - \sum_{m=0}^{M-1} p_m \right) + \beta \left(\bar{E} - \sum_{m=0}^{M-1} p_m E_m \right) \xrightarrow{\text{choose } \alpha \text{ and } \beta \text{ to enforce the constraints}} \begin{array}{l} \text{must be maximal} \\ \alpha \text{ and } \beta \text{ are Lagrange multipliers} \end{array} e^{-(\alpha+1)} \sum_{m=0}^{M-1} e^{-\beta E_m} = 1$$

$$\xrightarrow{1 + \ln \rho_m + \alpha + \beta E_m = 0} e^{-(\alpha+1)} \sum_{m=0}^{M-1} E_m e^{-\beta E_m} = \bar{E}$$

Lemma. it also holds that

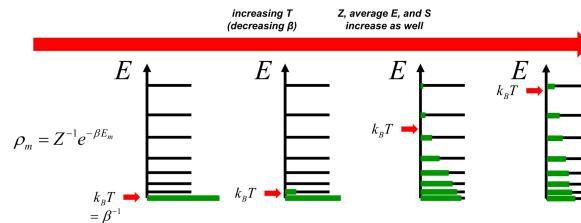
$$\sum_{m=0}^{M-1} \rho_m = 1$$

and $\bar{E} = \sum_{m=0}^{M-1} \rho_m E_m$

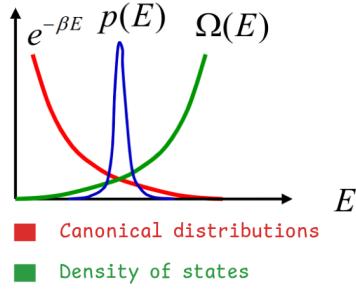
(450)

Feature

1. population decreases exponentially with increasing energy



2. The populated energies correspond to a peaky region, since density of states is a sharply increasing function of energy



7.9.3. Boltzmann Entropy

$$S = k_B \ln Z + k_B \beta \bar{E} \quad (451)$$

7.9.4. The Canonical Ensemble (Classical)

Distribution

- normalized probability of a classical phase-space point in the NVT ensemble
- units: $[\rho] = \frac{1}{\text{action}^{3N}}$

$$\begin{aligned} \rho(\mathbf{x}^{2N}) &= \xi Z^{-1} e^{-\beta \mathcal{H}(\mathbf{x}^{2N})} \\ \text{with } \int d\mathbf{x}^{2N} \rho(\mathbf{x}^{2N}) &= 1 \end{aligned} \quad (452)$$

Classical Partition Function

- unitless

$$Z = \xi \int d\mathbf{x}^{2N} e^{-\beta \mathcal{H}(\mathbf{x}^{2N})} \quad (453)$$

- the key quantity to connect statistical mechanics to thermodynamics
- knowing the **partition function** and its derivatives w.r.t. N, V, T , one can derive all **state functions** of the system

Gibbs Entropy

- classical Gibbs entropy for the NVT ensemble
- units: $[S] = \frac{\text{energy}}{\text{temperature}}$

$$S = -k_B \int d\mathbf{x}^{2N} \ln[\xi^{-1} \rho(\mathbf{x}^{2N})] \quad (454)$$

It also holds

$$\begin{aligned} S &= k_B \ln Z + k_B \beta \bar{E} \\ \text{with } \bar{E} &= \int d\mathbf{x}^{2N} \rho(\mathbf{x}^{2N}) \mathcal{H}(\mathbf{x}^{2N}) \end{aligned} \quad (455)$$

7.9.5. Connection to Thermodynamics

- the added QM zero-point energy U_o

$$U = - \left(\frac{\partial \ln Z}{\partial \beta} \right)_{N,V} + U_o \quad (456)$$

Average energy relative to ground state

$$\bar{E} = \sum_{m=0}^{M-1} \rho_m E_m \quad (457)$$

with

- $\rho_m = Z^{-1} e^{-\beta E_m}$
- $Z = \sum_{m=0}^{M-1} e^{-\beta E_m}$

Connection with the two laws of thermodynamics

- for a reversible process, the infinitesimal change in a closed system dU is reversible

$$dU = \begin{cases} dU_o + \sum_{m=0}^{M-1} \rho_m dE_m + \sum_{m=0}^{M-1} E_m d\rho_m \\ \delta W_{\text{rev}} + \delta Q_{\text{rev}} = -PdV + TdS \end{cases} \quad (458)$$

- from statistical mechanics it holds $U = \bar{E} + U_o$

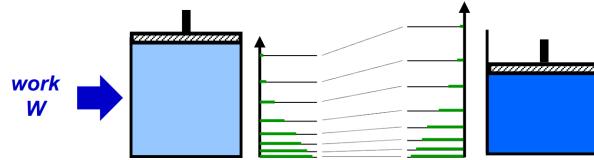
Interpretation Consider 1D particle in a box

$$E_n = \frac{\hbar^2 \pi^2}{2ma^2} n^2, n = 1, 2, \dots \quad (459)$$

Volume Work as Change of Levels

- volume work identified with a change of energy by changing the levels but not the populations

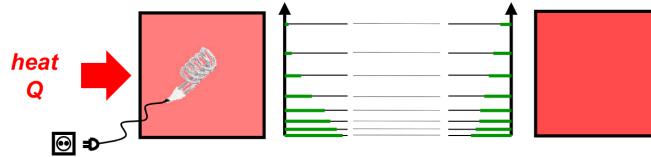
$$\delta W_{\text{rev}} = -PdV = dU_o + \sum_{m=0}^{M-1} \rho_m dE_m \quad (460)$$



Heat Work as Change of populations

- heat is identified with a change energy by changing the populations but not the levels

$$\delta Q_{\text{rev}} = TdS = \sum_{m=0}^{M-1} E_m d\rho_m \quad (461)$$



Parameter β

- Lagrange multiplier β

$$\beta = \frac{1}{k_B T} \quad (462)$$

Note: the following expressions all can be reformulated into expressions without explicit k_B usage

- The **thermodynamic variables** are directly connected to the **partition function** *and its derivatives*

→ **Internal energy**

$$U = - \left(\frac{\partial \ln Z}{\partial \beta} \right)_{N,V} + U_o$$

where

$$\beta = \frac{1}{k_B T}$$

and

→ **Entropy**

$$S = T^{-1} \left(\beta^{-1} \ln Z + U - U_o \right)$$

$$U_o$$

is the
quantum-mechanical
zero-point energy

→ **Helmholtz free energy**

$$F = -\beta^{-1} \ln Z + U_o$$

→ **Pressure**

$$P = \beta^{-1} \left(\frac{\partial \ln Z}{\partial V} \right)_{N,T} - \left(\frac{\partial U_o}{\partial V} \right)_N$$

Entropy (statistical-mechanical expression)

$$S = k_B \ln Z + \frac{U - U_o}{T} \quad (463)$$

from the established relation

$$S = k_B \ln Z + k_B \beta \bar{E} \quad (464)$$

Helmholtz Free Energy

$$F = -k_B T \ln Z + U_o \quad (465)$$

Derivation From the statistical-mechanical entropy expression

$$\begin{aligned} S &= k_B \ln Z + \frac{U - U_o}{T} \\ \Leftrightarrow TS &= Tk_B \ln Z + (U - U_o) \end{aligned} \quad (466)$$

One plug the above expression in

$$\begin{aligned} F &\stackrel{\Delta}{=} U - TS \\ \Leftrightarrow F &= U - (Tk_B \ln Z + (U - U_o)) \\ \Leftrightarrow F &= U - Tk_B \ln Z - (U - U_o) \\ \Leftrightarrow F &= U - Tk_B \ln Z - U + U_o \\ \Leftrightarrow F &= -k_B T \ln Z + U_o \end{aligned} \quad (467)$$

Pressure

$$P = k_B T \left(\frac{\partial \ln Z}{\partial V} \right)_{N,T} - \left(\frac{\partial U_o}{\partial V} \right)_N \quad (468)$$

Derivation

$$\begin{aligned} dF &= -PdV - SdT \\ \Rightarrow P &= - \left(\frac{\partial F}{\partial V} \right)_T \\ \Leftrightarrow P &= - \left(\frac{\partial (-k_B T \ln Z + U_o)}{\partial V} \right)_T \\ \Leftrightarrow P &= - \left(\frac{\partial (-k_B T \ln Z)}{\partial V} + \frac{\partial U_o}{\partial V} \right)_T \\ \Leftrightarrow P &= k_B T \left(\frac{\partial \ln Z}{\partial V} \right)_{N,T} - \left(\frac{\partial U_o}{\partial V} \right)_N \end{aligned} \quad (469)$$

7.9.6. Example: Calculation for Ideal Monoatomic Gas

Given the partition function for the ideal monoatomic gas

$$Z = \frac{V^N}{h^{3N} N!} \cdot \left(\frac{2\pi m}{\beta} \right)^{\frac{3N}{2}} \quad (470)$$

1. INTERNAL ENERGY
$U = -\frac{\partial \ln^{-\frac{3N}{2}}}{\partial \beta} = \frac{3N}{2} \beta^{-1} = \frac{3N}{2} k_B T$
2. Pressure
$P = \beta^{-1} \frac{\partial \ln V^N}{\partial V} = \beta^{-1} N V^{-1} = \frac{N k_B T}{V}$
3. Helmholtz Free Energy
$F = -\beta^{-1} \ln \left(\frac{V^N}{h^{3N} N!} \cdot \left(\frac{2\pi m}{\beta} \right)^{\frac{3N}{2}} \right)$ $\stackrel{\text{Stirling}}{=} -\beta^{-1} \ln \left(-N \ln N + N + N \ln V + N \ln \left(\frac{2\pi m}{\beta h^2} \right)^{\frac{3}{2}} \right)$ $= -N \beta^{-1} \left(1 + \ln \frac{V}{N} \left(\frac{2\pi m}{\beta h^2} \right)^{\frac{3}{2}} \right)$
4. Entropy (Sackur-Tetrode Equation)

$$S = k_B \left\{ \frac{3N}{2} + N \left(1 + \ln \frac{V}{N} \left(\frac{2\pi m}{\beta h^2} \right)^{\frac{3}{2}} \right) \right\} = Nk_B \left[\frac{5}{2} + \ln \frac{V}{N} \left(\frac{2\pi m}{\beta h^2} \right)^{\frac{3}{2}} \right] \quad (474)$$

Example derivation: for internal energy

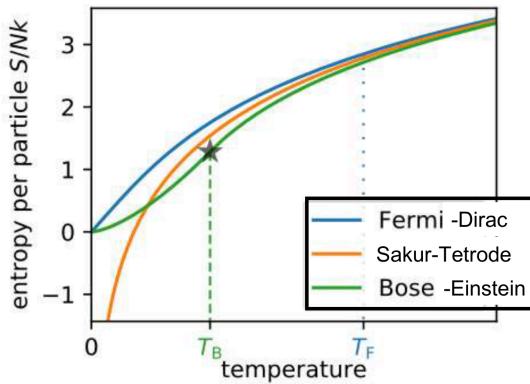
$$\begin{aligned} U &= - \left(\frac{\partial \ln Z}{\partial \beta} \right)_{N,V} \cancel{U_o} \\ &= \frac{3N}{2} \left(\frac{\partial \ln(\beta)}{\partial \beta} \right)_{N,V} \\ &= \frac{3N}{2} \beta^{-1} \end{aligned} \quad (475)$$

Sackur-Tetrode Equation

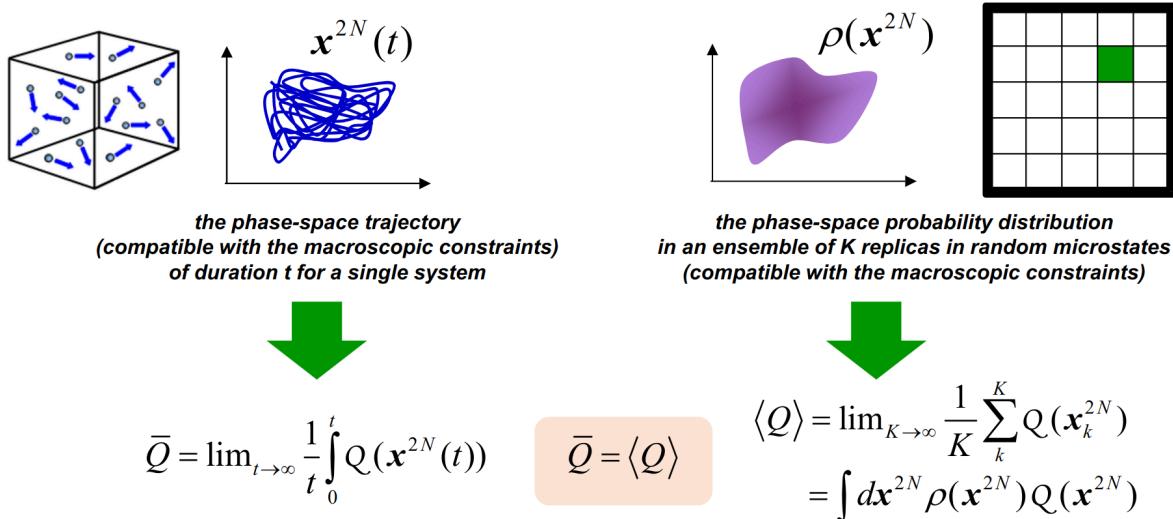
For the entropy at limit case, considering temperature at very low temperatures i.e. $T \rightarrow 0K$, with $\beta = \frac{1}{k_B T}$

$$\lim_{T \rightarrow 0} S = \lim_{T \rightarrow 0} \left\{ Nk_B \left[\frac{5}{2} + \ln \frac{V}{N} \left(\frac{2\pi m}{\beta h^2} \right)^{\frac{3}{2}} \right] \right\} \text{ diverges } \rightarrow -\infty \quad (476)$$

The assumption for very large density of states breaks down at very low temperatures!



7.9.7. The Ergodic Theorem



The equivalence between trajectory and ensemble averages

- valid for a dynamical system arising from **differential equations** on **smooth manifold**
- instead of averaging over **many system copies**, we can average over the **trajectory of a single system**
- limitations
 - holds for $K \rightarrow \infty$ and $t \rightarrow \infty$ (the latter is never true in MD simulations)
 - all thermodynamically accessible states must be dynamically accessible during observation time, each accessible state must be visited many times

7.9.8. The Ideal Gas Partition Function

The partition function of the system (gas) is a **product** of **single-molecule** partition functions, taking into account the indistinguishability of the molecules.

For pure gas consisting of only one type of molecules

$$Z := \frac{z^N}{N!} \quad (477)$$

Reasoning In an ideal gas there are no interactions between molecules or atoms, the energies are additive over the molecules

$$E = \sum_{i=1}^N E_i \quad (478)$$

Example: Factorizable single-molecule partition function

Given the energy partition additively

$$E = E^{\text{tra}} + E^{\text{rot}} + E^{\text{vib}} + E^{\text{ele}} + E^{\text{nuc}} \quad (479)$$

Then the single-molecule partition function can be factorized into a product of contributions from the various dof

$$Z = Z_{\text{tra}} \cdot Z_{\text{rot}} \cdot Z_{\text{vib}} \cdot Z_{\text{ele}} \cdot Z_{\text{nuc}} \quad (480)$$

Over states it holds

$$z_{\text{dof}} = \sum_{m=0}^{M_{\text{dof}}-1} e^{-\beta E_m^{\text{dof}}} \quad (481)$$

over levels it holds

$$z_{\text{dof}} = \sum_{j=0}^{J_{\text{dof}}-1} g_j^{\text{dof}} e^{-\beta E_j^{\text{dof}}} \quad (482)$$

8. Statistical Mechanics Part II

8.1. The Isothermal-isobaric (NPT) Ensemble

8.1.1. Constraints

1. Constant number of molecules $N \Rightarrow$ system constraint
 $\left\{ \begin{array}{l} 2. \text{ Constant average volume } \bar{V} \\ 3. \text{ Constant average energy } \bar{E} \Rightarrow \text{ensemble constraints} \end{array} \right.$ (483)

- these constraints amount to specifying N, P, T and result in a closed isothermal-isobaric system
 - the **most common** type of BC encountered for chemical systems in the **laboratory** and in **nature**

8.1.2. Probability Distribution

$$E_n = \frac{\hbar^2 \pi^2}{2ma^2} n^2, \text{ for } n = 1, 2, \dots \quad (484)$$

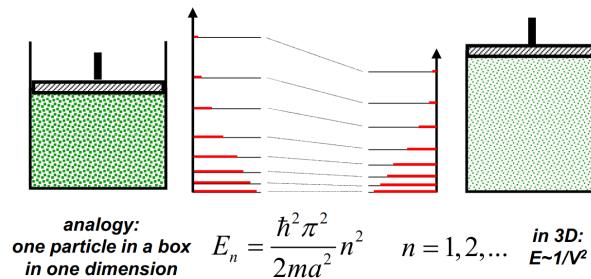
discrete volumes by summing over all possible volumes and associated energy states

$$\sum_{l,m} \dots = \sum_{l=0}^{L-1} \sum_{m=0}^{M-1} \dots \quad (485)$$

continuous volume by integrating over all possible volumes and sum over energy states at the given volume

$$\int d\mathcal{V} \sum_m \dots = \int_0^\infty d\mathcal{V} \sum_{m=0}^{M-1} \dots \quad (486)$$

Visualization



8.1.3. Quantum vs. Classical Expressions

QM-Expression using a continuous volume variable

- Given the no. molecules, pressure and absolute temperature N, P, T , the volume-dependent states with energies $E_m(\mathcal{V})$, one has

1. NPT PROBABILITY DISTRIBUTION
$\rho_m(\mathcal{V}) = Z_{NPT}^{-1} \cdot \varsigma \cdot e^{-\beta Y_m(\mathcal{V})}$
with normalization $\int d\mathcal{V} \sum_m \rho_m(\mathcal{V}) = 1$ (487)
and $\varsigma := \beta P$ with unit volume ⁻¹ for unit normalization
2. NPT Partition Function (unitless)
$Z_{NPT} = \varsigma \int d\mathcal{V} \sum_m e^{-\beta Y_m(\mathcal{V})}$ (488)
3. Enthalpy
$Y_m(\mathcal{V}) = E_m(\mathcal{V}) + PV$ (489)
4. NPT Ensemble Average
$A = \langle \mathcal{A} \rangle = \int d\mathcal{V} \sum_m \mathcal{A}_m(\mathcal{V}) \cdot \rho_m(\mathcal{V})$ (490)
• with the microscopic instantaneous observable $\mathcal{A}_m(\mathcal{V})$

Classical-Expression

- Given the no. molecules, pressure and absolute temperature N, P, T

1. NPT PROBABILITY DISTRIBUTION OVER PHASE-SPACE POINTS
$\rho(\mathbf{x}^{2N}, \mathcal{V}) = Z_{NPT}^{-1} \cdot \varsigma \cdot \xi \cdot e^{-\beta Y_m(\underline{\mathbf{x}}^{2N}, \mathcal{V})}$
with normalization $\int d\mathcal{V} \int d\mathbf{x}^{2N} \rho_m(\mathbf{x}^{2N}, \mathcal{V}) = 1$ (491)
and $\varsigma := \beta P$ with unit volume ⁻¹ for unit normalization
2. NPT Partition Function (unitless)
$Z_{NPT} = \varsigma \cdot \xi \int d\mathcal{V} \int d\mathbf{x}^{2N} \cdot e^{-\beta Y(\underline{\mathbf{x}}^{2N}, \mathcal{V})}$ (492)
3. Enthalpy
$Y(\mathbf{x}^{2N}, \mathcal{V}) = \mathcal{H}(\mathbf{x}^{2N}) + PV$ (493)
4. NPT Ensemble Average
$A = \langle \mathcal{A} \rangle = \int d\mathcal{V} \int d\mathbf{x}^{2N} \mathcal{A}(\mathbf{x}^{2N}, \mathcal{V}) \cdot \rho(\mathbf{x}^{2N}, \mathcal{V})$ (494)
• with the microscopic instantaneous observable $\mathcal{A}(\mathbf{x}^{2N}, \mathcal{V})$

8.1.4. Relating Partition Function Z_{NPT} to Z_{NVT}

The NPT partition function is a central quantity to connect to thermodynamics

QM

$$Z_{NPT} = \varsigma \int d\mathcal{V} \sum_m e^{-\beta Y_m(\mathcal{V})} \quad (495)$$

Classical

Consider the classical NPT partition function, we can replace some terms with the NVT partition function

$$\begin{aligned}
Z_{NPT} &= \varsigma \cdot \xi \int d\mathcal{V} \int dx^{2N} \cdot e^{-\beta Y(x^{2N}, \mathcal{V})} \\
&= \varsigma \cdot \int d\mathcal{V} \cdot \left(\xi \cdot \int dx^{2N} \cdot e^{-\beta(\mathcal{H}(x^{2N}) + P\mathcal{V})} \right) \\
&= \varsigma \cdot \int d\mathcal{V} \cdot e^{-\beta P\mathcal{V}} \left(\xi \cdot \int dx^{2N} \cdot e^{-\beta \mathcal{H}(x^{2N}, \mathcal{V})} \right) \\
&= \varsigma \cdot \int d\mathcal{V} \cdot e^{-\beta P\mathcal{V}} \cdot Z_{NVT}
\end{aligned} \tag{496}$$

Recall: NVT Partition Function

- QM

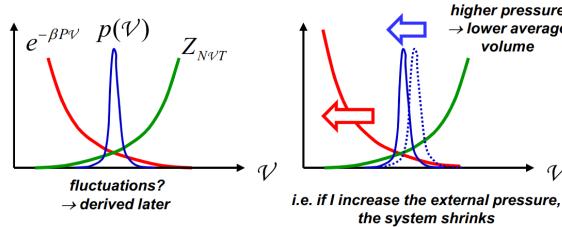
$$Z_{NVT} = \sum_{m=0} e^{-\beta E_m} \tag{497}$$

- Classical

$$Z_{NVT} = \xi \int dx^{2N} e^{-\beta \mathcal{H}(x^{2N})} \tag{498}$$

Interpretation

- we note that Z_{NVT} increases very sharply with the **volume**



- $e^{-\beta \mu P V}$ with $P > 0$ decreases very sharply with the **volume**

Example: compressibility

$$\left(\frac{\partial V}{\partial P} \right)_{N,T} = -V \kappa_T < 0 \tag{499}$$

8.2. The Grand-Canonical (μVT) Ensemble

8.2.1. Constraints

1. Constant volume $V \Rightarrow$ system constraint

$$\begin{cases}
2. \text{ Constant average no. particles } \bar{N} \\
3. \text{ Constant average energy } \bar{E}
\end{cases} \Rightarrow \text{ensemble constraints} \tag{500}$$

- these constraints amount to specifying μ, V, T and result in an open isothermal-isochoric system
 - the **very common** type of BC encountered for chemical systems
 - e.g. pH or humidity correspond to a given chemical potential of H^+ of $H_2O_{(g)}$

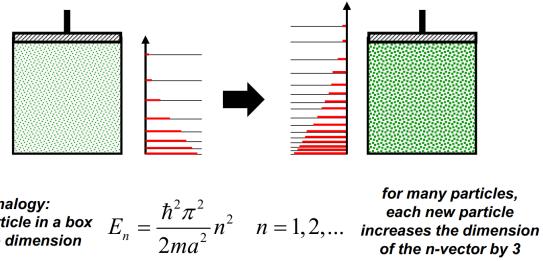
8.2.2. Probability Distribution

$$E_n = \frac{\hbar^2 \pi^2}{2ma^2} n^2, \text{ for } n = 1, 2, \dots \tag{501}$$

discrete **volumes** by summing over all possible **molecule numbers** and associated energy states

$$\begin{aligned}
\mathcal{N} &\Rightarrow E_{\mathcal{N}m} \\
\sum_{\mathcal{N}, m} \dots &= \sum_{\mathcal{N}=0}^{\infty} \sum_{m=0}^{M(\mathcal{N})-1} \dots
\end{aligned} \tag{502}$$

Visualization



8.2.3. Quantum vs. Classical Expressions

QM-Expression using a continuous volume variable

- Given the chemical potential, volume and the absolute temperature μ, V, T , the number-dependent states with energies $E_{\mathcal{N}m}$, one has

1. μVT PROBABILITY DISTRIBUTION

$$\rho_{\mathcal{N}m} = Z_{\mu VT}^{-1} \cdot e^{-\beta X_{\mathcal{N}m}}$$

$$\text{with normalization } \sum_{\mathcal{N},m} \rho_{\mathcal{N}m} = 1 \quad (503)$$

2. μVT Partition Function (unitless)

$$Z_{\mu VT} = \sum_{\mathcal{N},m} e^{-\beta X_{\mathcal{N}m}} \quad (504)$$

3. Enthalpy

$$X_{\mathcal{N}m} = E_{\mathcal{N}m} + \mu \mathcal{N} \quad (505)$$

4. μVT Ensemble Average

$$A = \langle \mathcal{A} \rangle = \sum_{\mathcal{N},m} \mathcal{A}_{\mathcal{N}m} \cdot \rho_{\mathcal{N}m} \quad (506)$$

- with the microscopic instantaneous observable $\mathcal{A}_{\mathcal{N}m}$

Classical-Expression

- Given the no. molecules, pressure and absolute temperature N, P, T

1. μVT PROBABILITY DISTRIBUTION OVER PHASE-SPACE POINTS

$$\rho(\mathbf{x}^{2N}, \mathcal{N}) = Z_{\mu VT}^{-1} \cdot \xi \cdot e^{-\beta X(\mathbf{x}^{2N}, \mathcal{N})}$$

$$\text{with normalization } \int d\mathcal{V} \int d\mathbf{x}^{2N} \rho_m(\mathbf{x}^{2N}, \mathcal{V}) = 1 \quad (507)$$

and $\xi := \beta P$ with unit volume^{-1} for unit normalization

2. μVT Partition Function (unitless)

$$Z_{\mu VT} = \xi \sum_{\mathcal{N}} \int d\mathbf{x}^{2N} \cdot e^{-\beta X(\mathbf{x}^{2N}, \mathcal{N})} \quad (508)$$

3. Enthalpy

$$X(\mathbf{x}^{2N}, \mathcal{N}) = \mathcal{H}(\mathbf{x}^{2N}, \mathcal{N}) - \mu \mathcal{N} \quad (509)$$

4. μVT Ensemble Average

$$A = \langle \mathcal{A} \rangle = \sum_{\mathcal{N}} \int d\mathbf{x}^{2N} \mathcal{A}(\mathbf{x}^{2N}, \mathcal{N}) \cdot \rho(\mathbf{x}^{2N}, \mathcal{N}) \quad (510)$$

- with the microscopic instantaneous observable $\mathcal{A}(\mathbf{x}^{2N}, \mathcal{N})$

8.2.4. Relating Partition Function $Z_{\mu VT}$ to Z_{NVT}

The NPT partition function is a central quantity to connect to thermodynamics

QM

$$Z_{\mu VT} = \sum_{\mathcal{N},m} e^{-\beta X_{\mathcal{N}m}} \quad (511)$$

Classical

Consider the classical NPT partition function, we can replace some terms with the NVT partition function

$$\begin{aligned}
Z_{\mu VT} &= \xi \sum_{\mathcal{N}} \int d\mathbf{x}^{2N} \cdot e^{-\beta X(\mathbf{x}^{2N}, \mathcal{N})} \\
&= \xi \sum_{\mathcal{N}} \int d\mathbf{x}^{2N} \cdot e^{-\beta(\mathcal{H}(\mathbf{x}^{2N}, \mathcal{N}) - \mu \mathcal{N})} \\
&= \sum_{\mathcal{N}} \left(\xi \cdot \int d\mathbf{x}^{2N} \cdot e^{-\beta \mathcal{H}(\mathbf{x}^{2N}, \mathcal{N})} \right) \cdot e^{+\beta \mu \mathcal{N}} \\
&= \sum_{\mathcal{N}} e^{\beta \mu \mathcal{N}} \cdot Z_{NVT}
\end{aligned} \tag{512}$$

Recall: NVT Partition Function using \mathcal{N} or N interchangeably

- QM

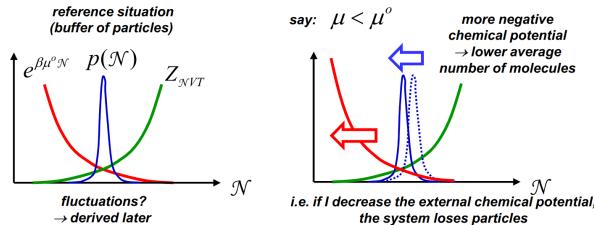
$$Z_{NVT} = \sum_{m=0} e^{-\beta E_m} \tag{513}$$

- Classical

$$Z_{NVT} = \xi \int d\mathbf{x}^{2N} e^{-\beta \mathcal{H}(\mathbf{x}^{2N})} \tag{514}$$

Interpretation

- we note that Z_{NVT} increases very sharply with the **no. molecules**
- $e^{\beta \mu \mathcal{N}}$ decreases very sharply with the **no. molecules**



Example: molar volume

$$\left(\frac{\partial N}{\partial \mu} \right)_{V,T} = \frac{N \kappa_T}{\nu} > 0 \tag{515}$$

9. Statistical Mechanics Part III

9.1. Gaussian Integrals

Integrals of monomials over a Gaussian distribution

General result for Gaussian Integral Given an integer $n \geq 0$ and a real $a > 0$, the integration over the positive x -axis reads

$$\begin{aligned} I_n(a) &= \int_0^\infty x^n e^{-ax^2} dx \\ &= \sqrt{c_n} \cdot (n-1)!! (2a)^{-\frac{n+1}{2}} \\ \text{with } c_n &:= \begin{cases} \frac{\pi}{2} & \text{if } n \text{ even} \\ 1 & \text{if } n \text{ odd} \end{cases} \end{aligned} \quad (516)$$

Special Cases

$n = 0$	(517)	$n = 2$	(518)	$n = 4$	(519)
$\frac{1}{2} \left(\frac{\pi}{a} \right)^{\frac{1}{2}}$	(520)	$\frac{1}{4} \left(\frac{\pi}{a^3} \right)^{\frac{1}{2}}$	(521)	$\frac{3}{8} \left(\frac{\pi}{a^5} \right)^{\frac{1}{2}}$	(522)
$n = 1$	(523)	$n = 3$	(524)	$n = 5$	(525)
$\frac{1}{2a}$	(526)	$\frac{1}{2a^2}$	(527)	$\frac{1}{a^3}$	(528)

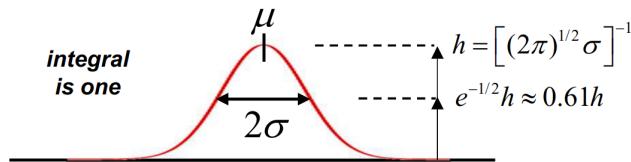
The integration over the whole real axis reads

- if n is even, the whole integrand is an even function

$$\begin{aligned} I_n(a) &= \int_{-\infty}^{\infty} x^n e^{-ax^2} dx \\ &= \begin{cases} 2I_n(a) & \text{if } n \text{ even} \\ 0 & \text{if } n \text{ odd} \end{cases} \end{aligned} \quad (529)$$

Normalized Gaussian

$$2I_{n=0}(a) = \frac{1}{\sqrt{2\pi}\sigma} e^{-\frac{(x-\mu)^2}{(2\sigma^2)}} \quad (530)$$



9.2. Statistical Mechanics of Many-Particle Systems

Ideal gas assumption (particles DO NOT interact)

1. Distinguishable Particles

- e.g. atoms in a macromolecule or in a solid

$$Z = \prod_n^N Z_n \quad (531)$$

2. Indistinguishable Particles

- e.g. identical particles in a liquid or gas
- neglecting QM symmetry issues (to account, Fermi-Dirac/Bose-Einstein statistics, at limit converge to Boltzmann)
 - Maxwell-Boltzmann statistics

$$Z = \frac{1}{N!} \prod_n^N z_n \quad (532)$$

- without ideal gas assumptions one needs to account for particle interactions via

1. Approximate analytical theories
 - e.g. perturbation, start from non-interacting, expand in successive powers of the interaction terms
2. Molecular Simulation
 - sample a finite Boltzmann-weighted ensemble numerically

9.3. The Ideal Monoatomic Gas

The gas is ideal if the interactions between the atoms are negligible

- only elastic collisions (with negligible self-volume) at contact that randomize velocities
- ideal-gas equation of state

$$PV = nRT \quad (533)$$

Note: this is different from the real gas (van der Waals) that accounts for corrections for interactions (a) and self-volume (b)

$$\left(P + a \left(\frac{n}{V} \right)^2 \right) (V - nb) - nRT \quad (534)$$

Ideal Monoatomic Gas

$$E_{\text{tot}} = E_{\text{kin}} + \cancel{E_{\text{pot}}} \quad (535)$$

- no potential energy, only kinetic

Statistical-mechanical description

- analytical derivation
- valid for ideal molecular gases to account for the contribution of **translation**
- thermodynamic properties U, P, F, S can be obtained by deriving the partition function Z accordingly (see canonical section)

9.3.1. Example: Partition Function Z of the Ideal Monoatomic Gas

1. Calculate the **canonical partition function**

- the exact QM-mechanical expression for a single atom in a monoatomic ideal gas

$$Z = \sum_{n_x=1}^{\infty} \sum_{n_y=1}^{\infty} \sum_{n_z=1}^{\infty} e^{-\beta E_n} \quad (536)$$

with $n^2 = n_x^2 + n_y^2 + n_z^2$ and the energy relative to ground state $E_n = \frac{\pi^2 \hbar^2}{2ma^2} (n^2 - 1)$

2. Use Gaussian integral for approximation at large density

- Note that the large density assumption is not valid at extremely low temperature!

$$\begin{aligned}
Z &= \int_0^\infty e^{-\beta E_n} dx \\
&= \left(\int_0^\infty e^{-\beta \frac{\pi^2 h^2}{2ma^2} x^2} dx \right)^3 \\
&= \left(\frac{1}{2} \left(\frac{\pi}{(\beta \frac{\pi^2 h^2}{2ma^2})} \right)^{\frac{1}{2}} \right)^3 \\
&= \left(\frac{1}{2} \left(\frac{2\pi ma^2}{\beta \pi^2 (\frac{h}{2\pi})^2} \right)^{\frac{1}{2}} \right)^3 \\
&= \left(a \frac{2\pi m}{\beta h^2} \right)^{\frac{3}{2}}
\end{aligned} \tag{537}$$

where we computed using

- $h = 2\pi\hbar \Leftrightarrow \hbar = \frac{h}{2\pi}$

$$I_0(a) = \int_0^\infty x^n e^{-ax^2} dx \stackrel{n=0}{=} \frac{1}{2} \left(\frac{\pi}{a} \right)^{\frac{1}{2}} \tag{538}$$

Thus the approximated result assuming a very large density of states is.

$$Z = V \cdot \left(\frac{2\pi m}{\beta h^2} \right)^{\frac{3}{2}} \tag{539}$$

3. Ideal Gas Assumption for **Indistinguishable Particles**

$$\begin{aligned}
Z &= \frac{V^N}{N!} \cdot \left(\frac{2\pi m}{\beta h^2} \right)^{\frac{3N}{2}} \\
&= \frac{V^N}{h^{3N} N!} \cdot \left(\frac{2\pi m}{\beta} \right)^{\frac{3N}{2}}
\end{aligned} \tag{540}$$

9.4. Factorization of the Partition Function

The momentum integral depends solely on the number of particles, their masses and the temperature, but not on the interactions within the system.

9.4.1. Classical Partition of the Canonical Ensemble

Classical partition function of the canonical ensemble

$$\begin{aligned}
Z = Z_{\text{NVT}} &= \xi \int d\mathbf{x}^{2N} e^{-\beta \mathcal{H}(\mathbf{x}^{2N})} \\
&= \xi \int d\mathbf{x}^{2N} e^{-\beta(\mathcal{K}(\mathbf{p}^N) + \mathcal{V}(\mathbf{r}^N))} \\
&= \xi \int d\mathbf{x}^{2N} e^{-\beta \mathcal{K}(\mathbf{p}^N)} \cdot e^{-\beta \mathcal{V}(\mathbf{r}^N)} \\
&= \dots \\
&= \underbrace{\left(\xi \int d\mathbf{p}^N e^{-\beta \mathcal{K}(\mathbf{p}^N)} \right)}_{Z_K} \underbrace{\left(\int d\mathbf{r}^N e^{-\beta \mathcal{V}(\mathbf{r}^N)} \right)}_{Z_V}
\end{aligned} \tag{541}$$

We factorize the partition function into a **momentum integral** for the kinetic energy component and a **configurational integral** for the potential-energy component using $\mathcal{H}(\mathbf{x}^{2N}) = \mathcal{K}(\mathbf{p}^N) + \mathcal{V}(\mathbf{r}^N)$

9.4.2. Momentum Integral

The **momentum integral** of the canonical ensemble is

$$Z_{\mathcal{K}} = \frac{1}{N!} \left(\frac{2\pi m}{\beta h^2} \right)^{\frac{3N}{2}} \quad (542)$$

Comparing to the partition function for ideal monoatomic gas

$$Z = \frac{V^N}{N!} \cdot \left(\frac{2\pi m}{\beta h^2} \right)^{\frac{3N}{2}} \quad (543)$$

It holds for the ideal gas that $Z_V = V^N$ and consequently $Z = Z_{\mathcal{K}} \cdot Z_V$ holds

Derivation From the momentum integral

- units: $[Z] = \text{length}^{-3N}$

$$\begin{aligned} Z_{\mathcal{K}} &= \left(\xi \int d\mathbf{p}^N e^{-\beta \mathcal{K}(\mathbf{p}^N)} \right) \\ &= \xi \left(\int_{-\infty}^{\infty} dp \cdot e^{-\beta \frac{p^2}{2m}} \right)^{3N} \\ &= \xi \left(2 \sqrt{\frac{\lambda}{2}} \left(\frac{\pi}{\frac{\beta}{2m}} \right)^{\frac{1}{2}} \right)^{3N} \\ &= \xi \left(\frac{2\pi m}{\beta} \right)^{\frac{3N}{2}} \\ &= \frac{1}{h^{3N} N!} \left(\frac{2\pi m}{\beta} \right)^{\frac{3N}{2}} \\ &= \frac{1}{N!} \left(\frac{2\pi m}{\beta h^2} \right)^{\frac{3N}{2}} \end{aligned} \quad (544)$$

with Gaussian integral for the even case $n = 0$

$$I_n(a) = \begin{cases} 2I_n(a) & \text{if } n \text{ even} \\ 0 & \text{if } n \text{ odd} \end{cases} \quad (545)$$

and we used

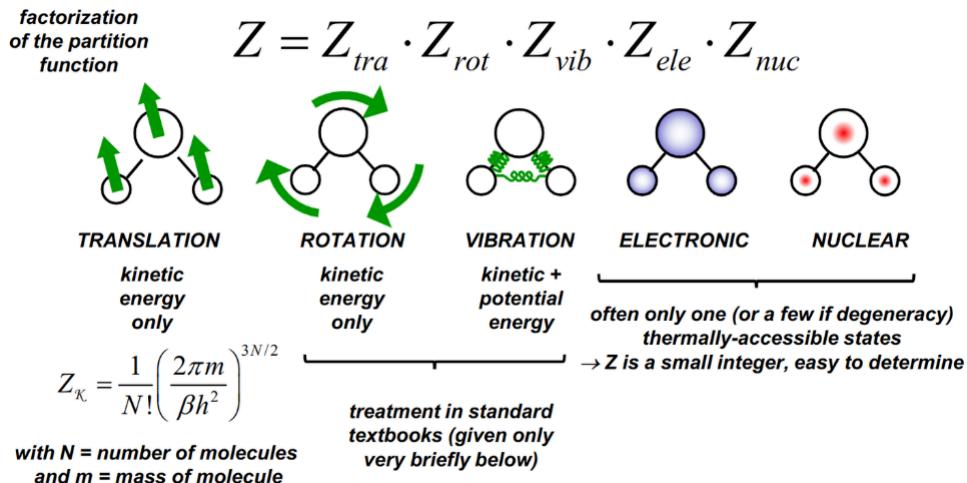
$$\xi = \frac{1}{h^{3N} N!} \quad (546)$$

9.4.3. Configuration Integral

The **configuration integral** of the canonical ensemble is

$$Z_V = \int d\mathbf{r}^N e^{-\beta V(\mathbf{r}^N)} \quad (547)$$

For gas molecules in an ideal gas, it can be further factored into contributions from **different motional modes**.



For liquids and solids, these modes cannot be decoupled from the intermolecular interactions and the partitioning is no longer strictly possible.

- MD simulations necessary!

1. Rotational Partition Function

QM partition function of the rigid linear rotor (exact)

$$Z_{RLR}^{\text{exact}} = \sum_{l=0}^{\infty} (2l+1) e^{-\frac{\beta\hbar^2}{2I} l(l+1)} \quad (548)$$

where $E_n = E_l$ arises as the solution of the TISE, considering energy levels and degeneracies

$$E_l = \frac{\hbar^2}{2I} l(l+1) = \begin{cases} I & \text{moment of inertia} \\ l = \{0, 1, \dots\} & \text{rotational quantum number } J \\ 2l+1 & \text{degeneracy} \\ \text{no zero-point energy} & \end{cases} \quad (549)$$

QM partition function (approximate)

- valid at sufficiently high temperatures (many levels populated)
 - e.g. generally no problem at room temperature
- if too low temperature, the explicit formula needs to be used

$$Z_{RLR} = \frac{2I}{\beta\hbar^2} \quad (550)$$

Derivation for the approximation

$$\begin{aligned} Z_{RLR}^{\text{exact}} &= \sum_{l=0}^{\infty} (2l+1) e^{-\frac{\beta\hbar^2}{2I} l(l+1)} \\ &\approx \int_{l=0}^{\infty} (2l+1) e^{-\frac{\beta\hbar^2}{2I} l(l+1)} dl \\ &= \int_{x=0}^{\infty} e^{-\frac{\beta\hbar^2}{2I} x} dx \\ &= \frac{I}{\beta\hbar^2} \end{aligned} \quad (551)$$

where we used a change of variable defining

$$x := l(l+1) \Rightarrow dx = (2l+1)dl \quad (552)$$

and use result for Gaussian integral for $n = 1$

$$I_1(a) = \int_0^{\infty} x^n e^{-ax^n} dx \stackrel{n=1}{=} \frac{1}{2a} \quad (553)$$

2. Vibrational Partition Function

QM partition function of the 1D harmonic oscillator (exact)

$$Z_{OHO} = \frac{1}{1 - e^{-\beta\hbar\omega n}} \quad (554)$$

- classical approximation is not necessarily valid at room temperature

where E_n as the solution of the TISE, also considering energy levels and degeneracies

$$\begin{aligned} E_l &= \hbar\omega \left(n + \frac{1}{2} \right) \\ &= \begin{cases} \omega & \text{angular frequency} \\ n = \{0, 1, \dots\} & \text{vibrational quantum number} \\ \text{no degeneracy} \rightarrow \text{one state per level} & \\ E_0 = \frac{1}{2}\hbar\omega & \text{zero-point energy} \end{cases} \end{aligned} \quad (555)$$

Derivation

$$Z_{OHO} = \sum_{n=0}^{\infty} e^{-\beta\hbar\omega n} \stackrel{*}{=} \frac{1}{1 - e^{-\beta\hbar\omega n}} \quad (556)$$

where in step (*) we used the infinite geometric series

$$\sum_{n=0}^{\infty} x^n = \frac{1}{1-x}, \text{ if } |x| < 1 \quad (557)$$

9.5. Momentum Distribution

9.5.1. Maxwell-Boltzmann Velocity Distribution

To investigate the **distribution of velocities** (momenta) in a molecular system, we followingly assume

- NVT expressions at the classical level
- Cartesian coordinate system

9.5.1.1. Single-Component Distribution

For one velocity component $\alpha = x, y, z$

$$\rho(\nu_\alpha) = \left(\frac{\beta m}{2\pi} \right)^{\frac{1}{2}} \cdot e^{-\frac{\beta m \nu_\alpha^2}{2}} \quad (558)$$

the **mean-square velocity component**

$$\langle \nu_\alpha^2 \rangle = \frac{1}{\beta m} \quad (559)$$

Derivation for $\rho(\nu_\alpha)$

Under the assumption that the mechanical system is unconstrained, the Hamiltonian $\mathcal{H}(\mathbf{x}^{2N}) = \mathcal{K}(\mathbf{p}^N) + \mathcal{V}(\mathbf{r}^N)$ implies that

Of the constrained case, one needs to work with generalized coordinates and take into account of metric-tensor effects

$$\begin{aligned} \rho(\mathbf{x}^{2N}) &= \rho_{\mathcal{K}}(\mathbf{p}^N) \cdot \rho_{\mathcal{V}}(\mathbf{r}^N) \\ &\stackrel{*}{=} \left(\prod_k^N \rho_k(p_k) \right) \cdot \rho_{\mathcal{V}}(\mathbf{r}^N) \end{aligned} \quad (560)$$

The step (\star) is valid because the probability distributions of **distinct momentum components** are **uncorrelated**

$$\begin{aligned} \mathcal{K}(\mathbf{p}^N) &= \sum_{i=1}^N \frac{p_i^2}{2m_i} \\ &= \sum_{k=1}^{3N} \frac{p_k^2}{2m_k} \end{aligned} \quad (561)$$

now we consider one velocity component $\rho_k(p_k)$

$$\begin{aligned} \rho_k(p_k) &\sim e^{-\frac{\beta p_k^2}{2m_k}} \\ \Leftrightarrow \rho_k(p_k) &\sim e^{-\frac{\beta m_k \nu_k^2}{2}} \end{aligned} \quad (562)$$

we normalize with the help of $\int_{-\infty}^{\infty} dx e^{-ax^2} = (\frac{\pi}{a})^{\frac{1}{2}}$ and obtain

$$\rho(\nu_\alpha) = \left(\frac{\beta m}{2\pi} \right)^{\frac{1}{2}} \cdot e^{-\frac{\beta m \nu_\alpha^2}{2}} \quad (563)$$

Derivation for mean-square velocity

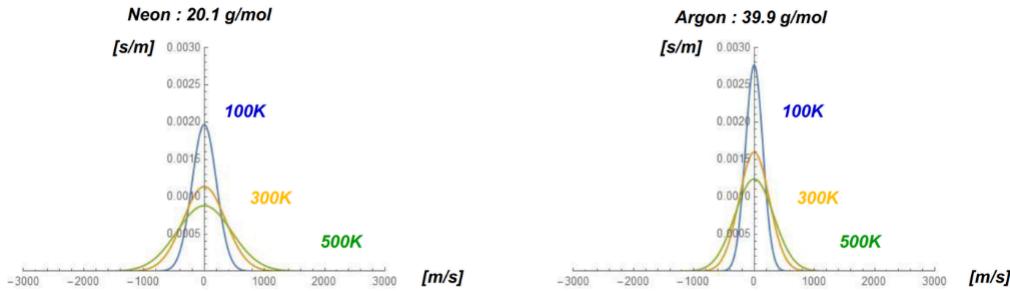
$$\begin{aligned}
\langle \nu_\alpha \rangle &= \int_{-\infty}^{\infty} \nu_\alpha \cdot \rho(\nu_\alpha) d\nu_\alpha \stackrel{\text{symmetric}}{=} 0 \\
\langle \nu_\alpha^2 \rangle &= \int_{-\infty}^{\infty} \nu_\alpha^2 \cdot \rho(\nu_\alpha) d\nu_\alpha \\
&= \int_{-\infty}^{\infty} \nu_\alpha^2 \cdot \left(\left(\frac{\beta m}{2\pi} \right)^{\frac{1}{2}} \cdot e^{-\frac{\beta m \nu_\alpha^2}{2}} \right) d\nu_\alpha \\
&= \left(\frac{\beta m}{2\pi} \right)^{\frac{1}{2}} \int_{-\infty}^{\infty} \nu_\alpha^2 \cdot \left(e^{-\frac{\beta m \nu_\alpha^2}{2}} \right) d\nu_\alpha \\
&= \frac{1}{\beta m}
\end{aligned} \tag{564}$$

where we used Gaussian integral $2I_2(a) = \frac{1}{2} \left(\frac{\pi}{a^3} \right)^{\frac{1}{2}}$

9.5.1.2. Vector Distribution

in terms of the 3D velocity vector

$$\rho(\nu) = \left(\frac{\beta m}{2\pi} \right)^{\frac{3}{2}} \cdot e^{-\frac{\beta m \nu^2}{2}} \tag{565}$$

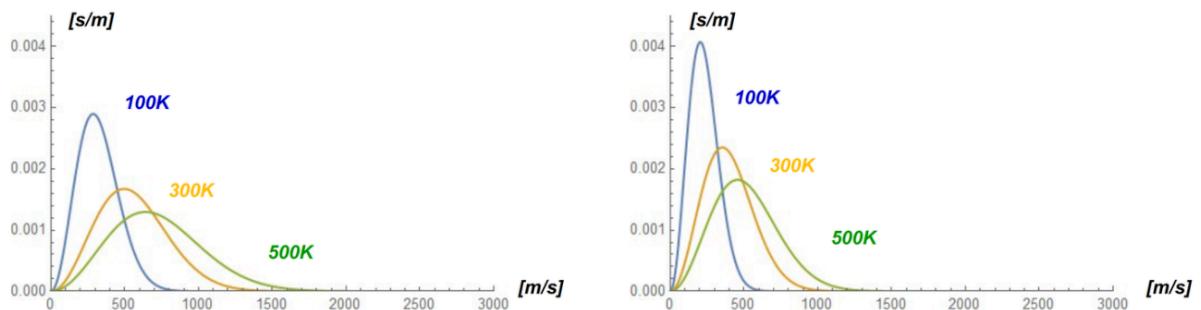


9.5.1.3. Norm Distribution

Distribution of the scalar velocity, i.e. the norm of the 3D velocity vector

$$\rho(\nu) = 4\pi \left(\frac{\beta m}{2\pi} \right)^{\frac{3}{2}} \cdot \nu^2 \cdot e^{-\frac{\beta m \nu^2}{2}} \tag{566}$$

with this normalization it holds that $\int_0^\infty d\nu \rho(\nu) = 1$



The **average atomic velocity**

$$\langle \nu \rangle = \left(\frac{8}{\pi \beta m} \right)^{\frac{1}{2}} \tag{567}$$

Derivation

$$\begin{aligned}
\langle \nu \rangle &= \int_{-\infty}^{\infty} \nu \cdot \rho(\nu) d\nu \\
&= \int_{-\infty}^{\infty} \nu \cdot \left(4\pi \left(\frac{\beta m}{2\pi} \right)^{\frac{3}{2}} \cdot \nu^2 \cdot e^{-\frac{\beta m \nu^2}{2}} \right) d\nu \\
&= 4\pi \left(\frac{\beta m}{2\pi} \right)^{\frac{3}{2}} \int_{-\infty}^{\infty} \nu^3 \cdot e^{-\frac{\beta m \nu^2}{2}} d\nu \\
&= \dots \\
&= \left(\frac{8}{\pi \beta m} \right)^{\frac{1}{2}}
\end{aligned} \tag{568}$$

where we used $I_3(a) = \frac{1}{2a^2}$

Root-mean-square atomic velocity

$$\langle \nu^2 \rangle^{\frac{1}{2}} = \left(\frac{3}{\beta m} \right)^{\frac{1}{2}} \tag{569}$$

Most probable atomic velocity

$$\nu^* = \left(\frac{2}{\beta m} \right)^{\frac{1}{2}} \tag{570}$$

Important Numbers

- $\left(\frac{8}{\pi} \right)^{\frac{1}{2}} \approx 1.60$
- $\sqrt{3} \approx 1.73$
- $\sqrt{2} \approx 1.41$

Relevant Phenomena Maxwell-Boltzmann distribution often used for monoatomic gases, but generally applicable for molecular systems and in all phases of matter in the classical limit (i.e. at sufficiently high temperature)

- speed of sound
- helium voice

9.5.2. Kinetic Theory of Gases

9.5.3. Equipartition Principle

In a molecular system at equilibrium and in the classical limit, the average kinetic energy stored in each degree of freedom amounts to $\frac{1}{2}k_B T$

Average Kinetic Energy

$$\langle \mathcal{K} \rangle = \frac{1}{2} \cdot N_{\text{dof}} k_B T \tag{571}$$

Generalized Equipartition Theorem

$$\langle x_m \frac{\partial \mathcal{H}}{\partial x_n} \rangle = \delta_{m,n} k_B T \tag{572}$$

Implications

- low temperatures \Rightarrow quantum effects
- constraints \Rightarrow metric-tensor effects

Examples:

For one degree of freedom of one atom it holds

$$\langle v_{\alpha}^2 \rangle = \frac{1}{\beta m} \tag{573}$$

thus the mean-square in this degree of freedom for one atom is

$$\langle \mathcal{K}_{i,\alpha} \rangle = \langle \frac{1}{2} m v_{i,\alpha}^2 \rangle = \frac{1}{2} m \langle v_{i,\alpha}^2 \rangle = \frac{1}{2\beta} \stackrel{\beta = \frac{1}{k_B T}}{=} \frac{1}{2} k_B T \tag{574}$$

Then in a 3D setup for one single atom, where $N_{\text{dof}} = 3$

$$\langle \mathcal{K}_i \rangle = 3 \cdot \langle \mathcal{K}_{i,\alpha} \rangle = \frac{3}{2} k_B T \quad (575)$$

9.6. Fluctuations

Discrete Fluctuations of a quantity Q

$$\langle Q \rangle = \sum_i P_i Q_i \quad (576)$$

Continuous Fluctuations of a quantity Q

$$\langle Q \rangle = \int dQ \cdot P(Q) Q \stackrel{\text{ergodic principle}}{\Leftrightarrow} \langle Q \rangle = \bar{Q} = \frac{1}{t} \int_0^t dt Q(t) \quad (577)$$

Standard Deviation Over Ensemble

$$\begin{aligned} \sigma_Q &= \left(\int dQ \cdot P(Q) (Q - \langle Q \rangle)^2 \right)^{\frac{1}{2}} \\ \stackrel{\text{ergodic principle}}{\Leftrightarrow} \sigma_Q &= \left(\frac{1}{t} \cdot \int_0^t dt \cdot (Q(t) - \bar{Q})^2 \right)^{\frac{1}{2}} \text{ if } t \rightarrow \infty \end{aligned} \quad (578)$$

By ergodic principle at $t \rightarrow \infty$, the standard deviation over ensemble is equivalent to root-mean-square fluctuation in time.

Equivalent Single-Sweep Equation

$$\begin{aligned} \sigma_Q^2 &= \langle (Q - \langle Q \rangle)^2 \rangle \\ &= \langle Q^2 - 2Q\langle Q \rangle + \langle Q \rangle^2 \rangle \\ &= \langle Q^2 \rangle - 2\langle Q \rangle \langle Q \rangle + \langle Q \rangle \langle Q \rangle \\ &= \langle Q^2 \rangle - \langle Q \rangle \langle Q \rangle \\ &= \langle Q^2 \rangle - \langle Q \rangle^2 \end{aligned} \quad (579)$$

9.6.1. Example: Fluctuation of Gaussian

Given the normalized Gaussian of mean μ and variances σ^2

$$P(Q) = \frac{1}{\sqrt{2\pi}\sigma} \cdot e^{-\frac{(Q-\mu)^2}{2\sigma^2}} \quad (580)$$

Using $\int_{-\infty}^{\infty} dx \cdot xe^{-ax^2} = 0$, we compute the fluctuations for Gaussian

$$\langle Q \rangle = \mu \quad (581)$$

Moreover, with $\int_{-\infty}^{\infty} dx \cdot x^2 e^{-ax^2} = \frac{1}{2} \left(\frac{\pi}{a^3} \right)^{\frac{1}{2}}$ it holds that

$$\langle (Q - \mu)^2 \rangle = \langle Q^2 \rangle - \mu^2 = \sigma^2 \quad (582)$$

9.6.2. Canonical Ensemble

$$\sigma_E^2 = k_B T^2 C_V \quad (583)$$

Derivation

- Calculate the fluctuations of the energy

$$\begin{aligned} \frac{\partial Z}{\partial \beta} &= \sum_m -E_m e^{-\beta E_m} = -Z \langle E \rangle \\ \Rightarrow \langle E \rangle^2 &= \frac{1}{Z^2} \left(\frac{\partial Z}{\partial \beta} \right)^2 \end{aligned} \quad (584)$$

second derivative

$$\begin{aligned}\frac{\partial^2 Z}{\partial \beta^2} &= \sum_m E_m^2 e^{-\beta E_m} = Z \langle E^2 \rangle \\ \Rightarrow \langle E^2 \rangle &= \frac{1}{Z} \frac{\partial^2 Z}{\partial \beta^2}\end{aligned}\tag{585}$$

2. Definition of variance

$$\begin{aligned}\sigma_E^2 &= \langle E^2 \rangle - \langle E \rangle^2 \\ &= \frac{1}{Z} \frac{\partial^2 Z}{\partial \beta^2} - \left(\frac{1}{Z^2} \left(\frac{\partial Z}{\partial \beta} \right)^2 \right) \\ &= -\frac{\partial}{\partial \beta} \langle E \rangle\end{aligned}\tag{586}$$

3. Isochoric heat-capacity

$$\begin{aligned}C_V &\triangleq \left(\frac{\partial U}{\partial T} \right)_{N,T} \\ &= \left(\frac{\partial U}{\partial \beta} \right)_{N,T} \frac{d\beta}{dT} \\ &= -\frac{1}{k_B T^2} \frac{\partial}{\partial \beta} \langle E \rangle\end{aligned}\tag{587}$$

then

$$\sigma_E^2 = (k_B T^2) \cdot \left(-\frac{1}{k_B T^2} \frac{\partial}{\partial \beta} \langle E \rangle \right) = k_B T^2 \cdot C_V\tag{588}$$

9.6.3. Isothermal-Isobaric Ensemble

$$\sigma_V^2 = k_B T V \kappa_T\tag{589}$$

Derivation similar derivation using the isothermal compressibility

$$\begin{aligned}\kappa_T &\triangleq -\frac{1}{V} \left(\frac{\partial V}{\partial P} \right)_{N,T} \\ &= -\frac{1}{\langle V \rangle} \frac{\partial}{\partial P} \langle V \rangle\end{aligned}\tag{590}$$

9.6.4. Grand-Canonical Ensemble

$$\sigma_N^2 = k_B T N \nu^{-1} \kappa_T\tag{591}$$

Derivation similar derivation using the molar volume

$$\left(\frac{\partial N}{\partial \mu} \right)_{V,T} = \frac{N \kappa_T}{\nu}\tag{592}$$

9.6.5. Scaling of Fluctuations with System Size

- with $\beta = \frac{1}{k_B T}$
- it holds that
 1. $C_V \propto N$
 2. $V \propto N$

1. CANONICAL ENSEMBLE
$\begin{aligned}\sigma_E^2 &= k_B T^2 C_V = \beta^{-1} C_V T \\ \Rightarrow \sigma_E &= (\beta^{-1} C_V T)^{\frac{1}{2}} \propto N^{\frac{1}{2}} \\ \Rightarrow \frac{\sigma_E}{\langle E \rangle} &\propto N^{-\frac{1}{2}}\end{aligned}\tag{593}$
2. Isothermal-Isobaric Ensemble

$$\begin{aligned}
\sigma_V^2 &= k_B T V \kappa_T = \beta^{-1} V \kappa_T \\
\Rightarrow \sigma_V &= (\beta^{-1} V \kappa_T)^{\frac{1}{2}} \propto N^{\frac{1}{2}} \\
\Rightarrow \frac{\sigma_V}{\langle V \rangle} &\propto N^{-\frac{1}{2}}
\end{aligned} \tag{594}$$

3. Grand-Canonical Ensemble

$$\begin{aligned}
\sigma_N^2 &= k_B T N \nu^{-1} \kappa_T = \beta^{-1} \nu^{-1} \kappa_T N \stackrel{?}{=} \beta^{-1} \rho \kappa_T N \\
\Rightarrow \sigma_N &= (\beta^{-1} \rho \kappa_T N)^{\frac{1}{2}} \propto N^{\frac{1}{2}} \\
\Rightarrow \frac{\sigma_N}{\langle N \rangle} &\propto N^{-\frac{1}{2}}
\end{aligned} \tag{595}$$

General principle

- the relative fluctuations of all dependent extensive quantities scale with the no. of particles N as $\propto N^{-\frac{1}{2}}$
 - the central-limit theorem leads to normal distribution of the quantities
 - the fluctuations of a sum of normal distribution scales as $N^{-\frac{1}{2}}$

$$\frac{\sigma(\sum_{i=1}^N R_i)}{\sum_{i=1}^N R_i} \propto \frac{1}{\sqrt{N}} \tag{596}$$

Thermodynamic limit $N \rightarrow \infty$ of large macroscopic systems

- In the thermodynamic limit, all observables become **fluctuation-free** in terms of relative fluctuations and a one-component one-phase system can be equivalently specified by **any combination** of three variables
- Example: Equivalent ensembles
 - water 1 kg, 1 liter, 300 K
 - water 1 kg, 1 bar, 300 K

9.7. Quantum Statistics

9.7.1. Preliminary: QM Mechanics - Bosons and Fermions

1. Fermions

- antisymmetric** wavefunction relative to particle interchange
 - e.g. electron, proton, neutron, nuclei with even numbers of proton + neutron

$$\hat{P}_{1,2} \cdot \Psi(\mathbf{r}_1, \mathbf{r}_2) = -\Psi(\mathbf{r}_2, \mathbf{r}_1) \tag{597}$$

- Generalized for an arbitrary no. identical non-interacting particles

$$\Psi(\mathbf{r}_1, \dots, \mathbf{r}_N) = (N!)^{-\frac{1}{2}} \underbrace{\sum_{\mathbf{P}} \sigma_{\mathbf{P}} \prod_n \varphi_{P_n}(\mathbf{r}_n)}_{\text{Slater determinant}} \tag{598}$$

where the Slater determinant can be written as

$$\det \begin{pmatrix} \varphi_1(\mathbf{r}_1) & \varphi_2(\mathbf{r}_1) & \dots & \varphi_N(\mathbf{r}_1) \\ \varphi_1(\mathbf{r}_2) & \varphi_2(\mathbf{r}_2) & \dots & \varphi_N(\mathbf{r}_2) \\ \vdots & \vdots & \ddots & \vdots \\ \varphi_1(\mathbf{r}_N) & \varphi_2(\mathbf{r}_N) & \dots & \varphi_N(\mathbf{r}_N) \end{pmatrix} \tag{599}$$

- Pauli Exclusion Principle**

There cannot be more than one fermion in a given quantum state

Interpretation

- in Slater determinant, if two (or more) of the single-particle φ -functions are the same, the determinant is zero
- no such constraints for bosons

2. Bosons

- symmetric** wavefunction relative to particle interchange
 - e.g. carrier bosons (e.g. photon), mesons, nuclei with odd numbers of proton + neutron

$$\hat{P}_{1,2} \cdot \Psi(\mathbf{r}_1, \mathbf{r}_2) = -\Psi(\mathbf{r}_2, \mathbf{r}_1) \tag{600}$$

- Generalized

$$\Psi(\mathbf{r}_1, \dots, \mathbf{r}_N) = (N!)^{-\frac{1}{2}} \sum_{P \in S_N} \prod_n^N \varphi_{P_n}(\mathbf{r}_n) \quad (601)$$

with S_N all permutations of N indices

3. The two-particle wavefunctions with appropriate parities

- assuming two identical independent particles where one-particle wavefunctions are $\varphi_1(\mathbf{r}_1)$ and $\varphi_2(\mathbf{r}_2)$

$$\Psi(\mathbf{r}_1, \mathbf{r}_2) = \frac{1}{\sqrt{2}} \cdot [\varphi_1(\mathbf{r}_1)\varphi_2(\mathbf{r}_2) \pm \varphi_2(\mathbf{r}_1)\varphi_1(\mathbf{r}_2)] \quad (602)$$

- + for symmetric bosons
- - for antisymmetric fermions

Features

Given a two-particle wave function $\Psi(\mathbf{r}_1, \mathbf{r}_2)$, and a particle-swapping operator denoted as $\hat{P}_{1,2}$ for which it holds that $\hat{P}_{1,2}^2 \Psi = \Psi$

$$\hat{P}_{1,2} \Psi(\mathbf{r}_1, \mathbf{r}_2) = \pm \Psi(\mathbf{r}_2, \mathbf{r}_1) \quad (603)$$

if eigenvalue of square operator is 1 \rightarrow eigenvalue of operator is ± 1 . The particles bear no “tag”, swapping them leads to an undistinguishable physical situation

9.7.2. Quantum Statistics

Given a system with N particles to distribute over **single-particle quantum state**. We assume that the particles are identical, independent (non-interacting & non-entangled \rightarrow separate quantum state to each particle available) and indistinguishable (same wavefunction within sign for fermions).

To determine the statistical weight $W(\mathbf{n})$

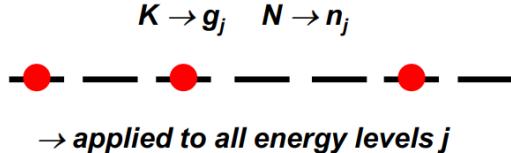
Fermi-Dirac Statistics

- weight of distribution

$$W_{FD}(\mathbf{n}) = \prod_j \frac{g_j!}{n_j!(g_j - n_j)!} \quad (604)$$

Derivation

$$N_{sel} = \binom{K}{N} = \frac{K!}{N!(K-N)!} \quad (605)$$



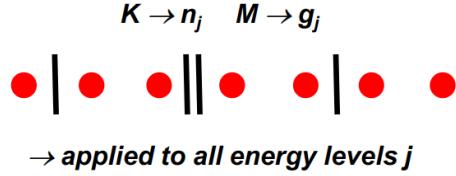
Bose-Einstein Statistics

- weight of distribution

$$W_{BE}(\mathbf{n}) = \prod_j \frac{(g_j + n_j - 1)!}{n_j!(g_j - 1)!} \quad (606)$$

Derivation

$$N_{dis} = \binom{K + M - 1}{K} = \frac{(K + M - 1)!}{K!(M - 1)!} \quad (607)$$



Maxwell-Boltzmann Limit

- if there are **many states available**, then for both cases, if $n_j \ll g_j, \forall j$

$$W_{BL(n)} = \prod_j \frac{g^{n_k}}{n_j!} \quad (608)$$

where

$$\frac{g_j!}{(g_j - n_j)!} \approx \frac{(g_j + n_j - 1)!}{(g_j - 1)!} \approx g^{n_k} \quad (609)$$

in practice, this corresponds to a low-density or high-temperature limit

9.7.3. Resulting Distribution Functions

Fermions (→ Fermi-Dirac)

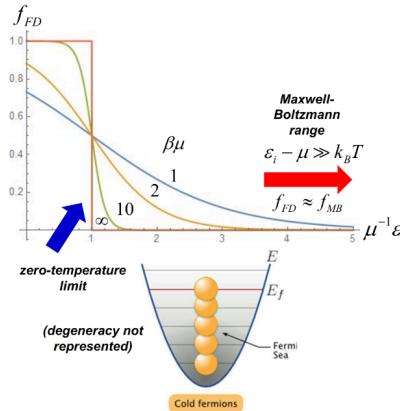
- with Fermi function $f = \frac{1}{e^{\beta(\varepsilon_i - \mu)} + 1}$

$$f_{FD,i} = \frac{1}{e^{\beta(\varepsilon_i - \mu)} + 1} \quad (610)$$

where the Fermi energy is defined by

$$\varepsilon_F = \lim_{T \rightarrow 0} \mu \quad (611)$$

in the limit $T \rightarrow 0$, all the energy levels are fully occupied from the lowest ε_0 to the Fermi level (i.e. chemical potential μ) $\varepsilon_F = \mu$



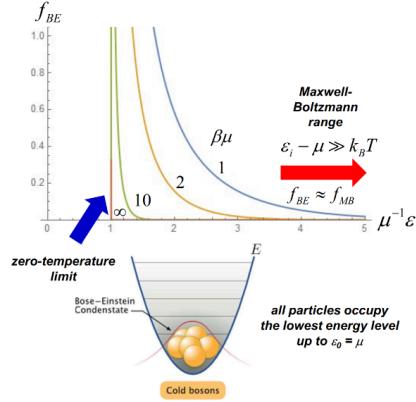
Bosons (Bose-Einstein)

$$f_{BE,i} = \frac{1}{e^{\beta(\varepsilon_i - \mu)} - 1} \quad (612)$$

where the lowest energy level is defined by

$$\varepsilon_0 = \lim_{T \rightarrow 0} \mu \quad (613)$$

in the limit $T \rightarrow 0$, all particles are found in the lowest energy level $\varepsilon_0 = \mu$



Maxwell-Boltzmann

- at low-occupancy limit

$$f_{MB,i} = Z^{-1} \cdot e^{-\beta \varepsilon_i} \quad (614)$$

with $Z = e^{-\beta \mu}$

9.7.3.1. Derivation for the Resulting Distribution Functions

$$\begin{aligned} W_{FD(n)} &= \prod_j \frac{g_j!}{n_j!(g_j - n_j)!} \\ W_{BE(n)} &= \prod_j \frac{(g_j + n_j - 1)!}{n_j!(g_j - 1)!} \\ W_{BL(n)} &= \prod_j \frac{g^{n_k}}{n_j!} \end{aligned} \quad (615)$$

1. Use Stirling approximation $\ln N! \approx N \cdot \ln N - N$ and differentiate

$$\begin{aligned} \frac{\partial}{\partial n_i} \ln W_{FD(n)} &= \ln \frac{g_i - n_i}{n_i} = \ln(f_{FD,i}^{-1} - 1) \\ \frac{\partial}{\partial n_i} \ln W_{BE(n)} &= \ln \frac{n_i + g_i - 1}{n_i} = \ln(f_{BE,i}^{-1} + 1) \\ \frac{\partial}{\partial n_i} \ln W_{MB(n)} &= \ln \frac{g_i}{n_i} = \ln f_{MB,i}^{-1} \end{aligned} \quad (616)$$

where

$$\begin{aligned} f_{FD,i} &\triangleq \frac{n_i}{g_i} \\ f_{BE,i} &\triangleq \frac{n_i}{g_i - 1} \\ f_{MB,i} &\triangleq \frac{n_i}{g_i} \end{aligned} \quad (617)$$

2. We maximize W with constraints in form of the Lagrange multipliers

$$\begin{aligned} \frac{\partial}{\partial n_i} \left(\ln W(n) - \alpha \sum_j n_j - \beta \sum_j n_j \varepsilon_j \right) &= 0, \forall i \\ \Rightarrow \begin{cases} f_{FD,i} = \frac{1}{e^{\alpha+\beta\varepsilon_i}+1} \\ f_{BE,i} = \frac{1}{e^{\alpha+\beta\varepsilon_i}-1} \\ f_{MB,i} = e^{-(\alpha+\beta\varepsilon_i)} \end{cases} \end{aligned} \quad (618)$$

the multipliers can be interpreted as

$$\begin{aligned} \beta &= \frac{1}{k_B T} \\ \alpha &= \frac{-\mu}{k_B T} \end{aligned} \quad (619)$$

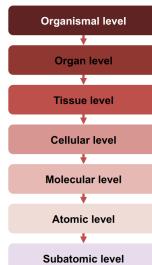
where μ is the chemical potential of particles, when the levels $\{\varepsilon_i\}$ and degeneracies $\{g_i\}$ are known, the value of μ is determined by the condition

$$N = \sum n_i \quad (620)$$

10. Molecular Dynamics Simulation

- Replace experiments when details of the process are inaccessible experimentally (e.g. chemical processes at the atomic level and femtosecond resolution)
- Complement to experiments in which:
 - approximate simulations may reduce the no. /cost of experiments and increase their likelihood of success (e.g. computer-aided drug design, protein engineering)
 - accurate simulations that reproduce available experimental data may provide additional insights into mechanisms. (e.g. properties of water, folding of peptides and proteins)

10.1. Biological Systems in a Nutshell



- COMPLEX HIERARCHY FROM MACROSCOPIC LIVING ORGANISMS TO MICROSCOPIC MOLECULAR WORLDS.

10.1.1. Biomolecules

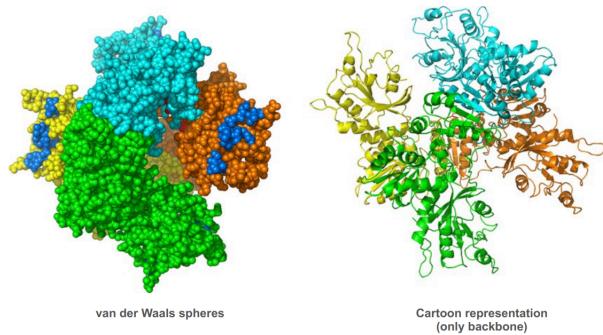
- Amino acids with side chains that have different characteristics (charged, polar, hydrophobic, aromatic)
- Carbohydrates
 - Monosaccharides (3-7 carbons)
 - Disaccharides
- Lipids
 - amphiphilic, it has *polar* (neutral or charged) head group and 1 or 2 (saturated/unsaturated) *apolar* tails
- Nucleic acids (DNA/RNA) with 4 bases in DNA (*adenine (A)*, *guanine (G)*, *cytosine (C)* and *thymine (T)*) and in RNA *uracil (U)* instead of *T*

10.1.2. Environment

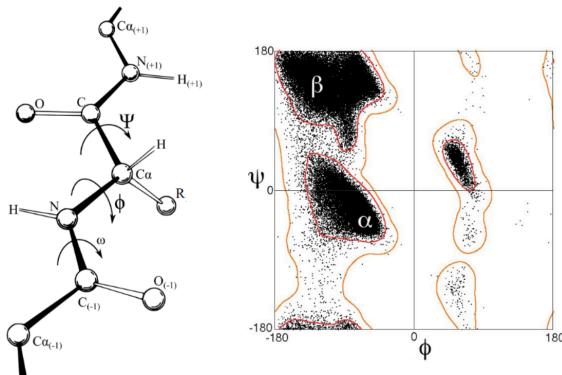
- Ions
 - Ca^{2+} : 1.5–2% of body mass, bones, teeth
 - Mg^{2+} : Bones and teeth, intracellular activity
 - Fe^{2+} : Hemoglobin (O_2 transport)
 - Cu^{2+} , Zn^{2+} : Cofactors in enzymes (catalytic activity)
 - Co^{3+} : In vitamin B12
 - Na^+ , K^+ : Water balance, nerve impulses, fluids inside and outside cells
 - Cl^- : Water balance
 - Nitrate: Involved in the production of amino acids
 - Phosphate: Involved in the production of nucleic acids, ATP (energy of the cells), phospholipids
- Water
 - high *heat capacity*: can act as a heat reservoir with
 - high *dipole moment*: very high dielectric constant ($\epsilon \approx 80$), has strong screening effect of charges
 - *hydrogen-bonding capacity*:
 1. relatively weak interaction, can be broken by thermal fluctuations
 2. long-range effects
 3. solid water is less dense than liquid water

10.1.3. Biomolecule Example: Representation of Proteins

- Protein can be represented
 1. using *Van der Waals* spheres
 2. Cartoon representation for only protein backbones



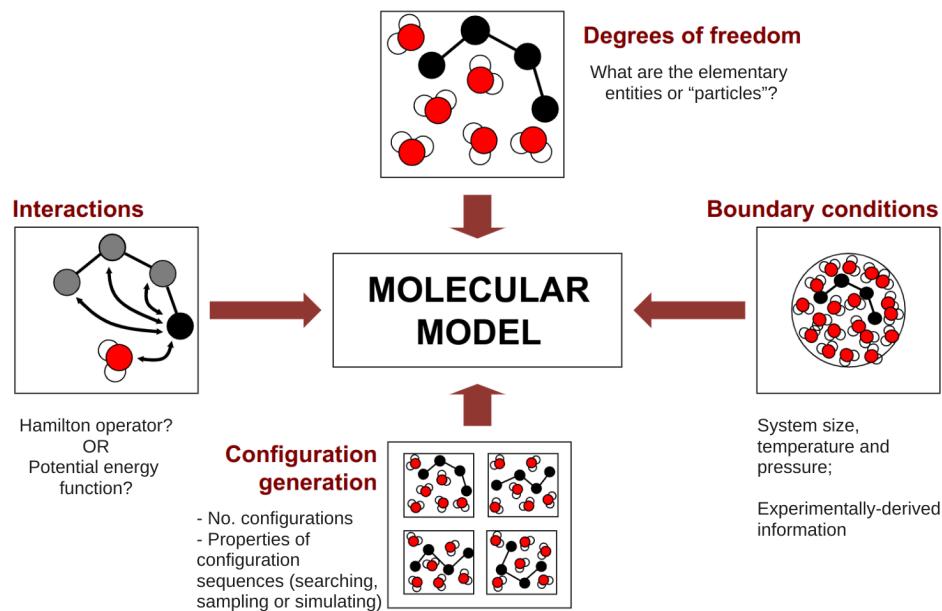
- Protein backbones contain **torsional angles**



- Proteins have **secondary structure motifs** (α -helix, π -helix, β -sheets)

10.2. Molecular Dynamics (MD) Simulations

- Numerically **integrate** over the **classical equations of motion**
- Using a Cartesian coordinate system based on the **Newton formulation**



- Simulating biological systems is essentially solving the **many-particle problem**

	Crystalline State	Liquid State / Macromolecules	Gas Phase
Quantum Mechanics	possible	very difficult	possible
Classical Mechanics	easy	essentially many-particle problem: simulation	trivial
 Reduced to just a few degrees of freedom by symmetry			 Reduced to just a few degrees of freedom by dilution

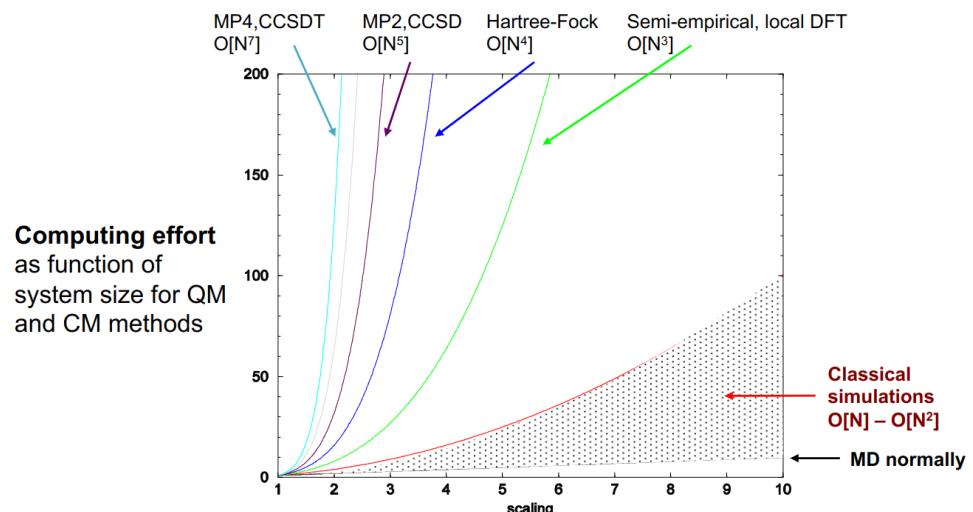
10.3. MD: Degrees of Freedom

10.3.1. Comparing quantum and classical descriptions

When is quantum description valid?

- A full quantum description is only possible for small systems (100s of atoms)
 - For **thermodynamic** properties of large systems, quantum effects are generally negligible

Performance



Degrees of Freedom

- Quantum (statistical) mechanics → Classical (statistical) mechanics

Level of resolution	I	II	III	IV	V
Particles	Sub-nuclear: nucleons + electrons	Sub-atomic: nuclei + electrons	Atomic	Supra-atomic	Supra-molecular
Mass [amu]	$10^{-3} - 1$	$10^{-3} - 10^2$	$1 - 10^2$	$10 - 10^2$	$10 - 10^2$
Size [nm]	10^{-6}	$10^{-6} - 10^{-5}$	$0.03 - 0.3$	$0.5 - 1.0$	$0.5 - 1.0$
Interactions	Strong, Coulomb, Pauli principle	Coulomb, Pauli principle	bonded terms, Coulomb, repulsive, van der Waals	Coulomb, repulsive, van der Waals	
Scaling effort	$N^{>3}$ nucleons	$N^{>3}$ electrons	N^{1-2} atoms	N^{1-2} beads	N^{1-2} beads
Reduction in number of DOF from previous level		$10 - 100$	$10 - 100$	$2 - 5$	$2 - 10$
Reduction in comp. effort from previous level		$\geq 10^3$	$\geq 10^3$	$2 - 25$	$2 - 100$

	QM	CM
Equation of motion?	Time-dependent Schrödinger equation: $i\hbar \frac{\partial \Psi(\mathbf{r}^N, t)}{\partial t} = \hat{H}\Psi(\mathbf{r}^N, t)$	Newton's equation of motion: $\mathbf{f}_i = m_i \mathbf{a}_i$ $\mathbf{f}_i = -\frac{\partial V(\mathbf{r}^N)}{\partial \mathbf{r}_i}$
Interactions?	Born-Oppenheimer approximation: Nuclei and electrons decoupled	Interaction potential energy function: Generally pairwise additive, but polarisation can be included
Coordinates?	Probabilistic nature of wave function: Uncertainty principle $ \Psi(\mathbf{r}_i, t) ^2$	Phase space trajectory: $\mathbf{r}^N, \mathbf{p}^N$
Statistics?	Bose-Einstein or Fermi-Dirac statistics (Pauli principle)	Boltzmann statistics

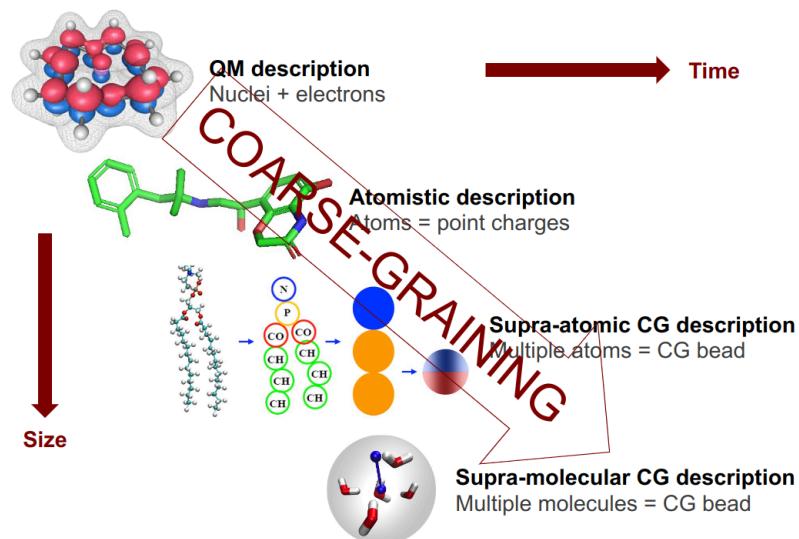
10.3.2. Coarse-Grained Models

Coarse-grain means to:

- Eliminating degrees of freedom (DOFs) and interactions.
- What to **coarse-grain** in order to eliminate **degrees of freedom** is dependent on:
 1. Properties of the concrete research question.
 2. Interactions governing **eliminated** DOFs must be largely decoupled from the system.
 3. Interactions governing **remaining** DOFs should be simply representable
 4. Eliminated DOFs must be large in number (great performance benefits)

Example: Coarse-graining

- From QM to atomistic description, abstracting electrons away eliminate **degrees of freedom**.
- From atomistic to supra-atomic or supra-molecular CG description, what can be abstracted away



10.3.3. Trade-offs in Coarse-graining

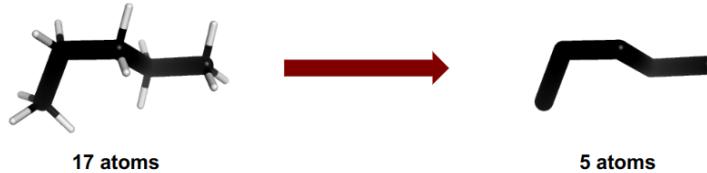
- **Trade-off:** accuracy and speed-up.
 - ▷ coarse-graining involves per se a loss of information

ACCURACY	SPEED-UP
<ul style="list-style-type: none"> • model parameters are less transferable (between similar sub-structures) • physical basic of a particular process may be changed • possible unphysical balance of entropy & energy 	<ul style="list-style-type: none"> • general reduction of the range of state points

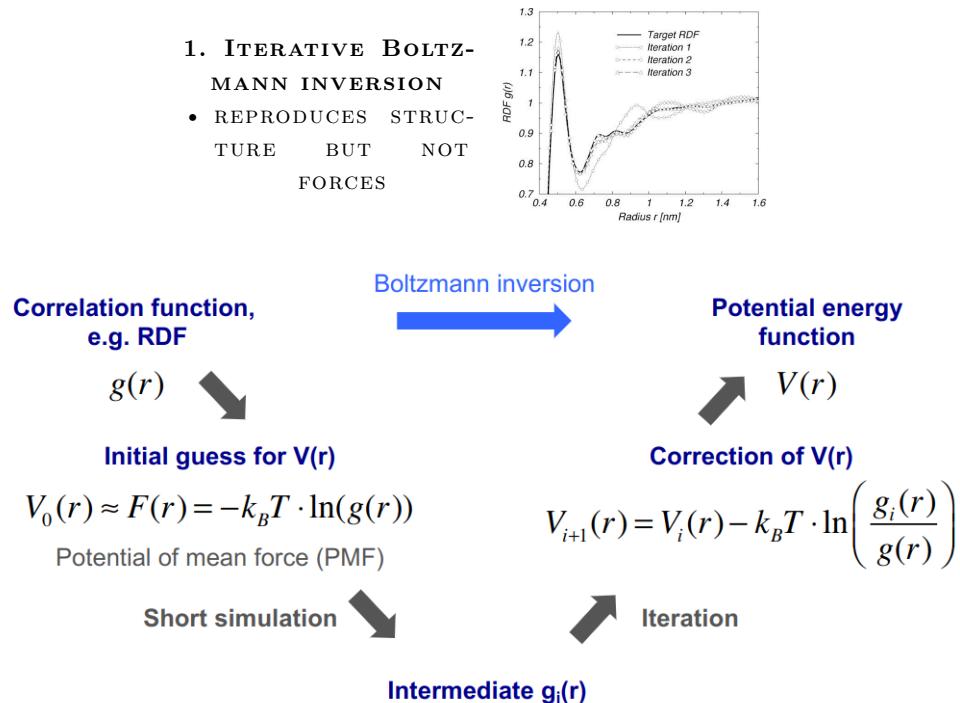
10.3.4. Coarse-Grain Strategy for atoms: United Atoms

Goal: reduce no. particles in the system

- common approach is to **remove atoms** that have no strong interactions with other atoms (*non-essential DOFs*)
 - e.g. remove hydrogen atoms in lipids
- one often **replace functional groups** with larger atoms too
 - e.g. replace CH, CH₂ and CH₃ with larger atoms, see **Pentane** example below



10.3.5. Coarse-Grain Strategies for Supra-Atomic CG Models



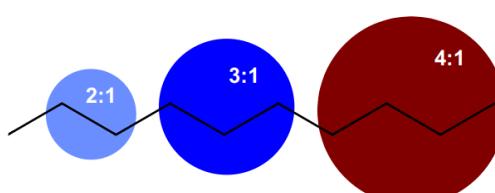
2. Force matching

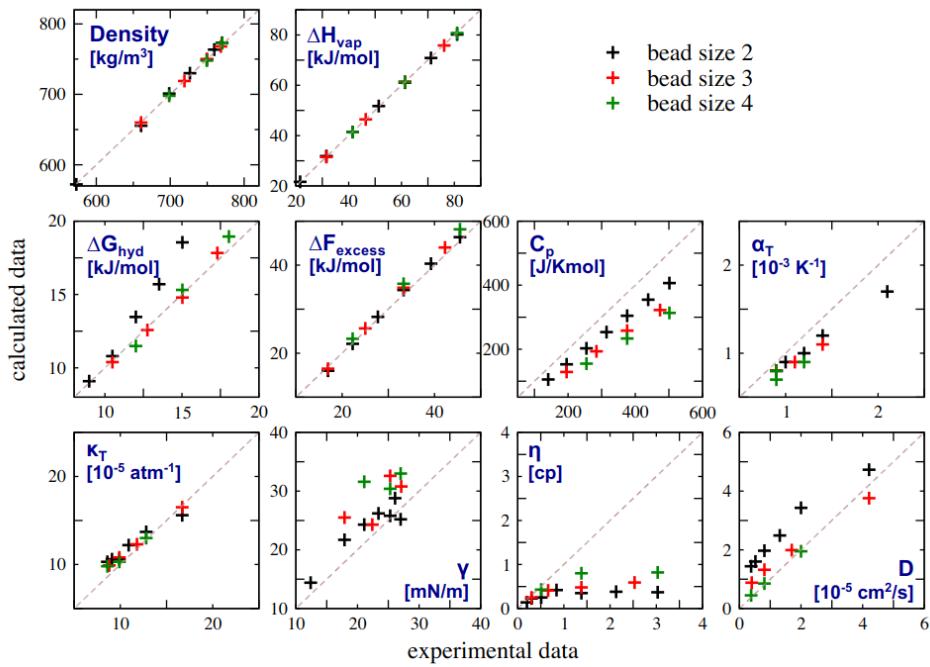
- reproduces forces but not structure
 - first compute **reference forces**, which is the average force on mapped atoms for each CG bead; next match using **least-square fitting** the force distributions by effective pair potentials
-

3. Fitting to thermodynamic properties

Typically, one select some **target properties** such as density, potential energy etc. One then provide some **initial guess** of parameters based on atomistic simulations. Then systematic scanning of parameters is performed.

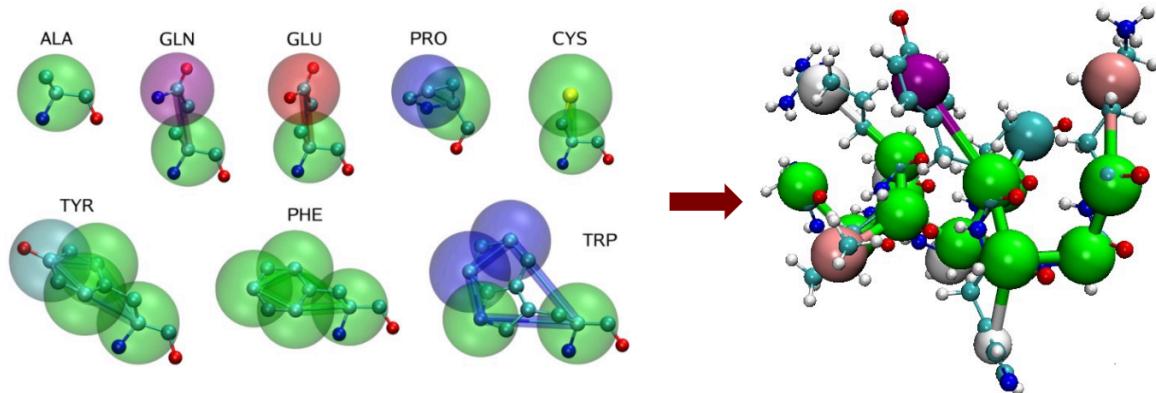
Example: Coarse-grained alkane model





Example: MARTINI CG force field

- fitting to thermodynamic properties
- Disadvantage:** requires the use of elastic network to keep secondary/tertiary protein structures, possible loss of essential degrees of freedom



10.4. MD: Interactions in Classical Atomistic Force Fields

- **System:** N particles classical

$$\text{Cartesian} = \begin{cases} \text{coordinates: } \mathbf{r}^N \equiv (\mathbf{r}_1, \mathbf{r}_2, \dots, \mathbf{r}_N) \\ \text{momenta: } \mathbf{p}^N \equiv (\mathbf{p}_1, \mathbf{p}_2, \dots, \mathbf{p}_N) \\ \text{mass: } (m_1, m_2, \dots, m_N) \end{cases} \quad (621)$$

1. FORMULATION: HAMILTONIAN

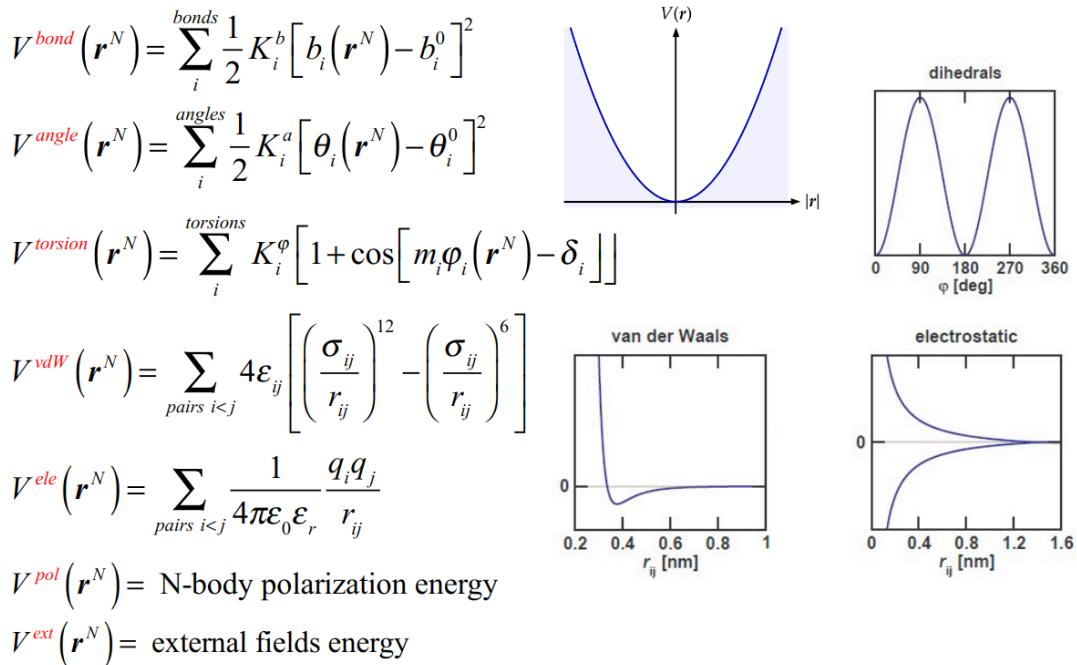
Recall from the section of classical mechanics where we had the expression for Hamiltonian in Cartesian coordinates.

$$\begin{aligned} \mathcal{H}(\mathbf{r}^N, \mathbf{p}^N) &= \mathcal{K}(\mathbf{r}^N, \mathbf{p}^N) + \mathcal{V}(\mathbf{r}^N) \\ &= \sum_i^N \frac{\mathbf{p}_i^2}{2m_i} + \mathcal{V}(\mathbf{r}^N) \\ &= \sum_i^N \frac{\mathbf{p}_i^2}{2m_i} + \mathcal{V}(\mathbf{r}_1, \mathbf{r}_2, \dots, \mathbf{r}_N) \end{aligned} \quad (622)$$

2. Formulation: Potential Energy Function

$$\mathcal{V}(\mathbf{r}^N) = \mathcal{V}^{\text{phys}}(\mathbf{r}^N) + \mathcal{V}^{\text{special}}(\mathbf{r}^N) \quad (623)$$

2.1 Physical Terms



2.2 Special Interaction Terms

- restraints on the system from experimental data (e.g. NMR)
- restraints on the system to bias the sampling

10.4.1. Classical Force Field

Generic force field terms for molecules

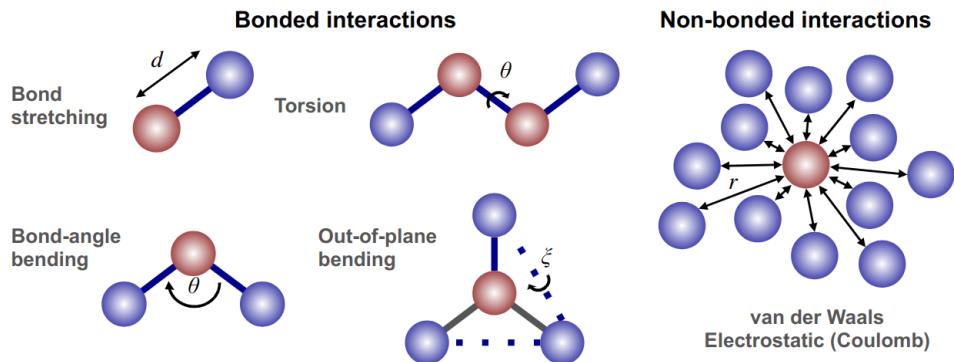
$$\mathcal{V}^{\text{phys}}(\mathbf{r}^N), \text{ with } \mathbf{r}^N = (\mathbf{r}_1, \mathbf{r}_2, \dots, \mathbf{r}_N) \quad (624)$$

Requirements for an effective force fields

- **Representative:** models underlying physics appropriately
- **Simple:** contains as few terms as possible
- **Computationally efficient:** avoids complex derivatives and exponential terms
- **Transferable:** parameters appropriate for a range of molecules

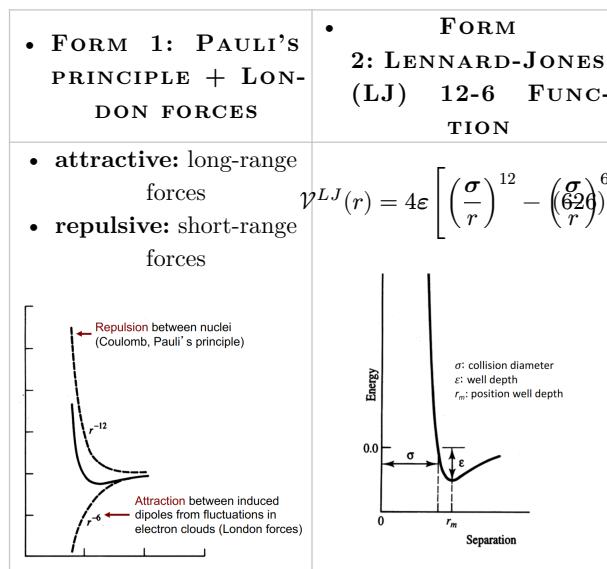
Example: Potential energy function for molecules

$$\begin{aligned}\mathcal{V}(\mathbf{r}^N) &= \mathcal{V}_{\text{bonded}} + \mathcal{V}_{\text{non-bonded}} \\ &= (\mathcal{V}_{\text{bonds}} + \mathcal{V}_{\text{angles}} + \mathcal{V}_{\text{torsions}} + \mathcal{V}_{\text{improper}}) + (\mathcal{V}_{\text{elec}} + \mathcal{V}_{\text{vdW}})\end{aligned}\quad (625)$$



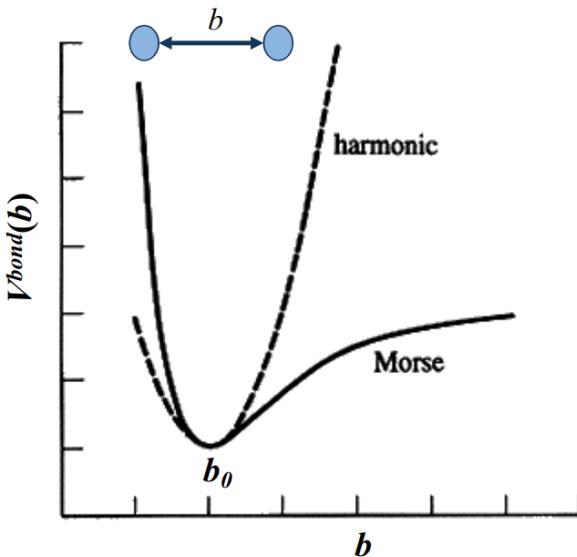
10.4.2. Non-bonded Terms

- **van der Waals interactions:** interactions between atoms independent of net charge.



10.4.3. Bonded Terms

- Covalent bond stretching
 - pairwise interaction: 2-body term
 - various forms possible



FORM 1: MORSE FUNCTION

- **Advantage:** Dissociation (bond breaking) possible

- **Disadvantage:** Computationally expensive

b_{ij} : length of the bond between atoms i and j

$$\mathcal{V}^{\text{Morse}}(\mathbf{r}(t); D_n; K_n^b; b_n^0) = \sum_n D_n \left\{ 1 - e^{\left(-\left(\frac{K_n^b}{2} \right)^{\frac{1}{2}} (b_{n(t)} - b_n^0) \right)^2} \right\} \quad (627)$$

• FORM 2: HARMONIC FUNCTION

- **Advantage:** simple, cheap and most commonly used

- **Disadvantage:** No dissociation possible

$$\mathcal{V}^{\text{harm}}(\mathbf{r}(t); K_n^b; b_n^0) = \sum_n \frac{1}{2} K_n^b (b_{n(t)} - b_n^0)^2 \quad (628)$$

10.4.4. Parameterization of Classical Force Fields

Force fields are often underdetermined due to too many parameters it may depend on (and the lack of experimental data). Moreover, multiple parameter combinations can give the same output.

Imposing Transferability to Improve Parametrization

- restrict no. LJ atom types
- use a combination rule for LJ parameters
- parametrize small molecules (liquids) and extrapolate to larger compounds
- use multiple compounds with same functional group



10.5. MD: Configuration Generation

Background: High-dimensional configuration space, where it is impossible to enumerate all the local energy minima or find the global minimum.

Goal: Have good initial coordinates of atoms and generate only relevant configurations that have

- **low energy:** unstable intermediates are normally not desirable
- **Boltzmann-weighted**

10.5.1. Classes of Methods

First two classes of methods, i.e. searching and sampling generally followed by **energy minimization** (EM). One search the configuration space as widely as possible for low-energy regions, and report all local energy minima found by energy minimization.

1. Searching

- search methods
 - eg. systematic search, random search, stepwise build-up, genetic algorithms, distance geometry, homology modeling
- downgraded MD
 - eg. simulated annealing, pot. ene. annealing (PEACS), soft-core atoms, 4D molecular dynamics, local elevation/metadynamics

2. Sampling

- metropolis Monte Carlo (MC)
- modified MD
 - eg. molecular dynamics with altered masses or biasing potentials, replica exchange (in temperature or Hamiltonian)

3. Simulating

- molecular dynamics (MD)
 - with thermostat
- stochastic dynamics (SD)
- Brownian dynamics (BD)
- Markov state models (MSM)

Key Properties of the Required Method

	SEARCHING	SAMPLING	SIMULATING
Boltzmann distribution	✗	✓	✓
Dynamical sequence	✗	✗	✓

1. **Boltzmann-weighted ensemble** of configurations
 - *thermodynamic properties* can be calculated
2. **Physically-based sequence** of configurations through a classical equation of motion
 - *dynamic properties* can be calculated

10.5.2. Integrators

In molecular dynamics (MD) simulations, computational costs and memory requirement are less important, as the main effort in MD is the force calculation but not the integration.

For convenience, **fixed timestep** is used and there are **not more than one** number of force evaluations per timestep.

To summarize, MD integrators should provide:

- stability and robustness
 - good accuracy for long time steps
 - conserve momentum and energy
 - reversible in time

- preserve constant T or P
 - compatible with thermostating/barostating

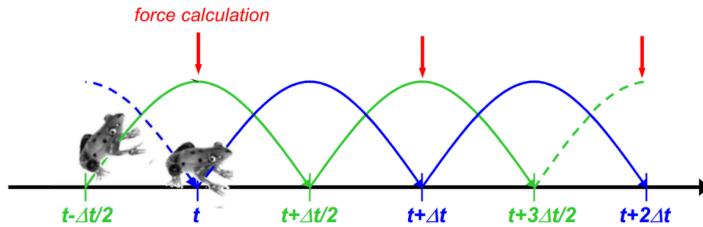
Time Reversibility One can follow the same algorithm backward in time and get the same trajectory

Symplectic algorithm Phase-space-volume preserving

10.5.2.1. Leap-Frog Integrator

$$\begin{aligned} v\left(t + \frac{1}{2}\Delta t\right) &= v\left(t - \frac{1}{2}\Delta t\right) + a(t)\Delta t \\ r(t + \Delta t) &= r(t) + v\left(t + \frac{1}{2}\Delta t\right)\Delta t \end{aligned} \quad (629)$$

- an interleaved **symplectic** algorithm that is common and good for MD
- time reversible
- third-order accurate, error of order Δ^3 in both coordinates and velocities



Coordinates and velocities are **not** available simultaneously

- to get the kinetic energy at time t , the velocities must be back-calculated

$$\begin{aligned} v(t) &= \frac{1}{2} \left[v\left(t - \frac{1}{2}\Delta t\right) + v\left(t + \frac{1}{2}\Delta t\right) \right] \\ &+ \frac{\Delta t}{16} \cdot [a(t - \Delta t) + a(t + \Delta t)] + (O(\Delta t))^4 \end{aligned} \quad (630)$$

10.5.2.2. Euler Forward/Backward

- not time reversible
- error of order Δ^2

$$\begin{aligned} v(t_n + \Delta t) &= v(t_n) + a(t_n)\Delta t \\ x(t_n + \Delta t) &= x(t_n) + v(t_n)\Delta t + \frac{1}{2}a(t_n)\Delta t^2 \end{aligned} \quad (631)$$

10.5.2.3. Runge-Kutta

- not time reversible
- more accurate, error of order Δ^4

Example: Solving ODE with Runge-Kutta time stepping

Consider an ODE, the spacing defined as $h := \Delta$

$$\frac{dy}{dt} = f(t, y) \quad (632)$$

Then at each time step, one calculates

$$\begin{aligned} k_1 &= h \cdot f(t_n, y_n) \\ k_2 &= h \cdot f\left(t_n + \frac{h}{2}, y_n + \frac{1}{2}k_1\right) \\ k_3 &= h \cdot f\left(t_n + \frac{h}{2}, y_n + \frac{1}{2}k_2\right) \\ k_4 &= h \cdot f(t_n + h, y_n + k_3) \end{aligned} \quad (633)$$

The variable update at next time step can be computed using

$$y_{n+1} = y_n + \frac{1}{6}[k_1 + 2k_2 + 2k_3 + k_4] + O(\Delta^5) \quad (634)$$

10.5.2.4. Example: Comparison of Integrators for Harmonic Oscillator

Physics of Harmonic Oscillators ($m = 2$)

Equation of motion with initial conditions:

$$\frac{d^2x(t)}{dt^2} = -x(t) \quad (635)$$

$$\begin{cases} x(0) = 1 \\ \frac{dx(0)}{dt} = v(0) = 0 \end{cases}$$

Kinetic Energy

$$\mathcal{K}(t) = \frac{1}{2}mv(t)^2 \propto v(t)^2 \quad (636)$$

Potential Energy

$$\mathcal{V}(t) = \frac{1}{2}kx(t)^2 \propto x(t)^2 \quad (637)$$

Total Energy is conserved

$$\begin{aligned} E_{\text{tot}}(t) &= \mathcal{K}(t) + \mathcal{V}(t) \\ &= v(t)^2 + x(t)^2 \\ &= 1 \end{aligned} \quad (638)$$

Exact Solutions

$$\begin{cases} x(t) = \cos(t) \\ v(t) = -\sin(t) \end{cases} \quad (639)$$

10.5.2.5. Energy Conservation in Numerical Simulations

- In general, the total energy resolved from numerical simulation may both **fluctuate** and **drift**, even though mathematically and physically it is not desirable.
- Reason for it is **limited accuracy** caused by
 - *sources of non-conservativeness* (e.g. cutoff noise, constraints applied with finite tolerance)
 - even assuming *full conservativeness*, there are still **integration errors** at finite Δt , caused by intrinsic accuracy of the integrator, where terms like $O(\Delta t^n)$ are ignored.
 - even in the limit $\Delta t \rightarrow 0$, computers work at a finite numerical precision.

10.5.3. Choice of the Time Step Size

- Rule of thumb: $\Delta t \approx \frac{\tau}{10}$, where τ is the period of the fastest motion in the system
- too short time steps → poor sampling
- too long time steps → poor energy conservation & program may overflow

Example: Recommended timestep choices Δt

- Biomolecule in water at 300 K
 - flexible bonds → 0.5 - 1 fs
 - constrained bonds → 2 fs
 - 1 fs = $1 \cdot 10^{-15}$ s

10.5.4. Initial Configuration

Initial configurations needed to begin a simulation consist of starting **coordinates** and **velocities**.

Choosing initial coordinates

- the initial (solute) coordinates are chosen carefully
 - e.g. experimentally from X-ray crystallography or NMR structure
- exception if the **equilibration time** preceding the run is longer than the **conformational relaxation time** of the system

Choosing initial velocities

- the choice is generally unimportant because the velocity relaxation time for most systems is short ($\sim ps = 10^{-12}s$)
→ mostly assigned randomly from a Maxwell-Boltzmann distribution at a given temperature

$$p(v_{ix}) = \left(\frac{m_i}{2\pi k_B T} \right)^{\frac{1}{2}} \cdot \exp\left(-\frac{m_i v_{ix}^2}{2k_B T} \right), \text{ with } T \text{ as initial temperature} \quad (640)$$

- except for determining the initial energy one may want to choose suitable initial velocities

10.5.5. Bond-Length Constraints

Applying constraints to bond-length means to **freeze** the bond vibrations. Freezing is valid if:

- bonds are dynamically weakly coupled to other degrees of freedom (rather irrelevant in large biomolecular systems)
- bonds are typically in the ground state at room temperature



- Advantage:** Bonds may vibrate fast and impose a short timestep of 0.5 – 1 fs. By applying bond-length constraints, timestep with all bonds constrained can be increased to 2 fs.

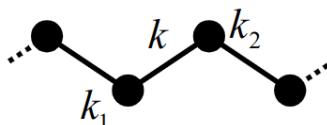
10.5.5.1. Bond-Length Constraints: The SHAKE Algorithm

SHAKE in Cartesian Coordinates

- To enforce geometric constraints in analytical (Lagrange) generalized coordinates is impractical.
- Most common bond-length constraint algorithm for numerical (iterative) methods in Cartesian coordinates

Algorithms

- $$\begin{cases} 1. \text{ Consider set of } N_c \text{ bond-length constraint equations} \\ 2. \text{ Insert within leap-frog equation with Lagrange multipliers} \\ 3. \text{ Solve the system approximately by assuming uncoupled + linearized} \\ 4. \text{ Apply approximate solution iteratively} \end{cases} \quad (641)$$



1. Constraint Equations

$$\sigma_k(\{r_i\}) = r_{k_1, k_2}^2 - d_{k_1, k_2}^2 \stackrel{!}{=} 0, \text{ for } k = 1, \dots, N_c \quad (642)$$

with partial derivatives

$$\frac{\partial}{\partial r_i} \sigma_k(\{r_i\}) = \frac{\partial}{\partial r_i} (r_{k_1, k_2}^2 - d_{k_1, k_2}^2) = 2(\delta_{ik_1} - \delta_{ik_2}) \cdot \underbrace{r_{k_1, k_2}(t)}_{\substack{\text{for each constraint } k, \\ \text{a constraint force acts} \\ \text{on the connected atoms } k_1 \text{ and } k_2}} \quad (643)$$

2. Lagrange Method of Undetermined Multipliers

Recall for computation of forces we have, $\mathbf{F}_i(\mathbf{r}^N, t) = -\frac{\partial}{\partial \mathbf{r}_i} \mathcal{V}(\mathbf{r}^N, t)$. We modify the system of equations by adding a “zero-term” using the constraint equations to the potential energy.

$$\begin{aligned} m_i \mathbf{a}_i(t) &= \tilde{\mathbf{F}}_i(\mathbf{r}^N, t) \\ m_i \mathbf{a}_i(t) &= \mathbf{F}_i^{uc}(\mathbf{r}^N, t) + \underbrace{\mathbf{F}_i^c(\mathbf{r}^N, t)}_{\text{constraint forces}} \\ m_i \frac{d^2 \mathbf{r}_i(t)}{dt^2} &= -\frac{\partial}{\partial \mathbf{r}_i} \mathcal{V}(\{\mathbf{r}_i\}) - \frac{\partial}{\partial \mathbf{r}_i} \sum_{k=1}^{N_c} l_k(t) \sigma_k(\{\mathbf{r}_i\}) \\ &= -\frac{\partial}{\partial \mathbf{r}_i} \mathcal{V}(\{\mathbf{r}_i\}) - 2 \sum_{k=1}^{N_c} l_k(t) (\delta_{ik_1} - \delta_{ik_2}) \mathbf{r}_{k_1, k_2}(t) \end{aligned} \quad (644)$$

where important identity for constraint forces is:

$$\mathbf{F}_i^c(\mathbf{r}^N) = -2 \sum_{k=1}^{N_c} l_k(t) (\delta_{ik_1} - \delta_{ik_2}) \mathbf{r}_{k_1, k_2}(t) \quad (645)$$

3. Comparing constrained and unconstrained time steps

$$\left\{ \begin{array}{l} \underline{\mathbf{r}_i^{uc}(t + \Delta t)} = \mathbf{r}_i(t) + \mathbf{v}_i(t - \frac{\Delta t}{2}) \Delta t + \Delta t^2 m_i^{-1} \mathbf{F}_i^{uc}(t) \text{ unconstrained} \\ \underline{\mathbf{r}_i^c(t + \Delta t)} = \underline{\mathbf{r}_i^{uc}(t + \Delta t)} + \Delta t^2 m_i^{-1} \mathbf{F}_i^c(t) \text{ constrained} \end{array} \right. \quad (646)$$

4. Plugging back to constraint equations

For all $k = 1, \dots, N_c$,

$$\begin{aligned} (r_{k_1, k_2}^c)^2 - d_{k_1, k_2}^2 &\stackrel{!}{=} 0 \\ \left[\frac{\mathbf{r}_{k_1, k_2}^{uc}(t + \Delta t)}{\mathbf{r}_{k_1, k_2}^{uc}(t + \Delta t) + \Delta t^2 \left(m_{k_1}^{-1} \underbrace{\mathbf{F}_{k_1}^c(t)}_{\substack{\text{can be replaced} \\ \text{by identity above}}}, m_{k_2}^{-1} \underbrace{\mathbf{F}_{k_2}^c(t)}_{\substack{\text{can be replaced}}} \right)} \right]^2 - d_{k_1, k_2}^2 &\stackrel{!}{=} 0 \end{aligned} \quad (647)$$

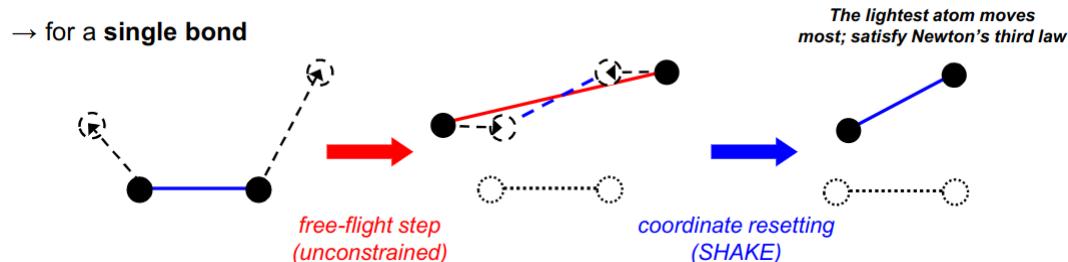
5. Solving the system of equations

The solution involve having the **assumption** that constraints are **uncoupled**, canceling terms with $(\delta_{ik_1} - \delta_{ik_2})$, and then linearize the equation.

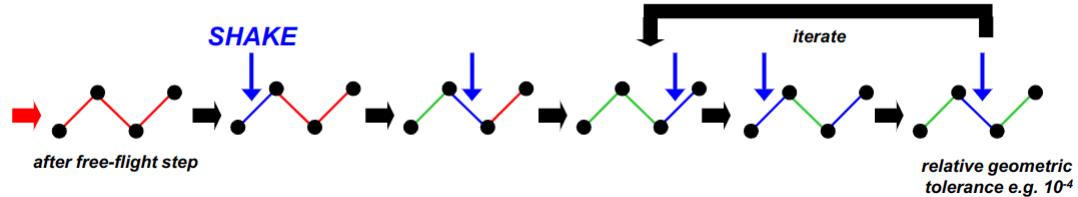
SHAKE in practice

The solution of system of equations in which we assume the constraints are decoupled and linearized the equation gives us the following coordinate update rules:

$$\begin{aligned} \mathbf{r}_{k_1}^c(t + \Delta t) &= \mathbf{r}_{k_1}^{uc}(t + \Delta t) - 2\Delta t^2 m_{k_1}^{-1} l_k(t) \mathbf{r}_{k_1, k_2}(t) \\ \mathbf{r}_{k_2}^c(t + \Delta t) &= \mathbf{r}_{k_2}^{uc}(t + \Delta t) - 2\Delta t^2 m_{k_2}^{-1} l_k(t) \mathbf{r}_{k_1, k_2}(t) \end{aligned} \quad (648)$$



→ for **multiple bonds**: iterate until all constraints are fulfilled within some relative tolerance



Corrections need to be applied to velocities and forces:

- Conserves total, linear, and angular momenta:

$$v\left(t + \frac{1}{2}\Delta t\right) = \frac{[r(t + \Delta t) - r(t)]}{\Delta t} \quad (649)$$

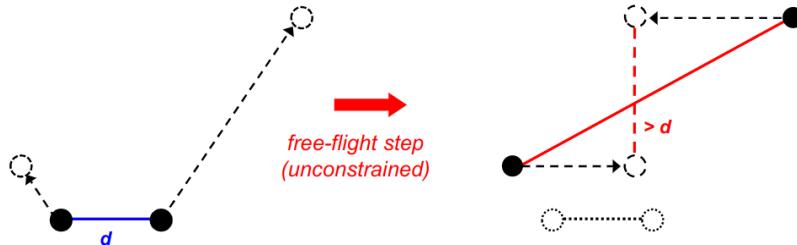
- Closely related to Lagrangian multipliers:

$$\mathbf{F}(t) = \mathbf{F}^{uc}(t) + \underline{\mathbf{M}} \frac{[r(t + \Delta t) - r^{uc}(t)]}{\Delta t^2} \quad (650)$$

Possible Failures when using SHAKE

- If atom(s) move too much in a single timestep, convergence cannot be guaranteed
 - commonly indicates bad simulation configuration setup (e.g. skip energy minimization) or a flaw method is used
- timestep is too long

Example: failure in simulating a single bond



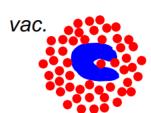
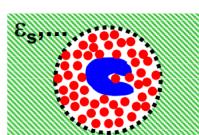
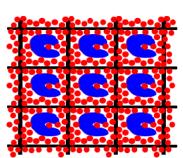
10.6. MD: Boundary Conditions

10.7. Spatial Boundary Conditions

MD simulations is plagued by

1. Finite-size effects
2. Surface effects

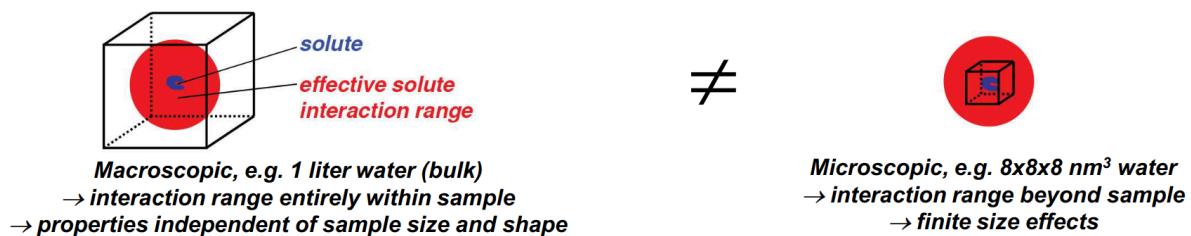
→ simulated properties may heavily depend on specific choices made in spatial boundary conditions

	FINITE-SIZE EFFECTS	SURFACE EFFECTS	
→ vacuum	vac. 	very large	very large → compactness → spherical shape → too strong electrostatics
→ implicit solvent	vac. 	none	large → boundary problem → parameter-sensitive → cheap
→ finite system (e.g. droplet or solvent layer)	vac. 	large	very large (at solvent-vacuum) → too high pressure → solvent evaporation → surface-layer artifacts → too strong electrostatics
→ finite system + implicit solvent	vac. 	none	large (at solvent-continuum) → boundary problem → poor parameter transferability
→ periodic <i>MOST USED NOWADAYS!</i>	vac. 	large	none → artificial anisotropy → artificial periodicity → high effective concentration → expensive → finite-size effects still present !

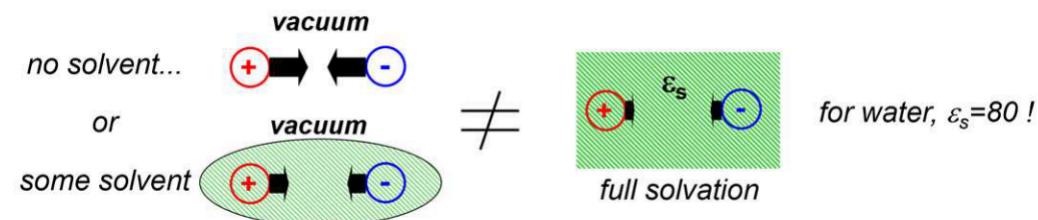
10.7.1. Finite-size and surface effects

Finite-Size Effect

- arises because the simulated system is truly microscopic



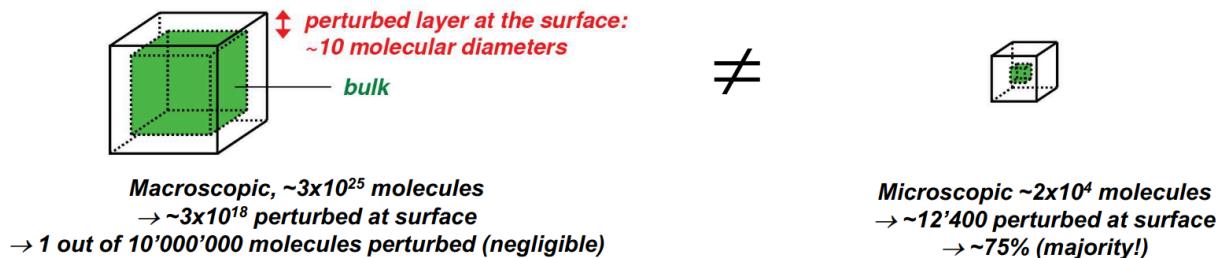
- the lack of solute-solvent interactions (e.g. the lack of dielectric screening) hinders full solvation
 - cannot model intra-solute ones (e.g. van der Waals and electrostatic)
 - electrostatic interactions such as ion pairing, hydrogen bonds are overweighted in the sample



Surface Effect

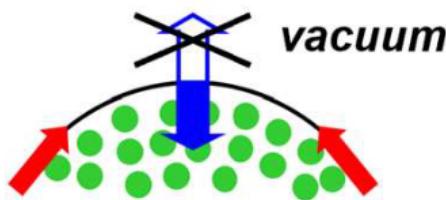
- arise when the simulated system has a large surface-to-volume ratio

- predominantly due to increased surface tension



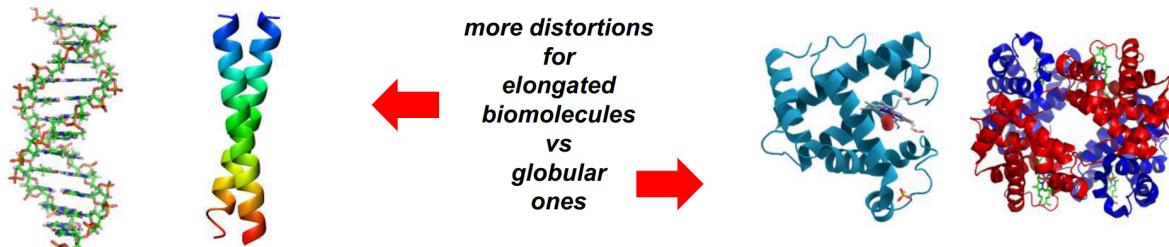
Example: Surface Tension

- to minimize the surface area of the sphere
 - increased pressure (compactness)
 - effects large for microscopic samples ($\sim 2 \times 10^4$ molecules, commonly $\sim 12,400$ perturbed at surface, $\sim 75\%$ (majority!))

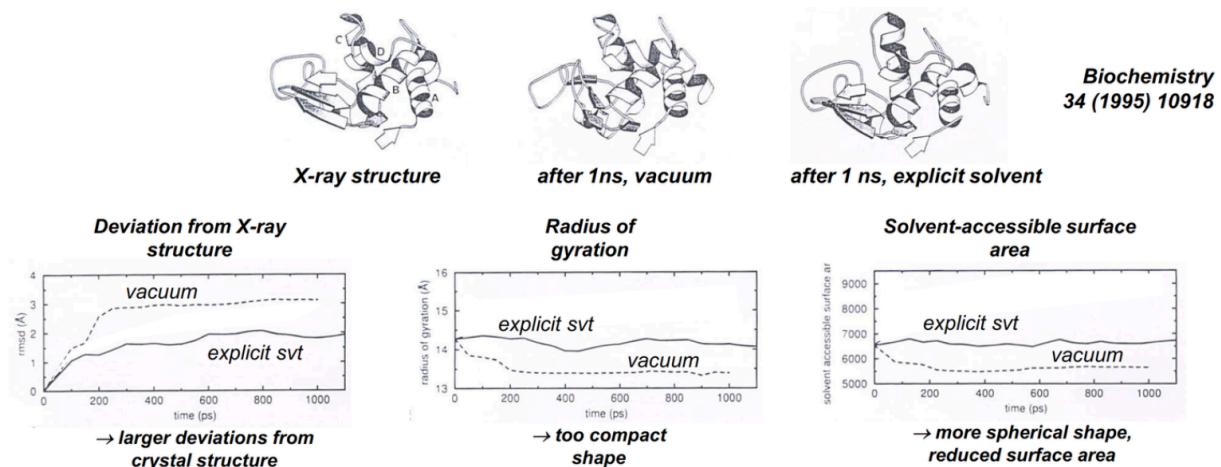


10.7.2. Vacuum boundary conditions

- strongly distortive effect on biomolecules → “locking” of the kinetics
 - Finite-size effects** → enhanced intramolecular interactions
 - Surface effects** → surface reduction and artificial sphericity



Example: Hen-egg-white Lysozyme (129 residues)



10.7.3. Implicit-solvent boundary conditions

- can be used under otherwise vacuum BC to **mimic** the effect of a **solvent** without including the solvent molecules explicitly

Approach:

- Add **solvation terms** in the potential-energy function of the solute to account implicitly for the **solvent-induced modulation** of both **electrostatic** and **non-polar** interactions



Example: dielectric screening (Electrostatics)

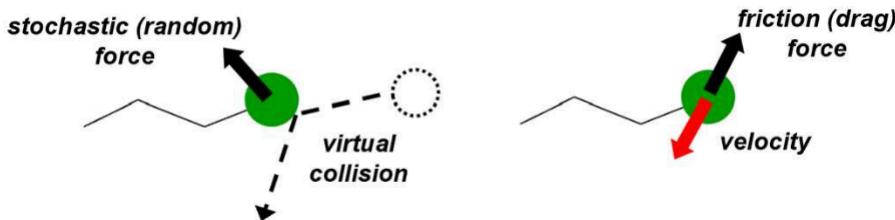
- reduce the atomic charges
- damp the Coulomb potential
- apply continuum electrostatics

Example: van der Waals competition + hydrophobic terms (Non-polar)

- term proportional to the solvent-exposed surface area (SASA)
- SASA sorted by identity of contributing atom

Example: Application with stochastics dynamics (SD)

- results in same equilibrium properties and improved dynamic properties



Key Issues for continuum models

- validity of macroscopic continuum electrostatics at the microscopic level
- exact location of solute-solvent boundary
- atomic parameters (charges, radii, surface-area parameters)
- solute dielectric constant, surface-area coefficient

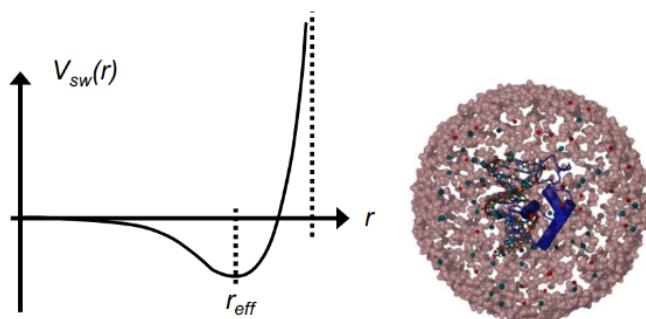
10.7.4. Finite-system boundary conditions

- simulate a finite solute-solvent system possibly surrounded by an implicit solvent model
 - e.g. droplet
- needs confinement potential
- may also need **orientational correction** potential

Example: Confinement Potential for Finite-System BC

- Using the Lennard-Jones wall, one can confine the sample, prevents evaporation and mimic dispersion

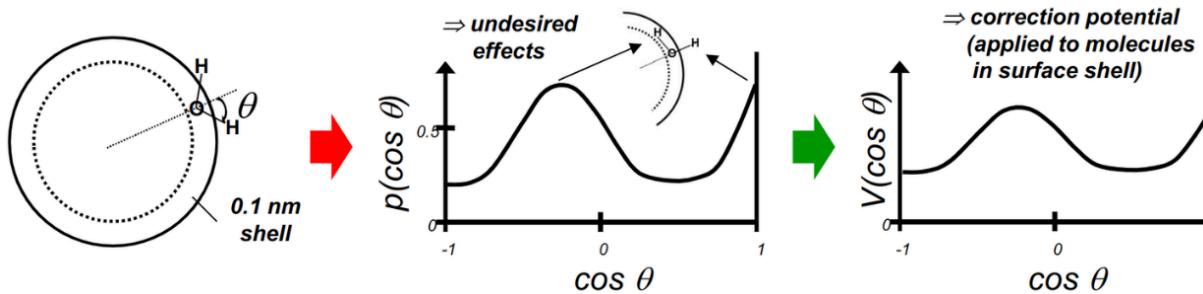
$$V_{SW(r;r_0)} = C_{12}(r_0 - r)^{-12} - C_6(r_0 - r)^{-6} \quad (651)$$



Example: Orientational Correction Potential

- water droplet + soft-wall + implicit-solvent outside

- prevents solvent preferential orientation and inhomogeneous distribution at surface
- rather ad hoc and poorly transferable
 - specific to one continuum model, takes time to calibrate and has to be redone for different droplet sizes or solutes in the droplet especially if charged

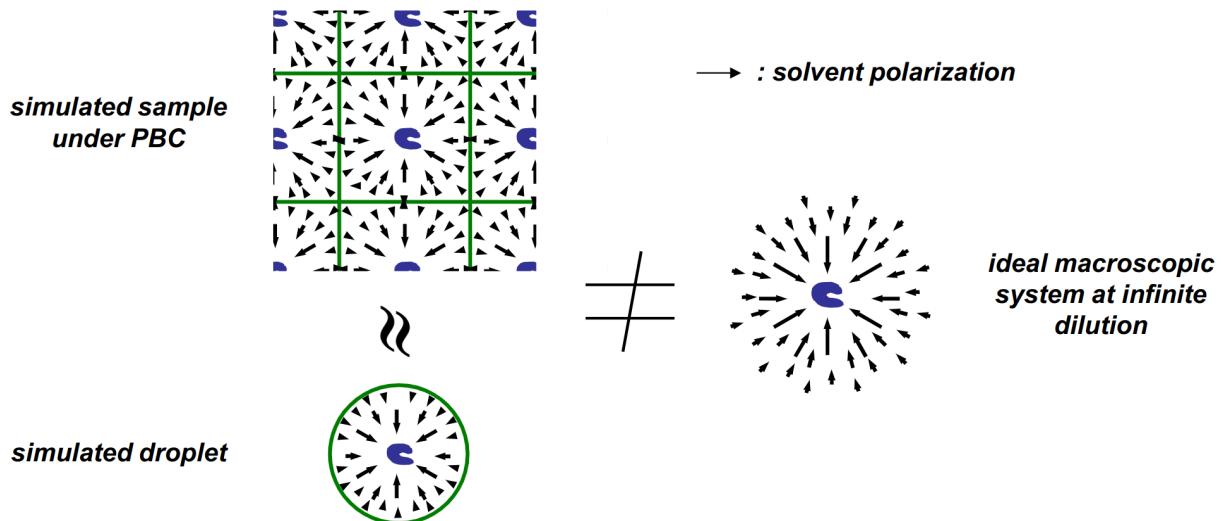


10.7.5. Periodic boundary conditions

- the most common choice for **explicit-solvent simulations** nowadays
- the simulated system (solute+solvent) mimics the **infinite lattice** of periodic copies of the reference box (pseudo-crystal)
 - consists of particles within a reference computational box of space-filling shape
 - at each simulation step, **particles exiting** the box through one face are **translated** so that they **reenter** the box through the opposing face

Periodic BC for Surface Effect

- probably the best remedy for surface effects
 - no interface to vacuum, the surface effects are entirely eliminated
- only a partial remedy for **finite-size effects** (effects dominated by long-range electrostatic interactions)

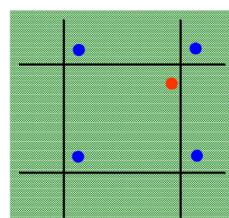


10.7.5.1. Common Box Shapes (space-filling)

- only particle coordinates in the reference box are stored in the computer

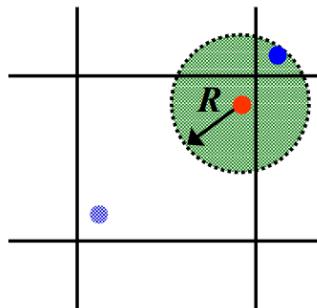
Interaction Evaluation

- each particle in the reference box has non-bonded interactions with all other particles that are in the reference box and all their replicas in the periodic system
 - interaction evaluated using lattice-sum methods (Fourier series)



Evaluation with Cutoff Distance R

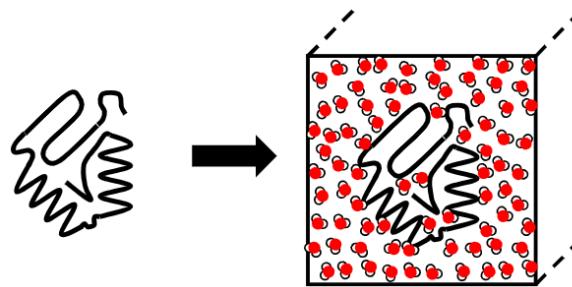
- interactions evaluated using a double sum over particles with a distance smaller than R
- R in general smaller than the half box edge to select a **subset** of the **minimum-image pairs**
 - e.g. **covalent interactions** are **short-ranged** and only act between minimum images



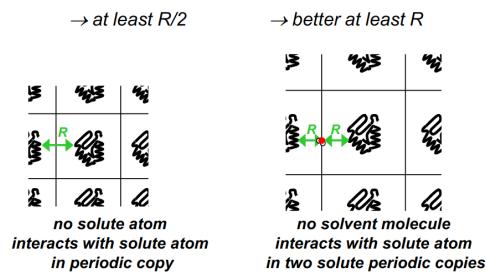
minimum-image pair: atom and the closest periodic replica of another one

1. RECTANGULAR PRISM	<ul style="list-style-type: none"> • FOR ELONGATED MACRO-MOLECULES • WATCH OUT IF THE MOLECULE ROTATES BY FIXING TRANSLATIONAL CONSTRAINTS
2. Hexagonal Prism	idem (may be used for DNA)
3. Cube	isotropic, but requires a lot of solvent
4. Truncated Octahedron	almost isotropic, and requires less solvent ($\sim 20\%$ less) for spherical molecules
5. Triclinic	for crystal simulations and more recently for implementing any (optimal) box shape into a single simulation code

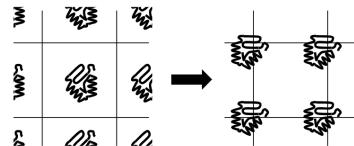
Example: Solvating a Macromolecule



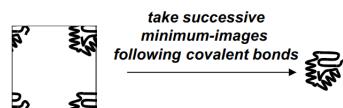
- minimum distance solute-to-wall should be chosen large enough



- since macromolecules may drift in the periodic system, one needs to restore the covalent connectivity before applying analyses



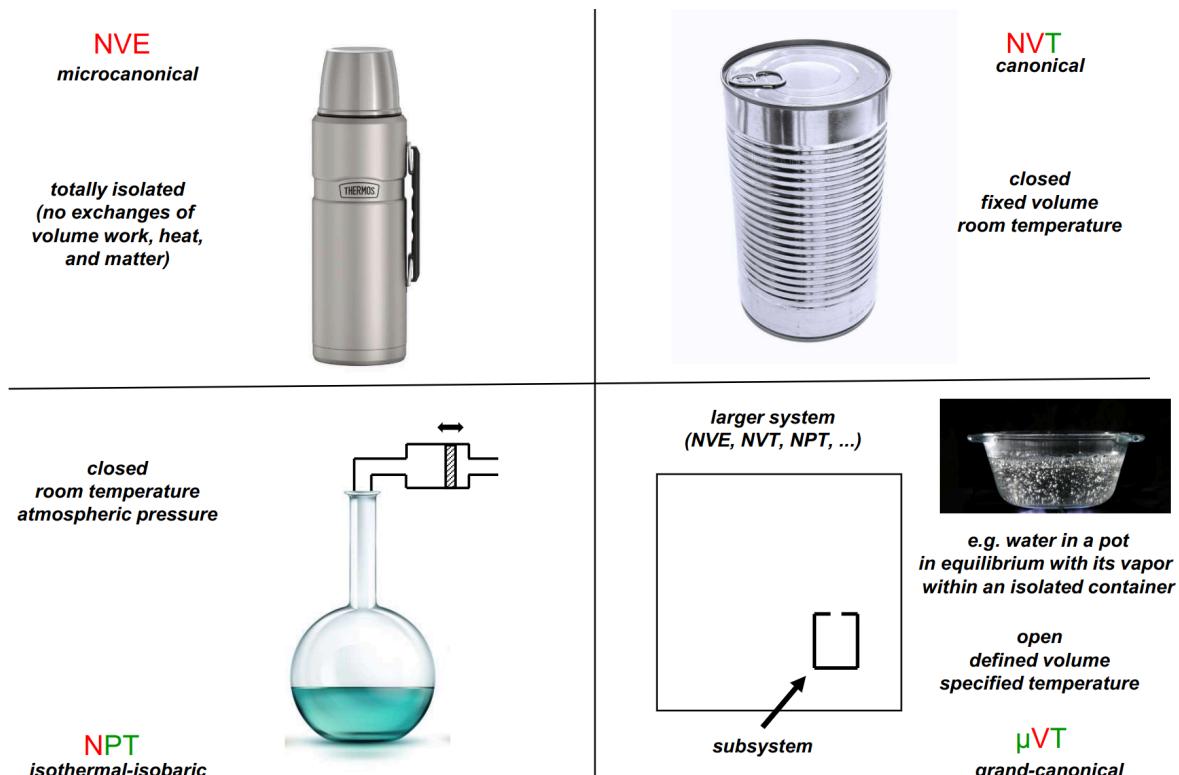
resolved by



10.8. Thermodynamic Boundary Conditions

- Main ensembles and characteristics (summary)

thermodynamic boundary conditions	ensemble (name, independent variables)	fluctuate	experiment	simulation (example of methods)
	NVE microcanonical		isolated system (uncommon)	<ul style="list-style-type: none"> plain MD MC + "ergostat"
	NVT canonical	E	closed system + thermostat (e.g. ambient T) + rigid container (more common)	<ul style="list-style-type: none"> MD + thermostat MC SD
	NPT isothermal-isobaric (Gibbs)	V,E	closed system + thermostat (e.g. ambient T) + barostat (e.g. atmospheric P) (most common)	<ul style="list-style-type: none"> MD + thermostat + barostat MC + barostat SD + barostat
	μ VT grand-canonical	N,E	open system + thermostat (e.g. ambient T) + fixed volume (also very common)	<ul style="list-style-type: none"> grand-canonical MD + thermostat grand-canonical MC



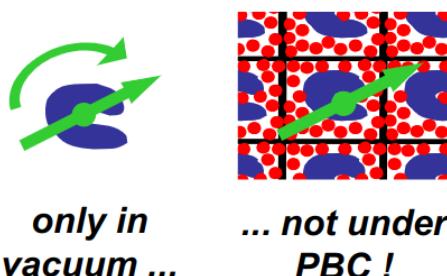
10.8.1. Plain (Newtonian) Molecular Dynamics

- plain MD follows the **Newtonian equations** of motion
- it samples the **microcanonical ensemble**
 - independent parameters** N, V, E_{tot} that are constant (zero fluctuations) and specified at simulation start.
The energy is specified via the starting coordinate (\rightarrow potential energy) and velocities (\rightarrow kinetic energy)
 - conserved quantities** E_{tot} , total linear momentum p_{tot} , and total angular momentum L_{tot}
 - Note: they may still drift due to numerical noise in the computation!
 - dependent quantities** T, P that are calculated as ensemble averages, and they have non-zero fluctuations for finite-systems

$$\begin{aligned} T &= \langle \mathcal{T} \rangle \\ P &= \langle \mathcal{P} \rangle \end{aligned} \tag{652}$$

Example: Conservation of the Total Angular Momentum

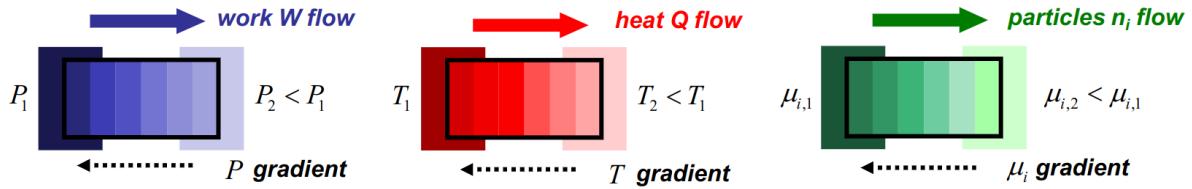
- for conservation of L_{tot}



10.8.2. Thermostating/barostating: Motivation

we need **temperature or pressure control** when

- performing simulations in NVT, NPT or μ VT ensembles
- studying T- or P-dependent properties/processes
 - e.g. processes such as phase or conformational transitions
- studying non-equilibrium processes



Controlling the temperature allows us to

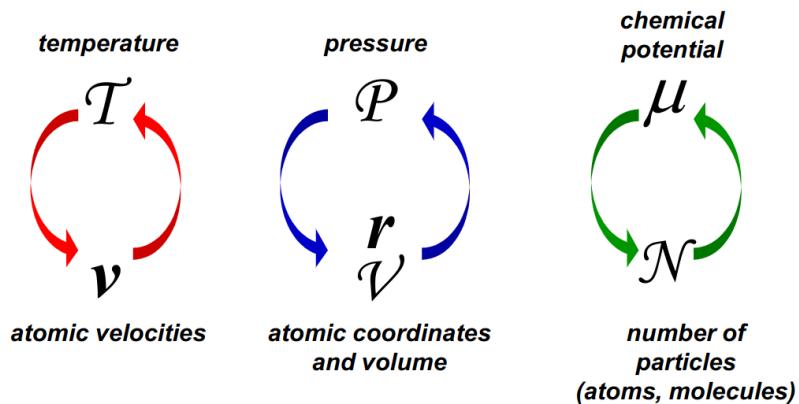
- stabilize the energy
- enhance conformational searches

Thermal BC should in principle be **soft** such that P and T have **non-negligible fluctuations** in microscopic systems

10.8.3. Thermostating/barostating: Basic Principle

The desirable mechanism should be a **negative-feedback mechanism**

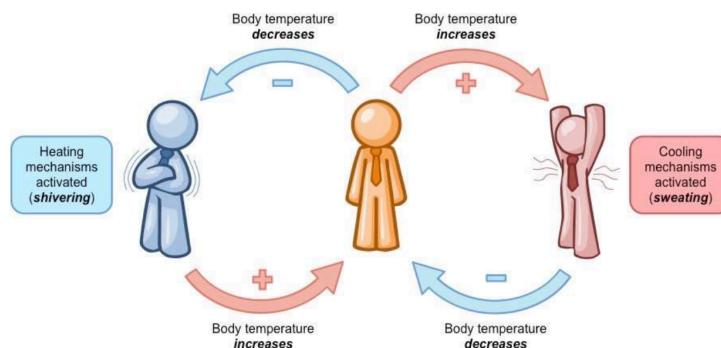
- variable to monitor instantaneous observables
- variable to adjust
 - configurational variable of the system



- various algorithms...

Example: A negative-feedback mechanism for body temperature

- to keep an intensive quantity (e.g. P, T, μ constant on average)



10.8.4. Instantaneous temperature

$$\mathcal{T} = \frac{2}{N_D k_B} \cdot \mathcal{K} \quad (653)$$

At equilibrium it holds that

$$\langle \mathcal{T} \rangle = T \quad (654)$$

in **three dimensions**, in the absence of **constraints** and **uncoupled dofs**. we consider the entire system consisting of N atoms and have

$$N_D = 3N \quad (655)$$

Interpretation

- does not fluctuate as much as pressure (temperature fluctuations in the order of ~ 10 K)
- the above definition holds for a system at equilibrium at temperature T . In which the **equipartition theorem** states that the average kinetic energy per degree of freedom is related to the **macroscopic temperature** as
- for one dof α (e.g. x, y, z Catesian dof of one atom)

$$\langle \mathcal{K}_\alpha \rangle = \left\langle \frac{1}{2} m_\alpha \nu_\alpha^2 \right\rangle = \frac{k_B T}{2} \quad (656)$$

- for a set of dofs, where \mathcal{N}_D is the number of degrees of freedom

$$\langle \mathcal{K} \rangle = \frac{\mathcal{N}_D k_B T}{2} \quad (657)$$

10.8.5. Instantaneous pressure

$$\mathcal{P} = \frac{2(\mathcal{K} - \mathcal{W})}{3V} = \frac{Nk_B T}{V} - \frac{2\mathcal{W}}{3V} \quad (658)$$

The **instantaneous isotropic virial** (GROMOS definition) of the system, considering all forces between the particles

$$\mathcal{W} = -\frac{1}{2} \sum_{i=1}^N \mathbf{r}_i \cdot \mathbf{F}_i \quad (659)$$

At equilibrium

$$\begin{aligned} \langle \mathcal{P} \rangle &= P \\ \Rightarrow P &= \left\langle \frac{2(\mathcal{K} - \mathcal{W})}{3V} \right\rangle \\ &= \underbrace{\frac{Nk_B T}{V}}_{\substack{\text{ideal gas} \\ \text{contribution} \\ \text{kinetic energy}}} - \underbrace{\left\langle \frac{2\mathcal{W}}{3V} \right\rangle}_{\substack{\text{intermolecular} \\ \text{forces}}} \end{aligned} \quad (660)$$

for the contribution from intermolecular forces it holds that

$$\begin{cases} \text{attractive} \rightarrow \text{pull inwards} \rightarrow W > 0 \Rightarrow P \downarrow \\ \text{repulsive} \rightarrow \text{pull outwards} \rightarrow W < 0 \Rightarrow P \uparrow \end{cases} \quad (661)$$

Interpretation

- the pressure is a highly fluctuating quantity (1 bar pressure fluctuations in the order of ~ 100 bar)
 - ▶ because the kinetic energy wants to expand the box and the virial wants to shrink the box
 - ▶ needs long simulations for a precise averaging
- above holds for a system at equilibrium at temperature P . From the **virial theorem**, we know that each dof contributes to the **isotropic macroscopic pressure** of the **entire system** with $\mathcal{N}_D = 3N$ as

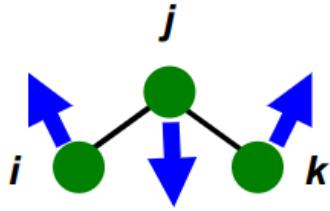
$$\left\langle \frac{2(\mathcal{K}_\alpha - \mathcal{W}_\alpha)}{3V} \right\rangle = \left\langle \frac{m_\alpha \nu_\alpha^2 + r_\alpha F_\alpha}{3V} \right\rangle \quad (662)$$

it implies that the pressure for the entire system is

$$\mathcal{P} = \left\langle \frac{2(\mathcal{K} - \mathcal{W})}{3V} \right\rangle \quad (663)$$

- the same equation can be used under **periodic BC**, but one has to select the right periodic images for the coordinates
 - ▶ covalent terms: gather the atoms by applying periodic shifts

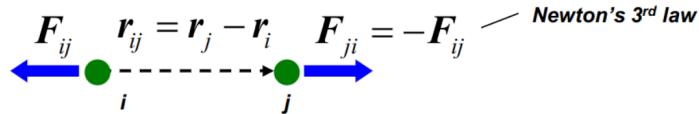
$$W_{ijk} = -\frac{1}{2} (\mathbf{r}_i \cdot \mathbf{F}_i + \mathbf{r}_j \cdot \mathbf{F}_j + \mathbf{r}_k \cdot \mathbf{F}_k) \quad (664)$$



- non-bonded minimum-image pairwise (e.g. bond-angle bending term)

$$\begin{aligned}
 W_{ij} &= -\frac{1}{2} \sum_i^N \sum_{j \neq i}^N \mathbf{r}_i \cdot \mathbf{F}_{ij} \\
 &= -\frac{1}{4} \sum_i^N \sum_{j \neq i}^N [\mathbf{r}_i \cdot \mathbf{F}_{ij} + \mathbf{r}_j \cdot \mathbf{F}_{ji}] \\
 &= \frac{1}{4} \sum_i^N \sum_{j \neq i}^N \mathbf{r}_{ij} \cdot \mathbf{F}_{ij} \\
 &= \frac{1}{2} \sum_i^N \sum_{j > i}^N \mathbf{r}_{ij} \cdot \mathbf{F}_{ij}
 \end{aligned} \tag{665}$$

e.g. repulsive as drawn $\rightarrow W < 0 \Rightarrow P \uparrow$



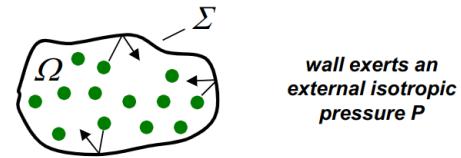
- constraint forces also have a virial contribution and can be calculated from the SHAKE Lagrange multipliers
Derivation skipped

• Derivation: the **virial theorem**

→ Consider a **finite system at equilibrium** that is bounded by a **confinement wall**

→ **Dynamical virial** definition

$$Q = \sum_{i=1}^N m_i \mathbf{r}_i \cdot \dot{\mathbf{r}}_i \quad \xrightarrow{\text{time derivative}} \quad \dot{Q} = 2(\mathcal{K} - \mathcal{W}^{tot})$$



because

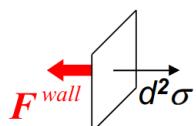
$$\left[\begin{array}{l} \mathcal{K} = \frac{1}{2} \sum_{i=1}^N m_i \dot{\mathbf{r}}_i^2 \\ \mathcal{W}^{tot} = -\frac{1}{2} \sum_{i=1}^N m_i \mathbf{r}_i \cdot \ddot{\mathbf{r}}_i = -\frac{1}{2} \sum_{i=1}^N \mathbf{r}_i \cdot \mathbf{F}_i^{tot} \end{array} \right] \begin{array}{l} \text{between particles} \\ + \text{from the wall} \end{array} \quad \begin{array}{l} \text{Newton} \end{array}$$

→ **Virial theorem**

$$\langle \dot{Q} \rangle = \lim_{t \rightarrow \infty} \frac{1}{t} \int_0^t dt \dot{Q}(t) = \lim_{t \rightarrow \infty} \frac{Q(t) - Q(0)}{t} = 0 \quad \begin{array}{l} \text{because } Q \text{ is always finite} \\ \rightarrow \text{coordinates are bounded to system volume} \\ \rightarrow \text{velocities are bounded by temperature} \end{array}$$

use long-time average to calculate ensemble average (ergodicity)

→ Virial of the **wall forces**



$d^3\omega$: volume element
 $d^2\sigma$: surface element

$$\begin{aligned}
 \langle \mathcal{W}^{wall} \rangle &= -\frac{1}{2} \sum_{n=1}^N \mathbf{r}_i \cdot \mathbf{F}_i^{wall} = \frac{1}{2} P \int_{\Sigma} d^2\sigma(\mathbf{r}) \cdot \mathbf{r} \\
 &= \frac{1}{2} P \int_{\Omega} d^3\omega(\mathbf{r}) \nabla \cdot \mathbf{r} = \frac{3}{2} P \langle \mathcal{V} \rangle
 \end{aligned}$$

divergence (Gauss) theorem

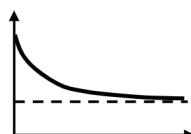
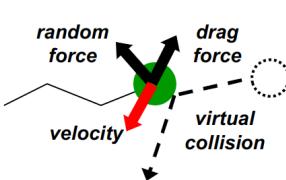
between particles
from the wall

$$\mathcal{W}^{tot} = \mathcal{W} + \mathcal{W}^{wall}$$

$$\rightarrow \langle \mathcal{W} \rangle = \left\langle \mathcal{K} - \frac{3}{2} P \mathcal{V} \right\rangle$$

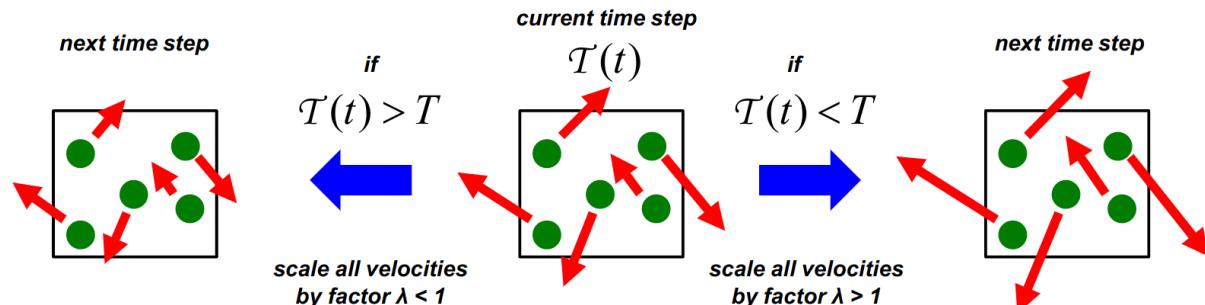
10.8.6. Thermostating/Barostating Algorithms

- common algorithms explained with thermostating

ALGORITHMS	ADVANTAGES	DISADVANTAGES
1. Constraining methods ▶ fix quantity exactly to target value with no fluctuations at all	▶ Hamiltonian form ▶ correct configuration distribution	▶ no fluctuations in temperature and kinetic energy (unphysical)
2. Weak-coupling methods ▶ relax quantity exponentially (1st order) towards target value	first-order exponential relaxation (physical)	ensemble depends on τ_T (only approximately canonical)
 3. Extended system methods ▶ relax quantity via extra variable (2nd order) around target value	correct ensemble (canonical)	second-order oscillatory relaxation (unphysical)
 4. Stochastic methods ▶ relax quantity using stochastic variables ▶ recommended if one only cares about the thermodynamics but not the dynamics	▶ correct ensemble (canonical) ▶ first-order exponential relaxation (physical) ▶ very efficient thermalization & few artifacts (very robust)	▶ non-deterministic (no constant of motion) ▶ “local” thermostating (unphysical dynamics)
		

10.8.7. Thermostating

Working principle by velocity scaling



Equations of motion

- isokinetic, closed, isochoric

$$\begin{aligned}
 \dot{\mathcal{N}} &= 0 \\
 \dot{\mathbf{r}} &= \nabla_{\mathbf{p}} \mathcal{K} \\
 \dot{\mathbf{p}} &= -\nabla_{\mathbf{r}} \mathcal{U} - \zeta_T \mathbf{p} \\
 \dot{\mathcal{V}} &= 0
 \end{aligned} \tag{666}$$

10.8.7.1. Temperature Constraining

In **temperature constraining**, we have $\zeta_T = \frac{-\nabla_r \mathcal{U} \cdot \nabla_p \mathcal{K}}{2K}$ as the effective friction coefficient, with the numerator showing the “tendency” of the forces to increase the kinetic energy

$$-\nabla_r \mathcal{U} \cdot \nabla_p \mathcal{K} = \mathbf{F} \cdot \dot{\mathbf{r}} \quad (667)$$

- if \mathbf{F} would increase, \mathcal{K} brakes particles
- if \mathbf{F} would decrease, \mathcal{K} accelerates particles

Lemma. kinetic energy stays constant at K if we start with $\mathcal{K}(0) = K$

- Proof

$$\begin{aligned} \dot{\mathcal{K}} &= \frac{d}{dt} \left(\frac{1}{2} \mathbf{p} \cdot \mathbf{M}^{-1} \mathbf{p} \right) \\ &= \dot{\mathbf{p}} \cdot \mathbf{M}^{-1} \mathbf{p} \\ &= -\nabla_r \mathcal{U} \cdot \nabla_p \mathcal{K} - \zeta_T \mathbf{p} \cdot \nabla_p \mathcal{K} \\ &= -\nabla_r \mathcal{U} \cdot \nabla_p \mathcal{K} \left(1 - \frac{\mathcal{K}}{K} \right) \\ &= 0 \end{aligned} \quad (668)$$

Practical Implementation

- leap-frog, velocity scaling

Given $\mathcal{K}(t - \frac{\Delta}{2}) = K$, the leap is

$$\mathbf{v}\left(t + \frac{\Delta}{2}\right) = \mathbf{v}\left(t - \frac{\Delta}{2}\right) + \mathbf{M}^{-1} \mathbf{F}(t) \Delta \quad (669)$$

to calculate $\mathcal{K}(t + \frac{\Delta}{2})$ while ensure the kinetic energy equals K after scaling, we perform the velocity scaling by scaling the calculated $\mathbf{v}(t + \frac{\Delta}{2})$ by the factor λ , where

$$\lambda := \left[\frac{\mathcal{K}(t - \frac{\Delta}{2})}{\mathcal{K}(t + \frac{\Delta}{2})} \right]^{\frac{1}{2}} \quad (670)$$

or using an alternative definition

$$\lambda := \left[\frac{K}{\mathcal{K}(t + \frac{\Delta}{2})} \right]^{\frac{1}{2}} \quad (671)$$

Interpretation

- correct canonical distribution of coordinates
- but incorrect (zero) temperature fluctuations
- one needs to remove one dof for the constraint when calculating T

10.8.7.2. Weak-Coupling (Berendsen) Thermostat

Consider the same equations of motion with a different effective friction coefficient defined as

$$\zeta_T = \frac{1}{2\tau_T} \frac{\mathcal{K} - K}{\mathcal{K}} \quad (672)$$

where τ_T is the thermostat coupling time

- if $\mathcal{K} > K$, brakes particles in proportion to the relative difference
- if $\mathcal{K} < K$, accelerates particles in proportion to the relative difference

Lemma. Given ideal-gas, the temperature **relaxes exponentially** towards its target

- Proof. since $\mathcal{U} = 0$ (?)

$$\begin{aligned} \dot{\mathcal{K}} &= \frac{d}{dt} \left(\frac{1}{2} \mathbf{p} \cdot \mathbf{M}^{-1} \mathbf{p} \right) \\ &= \dot{\mathbf{p}} \cdot \mathbf{M}^{-1} \mathbf{p} \\ &= -\zeta_T \mathbf{p} \cdot \nabla_p \mathcal{K} \\ &= -2\mathcal{K}\zeta_T \\ &= -\frac{1}{\tau_T} (\mathcal{K} - K) \end{aligned} \quad (673)$$

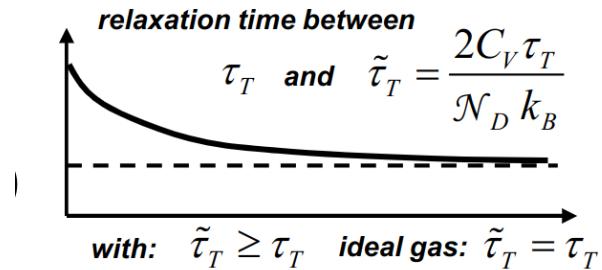
Example: Realistic relaxation time

- for long coupling times, the relaxation may be slower as the energy added/removed also redistributes to the potential energy
 - with $C_V = \left(\frac{\partial E}{\partial T}\right)_V$ it holds that

$$\dot{\mathcal{T}} \approx -\frac{1}{C_V \tau_T} \cdot (\mathcal{K} - K) \quad (674)$$

which then implies

$$\dot{K} \approx -\frac{\mathcal{N}_D k_B}{2C_V \tau_T} (\mathcal{K} - K) \quad (675)$$

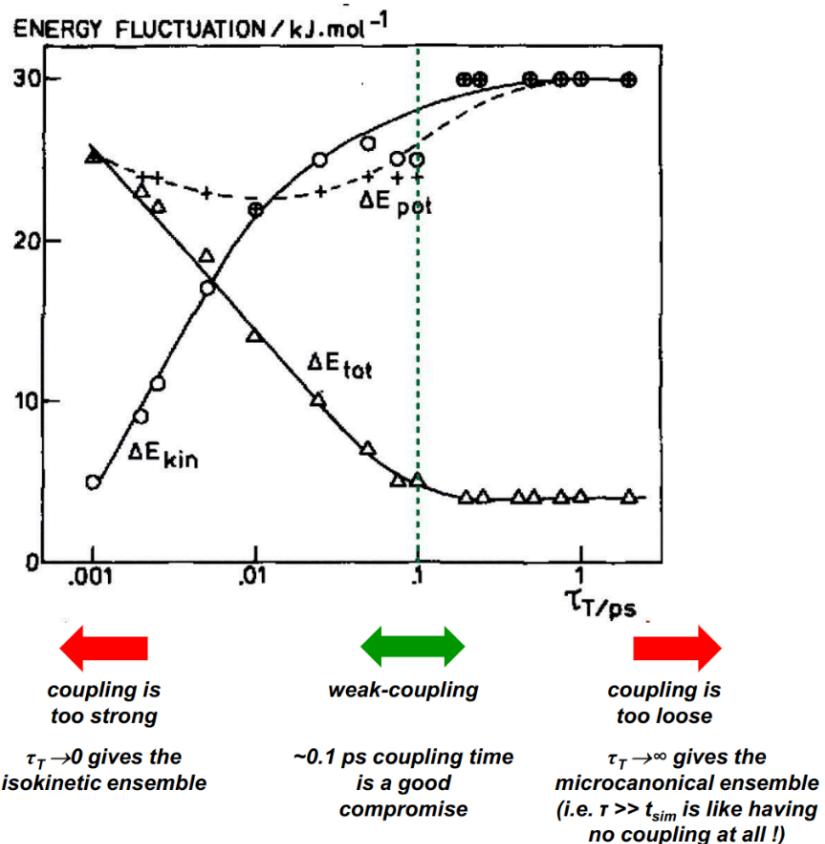


Interpretation

- properties depend on C_V and τ_T
 - ▶ configuration probability distribution is not rigorously canonical
 - ▶ temperature fluctuations are present but not rigorously correct
 - temperature relaxation dynamics is exponential and matches physical phenomenon

Effect of Coupling Strength

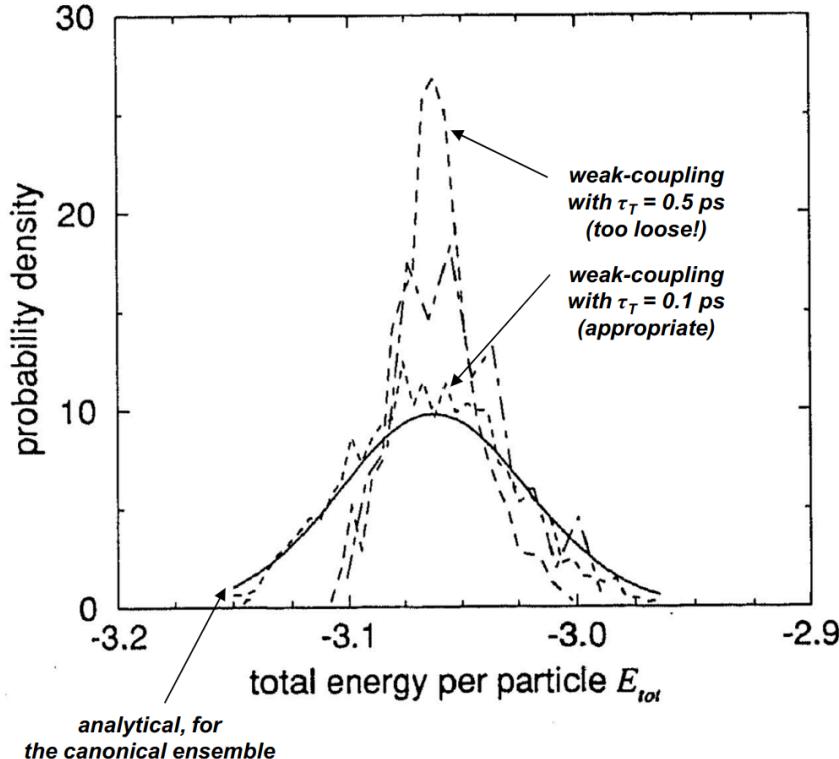
- Fluctuations of the kinetic, potential and total energies in simulations of water
 - desired sufficiently fast equilibration available
 - generally good enough but not rigorous



- Energy fluctuations of the total energy per particle in simulations of a Lennard-Jones fluid

- here the LJ reduced units are used ($N = 216$, $T = 1.3$, $C_V = 15.8$)

$$\begin{aligned}\sigma_E^2 &= \langle E^2 \rangle - \langle E \rangle^2 = \beta^{-1} C_V T \\ \Rightarrow \sigma_{\frac{E}{N}}^2 &= N^{-2} \beta^{-1} C_V T \text{ energy per particle}\end{aligned}\quad (676)$$



10.8.7.3. Extended-System (Nosé-Hoover) Thermostat

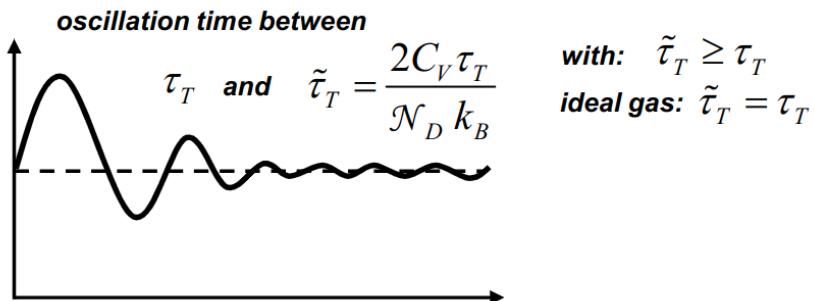
Now we have the effective friction coefficient as an extra variable in the dynamics with its own equation of motion

$$\dot{\zeta}_T = \frac{1}{\tau_T^2} \left(\frac{\mathcal{K}}{K} - 1 \right) \quad (677)$$

where τ_T is the thermostat coupling time and ζ_T is the thermostat variable in the units of time $^{-1}$

- if $\mathcal{K} > K$, friction is increased, brakes particles in proportion to the relative difference
- if $\mathcal{K} < K$, friction is decreased, accelerates particles in proportion to the relative difference

Lemma. In an ideal-gas the temperature relaxes with damped oscillations towards its target



Interpretation

- configuration probability distribution is canonical
- temperature fluctuations are present but not correct
- temperature relaxation dynamics is oscillatory, which is not very physical

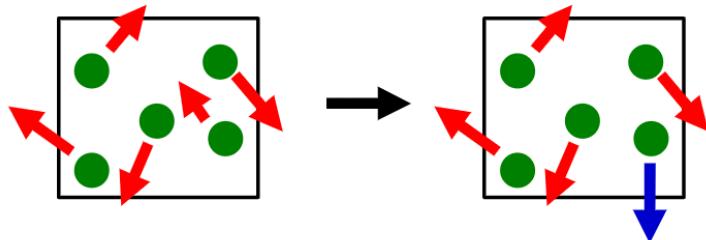
10.8.7.4. Stochastic Thermostats

- non-deterministic
- dynamics is heavily perturbed

- local thermostating not physical in terms of dynamics
- the collision thermostat does not even have continuous velocity trajectory
- needs many random numbers
 - watch out for possible series correlations in the random-number generator!
- leads to exponential temperature relaxation (physically ok)
- is efficient and homogeneous thermostating (very robust)

Collision Thermostat within every τ_T period

- pick an atom at random
- reassign its velocity at random from a Maxwell-Boltzmann distribution at T_{ref}
- results in $\langle T \rangle = T_{\text{ref}}$



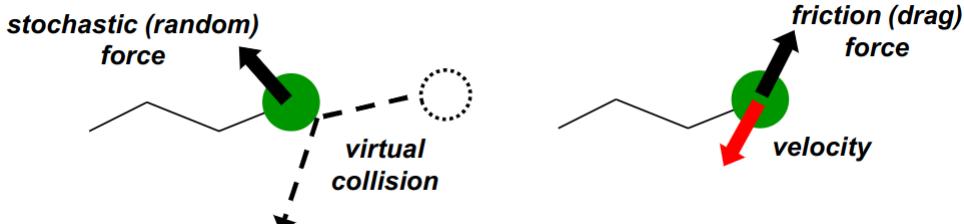
Langevin Thermostat

Recall the Langevin equation of motion

$$m_i \ddot{\mathbf{r}}_i = \mathbf{F}_i(\mathbf{r}(t)) + \mathbf{R}_i(t) - m_i \gamma_i \dot{\mathbf{r}}_i(t) \quad (678)$$

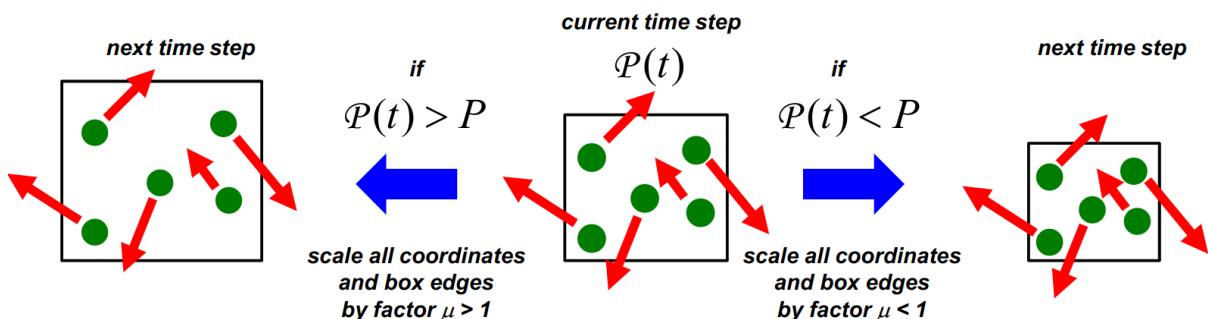
and results in

$$\langle T \rangle = \frac{\langle R_i^2 \rangle}{6m_i \gamma_i k_B} = T_{\text{ref}} \quad (679)$$



10.8.8. Barostating

Working principle by isotropic coordinate/box scaling



Equations of motion

$$\begin{aligned} \dot{\mathcal{N}} &= 0 \\ \dot{\mathbf{r}} &= \nabla_p \mathcal{K} + \underline{\chi} \mathbf{r} \\ \dot{\mathbf{p}} &= -\nabla_r \mathcal{U} - \underline{\chi} \mathbf{p} \\ \dot{\mathcal{V}} &= 3\underline{\mathcal{V}}\underline{\chi} \end{aligned} \quad (680)$$

10.8.8.1. Pressure Constraining

- difficulty lies in the calculation of the **virial derivative**
 - in essence boils down to calculate the instantaneous compressibility

Expression needs to be solved to obtain χ

$$\begin{aligned} 3P\dot{\mathcal{V}} &= 9P\mathcal{V}\chi \\ &= 2(\dot{\mathcal{K}} - \dot{\mathcal{W}}) \\ &= 2 \sum_{i=1}^N \frac{\mathbf{p}_i \cdot \dot{\mathbf{p}}_i}{m_i} + \sum_{i=1}^N (\dot{\mathbf{r}}_i \cdot \mathbf{F}_i + \dot{\mathbf{r}}_i \cdot \mathbf{F}_i) \end{aligned} \quad (681)$$

where the intermediate steps resulted from the virial theorem stating

$$\begin{aligned} P &= \left\langle \frac{2(\mathcal{K} - \mathcal{W})}{3\mathcal{V}} \right\rangle \\ \mathcal{K} &= \sum_{i=1}^N \frac{\mathbf{p}_i^2}{2m_i} \\ \mathcal{W} &= -\frac{1}{2} \sum_{i=1}^N \mathbf{r}_i \cdot \mathbf{F}_i \end{aligned} \quad (682)$$

10.8.8.2. Weak Coupling

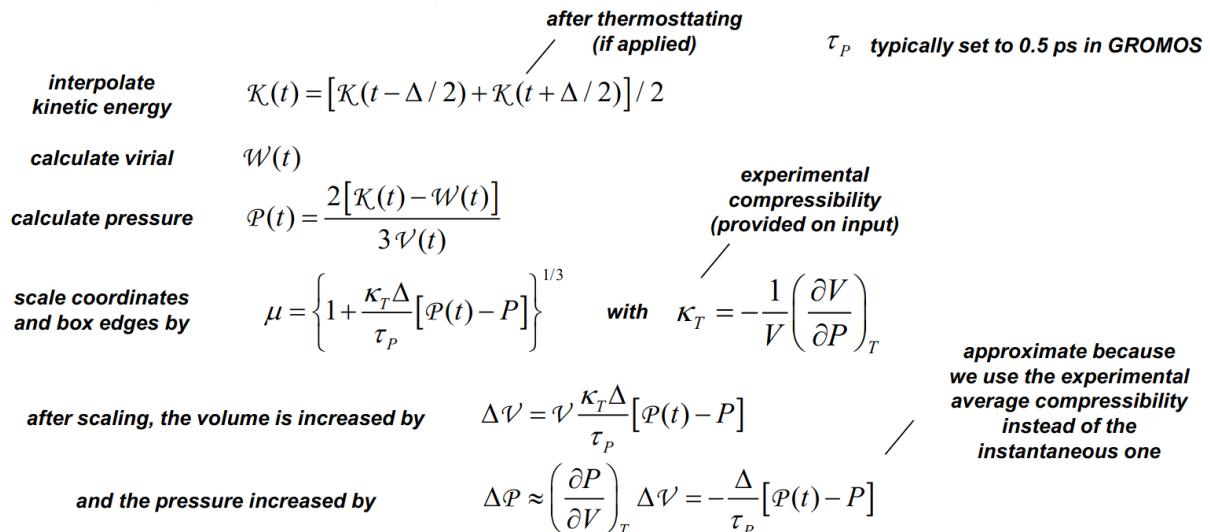
Equations of motion are modified to

$$\begin{aligned} \dot{\mathcal{N}} &= 0 \\ \dot{\mathbf{r}} &= \nabla_{\mathbf{p}} \mathcal{K} + \frac{1}{3\mathcal{V}} \dot{\mathcal{V}} \mathbf{r} \\ \dot{\mathbf{p}} &= -\nabla_{\mathbf{r}} \mathcal{U} \\ \dot{\mathcal{V}} &= \frac{\kappa_T}{\tau_P} (\mathcal{P} - P) \mathcal{V} \end{aligned} \quad (683)$$

this corresponds to an exponential relaxation of the volume

Practical Implementation

- leap-frog, GROMOS



10.8.8.3. Extended-System Coupling

- volume as an additional dof in the dynamics where \mathcal{V} is the volume variable and M_V the mass of the volume variable

Lagrangian of the extended system

$$\begin{aligned}\mathcal{L} &= \mathcal{K} - \mathcal{U} \\ &= \mathcal{L}_{\text{phys}} + \frac{1}{2} M_V \dot{V}^2 - P\mathcal{V}\end{aligned}\tag{684}$$

where the added kinetic energy and the added potential energy are

$$\begin{aligned}\mathcal{K}_V &= \frac{1}{2} M_V \dot{V}^2 \\ \mathcal{U}_V &= P\mathcal{V}\end{aligned}\tag{685}$$

with simplification of the Lagrangian equations of motion

$$\begin{aligned}\dot{\mathcal{N}} &= 0 \\ \dot{\mathbf{r}} &= \nabla_{\mathbf{p}} \mathcal{K} + \frac{1}{3} \frac{\dot{\mathcal{V}}}{\mathcal{V}} \mathbf{r} \\ \dot{\mathbf{p}} &= -\nabla_{\mathbf{r}} \mathcal{U} - \frac{1}{3} \frac{\dot{\mathcal{V}}}{\mathcal{V}} \mathbf{p} \\ \ddot{\mathcal{V}} &= W^{-1}(\mathcal{P} - P)\end{aligned}\tag{686}$$

where W is the parameter determining the coupling strength and P is the reference pressure of the barostat

Interpretation

- Parrinello-Rahman: anisotropic variant enabling the deformation of the box
- second-order method which correct ensemble but spurious oscillations

10.8.8.4. Stochastic Methods

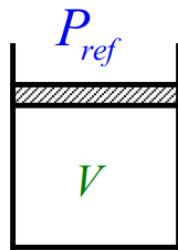
Langevin Barostat (Langevin piston)

- Equations of motion

$$\begin{aligned}\dot{\mathcal{N}} &= 0 \\ \dot{\mathbf{r}} &= \nabla_{\mathbf{p}} \mathcal{K} + \frac{1}{3} \frac{\dot{\mathcal{V}}}{\mathcal{V}} \mathbf{r} \\ \dot{\mathbf{p}} &= -\nabla_{\mathbf{r}} \mathcal{U} - \frac{1}{3} \frac{\dot{\mathcal{V}}}{\mathcal{V}} \mathbf{p} \\ \ddot{\mathcal{V}} &= W^{-1}(\mathcal{P} - P) - \underline{\gamma \dot{\mathcal{V}}} + R(t)\end{aligned}\tag{687}$$

where it holds that

$$\langle R(0)R(t) \rangle = \frac{2\gamma k_B T \delta(t)}{W}\tag{688}$$



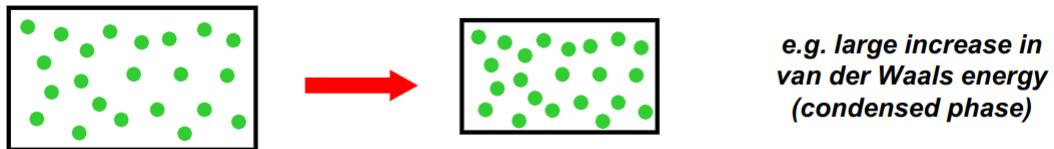
10.8.9. Selection of coupling times

for simultaneous barostating and thermostating

- thermostating should occur faster than the barostating
 - otherwise it would cause unphysically large fluctuations of temperature and consequently of all properties in the system

Example: Berendsen thermostat

- barostating through scaling provokes large changes in the potential energy
- partial conversion from E_{pot} to E_{kin} occurs on a very short timescale
- it must hold that $\tau_T < \tau_P$, where the typical values for weak coupling are $\tau_T \approx 0.1\text{ps}$ and $\tau_P \approx 0.5\text{ps}$

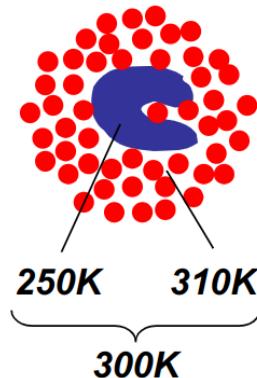


10.8.10. Violation: Equipartition

- when the temperature is heterogeneous, we have the equipartition violations, with two types of issues

1. Hot-solvent/Cold-solvent issue

- heterogeneous between different regions of the system



Interpretation

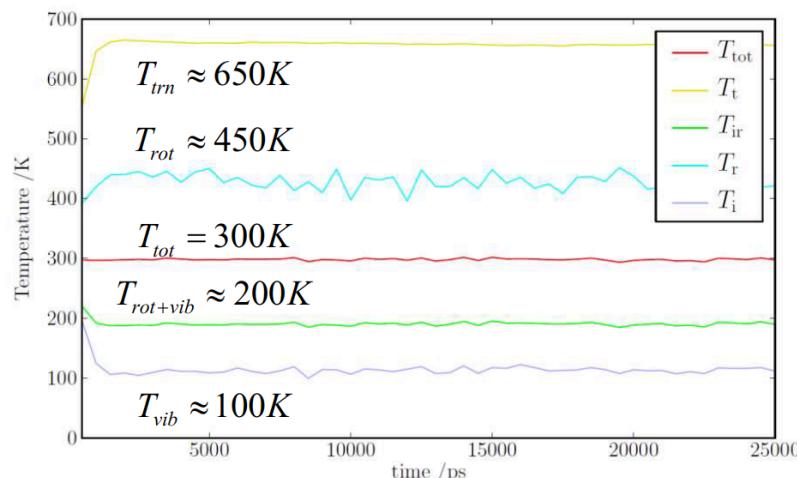
- The **solvent** is often subject to **more heating** (cutoff noise) than the solute, but the kinetic energy may **exchange slowly** between them
- Problem:** When using only one thermostat, the average system temperature may be correct, but the solute is simulated to be colder than the solvent which is not physical.
- Fix:** couple solute and solvent dof to **separate thermostats**

2. vibrationally-cold Gas Issue

- heterogeneous between different types of degrees of freedoms

Interpretation

- The **translation**, **rotation** and **vibration** modes coupled to the same thermostat should have **different temperatures** (different noise rates) in an **ideal gas**.
- Fix:** couple different modes to **separate thermostats** or use a **stochastic** one



MD of 512 molecules far apart (25 ns), joint thermostat coupling of translation, rotation and vibration

10.8.11. Violation: Uncoupled DOF Entered the Calculation

- **uncoupled dof** such as the system total linear or angular momentum can store arbitrary kinetic energies and should **not** enter the calculation of the temperature and pressure

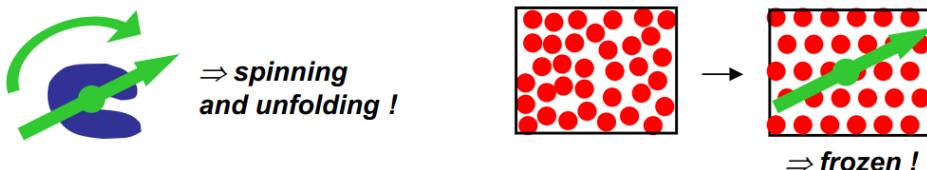
Example: Linear momentum has no effect on the system properties

- A glass of water that moves is not warmer than the one sitting on the table

Example: Angular momentum has no effect on the system properties

- e.g. centrifugal forces shall not be accounted

Flying Ice-Cube Issues



10.9. Grand-canonical sampling

Grand-canonical sampling are MD simulations where

- the no. particles \mathcal{N} in the system can vary
- the chemical potential μ is held constant (on average)

Disadvantages

- the no. particles varies and this is often unavailable in common simulation codes
- the variation is discrete and creates jumps in the dynamics
 - equilibration required after each jump
- the variable to monitor is a chemical potential μ , which is not an instantaneous observable

Recall: Chemical potential

- change of free energy upon adding a new particle

$$\mu = \frac{\partial F}{\partial N} \quad (689)$$

where the free energy is defined as

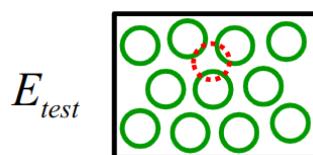
$$F = -\beta^{-1} \ln Z \quad (690)$$

Beutler-van-Gunsteren Weak-coupling Algorithm

- The chemical potential in excess to the ideal gas is estimated over a simulation period at constant N

$$\mu^{\text{ex}} = -\beta^{-1} \ln(\langle e^{-\beta E_{\text{test}}} \rangle)_N \quad (691)$$

where E_{test} is the energy for inserting a new particle at random position



The no. particles is possibly adjusted according to a weak-coupling expression

$$\frac{d\mathcal{N}(t)}{dt} = \text{round}\{\alpha_N [e^{-\beta\mu^{\text{ex}}} - e^{-\beta\mu_0^{\text{ex}}}] \} \quad (692)$$

where $\alpha_N \in \mathbb{R}^+$ is the coupling time and μ_0^{ex} is the reference excess chemical potential for which sit holds that

$$\begin{cases} \mu^{\text{ex}} > \mu_0^{\text{ex}} \Rightarrow \frac{dN}{dt} < 0 \rightarrow \text{tendency to lose particles} \\ \mu^{\text{ex}} < \mu_0^{\text{ex}} \Rightarrow \frac{dN}{dt} > 0 \rightarrow \text{tendency to gain particles} \end{cases} \quad (693)$$

And each adjustment is followed by an **equilibration period**

11. Monte Carlo Sampling & Stochastic Dynamics

11.1. Monte Carlo Sampling

- **stochastic methods** are methods where random numbers used in problem solving, MC sampling is a type of stochastic method used to sample a large configuration space
- **Importance Sampling** as a type of MC sampling is commonly used
 - **Motivation:** when performing uniform sampling with Boltzmann weighting, many configurations with high energy sampled do **not** contribute due to Boltzmann weighting used
 - inefficient and thus in importance sampling we sample directly in proportion to the Boltzmann weight

11.2. Markov Chain and Equilibrium Population

Markov Chain

- A system can exist in a **finite** no. of N states where any given instance of this system can **hop randomly** and **iteratively** from state to state.

The **transition probabilities** T_{mn} (from m to n) only depend on the **initial** and **final** state of the hop but not the history, with the normalization

$$\sum_m^N T_{mn} = 1, \forall n \quad (694)$$

Markov chain of states for a single system Assume we start from some state n , we select a new state m at random with

- the stochastic matrix $\underline{\alpha} := \{\alpha_{mn} \mid m, n = 1, \dots, N\}$ where $\alpha_{mn}(m \neq n)$ is the probability of selecting state m for a $n \rightarrow m$ transition attempt from state n , and $\alpha_{nn} = 0$
- the acceptance matrix $\underline{a} := \{a_{mn} \mid m, n = 1, \dots, N\}$ gives the probability of a transition attempt to be accepted

This generates a Markov chain with

$$\begin{cases} T_{mn} = \alpha_{mn} a_{mn} & \text{if } m \neq n \\ T_{nn} = 1 - \sum_{m \neq n}^N T_{mn} & \text{else} \end{cases} \quad (695)$$

11.2.1. Metropolis Monte Carlo Scheme

- in MD when people say “Monte Carlo sampling”, they often refer to “Metropolis sampling”

Markov chain of states with Boltzmann sampling (Metropolis)

- using a symmetric stochastic matrix $\alpha_{mn} = \alpha_{nm}$
- with the acceptance matrix a_{mn} defined as

$$a_{mn} = \begin{cases} 1 & \text{if } V_m \leq V_N \\ \exp\{-\beta(V_m - V_N)\} & \text{else} \end{cases} \quad (696)$$

Proof Using the microscopic reversibility, it holds for $n \neq m$ that

$$\frac{p_m}{p_n} = \frac{T_{mn}}{T_{nm}} = \frac{\alpha_{mn}}{\alpha_{nm}} \cdot \frac{a_{mn}}{a_{nm}} = \frac{a_{mn}}{a_{nm}} = \exp\{-\beta(V_m - V_N)\} \quad (697)$$

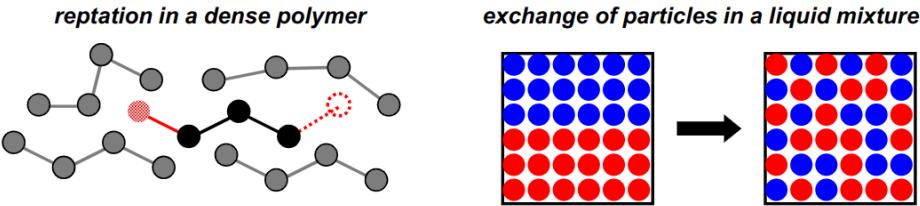
11.3. The Monte Carlo Method

Advantages

- a Boltzmann-weighted ensemble of configurations is generated that is canonical or NVT ensemble, so that thermodynamic observables can be computed with X being the macroscopic observable and x the corresponding microscopic observable

$$X = \langle x(\mathbf{r}) \rangle = \frac{1}{N_{\text{steps}}} \sum_{k=1}^{N_{\text{steps}}} x(\mathbf{r}(k)) \quad (698)$$

- easily extended to other isothermal ensembles (NPT, pVT, ...)
- no need for derivatives of the potential energy function for force calculation
 - simpler implementation
 - computationally less expensive
 - applicable to discontinuous potential energy functions
- efficient unphysical (but reversible) moves can be designed for improved sampling



Disadvantages

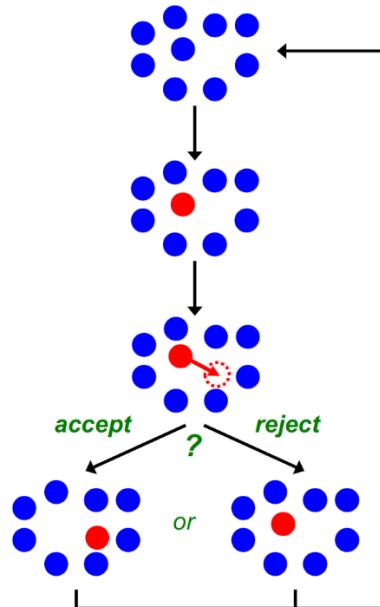
- non-deterministic
- no dynamic information
- the design of a reasonable acceptance ratio may be difficult for some systems (e.g. macromolecules)

11.3.1. Monte-Carlo Method Algorithm

```

1: FUNCTION MC_SAMPLING(A, N, V)
2:   ▷ Start at configuration  $r(0)$ 
3:   while  $k \leq N_{\text{steps}}$  do
4:     Select an atom  $i$  at random
5:      $i \leftarrow \text{int}[N \text{ rand}(0, 1) + 1]$ 
6:     Attempt a move for this atom  $r_i(k) \rightarrow r'_i(k)$ 
7:      $x'_i \leftarrow x_i + [2 \text{ rand}(0, 1) - 1] \cdot \Delta r$ 
8:      $y'_i \leftarrow y_i + [2 \text{ rand}(0, 1) - 1] \cdot \Delta r$ 
9:      $z'_i \leftarrow z_i + [2 \text{ rand}(0, 1) - 1] \cdot \Delta r$ 
10:    if  $V' = V[r'(k)] < V = V[r(k)]$  then
11:       $r(k+1) \leftarrow r'(k)$  accept
12:    else if  $\text{rand}(0, 1) \leq \exp\{-\beta(V' - V)\}$  then
13:       $r(k+1) \leftarrow r'(k)$  accept
14:    else
15:       $r(k+1) \leftarrow r(k)$  reject

```



Choice of the Step Size Δr

- too large \rightarrow small acceptance ratio (ideal ratio $\sim 50\%$)
- too small \rightarrow slow sampling

General Case: Moves for rigid molecules

- e.g. for molecular liquids
- 4 maximal displacement parameters $\Delta r, \Delta\alpha, \Delta(\cos\beta), \Delta\gamma$ optimizable

Special Case: Moves for flexible molecules

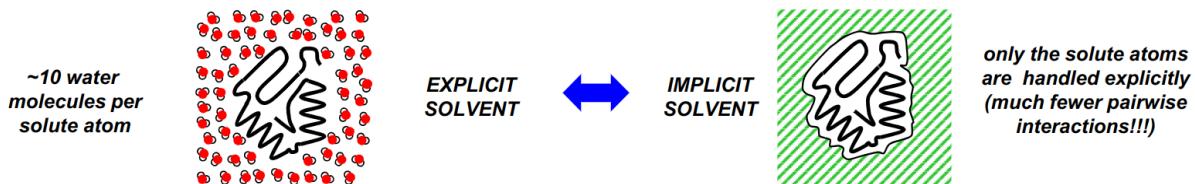
- random translation of the center of mass or the random rotation about the center of mass

11.4. Stochastic Dynamics (SD)

- **Motivation:** in MD, solvent has effect on the solute and need to be taken into account to obtain the correct thermodynamics for conformation and binding and dynamics across timescales
 - but simulating (macro)molecules in solution with an **explicit solvent** representation is **expensive**
- **Stochastic Dynamics** aims to mimic following effects **without** including the expensive solvent molecules **explicitly**, it samples a canonical (NVT) ensemble at a temperature T . The configurational sampling depends on T but not on the specific values of γ and σ .

1. Mean solvent effect \Rightarrow affects the thermodynamics

$$\left\{ \begin{array}{l} 2. \text{ Stochastic collisions} \\ 3. \text{ Frictional drag} \end{array} \right. \Rightarrow \text{affects the dynamics} \quad (699)$$

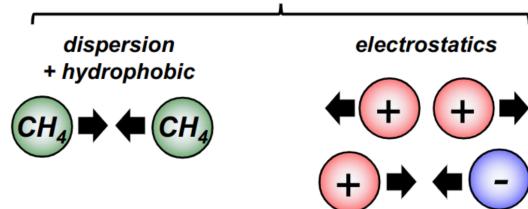


- Applications of SD are
 - commonly implicit-solvent simulation uses SD and explicit solvent uses MD
 - one can use SD as a robust thermostat in explicit-solvent simulation
 - use SD to simulate molecules in vacuum can avoid quasi-periodic motions and problems with poor translational/rotational/vibrational coupling (e.g. to calculate vaporization enthalpies)

11.4.1. Effects of Solvent

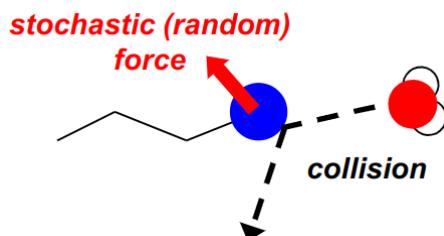
1. Mean solvent effect

- on the left the dispersive attraction is slightly reduced in non-polar solvent, and largely enhanced in polar solvents like water (hydrophobic effect)
- on the right Coulombic interactions are weakened by the solvent dipoles (dielectric screening, e.g. by a factor 80 for water!)



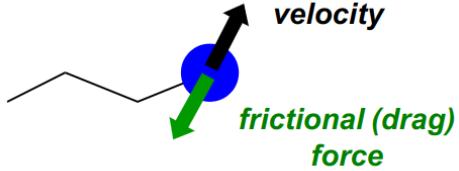
2. Stochastic collisions

- kicks by the solvent molecules on the solute atoms induce random forces (but this randomness still obeys some constraints!)



3. Frictional drag

- friction by the solvent molecules on the solute atoms reduces their velocities



11.4.2. The Langevin Equation

- the equation of motion for SD that accounts for all three effects
- stochastic differential equation (SDE) of second order with a first-order term

$$m_i \ddot{\mathbf{r}}_i = \underbrace{\mathbf{F}_i^{\sim}}_{\text{systematic force}} - \underbrace{m_i \gamma_i \dot{\mathbf{r}}_i}_{\text{frictional force}} + \underbrace{\sigma_i \boldsymbol{\eta}_i}_{\text{stochastic force}} \quad (700)$$

where $\boldsymbol{\eta}_i = \boldsymbol{\eta}_i(t)$ is the white-noise vector distributed using Gaussian in unit of time $^{-\frac{1}{2}}$, $\mathbf{F}_i^{\sim} = \mathbf{F}_i^{\sim}(\mathbf{r}(t))$ the systematic force vector.

Often one assume that the friction coefficient (unit time $^{-1}$) and the stochastic force amplitude σ_i (unit: force \times time $^{\frac{1}{2}}$) are identical for all atoms and independent of space and time

Formal Solution of the Langevin Equation

- w.l.o.g. in 1D the Langevin equation can be written in terms of the **velocity** as an inhomogeneous first-order SDE

$$m \frac{dv}{dt} = F - m\gamma v + \sigma \eta \quad (701)$$

Solution in 1D

$$v(t) = e^{-\gamma t} \left[v(0) + m^{-1} \int_0^t dt' \cdot e^{\gamma t'} (F(t') + \sigma \eta(t')) \right] \quad (702)$$

Verification by direct differentiation

It must hold that

$$\frac{dv}{dt} = -\gamma v + \frac{1}{m} (F + \sigma \eta) \quad (703)$$

We differentiate the solution above

$$\begin{aligned} \frac{dv}{dt} &= -\gamma \cdot e^{-\gamma t} \underbrace{\left[v(0) + m^{-1} \int_0^t dt' \cdot e^{\gamma t'} (F(t') + \sigma \eta(t')) \right]}_{v(t)} + \\ &\quad e^{-\gamma t} \frac{d}{dt} \left[v(0) + m^{-1} \int_0^t dt' \cdot e^{\gamma t'} (F(t') + \sigma \eta(t')) \right] \\ &= -\gamma \cdot v(t) + e^{-\gamma t} m^{-1} \cdot e^{\gamma t} (F(t) + \sigma \eta(t)) \\ &= -\gamma \cdot v(t) + m^{-1} \cdot (F(t) + \sigma \eta(t)) \end{aligned} \quad (704)$$

which matches the desired expression ■

Limit Cases of the Langevin Equation

- Zero-friction/zero-kick limit ($\gamma = 0, \sigma = 0$) corresponds to the Newton equation of MD
- High-friction limit corresponds to Brownian Dynamics

Interpretation of the Langevin Equation

- we can break the Langevin equation into parts and understand it

$$m_i \ddot{\mathbf{r}}_i = \underbrace{\mathbf{F}_i^{\sim}}_{\text{systematic force}} - \underbrace{m_i \gamma_i \dot{\mathbf{r}}_i}_{\text{frictional force}} + \underbrace{\sigma_i \boldsymbol{\eta}_i}_{\text{stochastic force}} \quad (705)$$

1. Mean force

- must incorporate the mean effect of the omitted solvent
- we define the **potential of mean force (PMF)** V^{\sim}

- if one instead takes the normal force field for explicit-solvent simulations without adding implicit-solvent terms, the results are wrong
- PMF are hard to construct/parameterize because the models are rather empirical and results often not accurate

$$\mathbf{F}_i^{\sim}(\mathbf{r}) = -\frac{\partial V^{\sim}(\mathbf{r})}{\partial \mathbf{r}_i} \quad (706)$$

2. Frictional force

- friction coefficient γ_i may depend on the particle identity or the position, but is often kept **constant**
- the value of γ for a solvent may be estimated by applying the Einstein equation of the Stokes law for a spherical solvent
- i). Einstein equation
- with D the diffusion coefficient

$$m\gamma = \frac{k_B T}{D} \quad (707)$$

ii). Stokes equation

- where a is the radius

$$m\gamma = 6\pi\eta a \quad (708)$$

3. Stochastic force

- the force coefficient σ_i may depend on the particle identity or position but is often kept as a **constant**

Steady-state balance of the frictional & stochastic forces the choice of σ is connected to the choice of γ via the temperature T . The following two effects balance each other at a specific temperature

- frictional forces dissipate** energy
- stochastic forces introduce** energy

$$T = \frac{\sigma^2}{2mk_B\gamma} \quad (709)$$

Choice of γ and T

- γ and T are used as input parameters
- one has free choice over γ , where it influences the dynamics of the system in which one tune between a low vs high frictional damping, but it does **not** effect the thermodynamics of the system! It is **always a canonical ensemble**.

11.4.3. Brownian Dynamics

- a first-order SDE that is valid in the **microscopic regime** with low Reynolds numbers where the viscosity dominates turbulent flow
 - i.e. for small objects, water is very “viscous”

$$m_i\gamma_i\ddot{\mathbf{r}}_i = \mathbf{F}_i^{\sim} + \sigma_i\boldsymbol{\eta}_i \quad (710)$$

Derivation from the Langevin equation

$$\begin{aligned} m_i\ddot{\mathbf{r}}_i &= \mathbf{F}_i^{\sim} - m_i\gamma_i\dot{\mathbf{r}}_i + \sigma_i\boldsymbol{\eta}_i \\ \Leftrightarrow m_i\gamma_i\dot{\mathbf{r}}_i &= \mathbf{F}_i^{\sim} + \sigma_i\boldsymbol{\eta}_i \end{aligned} \quad (711)$$

we neglect inertial term by setting the RHS to zero at the limit where $|m_i\ddot{\mathbf{r}}_i| \ll |m_i\gamma_i\dot{\mathbf{r}}_i|$

11.4.4. The Fokker-Plank Equation (FP)

- a statistical perspective on the time evolution

FP Equation

with the differentiation applies to the full product is denoted as

$$(\hat{O}B \times)C = \hat{O}(BC) \quad (712)$$

we define the Fokker-Plank equation (FP)

$$\dot{p}(x, t) = \left(-\frac{\partial}{\partial x} A(x, t) \times + \frac{1}{2} \frac{\partial^2}{\partial x^2} B^2(x, t) \times \right) p(x, t) \quad (713)$$

where the SDE used is

$$\dot{x}(t) = A(x, t) + B(x, t)\eta(t) \quad (714)$$

FP Equation for Brownian Dynamics (BD)

$$\dot{p}(x, t) = \left(-\frac{1}{m\gamma} \frac{\partial}{\partial x} \underbrace{F(x, t)}_{\text{drift term}} \times + D \frac{\partial^2}{\partial x^2} \times \right) p(x, t) \quad (715)$$

with the diffusion constant with units $\frac{\text{length}^2}{\text{time}}$ defined as

$$D := \frac{1}{2} \left(\frac{\sigma}{m\gamma} \right)^2 \quad (716)$$

where the SDE for BD is

$$m\gamma\dot{x} = F + \sigma\eta \quad (717)$$

Connection between γ, σ and T

$$\sigma^2 = 2\beta^{-1}m\gamma \quad (718)$$

Derivation

- Starting from the FPE for BD

$$\dot{p}(x, t) = \left(-\frac{1}{m\gamma} \frac{\partial}{\partial x} F(x, t) \times + D \frac{\partial^2}{\partial x^2} \times \right) p(x, t) \quad (719)$$

At equilibrium where $\dot{p}(x, t) = 0$ and $\tilde{p}(x) \sim e^{-\beta V(x)}$ hold it follows that

$$\begin{aligned} \dot{p}(x, t) &= \left(-\frac{1}{m\gamma} \frac{\partial}{\partial x} F(x, t) \times + D \frac{\partial^2}{\partial x^2} \times \right) e^{-\beta V(x)} \stackrel{!}{=} 0 \\ &\Rightarrow \frac{\partial}{\partial x} \times \underbrace{\left[\left(-\frac{1}{m\gamma} \frac{\partial}{\partial x} F(x, t) \times + D \frac{\partial}{\partial x} \times \right) e^{-\beta V} \right]}_{\text{flux of systems}} \stackrel{!}{=} 0 \\ &\Rightarrow \left(-\frac{1}{m\gamma} F(x, t) + D \frac{\partial}{\partial x} \times \right) e^{-\beta V} \stackrel{!}{=} 0 \quad (\star) \end{aligned} \quad (720)$$

We now solve the equation (\star) for σ

$$D \frac{\partial}{\partial x} e^{-\beta V} = \frac{1}{m\gamma} F e^{-\beta V} \quad (721)$$

for the LHS it we apply the chain rule, and use $F = -\frac{dV}{dx}$

$$D \frac{\partial}{\partial x} e^{-\beta V} = D \left(\frac{\partial}{\partial V} e^{-\beta V} \cdot \frac{\partial V}{\partial x} \right) = -D((-\beta)e^{-\beta V} \cdot F) = D(\beta e^{-\beta V} \cdot F) \quad (722)$$

plugging the LHS back to the equation (\star)

$$\underline{D\beta F e^{-\beta V}} = \frac{1}{m\gamma} F e^{-\beta V} \quad (723)$$

we use the definition of the diffusion coefficient $D := \frac{1}{2} \left(\frac{\sigma}{m\gamma} \right)^2$ which implies that

$$\begin{aligned} D\beta &\stackrel{!}{=} \frac{1}{m\gamma} \\ \Leftrightarrow \frac{1}{2} \left(\frac{\sigma}{m\gamma} \right)^2 \beta &= \frac{1}{m\gamma} \\ \Leftrightarrow \frac{\sigma^2}{(m\gamma)^2} &= \frac{2}{m\gamma\beta} \\ \Leftrightarrow \frac{\sigma^2}{m\gamma} &= \frac{2}{\beta} \\ \Leftrightarrow \sigma^2 &= 2\beta^{-1}m\gamma \end{aligned} \quad (724)$$

11.4.5. The Leap-Frog Integrator for SD

- Solution of the Langevin equations of motion

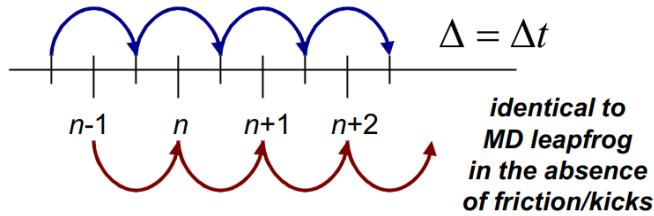
$$\begin{aligned} m \frac{dv}{dt} &= F - m\gamma v + \sigma \eta \\ \frac{dr}{dt} &= v \end{aligned} \tag{725}$$

with its formulation in 1D

$$\begin{aligned} v(t) &= e^{-\gamma(t-t_n)} \left[v(t_n) + m^{-1} \int_{t_n}^t dt' \cdot e^{\gamma(t_n-t')} (F(t') + \sigma \eta(t')) \right] \\ r(t) &= r(t_n) + \int_{t_n}^t dt' v(t') \end{aligned} \tag{726}$$

Leap-Frog Integrator

- We discretize using the leap-frog scheme



Leap-Frog velocity at half timestep

- we assume F to be constant over timestep, we incorporate the loss into the $O(\Delta^3)$ error

$$\begin{aligned} v\left(t_n + \frac{\Delta}{2}\right) &= e^{-\gamma\Delta} \cdot v\left(t_n - \frac{\Delta}{2}\right) + \frac{1 - e^{-\gamma\Delta}}{\gamma m} F(t_n) \\ &\quad + \frac{\sigma}{m} \left[\tilde{V}_n\left(\frac{\Delta}{2}\right) - e^{-\gamma\Delta} \tilde{V}_n\left(-\frac{\Delta}{2}\right) \right] + O(\Delta^3) \end{aligned} \tag{727}$$

with stochastic integral

$$\tilde{V}_n(\tau) := \int_{t_n}^{t_n+\tau} dt' \cdot e^{-\gamma(t_n+\tau-t')} \eta(t') \tag{728}$$

Leap-Frog coordinates at full timestep

$$\begin{aligned} r(t_n + \Delta) &= r(t_n) + \frac{e^{\frac{\gamma\Delta}{2}} - e^{-\frac{\gamma\Delta}{2}}}{\gamma} \cdot v\left(t_n + \frac{\Delta}{2}\right) \\ &\quad + \frac{\sigma}{m\gamma} \left[R_{n+\frac{1}{2}}\left(\frac{\Delta}{2}\right) - R_{n+\frac{1}{2}}\left(-\frac{\Delta}{2}\right) \right] + O(\Delta^3) \end{aligned} \tag{729}$$

with

$$r(t) = r\left(t_n + \frac{\Delta}{2}\right) + \int_{t_n+\frac{\Delta}{2}}^t dt' v(t') \tag{730}$$

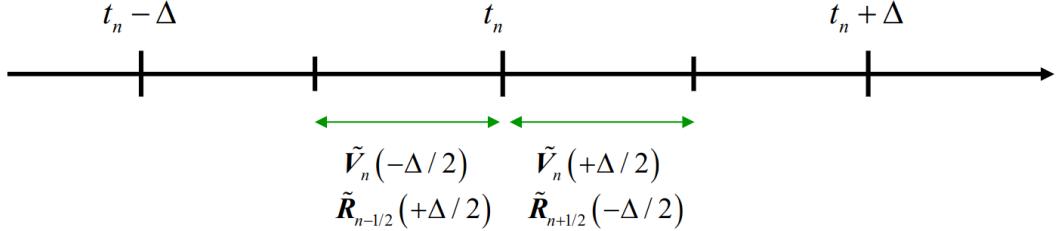
and the stochastic integral

$$\tilde{R}_{n+\frac{1}{2}}(\tau) := \int_{t_n+\frac{\Delta}{2}}^{t_n+\frac{\Delta}{2}+\tau} dt' \cdot \left(1 - e^{-\gamma(t_n+\frac{\Delta}{2}+\tau-t')}\right) \eta(t') \tag{731}$$

Stochastic Integrals

$$\begin{aligned} \tilde{V}_n(\tau) &= \int_{t_n}^{t_n+\tau} dt' \cdot e^{-\gamma(t_n+\tau-t')} \eta(t') \\ \tilde{R}_{n+\frac{1}{2}}(\tau) &= \int_{t_n+\frac{\Delta}{2}}^{t_n+\frac{\Delta}{2}+\tau} dt' \cdot \left(1 - e^{-\gamma(t_n+\frac{\Delta}{2}+\tau-t')}\right) \eta(t') \end{aligned} \tag{732}$$

Stochastic integrals are correlated by pairs



where the pairs obey bivariate Gaussian distributions

$$P\left(\tilde{R}_{n+\frac{1}{2}}, \tilde{V}_n\left(-\frac{\Delta}{2}\right)\right) \quad (733)$$

and

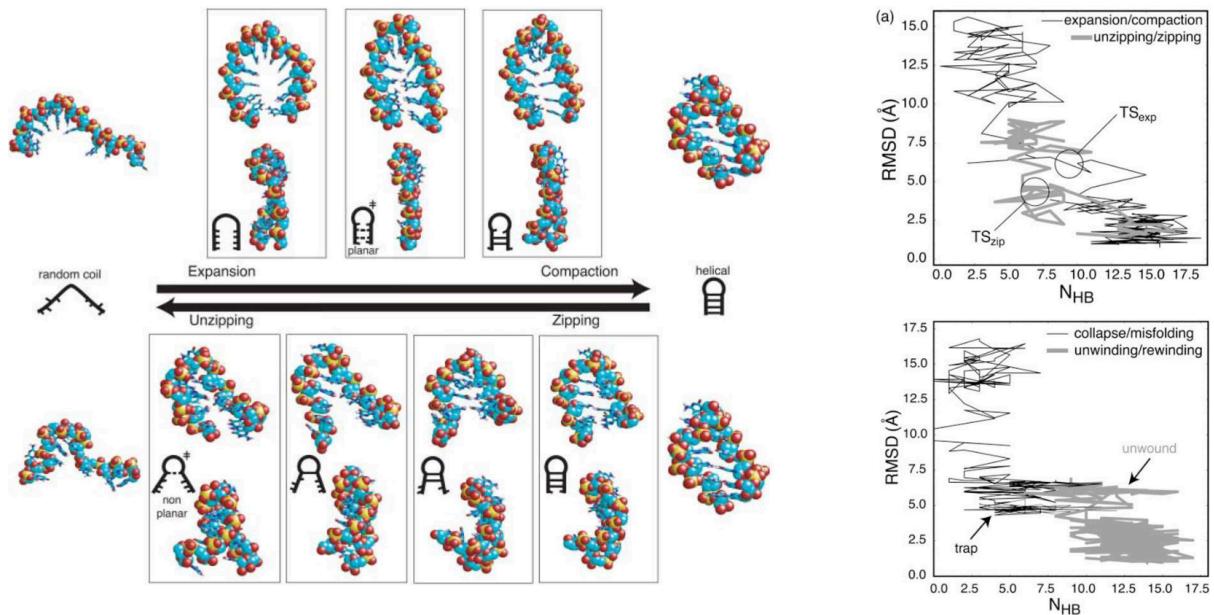
$$P\left(\tilde{R}_{n-\frac{1}{2}}, \tilde{V}_n\left(+\frac{\Delta}{2}\right)\right) \quad (734)$$

are drawn from a bivariate Gaussian distribution. In practice, this is done by having one and the other is sampled from the 1D conditional probability of the other.

Examples of SD Applications

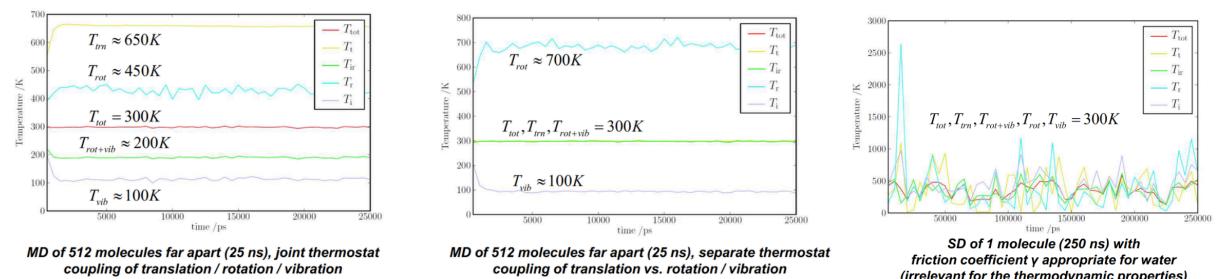
Example 1: RNA hairpin structures

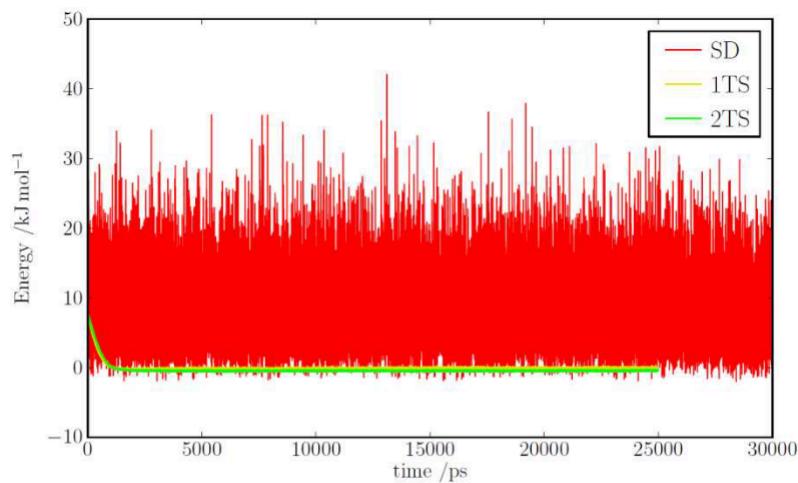
- using SD sampling with an implicit solvent model
- total simulation time over 400 μs



Example 2: Comparing 1-Thermostat, 2-Thermostat & SD

- for a test case of 1-butanol with separation of rot and vib approximated by fitting



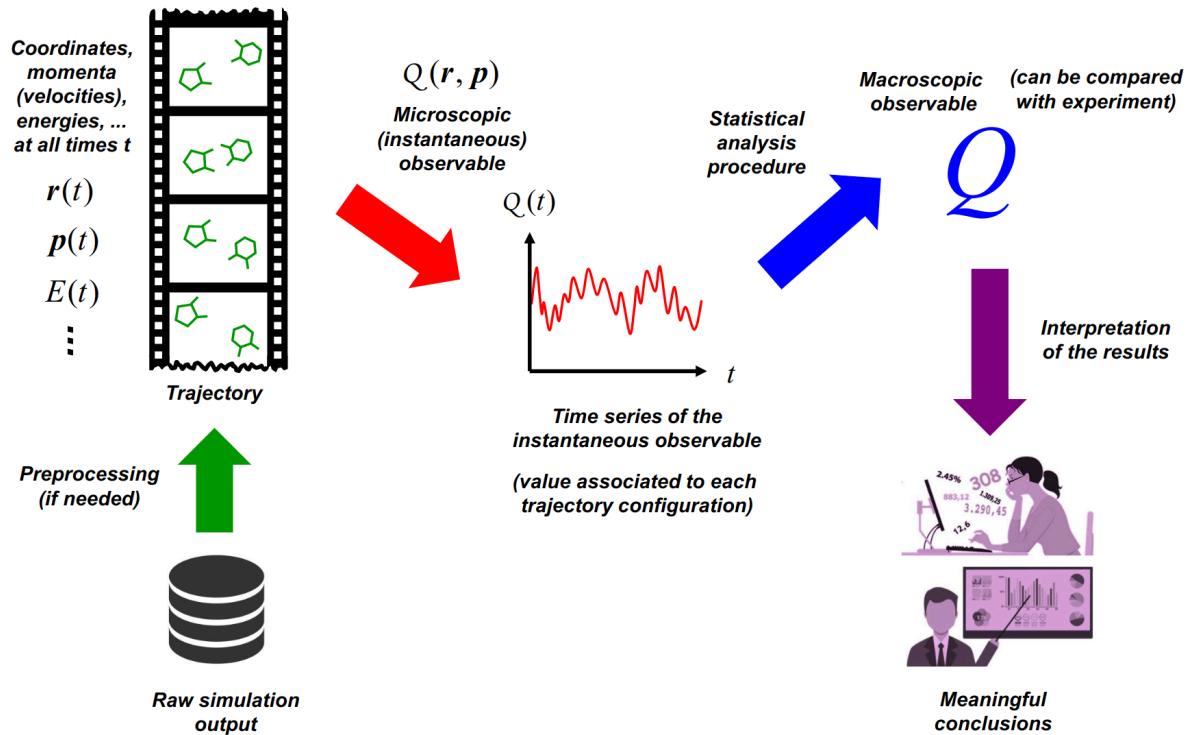


***Total potential energy is only correct with SD;
MD results may still be “about correct” if you start
at 300 K and simulate for a very short time***

12. Calculation of Properties from Simulations

Calculation of properties is a four-step process which consists of

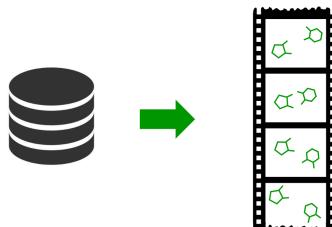
$$\left\{ \begin{array}{l} \text{Part I: Preprocessing of the raw simulation trajectories} \\ \text{Part II: Statistical analysis of time series} \\ \text{Part III: Types of properties that can be calculated} \\ \text{Part IV: Interpretation of simulation results} \end{array} \right. \quad (735)$$



12.1. Preprocessing

Preprocessing of the raw simulation trajectories is needed for calculation of specific structural observables

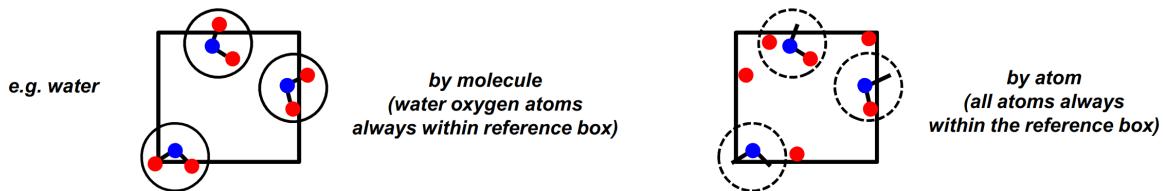
- periodic gathering (needed for all structural observables)
- roto-translational fitting (needed for comparing structures with each other)



12.1.1. Periodic Gathering

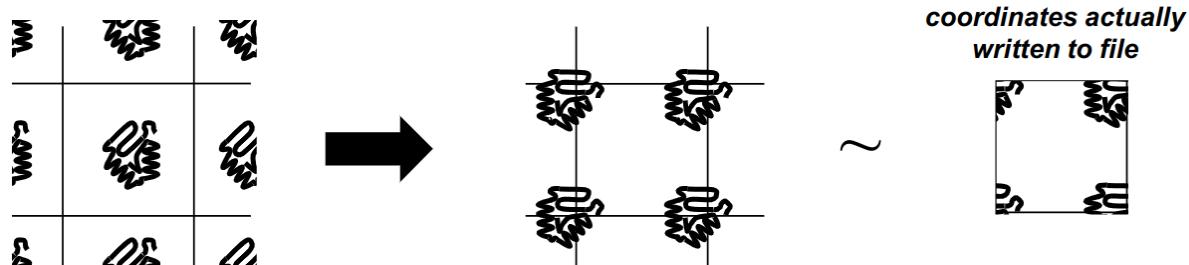
Periodic Boundary Conditions (PBC)

- by monitoring coordinates of **one periodic copy** of each particle, one simulate an **infinite periodic system**
 - no difference for the **momenta** (velocities)
 - for the coordinates, the restriction to a single copy in the output trajectory may be performed in different ways (e.g. by atoms, groups of molecules)



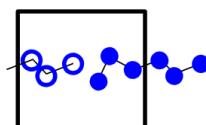
Periodic Gathering

- the trajectory of a molecule that is initially \ll gathered \gg may fail to remain so along time



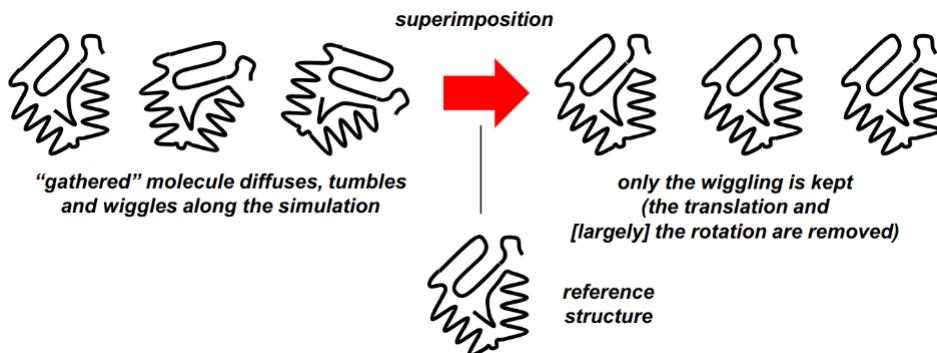
Approach 1: gather by following the covalent connectivity of the molecules

- pick a first (reference) atom that will always remain in the reference box and follow along bonds
- disadvantage: situations with multiple solute (macro-)molecules are not always obvious!



12.1.2. Roto-Translational Least-Squares Fitting

- Motivation: for observables of molecular structures, gathering is not sufficient
- compare **Cartesian coordinates**, but with the effect of the **translational** and **rotational diffusion** removed
- Disadvantage:
 - results may depend on the choice of the reference structure and of a subset of fitting atoms
 - rotational motion cannot be decoupled from the wiggling in an entirely strict fashion



Algorithm For each new structure, minimize

$$X = \sum_{i=1}^N [(C + Tr_i) - r_{i,\text{ref}}]^2 \quad (736)$$

with respect to

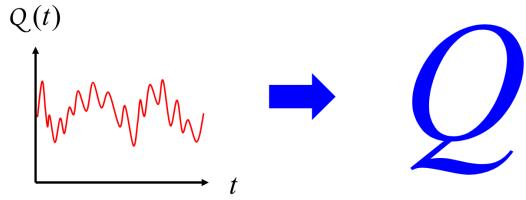
$$\begin{cases} C \text{ translation vector} \\ T \text{ rotation matrix} \end{cases} \quad (737)$$

12.2. Statistical Analysis

Following statistical analyses can be made based on the simulation results

- Time series

2. Distributions
3. Statistical moments
4. Fluctuation correlations
5. Time correlations
6. Occurrences and visiting/residence times



12.2.1. Time series

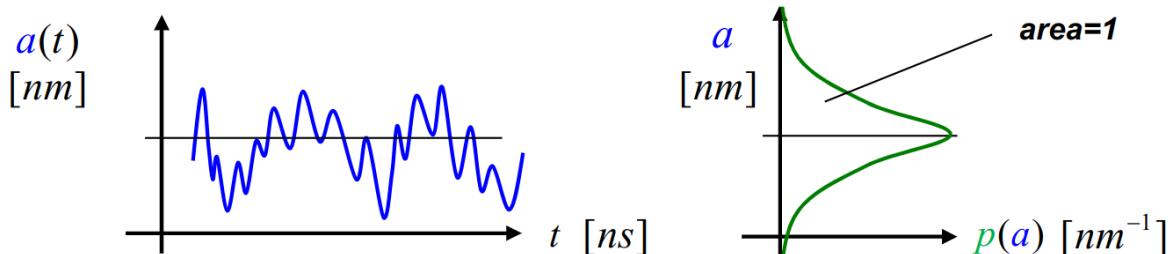
The basic result of monitoring an instantaneous observable Q is a time series.

- one can discard the time information while preserving everything else (e.g. probability distribution of Q over the simulation)

12.2.2. Distributions

- A probability distribution function should always be normalized
 - units: inverse of the units of the quantity

$$\int_{-\infty}^{\infty} da p(a) = 1 \quad (738)$$



Distribution of any function $f(a)$ of a

- Convolution of the two functions

$$p(f') = \int_{-\infty}^{\infty} da \cdot \delta(f(a) - f') p(a) \quad (739)$$

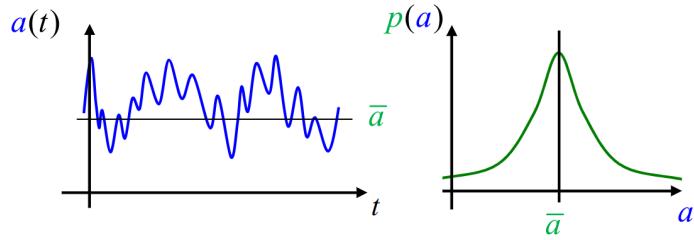
12.2.3. Statistical Moments

- The first two moment have the highest physical significance that are related to macroscopic observables or their temperature/pressure/composition derivatives etc.
- For a finite simulation, the higher the moment, the lower the accuracy

1. First moment: **mean** μ - measure of location
2. Second moment: **variance** σ^2 - measure of spread
3. Third moment: **skewness** - measure of asymmetry
4. Fourth moment: **kurtosis** - measure of peakedness

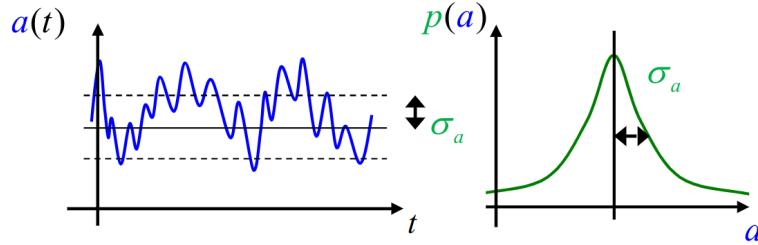
Average (mean value/first moment)

$$\bar{a} = \langle a \rangle = \int_{-\infty}^{\infty} da \cdot a p(a) \quad (740)$$



Variance (second moment)

$$\sigma_a^2 = \langle (a - \bar{a})^2 \rangle = \int_{-\infty}^{\infty} da \cdot (a - \bar{a})^2 p(a) \quad (741)$$



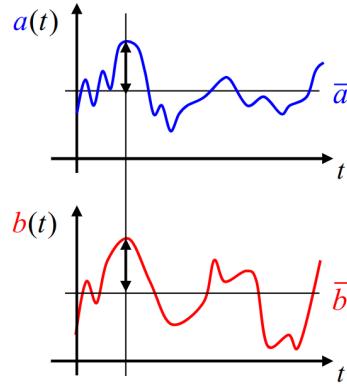
- the square-root of the variance is the standard deviation (i.e. root-mean-square/RMS or fluctuation)
 - often computed using a single-sweep over the data instead of two successive sweeps

12.2.4. Fluctuation correlations

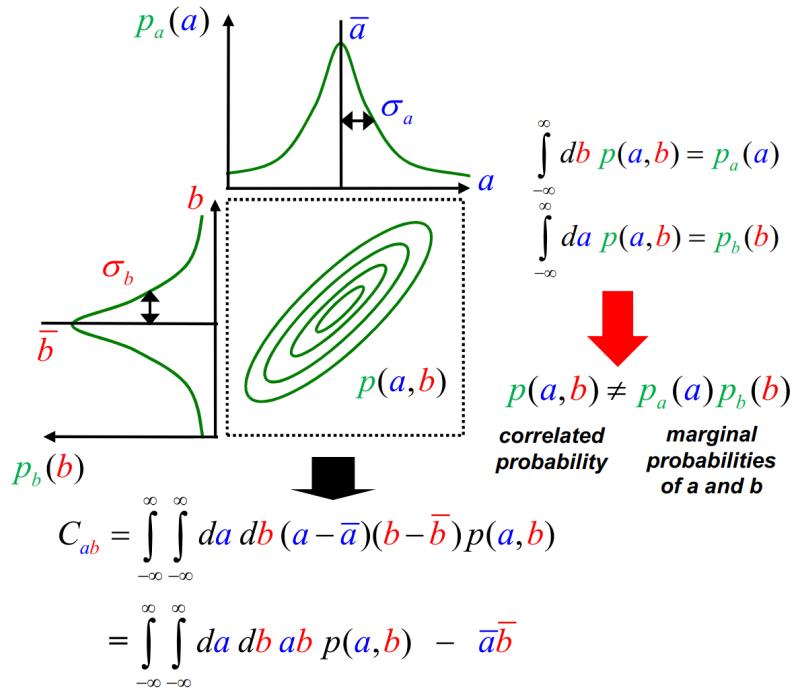
Covariance

- establish the extent of correlation in the probability distribution of two observables Q and R over the simulation
- "taking the mean"* of a two-dimensional probability distribution

$$\begin{aligned} C_{ab} &= \langle (a - \bar{a}) \cdot (b - \bar{b}) \rangle \\ &= \langle ab \rangle - \bar{a}\bar{b} \end{aligned} \quad (742)$$



Derivation



Cross-correlation

- a normalized covariance

$$c_{ab} = \frac{C_{ab}}{\sigma_a \sigma_b} \rightarrow \begin{cases} +1 & \text{perfect correlation} \\ 0 & \text{no correlation} \\ -1 & \text{perfect anticorrelation} \end{cases} \quad (743)$$

12.2.5. Time correlations

- used when the time information (relaxation) is important

Autocorrelation Function

$$C_Q(\tau) = \langle Q(t)Q(\tau + t) \rangle \quad (744)$$

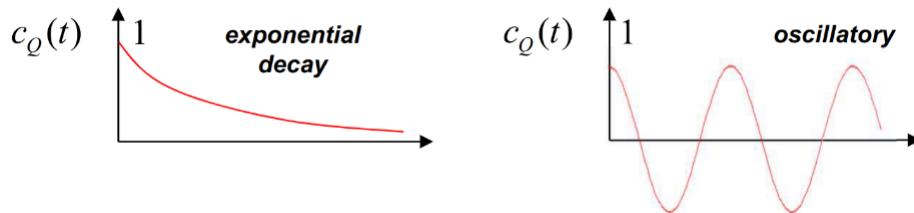
Normalized Autocorrelation Function

$$C_Q(t) = \frac{C_Q(t)}{C_Q(0)} \quad (745)$$

such that $C_Q(0) = 1$

Interpretation

- It holds that if $\langle Q \rangle = 0 \rightarrow C_Q(0) = \sigma_Q^2$
- example of extrem behaviors are the exponential decay (Lorenzian broadening) and the oscillatory (ω peaks)



Spectral Density

- Fourier transform of a time-correlation function (complex)

$$J_Q(\omega) = \int_0^\infty dt \cdot e^{-i\omega t} C_Q(t) \quad (746)$$

Time-crosscorrelation Function Between Two Observables

$$C_{QR}(\tau) = \langle Q(t)R(\tau + t) \rangle \quad (747)$$

and

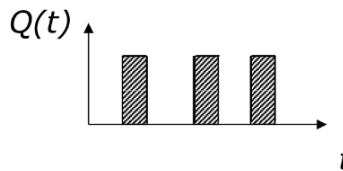
$$C_{QR}(t) = \frac{C_{QR}(t)}{C_Q^{\frac{1}{2}}(0) \cdot C_R^{\frac{1}{2}}(0)} \quad (748)$$

12.2.6. Occurrences and visiting/residence times

The time series can be used to derive specific **statistical characteristics**, the following apply to on-off coordinates defining events.

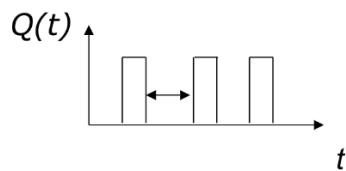
Occurrence

- Fraction of the trajectory configurations where the event condition is satisfied



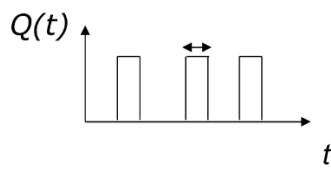
Visiting Time

- average time separating periods during which the event condition is satisfied

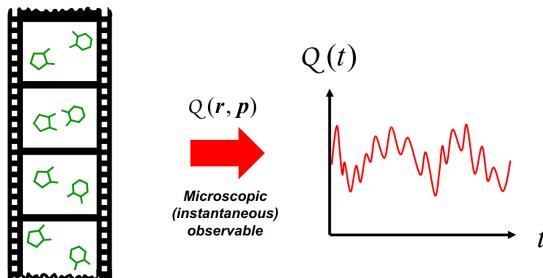


Residence Time

- average time during which the event condition is satisfied



12.3. Types of Properties



12.3.1. Structural Properties

quantities that solely depend on the **atomic positions**

- intramolecular or intermolecular
- local or global
- single structure along the trajectory or to multiple structures
- often **periodic gathering** needed and **roto-translational fitting** prior to the property calculation for structure comparisons

STRUCTURES
<ul style="list-style-type: none"> • internal coordinates <ul style="list-style-type: none"> ► distances, angles, dihedrals, hydrogen-bond, secondary structure, base pair arrangement

- radius of gyration R_{gyr}
- solvent-accessible surface area (SASA)

Intramolecular (averaged over a trajectory)

- average atomic positions
- atomic-positional RMS fluctuations (RMSF)
- covariance or cross-correlations of atomic positions
- atom-positional RMS deviation (RMSD)

Intermolecular (averaged over a trajectory)

- radial distribution functions (RDF)
- orientation correlation functions (OCF)

12.3.1.1. Radius of gyration of a (macro)molecule

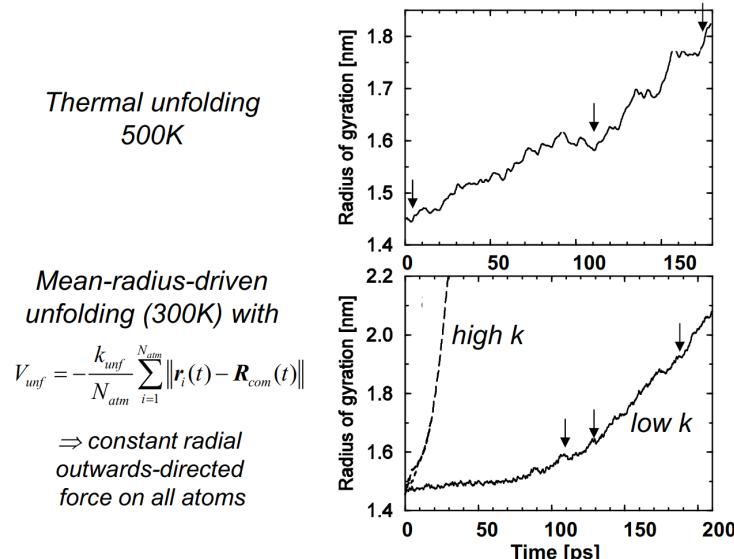
For a given trajectory frame at t_n

$$R_{\text{gyr}(t)} = \left[\frac{1}{N_{\text{atm}}} \sum_{i=1}^{N_{\text{atm}}} (\mathbf{r}_i(t) - \mathbf{R}_{\text{com}}(t))^2 \right]^{\frac{1}{2}} \quad (749)$$

where N_{atm} is the no. of atoms in the molecule and \mathbf{R}_{com} is the center of mass of the molecules. The mean radius/center of geometry is giving by

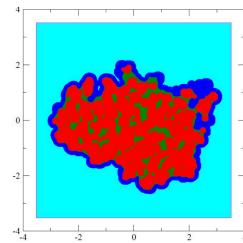
$$\mathbf{R}_{\text{com}} = M^{-1} \sum_{i=1}^{N_{\text{atm}}} m_i \mathbf{r}_i, \text{ with } M = \sum_{i=1}^{N_{\text{atm}}} m_i \quad (750)$$

Example: Unfolding lysozyme in water

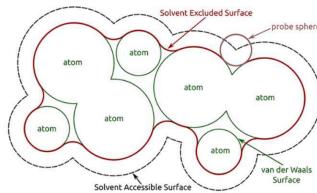


12.3.1.2. Solvent-accessible surface area of a (macro)molecule

- surface of the molecule exposed to the solvent
- depends on a set of atomic radii
- calculations
 - exact (time-consuming)
 - approximate (overlap-based formula)
- different surface definitions
 1. sas (center) in blue
 2. sas (contact) in green
 3. vdw in red



for solvent-accessible surface (sas):
probe radius 0.14 nm



12.3.1.3. Average atomic position of an atom in a (macro)molecule

- of an atom over a trajectory
- has little meaning per se due to distorted structure!

12.3.1.4. Atom-positional root-mean-square fluctuation (RMSF)

- of an atom along a trajectory, calculated after periodicity gathering and roto-translational fitting
- formally related to **B-factors** in crystallographic structures

$$\begin{aligned} \text{RMSF}(i) &= \langle (\mathbf{r}_i - \langle \mathbf{r}_i \rangle)^2 \rangle^{\frac{1}{2}} \\ &\approx \left[N_{\text{sim}}^{-1} \sum_{n=1}^{N_{\text{sim}}} (\mathbf{r}_i(t_n) - \langle \mathbf{r}_i \rangle)^2 \right]^{\frac{1}{2}} \end{aligned} \quad (751)$$

Can also be calculated with a single sweep over the atoms

$$= [\langle \mathbf{r}_i^2 \rangle - \langle \mathbf{r}_i \rangle^2]^{\frac{1}{2}} \quad (752)$$

12.3.1.5. Covariance or Cross-Correlations of Atomic Positions

- of a pair of atoms along a trajectory

12.3.1.6. Atom-positional RMS deviation

- between two conformations of the same (macro)molecule
- calculated after periodicity gathering and roto-translational fitting, for configurations m and n of the molecule

$$\text{RMSD}(m, n) = \left[N_{\text{atm}}^{-1} \sum_{n=1}^{N_{\text{atm}}} (\mathbf{r}_i(n) - \mathbf{r}_i(m))^2 \right]^{\frac{1}{2}} \quad (753)$$

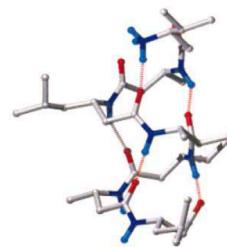
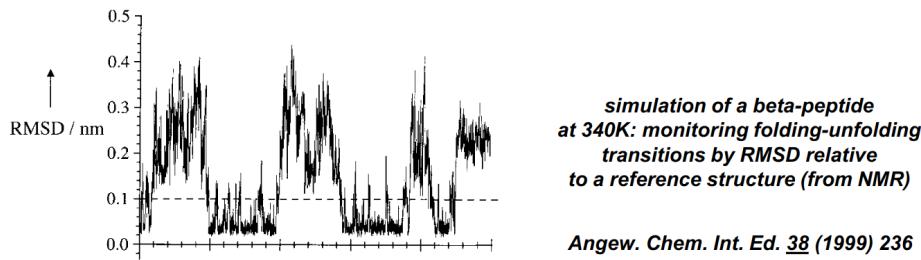
Interpretation

- definition includes the specification of both the (subset of) **atoms used for the roto-translational fitting** and the (subset of) **atoms to calculate the sum**

After periodicity gathering and roto-translational fitting of all successive frames to the reference structure one has

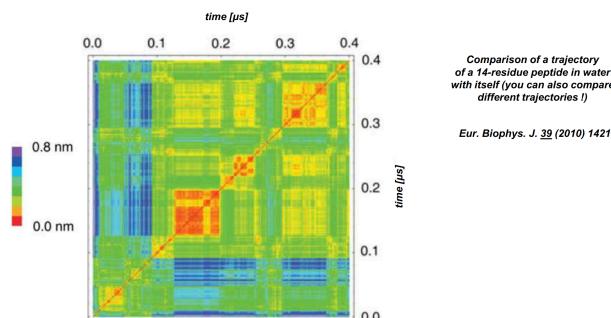
$$\text{RMSD}(t_n, \text{ref}) = \left[N_{\text{atm}}^{-1} \sum_{i=1}^{N_a} (\mathbf{r}_i(t_n) - \mathbf{r}_i^{\text{ref}})^2 \right]^{\frac{1}{2}} \quad (754)$$

Example 1: Simulation of a beta-peptide at 340K



Example 2: Along a trajectory

- monitor RMSD of all frames relative to all frames (RMSD matrix)

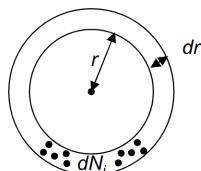


12.3.1.7. Radial Distribution Function (RDF)

- of a system over a trajectory

$$g(r) = \frac{1}{\eta} \left\langle \frac{dN_i(r, dr, t)}{4\pi r^2 dr} \right\rangle_{i,t} \quad (755)$$

where ρ is the average (bulk) number density in the system, $\eta := \frac{N_{\text{atm}}}{V_{\text{box}}}$ and $\langle \cdot \rangle_{i,t}$ is the average over central particles i and time frames and $dN_i(r, dr, t)$ for the no. atoms j in a shell of width dr at r around a reference atom i at time t

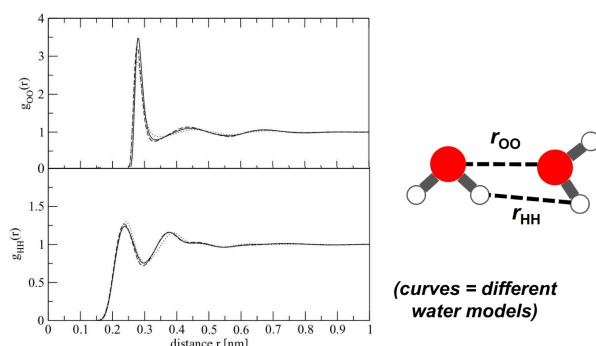


Interpretation

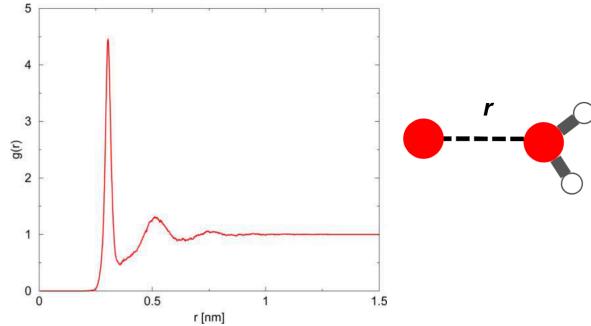
- it holds that $\lim_{r \rightarrow 0} g(r) \stackrel{!}{=} 0$, since atoms cannot overlap and $\lim_{r \rightarrow \infty} g(r) \stackrel{!}{=} 1$, in large distances \rightarrow no interaction & correlation
- For the local density of atoms at a given distance from a reference atom, given relative to the bulk
 - instead of N_{atm} , can also be N_{solt} for a solute in a solvent

$$\int_{V_{\text{box}}} dr \underbrace{4\pi r^2 \eta g(r)}_{\text{no. atoms in shell}} = N_{\text{atm}} - 1 \quad (756)$$

Example 1: Pure water



Example 2: Sodium ion in water



12.3.1.8. Orientational Correlation Function (OCF)

Ion-Dipole

- μ_i - vector at position r_i with size equals to μ
- $r_{ij} := \sqrt{[r_j - r_i]^2}$ - distance $i - j$
- $\cos(\theta) = \frac{\mu_i \cdot \mu_j}{\mu_i \mu_j}$

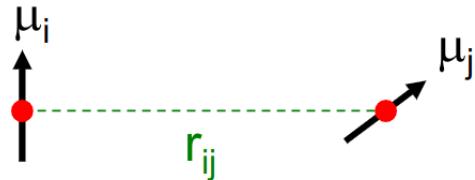
$$\langle \frac{\mu_i \cdot \mu_j}{\mu_i \mu_j} \rangle_r = \langle \cos \theta(r) \rangle_r \quad (757)$$



Dipole-Dipole

- $\cos(\theta) = \frac{\mu_i \cdot \mu_j}{\mu^2}$

$$\langle \frac{\mu_i \cdot \mu_j}{\mu^2} \rangle_r = \langle \cos \theta(r) \rangle_r \quad (758)$$



12.3.2. Thermodynamic Properties (with FD)

Given the basic thermodynamic observables $Q = \langle Q \rangle$, we consider the following properties

Isothermal compressibility

$$\kappa_T = -\frac{1}{V} \left(\frac{\partial V}{\partial P} \right)_T = \frac{1}{\rho} \left(\frac{\partial \rho}{\partial P} \right)_T = \left(\frac{\partial \ln \rho}{\partial P} \right)_T \quad (759)$$

with FD

$$\Rightarrow \left(\frac{\ln \left(\frac{\rho_2}{\rho_1} \right)}{P_2 - P_1} \right) \quad (760)$$

Isobaric expansivity

$$\alpha_P = \frac{1}{V} \left(\frac{\partial V}{\partial T} \right)_P = -\frac{1}{\rho} \left(\frac{\partial \rho}{\partial T} \right)_P = -\left(\frac{\partial \ln \rho}{\partial T} \right)_P \quad (761)$$

with FD

$$\Rightarrow - \left(\frac{\ln\left(\frac{\rho_2}{\rho_1}\right)}{T_2 - T_1} \right) \quad (762)$$

Isochoric heat capacity

$$c_V = \frac{1}{N} \left(\frac{\partial U}{\partial T} \right)_V \quad (763)$$

with FD

$$\Rightarrow c_V \approx \frac{E_{\text{tot},2} - E_{\text{tot},1}}{T_2 - T_1} + c_{V, \text{ QM-corr}} \quad (764)$$

Interpretation using experimental data for comparison

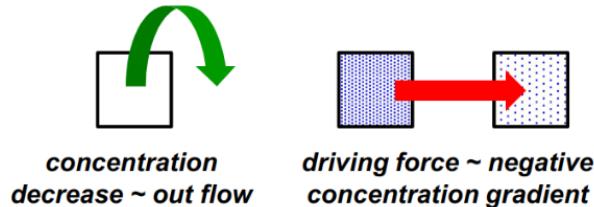
12.3.3. Transport/Dynamic/Kinetic Properties

- Calculation of transport coefficients
 - diffusion coefficient
 - viscosity
 - thermal/electrical conductivity
 - ionic conductivity
 - frequency-dependent dielectric permittivity

Continuity Equation

- c concentration of solute particles
- j flux of solute particles

$$\frac{\partial}{\partial t} c(\mathbf{r}, t) = -\nabla \cdot \mathbf{j}(\mathbf{r}, t) \quad (765)$$



Phenomenological Mass Transport Law (Fick)

- D diffusion constant
- mass flow governed by the concentration gradient

$$\mathbf{j}(\mathbf{r}, t) = -D \cdot \nabla c(\mathbf{r}, t) \quad (766)$$

Diffusion Equation

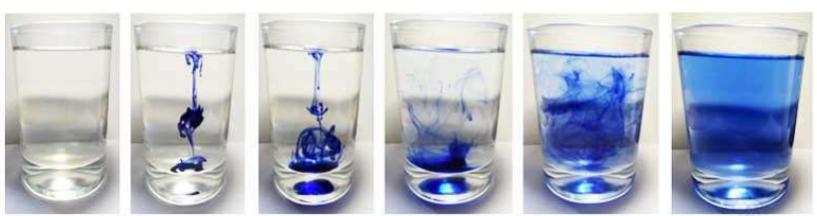
$$\frac{\partial}{\partial t} c(\mathbf{r}, t) = D \nabla^2 c(\mathbf{r}, t) \quad (767)$$

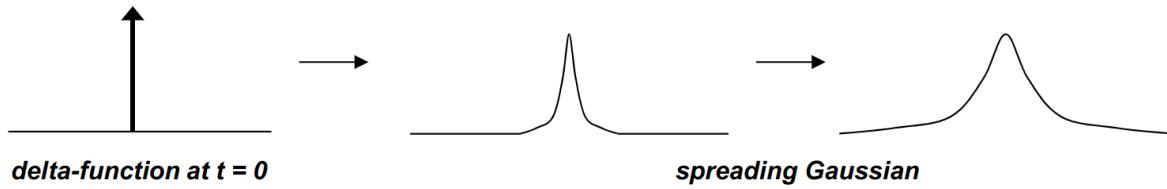
Example: Droplet Diffusion

Given the boundary condition $c(\mathbf{r}, t=0) = \delta(\mathbf{r})$, together with the diffusion equation, the resulting solution is

$$c(\mathbf{r}, t) = (4\pi Dt)^{-\frac{3}{2}} \cdot e^{-\frac{r^2}{4Dt}}$$

with normalization $\int c(\mathbf{r}, t) d\mathbf{r} = 1$ (768)

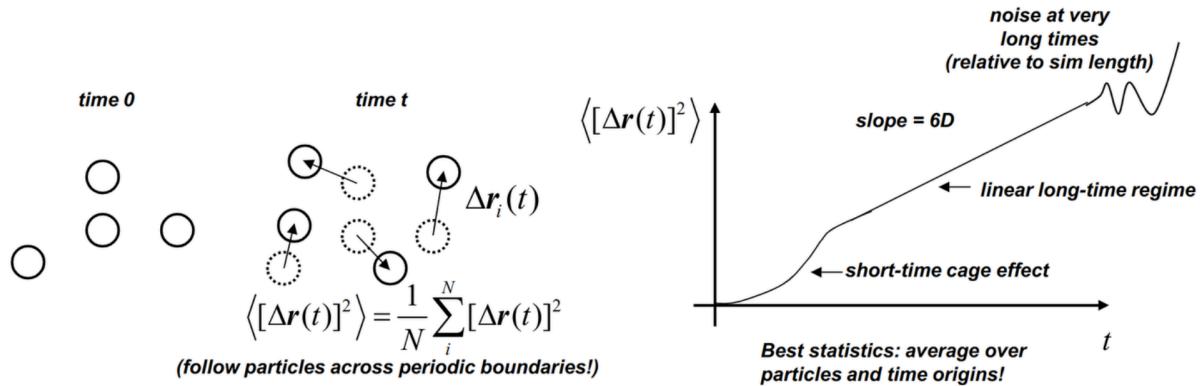




Einstein Relation

$$D = \frac{1}{6} \lim_{t \rightarrow \infty} \frac{d}{dt} \langle r^2(t) \rangle \quad (769)$$

Interpretation can be used to compute D from simulations

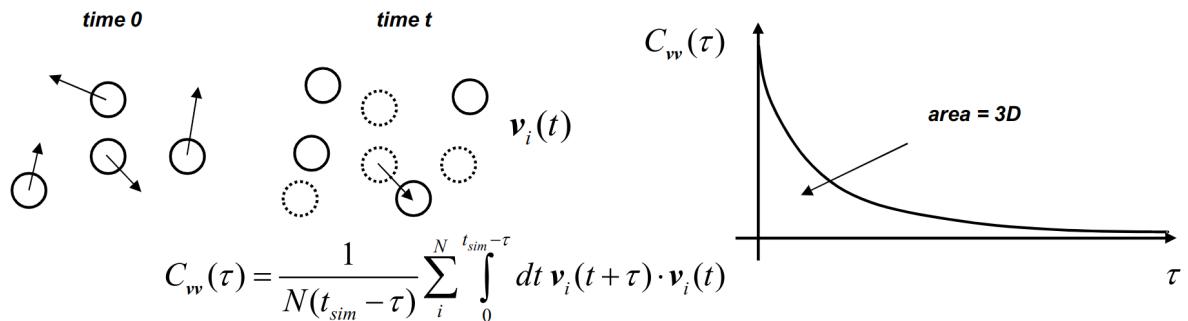


Green-Kubo Relation

$$D = \frac{1}{3} \lim_{\tau \rightarrow \infty} \int_0^\tau d\tau C_{vv}(\tau) \quad (770)$$

where

$$C_{vv}(\tau) = \langle \mathbf{v}(t) \cdot \mathbf{v}(\tau + t) \rangle \quad (771)$$



12.3.4. Dielectric Properties

Quantities for characterizing the response of a liquid (the solvent) to charges/dipoles (in a solute) are **Static Relative Dielectric Permittivity ϵ** and **Dielectric (Debye) Relaxation Time τ_D**

The main two calculation approaches are **dipole moment fluctuation** and **applied electric field**

1. Static Relative Dielectric Permittivity ϵ

Describes the ability to screen electrostatic interactions between charges

- In vacuum

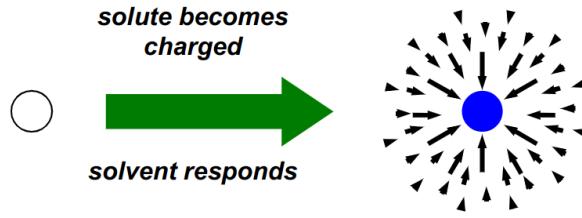
$$V(r) = \frac{qq'}{4\pi\epsilon_0} \cdot \frac{1}{r} \quad (772)$$

- In medium

$$V(r) = \frac{qq'}{4\pi\epsilon_0\epsilon} \cdot \frac{1}{r} \quad (773)$$

2. Dielectric (Debye) Relaxation Time τ_D

- describes how fast the medium responds to charge rearrangements in the solute



12.3.4.1. Method 1: Dipole Moment Fluctuation

Relative Permittivity ε to be calculated

- with ε_0 constant vacuum permittivity, ε_{RF} the simulation parameter reaction-field permittivity, V the box volume and M the box dipole moment

$$(\varepsilon - 1) \left(\frac{2\varepsilon_{\text{RF}} + 1}{2\varepsilon_{\text{RF}} + \varepsilon} \right) = \frac{\langle M^2 \rangle - \langle M \rangle^2}{3\varepsilon_0 V k_B T} \quad (774)$$

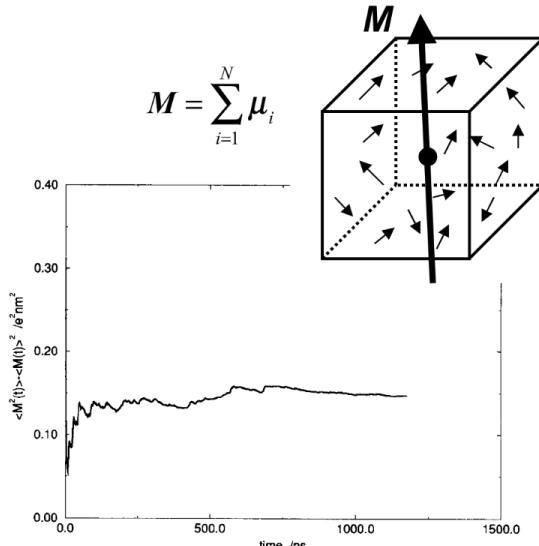


Figure 4. Cumulative average of the total dipole moment fluctuation of the system (Dietz model) as a function of time.

Relaxation Time τ_D

- auto-correlation function of M

$$\frac{\langle M(t') \cdot M(t'+t) \rangle_{t'}}{\langle M^2(t') \rangle_{t'}} = \exp\left(-\frac{t}{\tau_M}\right) \quad (775)$$

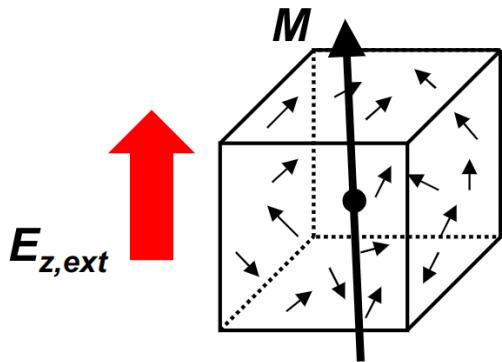
- with τ_M connected with Debye dielectric relaxation time τ_D

$$\tau_D \approx \left(\frac{2\varepsilon_{\text{RF}} + 1}{2\varepsilon_{\text{RF}} + \varepsilon} \right) \cdot \tau_M \quad (776)$$

12.3.4.2. Method 2: Applied Electric Field

Relative Permittivity ε

$$\varepsilon = 1 + \left(\frac{1}{\varepsilon_0} \right) \cdot \frac{\langle M_z \rangle}{V E_z^{\text{ext}}} \quad (777)$$



External field applied in z-direction

Relaxation Time τ_D

- build-up of box dipole moment when external field is applied
- auto-correlation function of M

$$\langle M_z(t) \rangle_{t_0} = \langle M_z(t = \infty) \rangle_{t_0} \cdot \exp\left[1 - \exp\left(-\frac{t - t_0}{\tau_M}\right)\right] \quad (778)$$

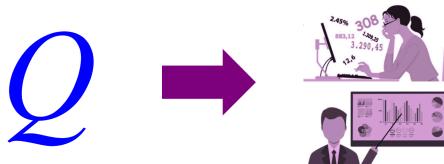
- with τ_M connected with Debye dielectric relaxation time τ_D , and C_{RF} the constant of the reaction field

$$\tau_D = \left[\frac{\varepsilon + 2 + C_{RF} \cdot (\varepsilon - 1)}{3} \right] \cdot \tau_M \quad (779)$$

12.4. Interpretation

there are things to pay attention to while interpreting the simulation results

1. Ergodicity, equilibration versus sampling
2. Roto-translational fitting artifacts
3. Choice of finite-difference intervals
4. Estimation of statistical errors
5. Analysis strategy: from the generic to the specific!

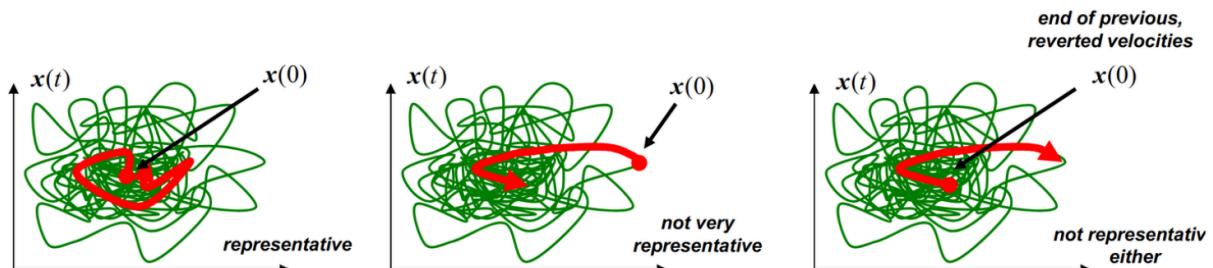


12.4.1. Ergodicity, equilibration versus sampling

Preliminary: Ergodic Hypothesis

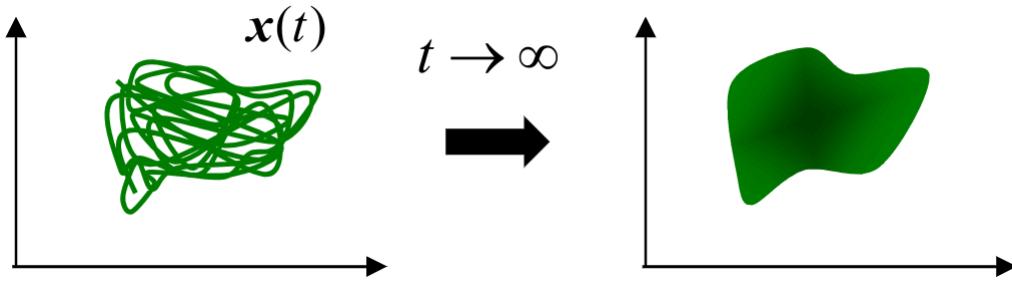
$$\bar{Q} = \langle Q \rangle \quad (780)$$

- In the limit of infinite time, any trajectory will end up visiting **all possible phase-space points** compatible with the hard macroscopic constraints \Rightarrow the choice of initial conditions should be irrelevant?
- No! Because we have only finite trajectory segments



Example: Postulate in the limit of infinite time

Given a single-system trajectory, an NVT ensemble $\mathbf{x} = \{\mathbf{r}, \mathbf{p}\}$, with some initial condition $\mathbf{x}(0)$ fixed



At equilibrium phase-space probability density, nowhere is zero

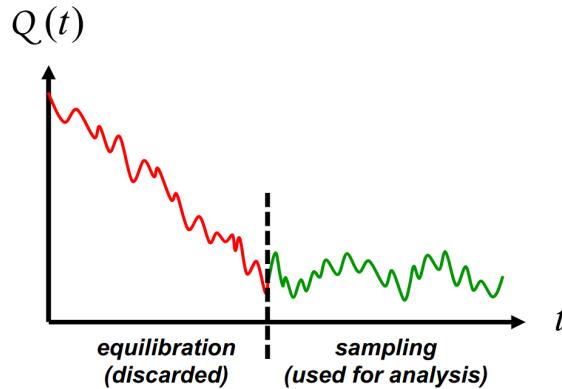
$$\bar{\rho}(\mathbf{x}) \sim \frac{\exp(-\beta\mathcal{H}(\mathbf{x}))}{\int d\mathbf{x} \exp(-\beta\mathcal{H}(\mathbf{x}))} \quad (781)$$

Equilibration vs sampling

- To cope with the limitation of finite simulation time

Equilibration discard the initial period of a simulation such that we lose memory of non-representative initial conditions

- equilibration is monitored by following a set of relevant observable and waiting for stabilization

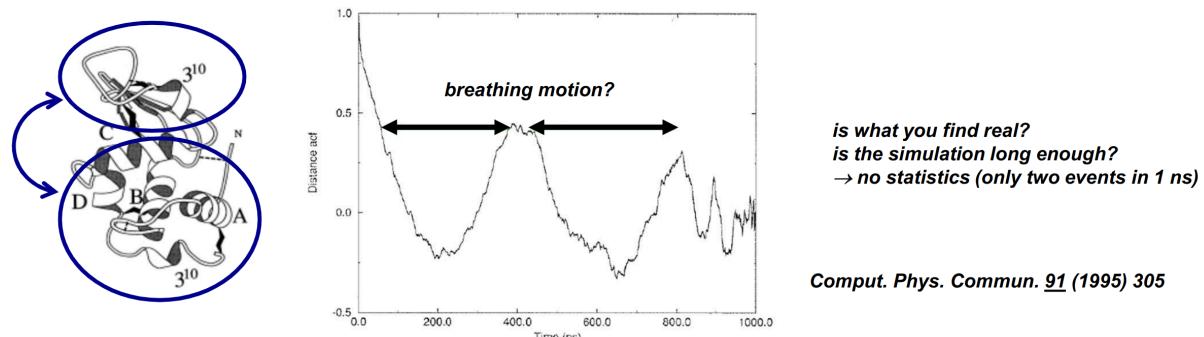


Disadvantage: still no guarantee, for complex systems equilibration is only possible within the available computer time if we start from an already reasonable initial configuration (e.g. protein structure from X-ray or NMR)

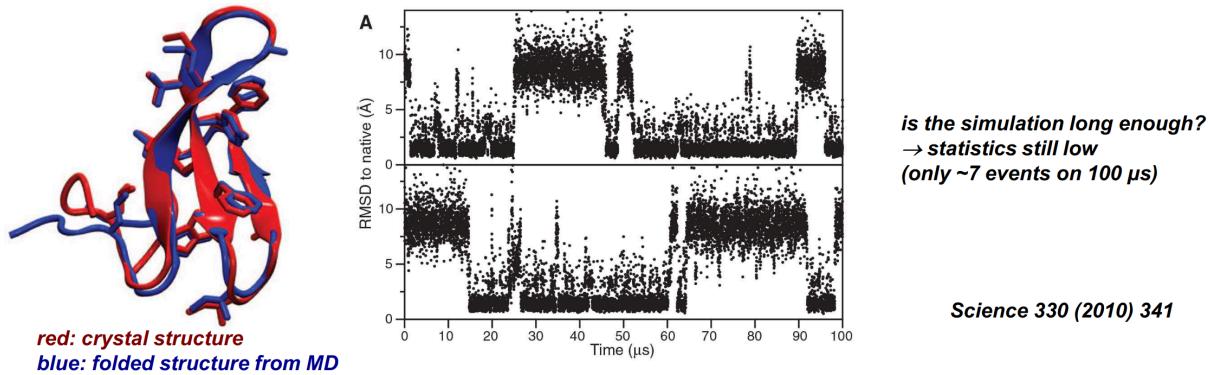
- the proper way is to perform multiple simulations from different initial conditions (in practice simulations too expensive)
- other remedies: increase simulation time, use sampling enhancement techniques

Example: Evaluating Simulation Results

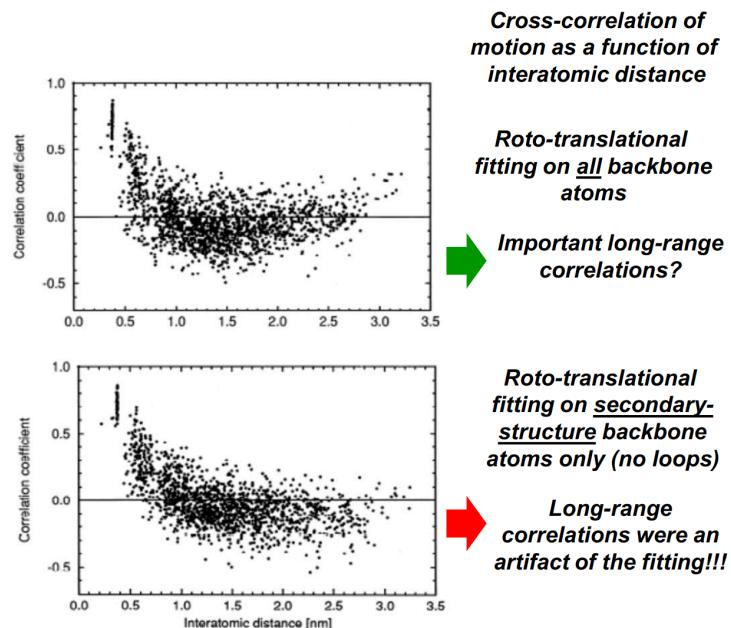
1. auto-correlation function of distance between centers of mass of domains (Lysozyme)



2. Folding and unfolding of Fip35

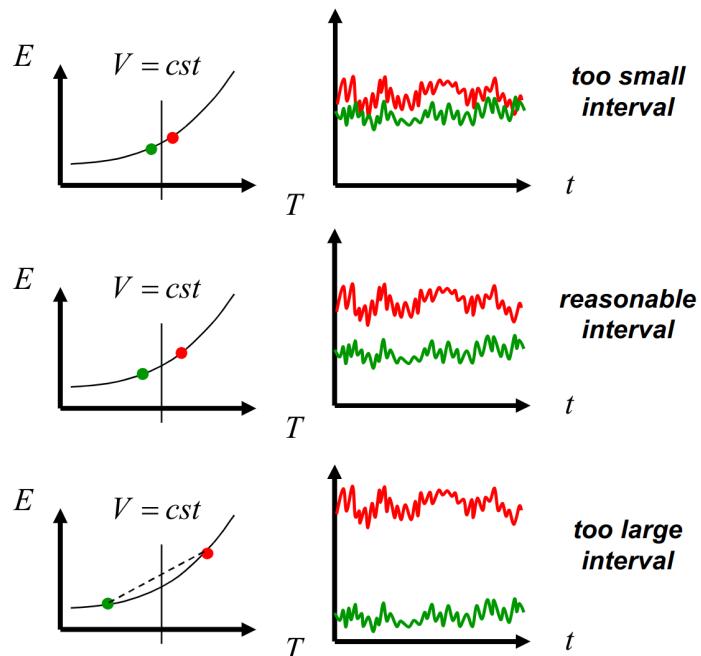


12.4.2. Roto-Translational Fitting Artifacts



12.4.3. Choice of FD Intervals

Example: Calculating $c_V \approx \frac{\Delta E_{tot}}{\Delta T}$



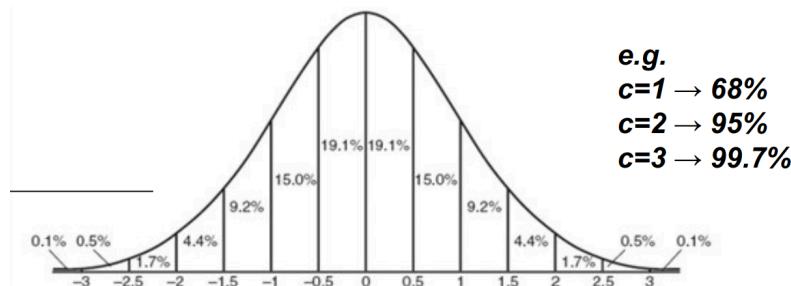
12.4.4. Estimation of Statistical Errors

When performing N independent experiments with results following a normal distribution, one can estimate the error on the mean by

$$\varepsilon = c \frac{\sigma}{N^{1/2}} \quad (782)$$

where N is no. experiments, σ the standard deviation and c the confidence factor

Example

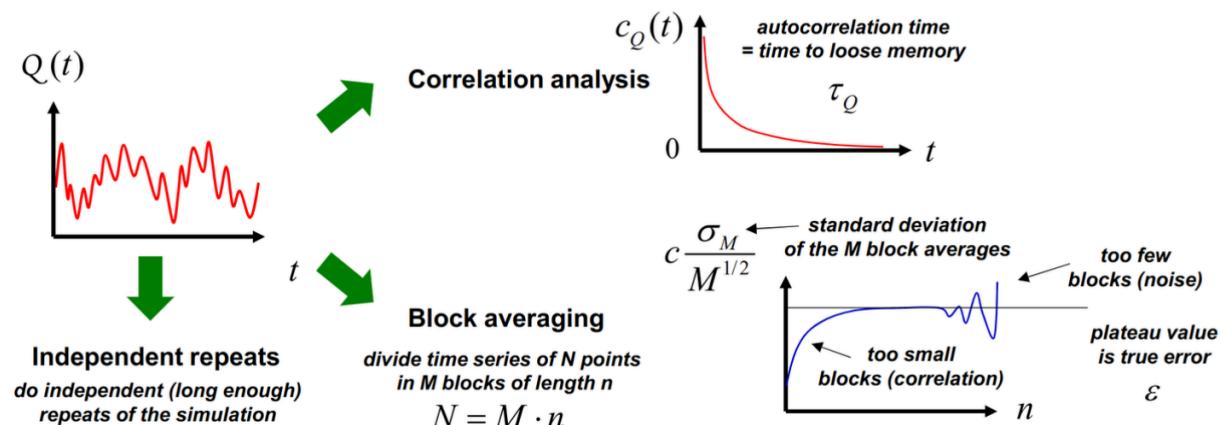


Performing many N -experiment sets, the mean one finds has a 95% chance to be within $\pm\varepsilon$ with $c = 2$ of the true mean μ that one obtains by having $N \rightarrow \infty$

Analysis Time Series

For correlation analysis, the effective number of independent samples is

$$\varepsilon = c \frac{\sigma_Q}{N_{\text{eff}}^{1/2}} \quad (783)$$



Example: Block averaging with butane dihedral time series

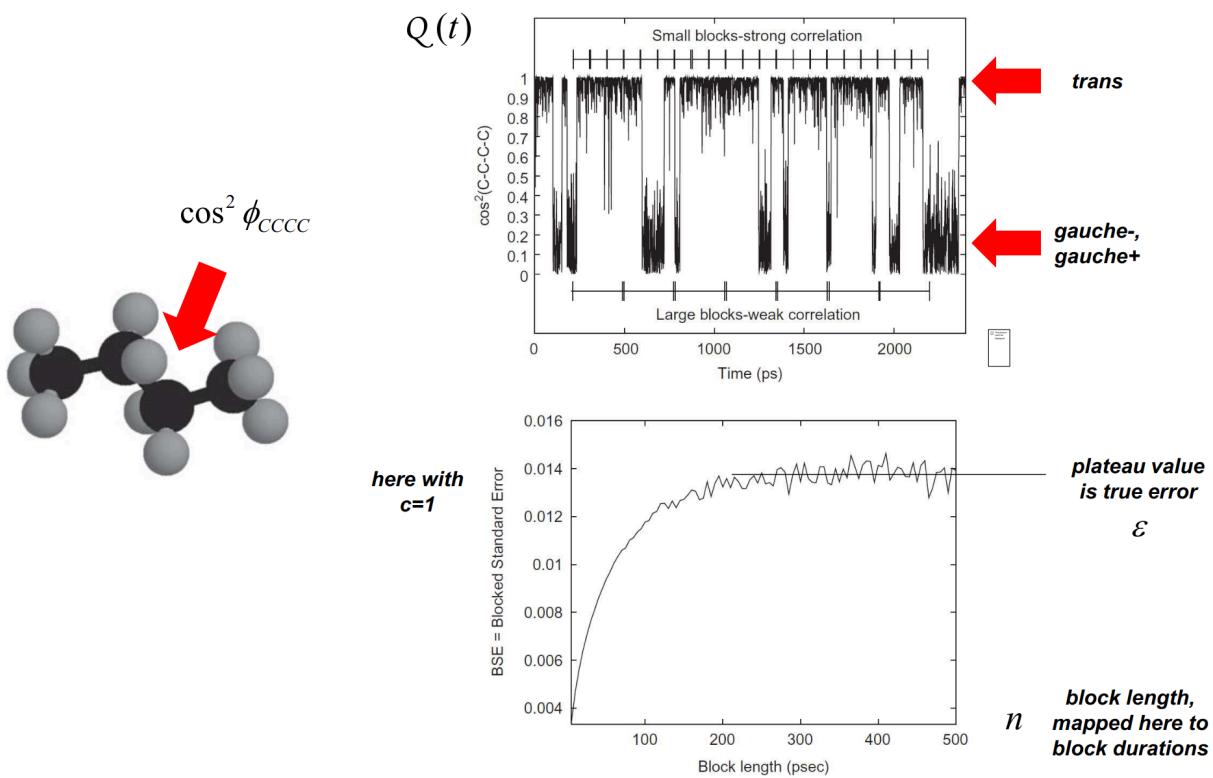


Figure 6 The block-averaging procedure considers a full range of block sizes. The upper panel shows the time series for the squared cosine of the central dihedral of butane, with two different block sizes annotated. The lower panel shows the block-averaged standard error for that times series, as a function of block size.

12.4.5. Analysis Strategy: From the Generic to the Specific!

- **Make a movie of the simulation:** Identify potential issues and points of interest.
- **Perform standard analyses:** Check for problems, equilibrium, and areas of interest.
- **Conduct tailored analyses:** Focus on specific observables relevant to your hypothesis.
- **Design clear graphs:** Ensure they effectively convey the main message.
- **Report error estimates:** Include them when possible to improve reliability.

Watch for common issues Addressing these issues early can save time and lead to more accurate conclusions.

- SHAKE failures
- Insufficient equilibration
- Temperature inconsistencies
 - e.g. by checking T_{solute} vs. T_{solvent}
- Unexpected center-of-mass motion
- Incorrect periodic gathering

13. Mathematics Cheat Sheet

Gradient

$$\frac{\partial}{\partial \mathbf{r}_i} = \nabla_i \quad (784)$$

Curl

$$\frac{\partial}{\partial \mathbf{r}_i} \times = \nabla_i \times \quad (785)$$

13.0.1. Total Differentials

Given a multivariate function,

$$f = f(\{z_i\}) = f(\{z_i \mid i = 1, \dots, n\}) \quad (786)$$

the **total differential** gives the infinitesimal change of the function for an infinitesimal change of all the variables.

$$df = f(\{z_i + dz_i\}) - f(\{z_i\}) \quad (787)$$

It can also be expressed as a sum over partial differentials

$$df = \sum_{i=1}^n \left(\frac{\partial f}{\partial z_i} \right)_{\{z_j \neq i\}} dz_i \quad (788)$$

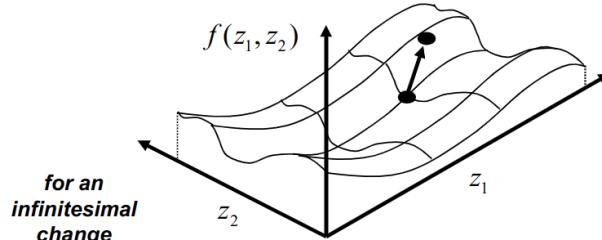
Example: 2D total differential

$$\begin{aligned} df &= \left(\frac{\partial f}{\partial z_1} \right)_{z_2} dz_1 + \left(\frac{\partial f}{\partial z_2} \right)_{z_1} dz_2 \\ &= \delta f_1 + \delta f_2 \end{aligned} \quad (789)$$

13.0.2. Integral of Total Differential

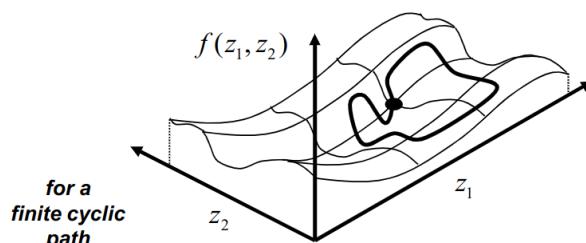
The integral of a total differential along any path gives the variation of the function *irrespective* of the path.

$$\int_{\{z_i\}}^{\{z'_i\}} df = \Delta f = f(\{z'_i\}) - f(\{z_i\}) \quad (790)$$



Along any circular path, the integral of a total differential is **zero**.

$$\oint df \stackrel{!}{=} 0 \quad (791)$$



- The **rule of Schwartz** (for differentials of second order)

$$f(x, y, \dots) \rightarrow \left(\frac{\partial}{\partial x} \left(\frac{\partial f}{\partial y} \right)_{x, \dots} \right)_{y, \dots} = \left(\frac{\partial}{\partial y} \left(\frac{\partial f}{\partial x} \right)_{y, \dots} \right)_{x, \dots}$$

loose notation $\frac{\partial^2 f}{\partial x \partial y} = \frac{\partial^2 f}{\partial y \partial x}$

- Die **chain rule**

$$f(x, \dots) = \tilde{f}(y(x), \dots) \quad \begin{matrix} \rightarrow \\ \text{independent of } x \end{matrix} \quad \left(\frac{\partial f}{\partial x} \right)_{\dots} = \left(\frac{\partial \tilde{f}}{\partial y} \right)_{\dots} \cdot \frac{dy}{dx}$$

*if the definition of f involves more functions depending on x
→ you get a sum of corresponding terms*

- The **variable exchange**

$$f(x, y, \dots) = \tilde{f}(x, z, \dots) \quad \begin{matrix} \rightarrow \\ z = z(x, y, \dots) \end{matrix} \quad \left(\frac{\partial f}{\partial x} \right)_{y, \dots} = \left(\frac{\partial \tilde{f}}{\partial x} \right)_{z, \dots} + \left(\frac{\partial \tilde{f}}{\partial z} \right)_{x, \dots} \left(\frac{\partial z}{\partial x} \right)_{y, \dots}$$

loose notation $\left(\frac{\partial f}{\partial x} \right)_y = \left(\frac{\partial f}{\partial x} \right)_z + \left(\frac{\partial f}{\partial z} \right)_x \left(\frac{\partial z}{\partial x} \right)_y$

- The **inversion**

$$z = z(x, y) \quad \begin{matrix} \rightarrow \\ y = y(x, z) \end{matrix} \quad \left(\frac{\partial z}{\partial y} \right)_x = \left[\left(\frac{\partial y}{\partial z} \right)_x \right]^{-1}$$

- The **permutation**

$$z = z(x, y) \quad \begin{matrix} \rightarrow \\ y = y(x, z) \end{matrix} \quad \left(\frac{\partial z}{\partial x} \right)_y = - \left(\frac{\partial z}{\partial y} \right)_x \left(\frac{\partial y}{\partial x} \right)_z$$

- The **Euler rule** (yes, another one ;-)

$$z = z(x, y) \quad \begin{matrix} \rightarrow \\ y = y(x, z) \end{matrix} \quad \left(\frac{\partial x}{\partial y} \right)_z \left(\frac{\partial y}{\partial z} \right)_x \left(\frac{\partial z}{\partial x} \right)_y = -1$$

*proof:
inversion + permutation*

- Der „**rule of Maxwell**“

$$f = f(x, y, \dots) \quad df = g(x, y, \dots)dx + h(x, y, \dots)dy + \dots \quad \begin{matrix} \rightarrow \\ \left(\frac{\partial g}{\partial y} \right)_{x, \dots} = \left(\frac{\partial h}{\partial x} \right)_{y, \dots} \end{matrix}$$

*proof:
use the rule of Schwartz*