Chimie Théorique: Mécanique Statistique

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Contents

Part I

Molecular Simulation (Damien Laage)

1 Chpt 1. Introduction to Molecular Dynamics

References:
- Statistical Mechanics, Mark Tukerman, chapter 3,4,5
- Understanding Molecular Simulations, Frenkel & Smith

1.1 Molecular Dynamics Simulations

We could not get all hamiltonian ...

1.1.1 A brief history of MD

- WWII, Computer for numerical simulation;
- 1950s, chains of oscillators;
- 1967, Liquid of Argon;
- 1971, Liquid of water;
- 1976, proteins;
- 2011, HIV capacid;
- 2013, Nobel Prize!

We should find a balance among speed/size/cost, or just design one specific computer only for MD.

1.1.2 Key steps of simulations

This is another kind of experiments, know where to pay attention.
1. prepare initial configurations;
2. calculate energies and forces;
3. integrate experience of motion, namely trajectory;
4. calculate (average) properties;

1.1.3 A numerical approach for Stat. Mech.

In a micro-canonical ensemble

$$\langle A \rangle = \frac{1/h \int dpdq A(p,q)\delta\left[H(p,q) - E\right]}{1/h \int dpdq\delta\left[H(p,q) - E\right]}$$

where the denominator is called the partition function

$$\Omega(N,V,E) = \int dpdq\delta\left[H(p,q) - E\right]$$

Only for very simple system, there would be analytical solutions; thus we turn to numerical simulations. For some observables, they are hard to measure experimentally, then numerical ... whose quality depends on what inputs.

1.1.4 Ergodicity

Main idea: Time average ~ sample average Hamiltonian equations of motion

$$\dot{q} = \frac{dq}{dt} = \frac{\partial \mathcal{H}}{\partial p} \qquad \dot{p} = \frac{dp}{dt} = -\frac{\partial \mathcal{H}}{\partial q}$$

Total energy is conserved $\frac{d\mathcal{H}}{dt} = 0$.

Analogy for micro-canonical ensemble, sample micro states of energy E.

Ergodicity hypothesis: Given on infinite time, system of energy E can visit **all** configurations on the constant energy hypersurface. Therefore, we address that micro-canonical ensemble average is equal to time average.

$$\langle A \rangle = \frac{\int dpdq A(p,q)\delta\left[H(p,q) - E\right]}{\int dpdq\delta\left[H(p,q) - E\right]} = \lim_{T\to\infty} \frac{1}{T} \int_0^T dt A\left[p(t),q(t)\right]$$

For example, it would be hard to move left to right due to the high energy barrier between. But for high-freedom system, there would always be possible passways.

1.2 Starting point of MD Simulation

Position: Lattice, Random arrangement, Protein crystal structure

How to simulate a few water molecules?

Droplet with strong boundary effect, it should keep all water molecules in the same condition.

Herein, we select the Periodical Boundary Condition, which is common for bulk simulation, meaning that the same particle would appear at the same position with each box cell.

How to simulate the vaporisation process? For instance, take vaporisation into consideration still, there would be no molecule loss inside a closed system with water and vapor at the same time.

Velocity: for example, draw from Maxwell-Boltzmann distribution

1.3 Energy and force calculations

Namely approximate solution to Schrödinger equation. There are several modern treatments:

- Density Functional Theory (DFT);
- partition system in quantum/classical (QM/MM);
- Artificial Intelligence;

the most popular approach is the classical force fields.

$$U = \sum_{i \in \text{bonds}} \frac{1}{2} k_i (\ell_i - \ell_i^0)^2 + \sum_{j \in \text{angles}} \frac{1}{2} k_j^\theta (\theta_j - \theta_j^0)^2 + \sum_{m \in \text{dihedral}} k_m^\phi \left[1 - \cos(n\phi + \delta) \right]$$

$$+ \sum_{i,j} \left\{ \frac{q_i q_j}{4\pi \epsilon_{ij} r_{ij}} + 4\epsilon_{ij} \left[\left(\frac{\sigma}{r_{ij}} \right)^{12} - \left(\frac{\sigma}{r_{ij}} \right)^6 \right] \right\}$$

where the last term with $4\epsilon_{ij}$ is called Lenard-Jones potential. Indeed, 6 is derived from the physical sense, while 12 is just derived for the sake of convenient calculation.

Since there would be too much parameters, we could ...

1. make fitting for coefficients
2. calculate them with DFT;
3. for AI, there are only a list of energies with configurations, hard to furnish analytical motion

for each time step, we should calculate force/potential/energy at each point. With forces described as $\vec{F} = -\vec{\nabla} U$, for pair potential $\propto N^2$.

1.4 Integrating the equations of motions

Too little step, longer time wasted; too large step, bigger calculation errors.

1.4.1 Verlet algorithm

We introduce Taylor series

$$\vec{r}(t + \Delta t) = \vec{r}(t) + \Delta t \dot{\vec{r}}(t) + \frac{1}{2} (\Delta t)^2 \ddot{\vec{r}}(t) + o(\Delta t^2)$$

$$= \vec{r}(t) + \Delta t \cdot \vec{v}(t) + \frac{1}{2m} (\Delta t)^2 \cdot \vec{F}(t) + o(\Delta t^2)$$

$$\vec{r}(t + \Delta t) = \vec{r}(t) - \Delta t \cdot \vec{v}(t) + \frac{1}{2m} (\Delta t)^2 \cdot \vec{F}(t) + o(\Delta t^2)$$

thus if the system memorize two steps, we could calculate the next by

$$\vec{r}(t + \Delta t) = 2\vec{r}(t) - \vec{r}(t - \Delta t) + \frac{1}{m}(\Delta t)^2$$

Similarly, we have the velocity verlet

$$\vec{r}(t + \Delta t) \simeq \vec{r}(t) + \Delta t \cdot \vec{v}(t) + \frac{(\Delta t)^2}{2m} \cdot \vec{F}(t)$$

$$\vec{v}(t + \Delta t) \simeq \vec{v}(t) + \frac{\Delta t}{2m} \left[\vec{F}(t) + \vec{F}(t + \Delta t) \right]$$

1.4.2 Key property

Goal:

- stability (no drift of E);
- time-reversibility $\vec{r}(t) \xrightarrow{+\Delta t} \vec{r}(t + \Delta t) \xrightarrow{-\Delta t} \vec{r}(t)$; however, the Euler algorithm mentioned above is not time-reversible ...
- sympletic: conserve magnitude of volume elements in phase space

1.4.3 Liouville formation of time-reversible algorithem

Liouville operator

$$i\mathcal{L} = \dot{q}\frac{\partial}{\partial q} + \dot{p}\frac{\partial}{\partial p}$$

for $F(p, q)$, $i\mathcal{L}f = \dot{f}$, thus we could make integration

$$f[p(t), q(t)] = e^{i\mathcal{L}t} f[p(0), q(0)]$$

however, $\mathcal{L}$ is also time-dependent.

Define two operators

$$i\mathcal{L}_q = \dot{q}\frac{\partial}{\partial q} \qquad i\mathcal{L}_q = \dot{p}\frac{\partial}{\partial p}$$

let's focus on $i\mathcal{L}_q$ at first

$$f[p(0), q(0)] = e^{i\mathcal{L}_q t} f(0) = f(0) + i\mathcal{L}_q t f(0) + \frac{(i\mathcal{L}_q t)^2}{2!} f(0) + \cdots = \sum_{n=0}^{\infty} \frac{[\dot{q}(0)t]^n}{n!} \frac{\partial^n}{\partial q^n} f(0)$$

$$= f[p(0), q(0) + \dot{q}(0)t]$$

namely $i\mathcal{L}_q$ could shift position. Similarly, $i\mathcal{L}_p$ could shift momenta. These two operators could not commute,

$$e^{i\mathcal{L}t} \neq e^{i\mathcal{L}_p t} e^{i\mathcal{L}_q t}$$

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However, we have Trotter identity

$$e^{A+B} = \lim_{P \to \infty} \left[e^{A/(2P)} e^{B/P} e^{A/(2P)} \right]^P$$

suppose that $\Delta t = t/P$,

$$\exp\left(i\mathcal{L}_p \frac{\Delta t}{2}\right) \exp\left(i\mathcal{L}_q \Delta t\right) \exp\left(i\mathcal{L}_p \frac{\Delta t}{2}\right) \sim \exp\left(i\mathcal{L}t\right) = \exp\left[i(\mathcal{L}_p + \mathcal{L}_q)t\right]$$

Therefore,

$$f\left[p(0), q(0)\right] \xrightarrow{+i\mathcal{L}_p \Delta t/2} f\left[p(0) + \frac{\Delta t}{2}\dot{p}(0), q(0)\right]$$

$$\xrightarrow{+i\mathcal{L}_q \Delta t} f\left[p(0) + \frac{\Delta t}{2}\dot{p}(0), q(0) + \Delta t \cdot \dot{q}\left(\frac{\Delta t}{2}\right)\right]$$

$$\xrightarrow{+i\mathcal{L}_p \Delta t/2} f\left[p(0) + \frac{\Delta t}{2}\dot{p}(0) + \frac{\Delta t}{2}\dot{p}(\Delta t), q(0) + \Delta t \cdot \dot{q}\left(\frac{\Delta t}{2}\right)\right]$$

so

$$p(0) \to p(0) + \frac{\Delta t}{2}\left[F(0) + F(\Delta)\right]$$

$$q(0) \to q(0) + \Delta t \cdot \dot{q}(0) + \frac{(\Delta t)^2}{2m}F(0)$$

1.5 MD Simulation in different ensemble

1.5.1 "Constant temperature"

System in constant with thermostat (heat bath), we have Maxwell-Boltzman stat.

$$\rho(p) = \left(\frac{\beta}{2m}\right)^{3/2} \exp\left(-\beta\frac{p^2}{2m}\right)$$

$$\langle p^2 \rangle = \frac{3m}{\beta} \qquad \langle p^4 \rangle = 15\left(\frac{m}{\beta}\right)^2 \qquad \frac{\sigma_p^2}{\langle p^2 \rangle^2} = \frac{\langle p^4 \rangle - \langle p^2 \rangle^2}{\langle p^2 \rangle^2} = \frac{2}{3}$$

and similarly we have

$$\frac{\sigma_T^2}{\langle T^2 \rangle^2} = \frac{2}{3N}$$

Hence, temperature does vary a little if N is large enough.

There exist some systems

- Andreson thermostat: random collision with heat bath;
- Nosé thermostat: extended Lagrangian, thus extend phase space, introduce coordinates + momenta

1.5.2 "Constant pressure"

We call NVT the canonical system, NVE the micro-canonical system.

1.6 A related simulation approach Monte Carlo

The main difference with molecular simulation is that Monte Carlo does not know about time. It is a way to sample the phase space.

1.6.1 Importance Sampling

$$\langle A \rangle = \frac{\int dp dq A(p,q) e^{-\beta H(p,q)}}{\int dp dq e^{-\beta H(p,q)}}$$

with such an equation above, we have to sample all points in the phase space to get each $A(p,q)$.

For Importance Sampling, we take

$$\langle A \rangle = \frac{1}{N} \sum_{i=1}^{N} A(p_i, q_i)$$

1.6.2 Metropolis method

Goal: generate points with related probability of $e^{-\beta H}$.
Here, we start from old configuration $\vec{q}$, in order to generate new trial configuration $\vec{q}'$, whose physical meaning is needed propre step distance.

With MB distribution, (n: new and o: old) we need to enforce <u>detailed balance</u> which imposes

$$\frac{P(o \rightarrow n)}{P(n \rightarrow o)} = e^{-\beta [U(n) - U(o)]}$$

- if $U(n) \leqslant U(o)$, the probability is equal to 1
- if $U(n) > U(o)$, the probability is equal to $e^{-\beta [U(n) - U(o)]}$

Numerically, pick a uniform random number $x \in [0, 1]$ and test if $x < e^{-\beta [U(n) - U(o)]}$.

1.7 Applications

1.7.1 Thermodynamics quantities

MC/MD, for heat capacity, surface tension, phase diagram, compressibility

1.7.2 Structural properties

Radical Distribution function, each peak show the radius of each solution layer, the curve would converge to the 1 finally.

1.7.3 Dynamical properties

MD, diffusion coefficient, viscosity, ...

2 Chpt 2. Advanced Simulation Techniques

MD is great but there are several limitations

- system size & length of trajectory due to computer resource;
- classical force fields could not describe electron rearrangement, thus no chemical reaction;
- Not efficient to model barriers, need to force MD sample around the boundary;
- Free energies are difficult to calculate;

2.1 Free energy calculations

$$\Delta F = F_B - F_A = (-k_B T \ln Q_B) - (-k_B T \ln Q_A)$$

$$= -k_B T \ln \frac{\int dpdq e^{-\beta(K+U_B)}}{\int dpdq e^{-\beta(K+U_A)}} = -k_B T \ln \frac{Z_B}{Z_A}$$

$$Z_B = \int dq e^{-\beta U_B(q)} = \int dq e^{-\beta U_B(q)} e^{+\beta U_A(q)} e^{-\beta U_A(q)} = \int dq e^{-\beta[U_B(q)-U_A(q)]} e^{-\beta U_A(q)}$$

$$\frac{Z_B}{Z_A} = \left\langle e^{-\beta[U_B(q)-U_A(q)]} \right\rangle_A = \frac{\int dq e^{-\beta[U_B(q)-U_A(q)]} e^{-\beta U_A(q)}}{\int dq e^{-\beta U_A(q)}}$$

we sample at state A, which is only a little area in phase space. Thus we need $A \sim B$, namely two states approach.

2.2 Thermodynamics Integration

For continuous (adiabatic) switching from A to B, we pose the parameter $\lambda \in [0, 1]$

$$U(q, \lambda) = (1 - \lambda)U_A(q) + \lambda U_B(q)$$

$$F_\lambda = -k_B T \ln \int dpdq e^{-\beta[K+U(q,\lambda)]} = -k_B T \ln Q_\lambda$$

$$\frac{\partial F}{\partial \lambda} = -\frac{k_B T}{Q_\lambda} \frac{\partial Q_\lambda}{\partial \lambda} = -\frac{k_B T}{Z_\lambda} \frac{\partial Z_\lambda}{\partial \lambda} = -\frac{k_B T}{Z_\lambda} \int dq \left(-\beta \frac{\partial U_\lambda}{\partial \lambda}\right) e^{-\beta U_\lambda} = \left\langle \frac{\partial U_\lambda}{\partial \lambda} \right\rangle_\lambda$$

$$\Delta F = F_B - F_A = \int_0^1 d\lambda \frac{\partial F}{\partial \lambda} = \int_0^1 d\lambda \left\langle \frac{\partial U_\lambda}{\partial \lambda} \right\rangle_\lambda$$

$$\boxed{\Delta F = \int_0^1 \langle U_B - U_A \rangle_\lambda d\lambda}$$

with that we could calculate the pKa. Note we could only calculate the energy difference, instead of the absolute value. Also, it is hard to calculate the entropy.

2.2.1 Biased potential methods

We need reaction coordinates!

Umbrella sampling

- define coordinates,
- then bias potential energy with $W\left[F(q^N), s^*\right] = \frac{k}{2}\left[f(q) - s\right]^2$, where s^* is the target coordinate
- run series of simulations biasing potential centered on q^N that shift from s_A to s_B;

Pick a coordinate $f(q)$ to go from A and B. We are biasing the original potential with an additional term $W\left[f(q), s\right] = k\left[f(q) - s\right]^2/2$. However, biasing implies to modify the averaging computation.

Probability along s in a biased simulations i, $(q \xrightarrow{f} s$, i is the index of the bias as there might be many) with $W_i\left[f(q), s\right] = k\left[f(q) - s_i\right]^2/2$

$$
\begin{aligned}
P_b^i(s) = \langle\delta\left[f(\vec{q}_i) - \vec{s}\right]\rangle_b &= \frac{\int dq\, e^{-\beta U(q)} e^{-\beta W_q\left[f(q), s_i\right]}\delta\left[f(q) - s_i\right]}{\int dq\, e^{-\beta U(q)} e^{-\beta W_i\left[f(q)_i, s_i\right]}} \\
&= \frac{\int dq\, e^{-\beta U(q)} e^{-\beta W_q\left[f(q), s_i\right]}\delta\left[f(q) - s_i\right]}{\int dq\, e^{-\beta U(q)}} \times \frac{\int dq\, e^{-\beta U(q)}}{\int dq\, e^{-\beta U(q)} e^{-\beta W_i\left[f(q)_i, s_i\right]}} \\
&= \frac{\left\langle e^{-\beta W_i\left[f(q), s_i\right]}\delta\left[f(q) - s\right]\right\rangle}{\left\langle e^{-\beta W_i\left[f(q), s_i\right]}\right\rangle} = \frac{e^{-\beta W_i(s, s_i)}\left\langle\delta\left[f(q) - s\right]\right\rangle_o}{\left\langle e^{-\beta W_i\left[f(q), s_i\right]}\right\rangle_o} \\
&= \frac{e^{-\beta W_i(s, s_i)} p_0(s)}{const.indep.of.s}
\end{aligned}
$$

$$
F_0(s) = -k_B T \ln p_0(s) = -k_B T \ln\left\{\frac{c p_b(s)}{\exp\left[-\beta W_i(s, s_i)\right]}\right\} = F_b(s) - W_i(s, s_i) + cst.
$$

Thus you can bias, then sample to obtain F_b, then correct the bias and repeat with a different bias. The choice of the strength of the added potential has an important influence on its effect: too soft and it has no effect; too hard and the sampling window becomes too small; so many such samplings will be needed, which required too much time.

Metadynamics Put small Gaussians (as penalty to avoid return the same position) to fill the unknown potential surface, until the Gaussian be flat, we draw the complete surface by adding all the Gaussians. * But it's hard to know when to end or continue exit.

All these methods still have limitations. In particular, they accelerate the sampling only along one coordinate that was picked. But there are many other coordinates! For example, take the

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catalysis reaction of enzyme. There are diff. conformations for the protein, each of them having diff. barriers for the reaction, so both coordinates (conformation and reaction) need be optimised.

Tempering approach   For a chemical reaction, the probability of going through a barrier $\propto e^{-\frac{\Delta G}{k_B T}}$, thus we could decrease ΔG or increase the temperature T in order to increase the probability.

Parallel tempering simulated replicas of the system at different temperatures. Periodically, we will attempt to swap the coordinate between pairs of replicas at diff. temperatures, with an acceptance probability. More exactly, the temperatures are swapped but the coordinates are kept the same for each replica. (Lionel)

Difficult to reconstruct neighbor simulation, we could arrive all positions under one temperature by adding extra heat going higher temperature. Need to put closer temperatures, low probability between two states with big temperature difference.

2.3   Describe Chemical Reactions

Perform electron structure calculation at each temperature to obtain free energies.

2.3.1   ab-initio

ab-initio molecular dynamics = DFT (density functional theory) based on MD. This method is quite expensive, at most for hundreds of atoms and one hundred picoseconds. Typically, this is useful tom simulate the solvatation of a proton in water. However, it is much too costly for complex systems such as a protein reaction.

2.3.2   QM/MM

QM/MM means quantum mechanics + molecular mechanics. The core of the system is solved with quantum chemistry while the rest is simulated using molecular dynamics. This is well suited for proteins for instance, where QM for enzymes, MM for the rest solvents/proteins.

Not discord the rest directly, for 1. rest structure could affect active sites; 2. possible charge transfer...

$$\mathcal{H} = \mathcal{H}_{QM} + \mathcal{H}_{MM} + \mathcal{H}_{QM/MM}$$

where the interaction part is based on Lenard-Jones potential.

2.4 Simulating Very Long Time

2.4.1 Coarse graining

group atoms together, namely united paticle. Proteins become a long string with beams. Faster but not easily transferable

2.4.2 Multiple time steps

at least low then fast frequent scale.
- fast motions, short timestep
- slow motions, long timestep

3 Chpt 3. Time Correlation Functions

Ref: Tuckerman chpt 13; Chanlder chpt 8 "Introduction to Meca. Stat."

3.1 Non-equilibrium Stat. Mech.

For micro-mechanic system,

$$\frac{\delta v}{\langle v \rangle} \simeq \frac{1}{\sqrt{N}}$$

the noise obey the Gaussian distribution

3.2 Definition of Time-Correlation Functoin

For observable A, $\langle A \rangle = \int dpdq\rho(p,q)A(p,q)$, its variance $\sigma^2 = \langle A^2 \rangle - \langle A \rangle^2$ is still not dynamical, since Gaussian could only furnish how the distribution is, but without time information. For example, triangle oscillators with different frequencies would have the same Gaussian distribution.

Mathematically, $\langle A(t)A(t + \Delta t) \rangle \neq \langle A(t) \rangle \langle A(t + \Delta t) \rangle$, because of time correlation.

Definition: Time-Correlation Function (TCF)

$$c_{AB}(\Delta t) = \langle A(0)B(\Delta t) \rangle = \int dpdq\rho(p,q)A(p,q)\exp(i\mathcal{L}\Delta t)(p,q)$$

with A, B two observables. Below are some properties

$$c_{AB}(0) = \langle A(0)B(0) \rangle = \langle AB \rangle$$

$$\lim_{\Delta t \to \infty} c_{AB}(\Delta t) = \lim_{\Delta t \to \infty} \langle A(0)B(\Delta t) \rangle = \langle A \rangle \langle B \rangle$$

where $\langle \cdots \rangle$ means time average. For auto-correlation $c_{AA}(\Delta t) = \langle A(0)A(\Delta t) \rangle$.

$$c_{AA}(\Delta t) = \frac{1}{N} \sum_{i=1}^{N} A(t_i)A(t_i + \Delta t)$$

it's the function to describe how fast the system loses its memory.

Time-Correlation Function of fluctuations around average

$$\delta A(t) = A(t) - \langle A \rangle$$

$$c_{\delta A \delta A}(t) = \langle \delta A(0)\delta A(t) \rangle = \langle [A(0) - \langle A \rangle] \cdot [A(t) - \langle A \rangle] = \langle A(0)A(t) \rangle - \langle A(0) \rangle \langle A \rangle$$

$$= \langle A(0)A(t) \rangle - \langle A(0) \rangle \langle A \rangle - \langle A \rangle \langle A(t) \rangle + \langle A \rangle^2$$

where we use the relation $\langle A(t) \rangle = \langle A \rangle$.

3.3 Some properties of TCF

Only depend on time interval Δt. At long decays, correlation is fast $c_{AA}(t) \to \langle A \rangle^2$, max amplitude (for auto-correlation) is at $t = 0$. For classical observable A, c_{AA} is a real and even function of time t.

$$c_{AA}(t) = \langle A(0)A(t) \rangle = \langle A(t)A(0) \rangle = \langle A(0)A(-t) \rangle = c_{AA}(-t)$$

We introduce Correlation Time

$$\tau = \int_0^\infty dt \frac{\langle \delta A(0) \delta A(t) \rangle}{\langle \delta A^2 \rangle}$$

since c_{AA} decay exponentially $\propto e^{-t/\tau}$

3.4 Examples of TCF

3.4.1 Gas velocity auto-correlation

$$v_x \to c(t) = \langle v_x(0) v_x(t) \rangle$$

Initial value

$$\begin{cases} c(0) = \langle v_x^2 \rangle \\ \frac{1}{2} m v_x^2 = \frac{1}{2} k_B T \end{cases} \quad \Rightarrow \quad c(0) = \frac{k_B T}{m}$$

Ideal gas   Ideal gas without interaction in an isolated system with the flat velocity curve, namely the velocity would not change along time t. Thus for the auto-correlation function, it keeps the initial value $c(t) = c(0) = \frac{k_B T}{m}$.

Dilute gas   There would be rare collisions: the velocity is constant by blocks (between each collision). As a consequence, $c(t)$ starts at $k_B T / m$ and decays to 0 at infinity. The shape between 0 and ∞ is not quite known.

3.4.2 Harmonic oscillator

$$q(t) = q(0) \cos(\omega t)$$

hence the auto-correlation is also a periodic function with the same frequency, it also keeps memory. In reality, the envelope exponentially decays.

3.4.3 Dopole moment of a diatomic molecule in a gas

$$\langle \vec{\mu}(0) \cdot \vec{\mu}(t) \rangle = \mu_0^2 \langle \vec{v}(0) \vec{v}(t) \rangle$$

$$v_x(t) = \frac{\vec{\mu} \cdot \vec{e}_x}{\mu_0}$$

3.5 Application to diffusion coefficient

We first introduce the probability $p(\vec{r}, t)$ to find a particle in $\vec{r}$ at time t. Reminder, we have the conservation law (like that from Hydrodynamics)

$$\frac{\partial p(\vec{r}, t)}{\partial t} + \vec{\nabla} \cdot \vec{j}(\vec{r}, t) = 0$$

also we have the Fick law of diffusion, where D is the coefficient of diffusion

$$\vec{j}(\vec{r}, t) = -D\vec{\nabla}p(\vec{r}, t)$$

this equation is not strictly obeyed, only empirical.

We then have

$$\frac{\partial p(\vec{r}, t)}{\partial t} = D\nabla^2 \frac{\partial p(\vec{r}, t)}{\partial t}$$

for Mean Square displacement, $\vec{r}(0) = \vec{0}$

$$\left\langle \Delta r^2(t) \right\rangle = \left\langle |\vec{r}(t) - \vec{r}(0)|^2 \right\rangle = \int d\vec{r} r^2 p(\vec{r}, t)$$

$$\frac{d}{dt} \left\langle \Delta r^2(t) \right\rangle = D \int dxdydz(x^2 + y^2 + z^2)\left(\frac{\partial^2 p}{\partial x^2} + \frac{\partial^2 p}{\partial y^2} + \frac{\partial^2 p}{\partial z^2}\right) = 3D \int dxdydz \cdot x^2 \frac{\partial^2 p}{\partial x^2} \cdots\cdots ①$$

$$+ 6D \int dxdydz \cdot x^2 \frac{\partial^2 p}{\partial y^2} \cdots\cdots ②$$

for the term 2, it equals to 0; for the term 1, we make integrals by parts twice

$$① \rightarrow 3D \int dydz \left\{ \left[x^2 \frac{\partial p}{\partial x}\right]_{xmin}^{xmax} - \int dx 2x \frac{\partial p}{\partial x} \right\}$$

thus $①+② \rightarrow 6D \int dxdydz p(x, y, z, t) = 6D$. We obtain Einstein's equation

$$\frac{d}{dt} \left\langle \Delta r^2(t) \right\rangle = 6D$$

$$\boxed{\left\langle \Delta r^2(t) \right\rangle = 6Dt}$$

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Note that $6 = 2 \times 3$, namely 2 times the number of dimensions.

Yet, this whole derivation requires Fick's law, which is not always valid. In particular, at small time (ie the inertial regime), the mean square displacement is quadratic. Indeed, in the inertial regime, $\vec{F} = 0$ so $\Delta\vec{r}(t) = \vec{v}(0)t$, and $\Delta r^2(t) = v^2(0)t^2$.

- In the initial region, $\Delta r^2(t) \propto t^2$
- In the diffusive region, $\Delta r^2(t) \propto t$

Connection between diffusion and time-correlation diffusion.

Collisions randomize velocity, and diffusion faster when velocity remains correlated

$$\Delta\vec{r}(t) = \int_0^t d\tau\,\vec{v}(\tau)$$

$$\frac{d}{dt}\left\langle \Delta r^2(t) \right\rangle = \frac{d}{dt}\left\langle |\vec{r}(t) - \vec{r}(0)|^2 \right\rangle = 2\left\langle \vec{v}(t) \cdot |\vec{r}(t) - \vec{r}(0)| \right\rangle = 2\left\langle \vec{v}(0) \cdot [\vec{r}(0) - \vec{r}(-t)] \right\rangle$$

$$= 2\int_{-t}^0 \langle \vec{v}(0) \cdot \vec{v}(\tau)\rangle d\tau = 2\int_0^t \langle \vec{v}(0) \cdot \vec{v}(\tau)\rangle d\tau$$

thus we find the relation

$$\lim_{t\to\infty} \frac{d}{dt}\left\langle \Delta r^2(t) \right\rangle = 2\int_0^\infty \langle \vec{v}(0) \cdot \vec{v}(\tau)\rangle d\tau = 6D$$

and we call the equation below as Green-Kubo relation, where 3 originates from the number of dimensions.

$$\boxed{D = \frac{1}{3}\int_0^\infty \langle \vec{v}(0) \cdot \vec{v}(\tau)\rangle d\tau}$$

If $D = 0$, it means the integrals compensate with each other. It is sensitive to long tails. Einstein relation is available only if t is large enough.

At a certain temperature T_0, NVT not correct for kinetic, thus we sample to NVE system, then T would fluctuate around T_0 average.

4 Rate Theory

biblio:

Chandler, Intro to Modern Stat. Mech., chpt 8

Peters, Reaction Rate Theory and Rate Events, chpt 10 13 16 17

4.1 Rate laws and Time-Correlation Functions

4.1.1 Phenomenological rate laws

We consider the most simple reaction below, with two rate constant k_{AB} and k_{BA} for the toward and backward reaction, respectively

$$A \leftrightarrow B$$
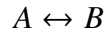
thus we could write the concentration function

$$[A](t) = \langle [A] \rangle + \{[A](0) - \langle [A] \rangle\} e^{-t/\tau}$$

$$[B](t) = \langle [B] \rangle - \{[A](0) - \langle [A] \rangle\} e^{-t/\tau}$$

and we have the decay time τ and its expression $\frac{1}{\tau} = k_{AB} + k_{BA}$

4.1.2 Microscopic Approach

Consider a reaction system with N particles in total, the number of particles in A could be expressed as

$$n_A(t) = \sum_{i=1}^{N} h_A \left[q_i(t) \right]$$

where q_i is the reaction coordinate, and h_A is the modified Heaviside function. If $q < q^*$, $h_A(q) = 1$, else $h_A(q) = 0$.

Introduce Relaxation following initial perturbation hamiltonian, $H = H_0 - \epsilon n_A$. The relaxation after perturbation is turned off.

$$\bar{n}_A(t) = \frac{\int dpdq e^{-\beta(H_0 - \epsilon n_A)} e^{i\mathcal{L}_0 t} n_A(0)}{\int dpdq e^{-\beta(H_0 - \epsilon n_A)}}$$

where we use the relation that $e^{i\mathcal{L}_0 t} n_A(0) \simeq n_A(t)$. Then we make perturbation expansion of ϵ, the o represents equilibrium

$$\bar{n}_A(t) = \frac{\langle e^{\beta \epsilon n_A} n_A(t) \rangle_o}{\langle e^{\beta \epsilon n_A} \rangle_o} \simeq \frac{\langle n_A \rangle_o + \beta \epsilon \langle n_A(0) n_A(t) \rangle_o}{1 + \beta \epsilon \langle n_A \rangle_o} \simeq \langle n_A \rangle_o + \beta \epsilon \left[\langle n_A(0) n_A(t) \rangle - \langle n_A \rangle_o^2 \right]$$

where we've seen $\left[\langle n_A(0)n_A(t)\rangle - \langle n_A\rangle_o^2\right] = \langle \delta n_A(0)\delta n_A(t)\rangle$, with $\delta n_A(t) = n_A(t) - \langle n_A\rangle$.

$$\boxed{\frac{\bar{n}_A(t) - \langle n_A\rangle_o}{\bar{n}_A(0) - \langle n_A\rangle_o} = \frac{\langle \delta n_A(0)\delta n_A(t)\rangle_o}{\langle \delta n_A^2\rangle_o}}$$

Such an equation told us that! The system loses microscopic memory ~ macro system perturbation correlation. We call the linear response above as Onsager regression.

4.1.3 Reaction flux

From Rate Law

$$\frac{\bar{n}_A(t) - \langle n_A\rangle_o}{\bar{n}_A(0) - \langle n_A\rangle_o} = e^{-t/\tau} = \frac{\langle \delta n_A(0)\delta n_A(t)\rangle_o}{\langle \delta n_A^2\rangle_o} = \frac{N\langle \delta h_A[q(0)] \cdot \delta h_A[q(t)]\rangle}{N\langle (\delta h_A)^2\rangle}$$

then we add d/dt, note $C(t) = C(-t)$ and $\dot{C}(t) = -\dot{C}(-t)$

$$-\frac{1}{\tau}e^{-t/\tau} = \frac{\langle \delta h_A[q(0)] \frac{d}{dt}\delta h_A[q(t)]\rangle}{\langle (\delta h_A)^2\rangle} = \frac{-\langle \delta h_A[q(t)] \frac{d}{dt}\delta h_A[q(0)]\rangle}{\langle (\delta h_A)^2\rangle}$$

then we use the property of Heaviside funciton $h_A = h_A^2$

$$\langle (\delta h_A)^2\rangle = \langle (h_A)^2\rangle - 2\langle h_A\rangle^2 + \langle h_A\rangle^2 = \langle h_A\rangle - \langle h_A\rangle^2 = (1 - \langle h_A\rangle)\langle h_A\rangle^2 = \langle h_A\rangle\langle h_B\rangle$$

$$-\frac{1}{\tau}e^{-t/\tau} = -\frac{\langle \overline{\dot{\delta h_A}}(0)\delta h_A(t)\rangle}{\langle h_A\rangle\langle h_B\rangle}$$

take the hypothesis $t \ll \tau$, we have $e^{-t/\tau} \simeq 1$, and $\langle h_A\rangle + \langle h_B\rangle = 1$ as well,

$$\frac{1}{\tau} = k_{AB} + k_{BA} = k_{AB}\left(1 + \frac{\langle h_A\rangle}{\langle h_B\rangle}\right) = \frac{k_{AB}}{\langle h_B\rangle}$$

thus we have

$$k_{AB} = \frac{\langle \overline{\dot{\delta h_A}}(0)\delta h_A(t)\rangle}{\langle h_A\rangle}$$

note the Heaviside function is the integration of delta distribution

$$\overline{\dot{\delta h_A}}(0) = \frac{d}{dt}\delta h_A[q(t)]\,|_{t=0} = \frac{dq}{dt}\,|_{t=0}\{-\delta[q(0) - q^*]\}$$

$$k_{AB} = \frac{1}{\langle h_A\rangle}\langle \dot{q}(0)\{-\delta[q(0) - q^*]\}\delta h_A(t)\rangle$$

$$\delta h_A(t) = h_A[q(t)] - \langle h_A\rangle = 1 - h_B[q(t)] - \langle h_A\rangle$$

$$\boxed{k_{AB} = \frac{1}{\langle h_A\rangle}\langle \dot{q}(0)\delta[q(0) - q^*]h_B[q(t)]\rangle}$$

where $\langle h_A \rangle$ is the normalized factor with probability in A, $\dot{q}(0)\delta\left[q(0) - q^*\right]$ is the flux through Transition State at $t = 0$, and $h_B\left[q(t)\right]$ is the probability to be in B after delay time t.

It seems weird that k_{AB} is a function of time t, rather than a constant. Indeed, in short delay t, rate to B is just depends on the initial velocity, because we start from q^* inside the delta function. Only if $h_B\left[q(t)\right]$ is not correlated with initial velocity, we could extract that from average $\langle \cdots \rangle$.

4.2 Transition State Theory

Eying, Wigner, Polary, 1930-1935

Central hypothesis:

- No recrossing;
- quasi-eq on reactant side, MB distribution
- Born-Oppenhemier approximation
- classical separable motion algorithm coordination at TS

TST rate constant, no recrossing $h_B(t) = \theta\left[\dot{q}(0)\right]$

$$k_{TST} = \frac{1}{\langle h_A \rangle}\langle \dot{q}(0)\delta\left[q(0) - q^*\right]\theta\left[\dot{q}(0)\right]\rangle = \langle j_X^{\neq}\rangle_R$$

the real rate constant $k = \kappa k_{TST}$ with $\kappa \in [0, 1]$

$$\kappa = \frac{k}{k_{TST}} = \frac{\langle \delta\left[q(0) - q^*\right]\dot{q}(0)h_B(t)\rangle}{\langle \delta\left[q(0) - q^*\right]\dot{q}(0)\theta\left[q(0)\right]\rangle}$$

$\dot{q}(0)$	$h_B(t)$	$\dot{q}(0)h_B(t)$		$\theta\left[\dot{q}(0)\right]$
+	1	+	=	+
+	0	0	<	+
−	1	−	<	0
−	1	0	=	0

4.3 Correction to TST

NB: TST is usually very good approximations of k

4.3.1 Kramer theory (1940s)

with Langevin equation

$$m\ddot{q} = -\frac{\partial V}{\partial q} - m\gamma\dot{q} + F$$

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Kramers result for

$$\kappa = \frac{\gamma}{\omega^{\neq}}\left(\sqrt{\frac{1}{4} + \frac{\omega^{\neq 2}}{\gamma^2}} - \frac{1}{2}\right)$$

where $\omega^{\neq}$ is supposed the frequency for harmonic potential at the peak.

- low friction $\kappa \sim 1$
- high friction $\kappa \sim \frac{\omega^{\neq}}{\gamma} \to 0$

4.3.2 Grote-Hynes (1980s)

Hynes was in ENS before

GLE used, coordinate would not respond simultaneously, decay exist. If environment could not respond quickly enough, species cross the barrier without recrossing before solvent response.

$$m\ddot{q} = -\frac{\partial V}{\partial q} - m\int_0^t \zeta(t-\tau)\dot{q}(\tau)d\tau + F(t)$$

where $\int \cdots$ is the decay force due to solvent, $\langle F(0)F(t)\rangle = mk_BT\zeta(t)$.

$$\omega_r^2 - \omega^{\neq 2} + \omega_r\int_0^\infty e^{-\omega_r t}\zeta(t)dt = 0$$

where ω_r is the effective barrier frequncy. This is Grote-Hynes equation, and we have $\kappa_{GH} = \frac{\omega_r}{\omega^{\neq}}$

Limiting regimes:

1. Solvent fast with respect barrier crossing time

   $\zeta(t) = \zeta_0\delta(t)$, Kramer result, full friction

2. Very slow solvent, $\tau \gg 1/\omega^{\neq}$.

$$m\ddot{q} = -\frac{\partial V}{\partial q} - m\int_0^t \zeta(t-\tau)\dot{q}(\tau)d\tau + F(t)$$

we expand that with harmonic approximation, where

$$\zeta(t-\tau)\dot{q}(\tau) \sim -m\zeta(0)\left[q(t) - q(0)\right] \sim -\frac{m}{2}\frac{d}{dq}\left[\zeta(0)\left(q(t)-q(0)\right)^2\right]$$

$$m\ddot{q} = -\frac{\partial}{\partial q}\left[V(q) + \frac{m}{2}\zeta(0)\left(q(t)-q(0)\right)^2\right] + F(t)$$

at the top of barrier $V(q) \simeq V(q^{\neq}) - \frac{1}{2}m\omega^{\neq}(q - q^{\neq})^2$, and the effective frequency at barrier $\omega_r = \sqrt{\omega^{\neq 2} - \zeta(0)}$

Weak friction $\kappa_{GH} = \frac{\omega_r}{\omega^{\neq}} = \sqrt{1 - \zeta(0)/\omega^{\neq 2}}$, so $\kappa_{GH} \sim 1$

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Strong friction called dynamical caging, system is trapped at the Transition State by solvent even though it is more stable to cross the barrier toward reactant of product

In general, $k_{TST} > k$ and $\kappa_{Kramer} < \kappa_{GH}$, since the system is not so fast in general, Kramer overestimate. Reaction faster inside enzyme than in solution ? block box, potential barrier, enzyme dynamical.

5   Quantum Time-Dependent Stat. Mech. Application to Spectroscopy & Energy transfer

Ref: Tuckerman chpt. 14; Notes A. Tokmokoff (UChicago)

5.1   Introduction

Note that $\langle \cdots \rangle$ means ensemble average, but bra-ket in Quantum Mechanics (QM).

5.2   Time-Dependent Perturbation Theory

Allow transition without disturbing original states. We pose $\hat{H}_0$ the unperturbed Hamiltonian, $\hat{H}_1(t)$ the time-dependent hamiltonian, the total hamiltonian $\hat{H}(t) = \hat{H}_0 + \hat{H}_1(t)$, and the time-dependent Schrödinger equation $\hat{H}(t)|\psi(t)\rangle = -i\hbar\partial_t |\psi(t)\rangle$. There are two approaches / pictures of QM.

- Time-dependence in state vector?
- Time-dependence in operator?
- Time-dependence in both?

Schrödinger picture Operator $\hat{H}$ time-independent, state vector time-dependent

$$\hat{H}(t)|\psi(t)\rangle = -i\hbar\partial_t |\psi(t)\rangle \qquad \Rightarrow \qquad |\psi(t)\rangle = \exp\left[-\frac{i}{\hbar}\hat{H}(t - t_0)\right]|\psi(t)\rangle$$

and the observable $\langle \hat{A}(t)\rangle = \langle \psi(t)|\hat{A}|\psi(t)\rangle$

Heisenberg picture Operator time-dependent, state vector time-independent

$$\frac{d\hat{A}}{dt} = \frac{1}{i\hbar}\left[\hat{A}, \hat{H}\right] \qquad \Rightarrow \qquad \hat{A}(t) = \exp\left[+\frac{i}{\hbar}\hat{H}(t - t_0)\right]\hat{A}(t_0)\exp\left[-\frac{i}{\hbar}\hat{H}(t - t_0)\right]$$

and the observable $\langle \hat{A}(t)\rangle = \langle \psi(t)|\hat{A}(t)|\psi(t)\rangle$

Interaction picture   We treat $\hat{H}_0$ with Schrödinger picture, $\hat{H}_1$ with Heisenberg picture, namely operator and state vector all time-dependent. Operator evolves according to $\hat{H}_0$, while state vector evolves according to $\hat{H}_1$

$$|\psi_S(t)\rangle = \exp\left[-\frac{i}{\hbar}\hat{H}(t - t_0)\right]|\psi_S(t_0)\rangle$$

$$\hat{A}_I(t) = \exp\left[+\frac{i}{\hbar}\hat{H}_0(t - t_0)\right]\hat{A}_I(t_0)\exp\left[-\frac{i}{\hbar}\hat{H}_0(t - t_0)\right]$$

$$|\psi_I(t)\rangle = \exp\left[+\frac{i}{\hbar}\hat{H}_0(t - t_0)\right]|\psi_S(t)\rangle$$

5.3   Time Correlation Function and frequency spectroscopy

5.3.1   Thermal average

$$|\psi_I(t)\rangle = \exp\left[-\frac{i}{\hbar}(\hat{H} - \hat{H}_0)(t - t_0)\right]|\psi_S(t_0)\rangle$$

$$= \exp\left[+\frac{i}{\hbar}\hat{H}_0(t - t_0)\right]|\psi_S(t)\rangle$$

For Average transition rate, we use Fermi Golden Rule $R(\omega) = \sum_i p_i \sum_f R_{i \to f}(\omega)$ where p_i is the thermal probability.

$$R(\omega) = \frac{2\pi}{\hbar}|F(\omega)|^2\sum_{i,f}p_i\left|\langle\psi_f|\hat{V}|\psi_i\rangle\right|^2\delta(E_f - E_i - \hbar\omega)$$

where $F(\omega)$ is the amplitude of incoming field, $\hat{V}$ is the perturbation due to interaction with fields, $\delta()$ allows the energy conservation

5.3.2   Time Correlation Function

Note the Fourier transform $\delta(E) = \frac{1}{2\pi\hbar}\int_{-\infty}^{+\infty} dE\exp(iEt/\hbar)$

$$R(\omega) = \frac{1}{\hbar^2}\int_{-\infty}^{+\infty}dt\,|F(\omega)|^2\sum_{i,f}p_i\exp\left[\frac{i}{\hbar}(E_f - E_p - \hbar\omega)t\right]\left|\langle\psi_f|\hat{V}|\psi_i\rangle\right|^2$$

$$= \frac{1}{\hbar^2}|F(\omega)|^2\int_{-\infty}^{+\infty}dt\,e^{-i\omega t}\sum_{i,f}p_i\langle\psi_i|\hat{V}|\psi_f\rangle\langle\psi_f|\hat{V}|\psi_i\rangle\exp(\frac{it}{\hbar}E_f)\exp(-\frac{it}{\hbar}E_i)$$

$$= \frac{1}{\hbar^2}|F(\omega)|^2\int_{-\infty}^{+\infty}dt\,e^{-i\omega t}\sum_{i,f}p_i\langle\psi_i|\hat{V}|\psi_f\rangle\langle\psi_f\left|e^{iE_f t/\hbar}\cdot\hat{V}\cdot e^{-iE_i t/\hbar}\right|\psi_i\rangle$$

note that $\sum_f |\psi_f\rangle\langle\psi_f| = \mathbf{1}$

$$R(\omega) = \frac{1}{\hbar^2} |F(\omega)|^2 \int_{-\infty}^{+\infty} dt e^{-i\omega t} \sum_{i,f} p_i \langle\psi_i|\hat{V}|\psi_f\rangle\langle\psi_f|\hat{V}_I(t)|\psi_i\rangle$$

$$= \frac{1}{\hbar^2} |F(\omega)|^2 \int_{-\infty}^{+\infty} dt e^{-i\omega t} \sum_{i,f} p_i \langle\psi_i|\hat{V}_I(0)\hat{V}_I(t)|\psi_i\rangle$$

$$R(\omega) = \frac{1}{\hbar^2} |F(\omega)|^2 \int_{-\infty}^{+\infty} dt e^{-i\omega t} \langle\hat{V}_I(0)\hat{V}_I(t)\rangle$$

5.3.3   Some aspects of quantum TCFs

Microscopic reversibility requires $R_{i\to f}(\omega) = R_{f\to i}(\omega)$, but note $R(\omega) \neq R(-\omega)$. We then repeat the process before [suppose $F(-\omega) = F(\omega)$]

$$R(-\omega) = \frac{2\pi}{\hbar} |F(\omega)|^2 \sum_{i,f} p_i \left|\langle\psi_f|\hat{V}|\psi_i\rangle\right|^2 \delta(E_f - E_i + \hbar\omega)$$

$$= \frac{2\pi}{\hbar} |F(\omega)|^2 \sum_{i,f} p_f \left|\langle\psi_i|\hat{V}|\psi_f\rangle\right|^2 \delta(E_i - E_f + \hbar\omega)$$

$$= \frac{2\pi}{\hbar} |F(\omega)|^2 \sum_{i,f} p_i e^{-\beta\hbar\omega} \left|\langle\psi_i|\hat{V}|\psi_f\rangle\right|^2 \delta(E_f - E_i - \hbar\omega) = e^{-\beta\hbar\omega} R(\omega)$$

$$R(-\omega) = \frac{1}{\hbar^2} |F(\omega)|^2 \int_{-\infty}^{+\infty} dt e^{+i\omega t} \langle\hat{V}_I(0)\hat{V}_I(t)\rangle = \frac{1}{\hbar^2} |F(\omega)|^2 \int_{-\infty}^{+\infty} dt e^{-i\omega t} \langle\hat{V}_I(t)\hat{V}_I(0)\rangle$$

we could find the relation $\left[\hat{V}_I(0), \hat{V}_I(\omega)\right] \neq 0 \quad \leftrightarrow \quad R(-\omega)$.

For Energy Absorption spectrum, "Net" energy absorbed by unit of time at frequency ω

$$Q(\omega) = [R(\omega) - R(-\omega)]\hbar\omega = \hbar\omega(1 - e^{-\beta\hbar\omega})R(\omega)$$

$$R(\omega) + R(-\omega) = (1 + e^{-\beta\hbar\omega})R(\omega) = \frac{1}{\hbar^2} |F(\omega)|^2 \int_{-\infty}^{+\infty} dt e^{-i\omega t} \left[\langle\hat{V}_I(0)\hat{V}_I(t)\rangle + \langle\hat{V}_I(t)\hat{V}_I(0)\rangle\right]$$

therefore

$$Q(\omega) = \frac{2\omega}{\hbar} |F(\omega)|^2 \tanh\left(\frac{\beta\hbar\omega}{2}\right) \int_{-\infty}^{+\infty} dt e^{-i\omega t} \left\langle \frac{1}{2}\left\{\hat{V}_I(0), \hat{V}_I(t)\right\} \right\rangle$$

at the classical limit, we have $\hbar \to 0$

$$Q_{cl}(\omega) = \beta\omega^2 |F(\omega)|^2 \int_{-\infty}^{+\infty} dt e^{-i\omega t} \left\langle\hat{V}(0)\hat{V}(t)\right\rangle_{cl}$$

finally we connect with TCF !!!

5.4 Optical Absorption Coefficient

5.4.1 Derivation

Introduction of system with incident light wave interaction hamiltonian, where $E(t)$ is the amplitude

$$\hat{H}_I(t) = -\hat{\mu} \cdot \hat{\epsilon} \cdot E(t)$$

$$\text{absorption coefficient} = \frac{\text{net absorbed energy/unit of time}}{\text{incident energy flux (Poynting vector)}}$$

$$\alpha(\omega) \propto \frac{\omega}{\hbar c} \tanh\left(\frac{\beta \hbar \omega}{2}\right) \int_{-\infty}^{+\infty} dt\, e^{-i\omega t} \left\langle \frac{1}{2} \{\hat{\mu}(0), \hat{\mu}(t)\} \right\rangle$$

$$\alpha_{cl}(\omega) \propto \frac{\beta \omega^2}{c} \int_{-\infty}^{+\infty} dt\, e^{-i\omega t} \langle \hat{\mu}(0), \hat{\mu}(t) \rangle_{cl}$$

and the linescope

$$\sigma(\omega) = \frac{1}{2\pi} \int_{-\infty}^{+\infty} dt\, e^{-i\omega t} \langle \vec{\mu}(0) \cdot \vec{\mu}(t) \rangle$$

spontaneous fluctuation of $\vec{\mu}$, molecule of field

5.4.2 Application to IR spectroscopy

$$\vec{\mu} = \vec{\mu}_0 + \frac{\partial \vec{\mu}}{\partial q}\Big|_{q=0} \cdot q + \mathcal{O}(q^2)$$

where $\vec{\mu}_0$ is the permanent dipole moment

$$\sigma(\omega) = \frac{1}{2\pi} \left|\frac{\partial \mu}{\partial q}\right|^2 \int_{-\infty}^{+\infty} dt\, e^{-i\omega t} \langle q(0) \cdot q(t) \rangle$$

where q refers to the nuclear displacement

5.4.3 Application to Raman Spectroscopy

Track: Replace dipole with dipole induced by the 1st interaction

$$\vec{\mu}_{\text{int}} = \alpha \cdot \vec{E}(t) \qquad \alpha = \alpha_0 + \frac{\partial \alpha}{\partial q}\Big|_{q=0} \cdot q + \mathcal{O}(q^2)$$

linescope

$$\sigma(\omega) = \frac{1}{2\pi} \int_{-\infty}^{+\infty} dt\, e^{-i\omega t} \langle q(0) \cdot q(t) \rangle \left|\frac{\partial \alpha}{\partial q}\right|^2$$

Both IR & Raman spectroscopy are related to the nuclear displacement.

Selection Rule Difference?

Part II

Stat. Mech. (Guilluam Stirnemann)

6   Chpt 1. Basic Conceptions of Stat. Mech.

6.1   Why Stat. Mech.?

Biochemical systems contain many ($\sim 10^{23}$) particles, + non-trivial interactions among them.

Q: How to extract valuable information about the system?

A: Probability approach = Stat. Mech.

Developed in 19th century (Maxwell, Gibbs), thermodynamics, we will focus on dynamical aspects, which is important in chemistry.

Stat. Mech.: probabilities based on positions (r^N) and momenta (P^N), we will be working with phase space $\Pi(r^N, P^N)$ in $6N$ dimensions, where N is the number of particles. In stat. mech.,

$$Proba(r^N) \propto \exp\left[-\mathcal{H}(r)\right]$$

where $\mathcal{H}$ is the classical hamiltonian of the system.

6.2   From Newton equations to the Lagrangian formulations

6.2.1   Newtown's equation

For a system with N particles in 3D, we have positions $\{r_i\}_{i=1,\cdots,N}$ and velocities $\{v_i\}_{i=1,\cdots,N}$. Suppose F_i as the forces acting on particles, in principle, it depends no the positions and velocities. We have the Newton second law

$$m\frac{dv_i}{dt} = F_i$$

or another form

$$m\ddot{r}_i = F_i$$

We have N such equations. Introduce $p_i = m_i v_i$,

$$\frac{dp_i}{dt} = F_i \quad \forall i$$

the classical evolution of N-particles system is fully determined by a total $6N$ equations.

6.2.2 Conservative forces

To go further, we now make the assumption that all forces in the system are conservative.

Define. A conservative forces is a force that is derives from a function called potential energy.

$$F_i(r_1, r_2, \cdots, r_N) = -\nabla_i U(r_1, r_2, \cdots, r_N)$$

it does not depend on velocity at anytime.

Why is it conservative? Suppose that $W_{AB} = \int_A^B \vec{F}_i d\vec{r}_i$, if $\vec{F}_i = -\vec{\nabla} U_i$, we have $W_{AB} = U_A - U_B$, therefore

$$\oint \vec{F} d\vec{l} = 0$$

6.2.3 Lagrangian formulations

We have seen the potential energy. We also introduce a quantity called kinetic energy

$$K(\dot{r}_1, \dot{r}_2, \cdots, \dot{r}_N) = \frac{1}{2} \sum_{i=1}^{N} m_i \dot{r}_i^2$$

Define. The Lagrangian $\mathcal{L}$ in the difference between kinetic and potential energy expressed

$$\mathcal{L}(r_1, r_2, \cdots, r_N, \dot{r}_1, \dot{r}_2, \cdots, \dot{r}_N) = K(\dot{r}_1, \dot{r}_2, \cdots, \dot{r}_N) - U(r_1, r_2, \cdots, r_N)$$

The equations of motion are generalized via Euler-Lagrange equation

$$\frac{d}{dt}\left(\frac{\partial \mathcal{L}}{\partial \dot{r}_i}\right) - \frac{\partial \mathcal{L}}{\partial r_i} = 0$$

$$\frac{\partial \mathcal{L}}{\partial \dot{r}_i} = m\dot{r}_i \quad \Rightarrow \quad \frac{d}{dt}\left(\frac{\partial \mathcal{L}}{\partial \dot{r}_i}\right) = m\ddot{r}_i$$

$$\frac{\partial \mathcal{L}}{\partial r_i} = -\frac{\partial U}{\partial r_i} = F_i$$

You could use any conjugate variables inside Euler-Lagrange equations, including position & momentum, energy & time. For more details, see Tuckerman page 12-13.

6.2.4 Energy Conservation

An important sequence of conservative forces is that energy is conserved. The total energy is the sum of kinetic energy and potential energy:

$$E = K + U = \frac{1}{2} \sum_i m_i \dot{r}_i^2 + U$$

we have the derivative

$$\frac{dE}{dt} = \sum_i m_i \dot{r}_i \ddot{r}_i + \frac{dU}{dt}$$

$$\frac{dU}{dt} = \frac{dU}{dr_i}\frac{dr_i}{dt} = \frac{dU}{dr_i}\dot{r}_i$$

thus

$$\frac{dE}{dt} = \sum_i \dot{r}_i \left(m_i \ddot{r}_i + \frac{\partial U}{\partial r_i} \right) = 0$$

since $m_i \ddot{r}_i = -\partial U / \partial r_i = F_i$ is always valid. Therefore E is conserved.

6.3 Hamiltonian formulations

We will now use another formulations, which is connected to the Lagrangian formulation but often more useful. Indeed, Hamiltonian could be derived from Lagrangian by Legendre Transform.

6.3.1 Legendre transform

Suppose $f : x \rightarrow f(x)$, if $s = \frac{\partial f}{\partial x}$, then we have the transform

$$\hat{f}(s) = f(x) - sx$$

if $s_i = \frac{\partial f}{\partial x_i}$, then we have the Legendre transform of f:

$$\hat{f}(s_1, \cdots, s_N) = f(x_1, \cdots, x_N) - \sum_i s_i x_i$$

6.3.2 Construction of Hamiltonian

According to Lagrangian

$$\frac{\partial \mathcal{L}}{\partial \dot{r}_i} = m_i \dot{r}_i = p_i$$

we then make Legendre transform

$$\hat{\mathcal{L}} = \mathcal{L} - \sum_i p_i r_i = K - U - \sum_i p_i r_i = \frac{1}{2}\sum_i m_i \dot{r}_i^2 - U - \sum_i p_i r_i = -\frac{1}{2}\sum_i m_i \dot{r}_i^2 - U = -\mathcal{H}$$

we call the Hamiltonian

$$\mathcal{H}(r_1, \cdots, r_N, p_1, \cdots, p_N) = \frac{1}{2}\sum_i \frac{p_i^2}{2m_i} + U(r_1, r_2, \cdots, r_N)$$

This is the total energy of the system expressed in terms of positions and momenta. One can easily know that

$$\dot{r}_i = \frac{\partial \mathcal{H}}{\partial p_i} \qquad \dot{p}_i = -\frac{\partial \mathcal{H}}{\partial r_i}$$

there are $6N$ equations in total.

Like the Lagrangian formulations, the proof of the Hamiltonian is that we can write such equations for any set of conjugated coordinations, prove

$$\dot{q}_\alpha = \frac{\partial \mathcal{H}}{\partial p_\alpha} \qquad \dot{p}_\alpha = -\frac{\partial \mathcal{H}}{\partial q_\alpha}$$

6.3.3 Energy Conservation

Hamiltonian is conserved, since

$$\frac{d\mathcal{H}}{dt} = \sum_i \left(\frac{\partial \mathcal{H}}{\partial r_i} \frac{\partial r_i}{\partial t} + \frac{\partial \mathcal{H}}{\partial p_i} \frac{\partial p_i}{\partial t} \right) = \sum_i \left(-\dot{p}_i \frac{\partial r_i}{\partial t} + \dot{r}_i \frac{\partial p_i}{\partial t} \right) = 0$$

If we take a point in phase space X with $X(t = 0) = \{r_1(0), \cdots, r_N(0), p_1(0), \cdots, p_N(0)\}$, the phase space trajectory will satisfy $\mathcal{H}[X(t)] = const$; constant energy on a $6N - 1$ hypersurface.

6.4 Phase Space Motion

6.4.1 Poissons Bracket & Liouville

In phase space, we suppose $\Gamma(q, p) = (q_i, p_i)_{i=1,\cdots,N}$. Let's consider a function $F(\Gamma, t)$

$$\frac{dF}{dt} = \frac{\partial F}{\partial t} + \sum_i \left(\frac{\partial F}{\partial q_i} \dot{q}_i + \frac{\partial F}{\partial p_i} \dot{p}_i \right) = \frac{\partial F}{\partial t} + \sum_i \left(\frac{\partial F}{\partial q_i} \frac{\partial \mathcal{H}}{\partial p_i} - \frac{\partial F}{\partial q_i} \frac{\partial \mathcal{H}}{\partial q_i} \right) = \frac{\partial F}{\partial t} + \{F, \mathcal{H}\}$$

with Poisson Bracket

$$\{F, G\}_i = \frac{\partial F}{\partial q_i} \frac{\partial G}{\partial p_i} - \frac{\partial F}{\partial p_i} \frac{\partial G}{\partial q_i}$$

We can also define the so-called Liouville operator

$$i\mathcal{L}\cdot = \{\cdot, \mathcal{H}\}$$

thus

$$\frac{dF}{dt} = \frac{\partial F}{\partial t} + i\mathcal{L}F$$

F is a constant of motion if $\partial F/\partial t = 0$ and $i\mathcal{L}F = 0$ for all t. We can also write

$$i\mathcal{L} = \sum_i \left(\dot{q}_i \frac{\partial}{\partial q_i} + \dot{p}_i \frac{\partial}{\partial p_i} \right)$$

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In general, $\partial F/\partial t = 0$ therefore

$$\frac{dF}{dt} = i\mathscr{L}F$$

$$F\left[\Gamma(t)\right] = \exp\left[i\mathscr{L}(t - t_0)\right] F\left[\Gamma(t_0)\right]$$

where $\exp\left[i\mathscr{L}(t - t_0)\right]$ is the propagator, and $F\left[\Gamma(t_0)\right]$ is Heisenberg formulation. In particular, we have the trajectory in phase space

$$\Gamma(t) = \exp\left(i\mathscr{L}t\right) \cdot \Gamma(0)$$

6.4.2   Conservation Laws

System without external forces $\sum_i F_i = 0$, and $\sum_i -\frac{\partial \mathcal{H}}{\partial q_i} = 0$. Consider the total momenta $P = \sum_i p_i$,

$$i\mathscr{L}P = \sum_i \{p_i, \mathcal{H}\} = \sum_i \dot{p}_i = \sum_i F_i = 0$$

thus the momenta is conserved.

We will make the analogy with hydrodynamics, $\nabla\vec{\sigma} = 0$ means incompressible flow,

$$\nabla_x \dot{X} = \sum_i \left(\frac{\partial \dot{q}_i}{\partial q_i} + \frac{\partial \dot{p}_i}{\partial p_i}\right) = \sum_i \left[\frac{\partial}{\partial q_i}\left(\frac{\partial \mathcal{H}}{\partial p_i}\right) - \frac{\partial}{\partial p_i}\left(\frac{\partial \mathcal{H}}{\partial q_i}\right)\right] = \sum_i \left(\frac{\partial^2 \mathcal{H}}{\partial q_i \partial p_i} - \frac{\partial^2 \mathcal{H}}{\partial p_i \partial q_i}\right) = 0$$

we have shown that motion in phase space is incompressible; in other word, the volume is conserved. This is one form of the Liouville theorem.

6.4.3   Phase Space Density & Liouville equation

We will now adapt a probability approach, namely "phase space density" $\rho(\Gamma, t)d\Gamma$, the probability of observing the system between Γ and $\Gamma + d\Gamma$

What's the time evolution of ρ? $\rho(\Gamma, 0) \to \rho(\Gamma, t)$, this is given by the Liouville equation

$$\frac{\partial \rho(\Gamma, t)}{\partial t} + i\mathscr{L}\rho(\Gamma, t) = 0$$

See Tukermann page 64-70 for demonstration.

At equilibrium, $\frac{\partial \rho}{\partial t} = 0$, also we should have

$$i\mathscr{L}\rho = 0 \qquad \leftrightarrow \qquad \rho(\Gamma, t) = \rho(\Gamma, 0)$$

this is another version of Liouville theorem, ρ the phase space density is conserved.

6.4.4 Ensemble average at equilibrium

$$\langle A \rangle = \int d\Gamma \rho(\Gamma, t) A(\Gamma)$$

One can show that the general solution of the Liouville $i\mathscr{L}\rho = 0$, is any function of the Hamiltonian

$$\rho(\Gamma) = F\left[\mathcal{H}(\Gamma)\right]$$

This function F should generate the fact that ρ is normalized $\int d\Gamma \rho(\Gamma) = 1$, and that is adversed of

$$\rho(\Gamma) = \frac{1}{Z}F(\mathcal{H})$$

with the partition function $Z = \int d\Gamma F\left[\mathcal{H}(\Gamma)\right]$ For the canonical ensemble for example, $\beta = 1/(k_B T)$

$$\rho(\mathcal{H}) = \frac{\exp(-\beta\mathcal{H})}{Z}$$

7 Chpt 2. Brownian motion and diffusion processes

7.1 From early experimental observation to the Einstein theory

7.1.1 Brown (1827)

Brown, British botanant, reported on the random motion of pollen particles under a microscope. The same thing happens with coal dust, leading to nothing about alive matters. This matches earlier observations. Brown speculates this is due to impact with solvent molecules, implying indirect evidences of atoms. *** Echoes agnostic theory developed around that time by Dalton & others, but there was no direct measurement or observation of atoms.

7.1.2 Einstein (1905), Theory of Brownian Motion

Clean connection with the motion of impacts with atoms. Einstein proposes a stochastic model for Brownian motion. There are two main results:

1. $D \leftrightarrow$ mobility of the particle;
2. $D \leftrightarrow$ mean square of displacement;

for

1. he looks at flux conservation;
2. he makes the following demonstration; (and also recovers the diffusion equation)

As for a system with N particles at time $t = 0$, we have the positions $\{x_i^0, y_i^0, z_i^0\}$, after the time τ, each of these particles has experienced a displacement Δ_i.

Δ follows a probability distribution ϕ, with $dn = N\phi(\Delta)d\Delta$, where dn is the number of particles that experience a jump between Δ and $\Delta + d\Delta$ during τ. Note $\phi(\Delta) = \phi(-\Delta)$, and we have normalized condition

$$\int_{-\infty}^{+\infty} \phi(\Delta)d\Delta = 1$$

We now introduce the probability density of particles $\rho(x, t)$

$$dx\rho(x, t + \tau) = dx \int_{-\infty}^{+\infty} \rho(x + \Delta)\phi(-\Delta)d\Delta$$

I can also write

$$\rho(x, t + \tau) = \rho(x) + \frac{\partial \rho}{\partial t}\tau + \cdots$$

$$\rho(x + \Delta, t) = \rho(x) + \frac{\partial \rho}{\partial x}\Delta + \frac{\partial^2 \rho}{\partial x^2}\frac{\Delta^2}{2} + \cdots$$

thus we obtain

$$\rho(x) + \frac{\partial \rho}{\partial t}\tau = \int_{-\infty}^{+\infty}\left[\rho(x) + \frac{\partial \rho}{\partial x}\Delta + \frac{\partial^2 \rho}{\partial x^2}\right]\phi(\Delta)d\Delta$$

$$\rho(x) + \frac{\partial \rho}{\partial t}\tau = \rho(x)\int_{-\infty}^{+\infty}\phi(\Delta)d\Delta + \rho(x)\int_{-\infty}^{+\infty}\Delta\phi(\Delta)d\Delta + \frac{\partial^2 \rho}{\partial x^2}\int_{-\infty}^{+\infty}\Delta^2\frac{\phi(\Delta)}{2}d\Delta$$

since $\phi(\Delta)$ is even function of Δ, $\int_{-\infty}^{+\infty}\Delta\phi(\Delta)d\Delta = 0$, we solve

$$\frac{\partial \rho}{\partial t} = \frac{1}{2\tau}\frac{\partial^2 \rho}{\partial x^2}\int_{-\infty}^{+\infty}\Delta^2\phi(\Delta)d\Delta$$

Below is microscopic diffusion equation

$$\boxed{\frac{\partial \rho}{\partial t} = D\frac{\partial^2 \rho}{\partial x^2}}$$

we get the diffusion coefficient

$$D = \frac{1}{2\tau}\int_{-\infty}^{+\infty}\Delta^2\phi(\Delta)d\Delta = \frac{\langle \Delta X^2\rangle}{2\tau}$$

Einstein's conlusion:

one can measure the average deplacement after a delay τ, $\lambda = \sqrt{2D\tau}$

at the same time he also obtained (η refers to viscocity , r is the radius of particle)

$$D = \frac{RT}{N_A \cdot 6\pi\eta r}$$

which allows us to measure N_A Avogadro number.

7.1.3   Jean Perrin (1908)

Nobel Prize in 1926. He measured N_A with different techniques, which confirmed Einstein's theory, and the existence of atoms.

7.1.4   Paul Langevin (1908)

Formation in term of equations of motions and laws of mechanism.

Brillant idea: introduce the concept of a random force.

7.2 Langevin equation

7.2.1 Friction is not enough

The force required to move this particle in the fluid is

$$\vec{F} = \zeta \vec{a}$$

with ζ as the friction coefficient. Stockes worked on that in 1850s, $\zeta = 6\pi\eta r$.

Thus the equation of motion ($\gamma = \zeta/m$)

$$m\dot{v} = -\zeta v \quad \rightarrow \quad \dot{v} = -\frac{\zeta}{m}v \quad \rightarrow \quad \dot{v} = -\gamma v \quad \rightarrow \quad v(t) = v(0)e^{-\gamma t}$$

This result cannot explain Brown mechanism, since :

1. $v(t) \rightarrow 0$ if $t \rightarrow \infty$, but particles would not stop;
2. $\langle v^2 \rangle = \langle v^2(0) \rangle e^{-2\gamma t} \rightarrow 0$ if $t \rightarrow \infty$, but it should be $\frac{k_B T}{m}$;

Langevin equation is to introduce random forces

$$\boxed{m\frac{dv}{dt} = -\zeta v + \delta F}$$

where the first term refers to systematic put of the environment influence, and the second term δF refers to fluctuation / random put.

What can we write about δF?

- random impacts with solvent molecules;
- very sudden effect, no correlation in space and in time $\langle \delta F(t) \rangle = 0$

or we write $\langle \delta F(t)\delta F(t') \rangle = 2B\delta\left(|t' - t|\right)$, furnished as Gaussian white noise.

7.2.2 Solution of Langevin equation

Introduce Laplace transforms

$$\tilde{f}(s) = \int_0^{+\infty} f(t)e^{-st}\,dt \qquad \tilde{f}'(s) = s\tilde{f}(s) - f(0)$$

then we will use that to use the Langevin equation

$$\frac{dv}{dt} = -\gamma v + \frac{\delta F}{m}$$

$$s\tilde{v}(s) - v(0) = -\gamma v(s) + \frac{\delta F(s)}{m}$$

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$$\tilde{v}(s) = \frac{v(0)}{s + \gamma} + \frac{\delta \tilde{F}(s)}{m(s + \gamma)}$$

then we do the inverse transform by $\mathscr{L}^{-1}\{\tilde{F}(s)\tilde{G}(s)\} \to \int_0^t F(t - \tau)G(\tau)d\tau$

$$\boxed{v(t) = v(0)e^{-\gamma t} + \int_0^t dt' \frac{\delta F(t')}{m} \exp\left[-\gamma(t - t')\right]}$$

We check $\langle v(t) \rangle$ while $t \to \infty$

$$\langle v(t) \rangle = \langle v(0) \rangle e^{-\gamma t} + \int_0^t dt' \frac{\langle \delta F(t') \rangle}{m} \exp\left[-\gamma(t - t')\right] = \langle v(0) \rangle e^{-\gamma t} \to 0$$

as well as $\langle v^2(t) \rangle$

$$\langle v^2(t) \rangle = \langle v^2(0) \rangle e^{-2\gamma t} + 2e^{-\gamma t} \int_0^t dt' \frac{\langle \delta F(t)v(0) \rangle}{m} e^{-\gamma(t-t')} + \int_0^t dt_1 \int_0^t dt_2 e^{-\gamma(t-t_1)} e^{-\gamma(t-t_2)} \frac{\langle \delta F(t_1)\delta F(t_2) \rangle}{m^2}$$

$$= \langle v^2(0) \rangle e^{-2\gamma t} + \int_0^t dt_1 e^{-2\gamma(t-t_1)} \frac{2B}{m^2}$$

$$= \langle v^2(0) \rangle e^{-2\gamma t} - \frac{1}{2\gamma}(e^{-2\gamma t} - 1) \times \frac{2B}{m^2}$$

$$= \langle v^2(0) \rangle e^{-2\gamma t} + \frac{B}{\zeta m}(1 - e^{-2\gamma t})$$

7.2.3   Fluctuation dissipation theorem

Long time limit $\langle v^2(t) \rangle \to \frac{k_B T}{m}$, but now we have $\langle v^2(t) \rangle \to \frac{B}{\zeta m}$, leading to

$$B = k_B T \zeta$$

We also have $\langle \delta F(0)\delta F(t) \rangle = 2k_B T \zeta \delta(t)$. Hence we obtain the fluctuation dissipation theorem

$$\boxed{\zeta = \frac{1}{k_B T} \int_0^\infty \langle \delta F(0)\delta F(t) \rangle dt}$$

7.2.4   Kubo and Stokes-Einstein relationship

Now let's consider the condition function of v

$$\langle v(0)v(t) \rangle = \langle v^2(0) \rangle e^{-\gamma t}$$

but $\frac{1}{2}m\langle v^2(0) \rangle = \frac{k_B T}{2}$, thus

$$\langle v(0)v(t) \rangle = \frac{k_B T}{m} e^{-\gamma t}$$

$$\Delta x(t) = \int_0^t v(\tau_1)d\tau_1$$

$$\langle \Delta x^2(t) \rangle = \left\langle \int_0^t d\tau_1 \int_0^t d\tau_2 v(\tau_1)v(\tau_2) \right\rangle$$

we have its derivative

$$\frac{d}{dt}\langle \Delta x^2(t) \rangle = 2\int_0^t d\tau \langle v(0)v(\tau) \rangle = 2\int_0^t dt' \langle v^2(0) \rangle e^{-\gamma t'} = \frac{2\langle v^2(0) \rangle}{\gamma}\left(1 - e^{-\gamma t}\right)$$

$$\boxed{\frac{d}{dt}\langle \Delta x^2(t) \rangle = \frac{2k_B T}{\zeta}\left(1 - e^{-\gamma t}\right)}$$

then we integrate a second time

$$\langle \Delta x^2(t) \rangle = \langle \Delta x^2(0) \rangle + \frac{2k_B T}{\zeta}\left[t + \frac{1}{\gamma}\left(e^{-\gamma t} - 1\right)\right] = 0 + \frac{2k_B T}{\zeta}\left[t + \frac{1}{\gamma}\left(e^{-\gamma t} - 1\right)\right]$$

$$\xrightarrow{t \ll 1/\gamma} \frac{2k_B T}{\zeta}\left[t + \frac{1}{\gamma}(1 - \gamma t)\right] = \frac{k_B T \gamma}{\zeta}t^2 = \frac{k_B T}{m}t^2$$

$$\xrightarrow{t \gg 1/\gamma} \frac{2k_B T}{\zeta}(t + \frac{1}{\gamma}) = \frac{2k_B T}{\zeta}t$$

Hence

- at short time, $\langle \Delta x^2 \rangle \propto t^2$, refers to ballistic regime;
- at long time, $\langle \Delta x^2 \rangle \propto t$, refers to diffusive regime;

We also recover Einstein's relation

$$\lim_{t \to \infty} \frac{\langle \Delta x^2 \rangle}{2t} = \frac{k_B T}{\zeta} = D$$

It also follows from the expression of $\langle v(0)v(t) \rangle$

$$\boxed{\int_0^\infty \langle v(0)v(t) \rangle dt = \frac{k_B T}{\zeta} = D}$$

which is called Kubo relation

7.2.5 Limitation of Langevin equation

Markovian The Langevin equation is Markovian, the random force is white noise, the friction at time t is only connected to the velocity at time t.

But the friction could depend on $v(s)$ with $s < t$, namely the memory effect in the friction. We replace

$$\zeta v(t) \to -\int_{-\infty}^t K(t - s)v(s)ds$$

where K is the friction memory kernel.

This will suppose new conditions on time random force to satisfy an equivalent version of the "fluctuation dissipation" theorem. Giving up longer white noise, but colored noise, namely non-Markovian, we would step into Generalized Langevin.

External potential and we assume "free" diffusion In reality, the molecule is always moving under a potential, with the force $\vec{F} = -\vec{\nabla}U$. Therefore, we modify the Langevin equation as

$$\frac{dp}{dt} = -\zeta\frac{p}{m} - U'(x) + \delta F$$

In practice, very complicated to solve the equation. For example, one issue is that $\langle F(x)\rangle$; it can only be solved in very specific case. An alternative consists in taking a probabilistic picture, and we can adopt a stochastic approach, leading to Fokker-Planck equation.

7.3 The Generalized Langevin Equation

GLE, see Tuckerman chpt. 15

7.3.1 Model of a system + a bath

* Solvent is very important in chemistry (e.g. the rate limiting step of reactions can be the reorientation of the solvent molecule.) $\Rightarrow$ Hence the solvent should be taken into account as a "bath".

* So far, we have seen a simple description of a bath effect.

- a systematic effect = friction;
- a random effect = random force;

Now we will focus the GLE that will evidence a more complex treatment of a bath. Note GLE is very useful for some theories of chemical rate + vibrational dephasing & relaxation.

The Hamiltonian of the particle in the absence of bath

$$H = \frac{p^2}{2\mu} + V(q)$$

In the presence of a bath, solvent positions $\{y_i\}_{i=1,\cdots,N}$, and we have

$$U_{total}(q, y_1, \cdots, y_N) = V(q) + U_{bath}(q, y_1, \cdots, y_N)$$

where the last term is for example a sum of 2-body interaction $U_{bath} = \sum_i \sum_{j\neq i} U(y_i - y_j)$.

Now let's assume we have an equilibrium position for U,

$$\{\bar{q}_\alpha\} = \{\bar{q}, \bar{y}_1, \cdots, \bar{y}_n\}$$

$$\frac{\partial U_{bath}}{\partial q_\alpha}\Big|_{\{\bar{q}\}} = 0 \quad \forall \alpha$$

then we compute 2nd order expression of U_{bath}

$$U_{bath}(q, y_1, \cdots, y_N) = U_{bath}\{\bar{q}, \bar{y}_1, \cdots, \bar{y}_n\} + \sum_\alpha \frac{\partial U_{bath}}{\partial q_\alpha}\Big|_q (q_\alpha - \bar{q}_\alpha) + \frac{1}{2}\sum_{\alpha,\beta}(q_\alpha - \bar{q}_\alpha)\frac{\partial^2 U_{bath}}{\partial q_\alpha \partial q_\beta}(q_\beta - \bar{q}_\beta)$$

For simplification, we will shift the potential scale $U_{bath}(\bar{q}, \bar{y}_1, \cdots, \bar{y}_n) = 0$, and we replace $q_\alpha - \bar{q}_\alpha \to q_\alpha$; and we separate q from other coordinates. Pose $H_{\alpha\beta} = \frac{\partial^2 U}{\partial q_\alpha \partial q_\beta}\big|_{eq.}$, we can finally write

$$U_{bath}(q, y_1, \cdots, y_N) = \sum_{\alpha=1}^{n} c_\alpha q y_\alpha + \frac{1}{2}\sum_{\alpha=1}^{n}\sum_{\beta=1}^{n} H_{\alpha\beta}y_\alpha y_\beta$$

where $c_\alpha = H_{\alpha q}/2$. The only term left $H_{00} \sim H_{qq}$ would be added into $V(q)$.

There exist the coordinate transformation such that $\{y_\alpha\} \to \{x_\alpha\}$, and the quadratic term $H_{\alpha\beta}y_\alpha y_\beta \to k_\alpha x_\alpha^2$, namely diagonalization. Thus we could make conclusion that for the total Hamiltonian

$$\mathcal{H} = \frac{p^2}{2\mu} + V(q) + \sum_{\alpha=1}^{n}\left(\frac{p_\alpha^2}{2m_\alpha} + g_\alpha q x_\alpha + \frac{1}{2}m_\alpha \omega_\alpha^2 x_\alpha^2\right)$$

7.3.2 Derivation of GLE

$$\dot{q} = \frac{\partial H}{\partial p} = \frac{p}{\mu} \qquad \dot{p} = -\frac{\partial H}{\partial q} = -\frac{dV}{dq} - \sum_\alpha g_\alpha x_\alpha$$

$$\dot{x}_\alpha = \frac{\partial H}{\partial p_\alpha} = \frac{p_\alpha}{m_\alpha} \qquad \dot{p}_\alpha = -\frac{\partial H}{\partial q_\alpha} = -g_\alpha q - m_\alpha \omega_\alpha^2 x_\alpha$$

$$\mu\ddot{q} = \dot{p} = -\frac{dV}{dq} - \sum_\alpha g_\alpha x_\alpha$$

$$m_\alpha \ddot{x}_\alpha = \dot{p}_\alpha = -g_\alpha q - m_\alpha \omega_\alpha^2 x_\alpha$$

Reminder, for Laplace transform

$$\tilde{f}(s) = \int_0^{+\infty} f(t)e^{-st}dt \qquad \tilde{f}'(s) = s\tilde{f}(s) - f(0)$$

hence we do that twice

$$s^2 \tilde{x}_\alpha(s) - \dot{x}_\alpha(0) - s x_\alpha(0) = -\frac{g_\alpha}{m_\alpha}\tilde{q}(s) - \omega_\alpha^2 \tilde{x}_\alpha(s)$$

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$$\tilde{x}_\alpha(s) = \frac{s}{s^2 + \omega_\alpha^2} x_\alpha(0) + \frac{\dot{x}_\alpha(0)}{s^2 + \omega_\alpha^2} - \frac{g_\alpha \tilde{q}(s)}{m_\alpha(s^2 + \omega_\alpha^2)}$$

since $\mathscr{L}(\cos bt) = \frac{s}{b^2 + s^2}$ and $\mathscr{L}(\sin bt) = \frac{b}{b^2 + s^2}$, we solve

$$x_\alpha = x_\alpha(0)\cos(\omega_\alpha t) + \frac{\dot{x}_\alpha(0)}{\omega_\alpha}\sin(\omega_\alpha t) - \frac{g_\alpha}{m_\alpha \omega_\alpha}\int_0^t d\tau\, q(\tau)\sin\left[\omega_\alpha(t - \tau)\right]$$

after Integration by part for the last term,

$$\to\to\to \frac{1}{\omega_\alpha}\left[q(t) - q(0)\cos(\omega_\alpha t)\right] - \frac{1}{\omega_\alpha}\int_0^t \dot{q}_\alpha(\tau)\cos\left[\omega_\alpha(t - \tau)\right]d\tau$$

Now we insert that to the first equation, obtaining the GLE:

$$\mu\ddot{q} = -\frac{dV}{dq} - \sum_\alpha q_\alpha x_\alpha = -\frac{dV}{dq} - \sum_\alpha g_\alpha\left[x_\alpha(0)\cos(\omega_\alpha t) + \frac{p_\alpha(0)}{m_\alpha \omega_\alpha}\sin(\omega_\alpha t) + \frac{g_\alpha}{m_\alpha \omega_\alpha^2}q(0)\cos(\omega_\alpha t)\right]$$
$$- \sum_\alpha \frac{g_\alpha^2}{m_\alpha \omega_\alpha^2}\int_0^t d\tau\, \dot{q}(\tau)\cos\left[\omega_\alpha(t - \tau)\right] + \sum_\alpha \frac{g_\alpha^2}{m_\alpha \omega_\alpha^2}q(t)$$

This corresponds to a form of the GLE

$$\mu\ddot{q} = -\frac{dW}{dq} - \int_0^t d\tau\, \dot{q}(\tau)\zeta(t - \tau) + R(t)$$

where $W(q), \zeta(t), R(t)$ represents the potential of mean force, friction, random force.

$$W(q) = V(q) - \sum_\alpha \frac{g_\alpha}{2m_\alpha \omega_\alpha^2}q^2$$

$$\zeta(t) = \sum_\alpha \frac{g_\alpha^2}{m_\alpha \omega_\alpha^2}\cos(\omega_\alpha t)$$

$$R(t) = -\sum_\alpha g_\alpha\left[\left(x_\alpha(0) + \frac{g_\alpha^2 q(0)}{m_\alpha \omega_\alpha^2}\right)\cos(\omega_\alpha t) + \frac{p_\alpha(0)}{m_\alpha \omega_\alpha^2}\sin(\omega_\alpha t)\right]$$

- Potential of mean force. "Effective" potential along q, basically a projection of the system force-energy along q.

- Random force. Does not seem random but in practice, we have so many solvent particles, so many frequencies and the total friction, $R(t)$ will look random.

  By taking average in the canonical ensemble, $\langle q(0)R(t)\rangle = 0$, $\langle \dot{q}(0)R(t)\rangle = 0$ for all t. We can also estimate $\langle R(0)R(t)\rangle = \frac{1}{\beta}\sum_\alpha \frac{g_\alpha^2}{m_\alpha \omega_\alpha^2}\cos(\omega_\alpha t)$, as well as $\boxed{\langle R(0)R(t) = k_B T \zeta(t)\rangle}$. The fluctuation-dissipation theorem is recovered!

- The dynamical friction kernel. $\int_0^t d\tau\, \dot{q}(\tau)\zeta(t - \tau)$ means that the bath has a finite time response to the fluctuation of the motion along q. The characterization of $\zeta(t)$ are given by the TCF of the random force.

Limitations

- As for Infinitely fast response $\zeta(t) = 2\zeta_0\delta(t)$, $\langle R(0)R(t)\rangle = 2k_BT\zeta_0\delta(t)$

$$\mu\ddot{q} = -\frac{dW}{dq} - \int_0^t d\tau\,\dot{q}(\tau) \times 2\zeta_0\delta(t-\tau) + R(t)$$

we recover the Langevin equation

$$\mu\ddot{q} = -\frac{dW}{dq} - \zeta_0\dot{q}(t) + R(t)$$

- As for Infinitely slow response, $\zeta(t)$ = constant along the motion

$$\int_0^t d\tau\,\zeta(t-\tau) = \int_0^t \tau\dot{q}(\tau)\zeta = \zeta\,[q(t) - q(0)]$$

$$\mu\ddot{q} = -\frac{d}{dq}\left[W(q) + \frac{\zeta}{2}(q(t) - q(0))^2\right] + R(t)$$

where the extra term $(q(t) - q(0))^2$ represents the dynamic caging effect, which means that the particle would be trapped inside solvent cage.

7.4 Fokker-Planck equations & applications

7.4.1 Derivation of the Fokker-Planck

Ref: Zwanzig ch 2.2

WHat's FP?

Form of Liouville equation to study stochastic motion of a dynamical system obeying a GLE with white noise.

Interest?

To study "non-linear" Langevin equation (when a potential is added)

... Fokker obtained PhD in 1913. Kolmegorov (1931) got the same equation but in a more general form.

***

We will the very general derivation $a = (a_1, \cdots, a_n)$ set variables that obeys a Langevin Equation withe white noise $\langle F(0)F(t)\rangle = 2B\delta(t)$, $\frac{da}{dt} = v(a) + F(t)$ for any function $v(a)$ of a.

Let's consider the probability density of a at time t, $f(a,t)$, where we have the normalized condition $\int f(a,t)da = 1$. According to the conservation law

$$\frac{\partial f}{\partial t} + \text{div}(Vf) = 0 \qquad \leftrightarrow \qquad \frac{\partial f}{\partial t} + \frac{\partial}{\partial a}\left(\frac{da}{dt}f\right) = 0$$

which is just the Liouville equation, and $V = \frac{da}{dt}$. Thus we have

$$\frac{\partial f}{\partial t} = -\frac{\partial}{\partial t}[v(a)f(a,t) + F(t)f(a,t)]$$

Let's call $\mathcal{L} \cdot = \frac{\partial}{\partial a}v(a)\cdot$, this equation can be solved and the solution is

$$f(a,t) = e^{-t\mathcal{L}}f(a,0) - \int_0^t ds e^{-(t-s)\mathcal{L}}\frac{\partial}{\partial a}F(s)f(a,s)$$

we now inject that into the expression mentioned above, obtaining

$$\frac{\partial f}{\partial t} = -\mathcal{L}f(a,t) - \frac{\partial}{\partial a}F(t)f(a,0)e^{-t\mathcal{L}} + \frac{\partial}{\partial a}F(t)\int_0^t ds e^{-(t-s)\mathcal{L}}\frac{\partial}{\partial a}F(s)f(a,s)$$

We will now take the ensemble average $\langle \cdots \rangle$ (average over noise)

$$\frac{\partial\langle f(a,t)\rangle}{\partial t} = -\mathcal{L}\langle f(a,t)\rangle - \frac{\partial}{\partial a}\left\langle F(t)f(a,0)e^{-t\mathcal{L}}\right\rangle + \frac{\partial}{\partial a}\left\langle F(t)\int_0^t ds e^{-(t-s)\mathcal{L}}\frac{\partial}{\partial a}F(s)f(a,s)\right\rangle$$

where the second term vanishes since we have random force with zero ensemble average. As for the third term, we have $\langle F(t)F(s)\rangle = 2B\delta(t-s)$. Finally, we got General form of Fokker-Planck equation

$$\frac{\partial\langle f(a,t)\rangle}{\partial t} = -\frac{\partial}{\partial a}v(a)\langle f(a,t)\rangle + \frac{\partial}{\partial a}B\frac{\partial}{\partial a}\langle f(a,t)\rangle$$

Note that we made an assumption between B and $v(a)$ (such as a fluctuation-dissipation theorem). In practice, one can imagine that B need not compensate for friction.

- If B is too big, system expands in phase space;
- If B is too small, system will shrink in phase space
- If B exactly compensate for friction, we got FD theorem, we reach a steady state.

7.4.2 Brownian motion and Smoluchowski equation

$$a = \begin{pmatrix} x \\ p \end{pmatrix} \qquad \dot{a} = \begin{pmatrix} \dot{x} \\ \dot{p} \end{pmatrix}$$

$$\dot{x} = \frac{p}{m} \qquad \dot{p} = -U'(x) - \zeta\frac{p}{m} + F_p(t) \qquad \langle F_p(t)F_p(t')\rangle = 2\zeta k_B T\delta(t-t')$$

$$F(t) = \begin{pmatrix} 0 \\ F_p(t) \end{pmatrix} \qquad B = \begin{pmatrix} 0 & 0 \\ 0 & \zeta k_B T \end{pmatrix}$$

thus FP eq. turns to

$$\frac{\partial f}{\partial t} = -\frac{\partial}{\partial x}\frac{p}{m}f - \frac{\partial}{\partial p}\left[\left(-U'(x) - \frac{\zeta p}{m}\right)f\right] + \zeta k_B T\frac{\partial^2}{\partial p^2}f$$

if $\zeta = 0$, we recover the Liouville equation

$$\frac{\partial f}{\partial t} = -\frac{\partial}{\partial x}\frac{p}{m}f - \frac{\partial}{\partial p}[-U'(x)f]$$

$$\frac{\partial f}{\partial t} + \frac{\partial}{\partial x}\frac{p}{m}f + \frac{\partial}{\partial p}[-U'(x)f] = 0$$

* In the general case where we have noise and friction, the solution of this equation, where "ss" means steady state $\frac{\partial f}{\partial s} = 0$

$$f_{ss}(x,p) = \frac{\exp[-\beta \mathcal{H}(x,p)]}{\iint \exp[-\beta \mathcal{H}(x,p)]\,dx\,dp}$$

Smoluchowski: similar motion (LE) but even simple, we neglect the inertial motion due to acceleration, namely we are in diffusion regime, so $\dot{x}^2 = 0$, and $t \gg \frac{1}{\gamma}$. Thus the LE is just the function of x

$$\dot{x} = -\frac{U'(x)}{\zeta} + \frac{F(x)}{\zeta}$$

where $v(x) = -\frac{U'(x)}{\zeta}$, and the random force $\frac{F(x)}{\zeta} \leftrightarrow B = \frac{k_B T}{\zeta}$

$$\frac{\partial f(x,t)}{\partial t} = -\frac{\partial}{\partial x}\left[-\frac{U'(x)}{\zeta}f(x,t)\right] + \frac{k_B T}{\zeta}\frac{\partial^2}{\partial x^2}f(x,t)$$

$$\boxed{\frac{\partial f}{\partial t} = \frac{1}{\zeta}\frac{\partial}{\partial x}U'(x)f + \frac{k_B T}{\zeta}\frac{\partial^2 f}{\partial x^2}}$$

$$\boxed{\frac{\partial f}{\partial t} = D\frac{\partial}{\partial x}e^{-\beta U(x)}\frac{\partial}{\partial x}e^{\beta U(x)}f}$$

This is Smoluchowski equation, where $D = \frac{k_B T}{\zeta}$. If $U(x)$ is constant, we have the diffusion equation again

$$\frac{\partial f}{\partial t} = D\frac{\partial^2 f}{\partial x^2}$$

7.4.3 Determination of mean first passage times (mfpt)

Let's work in a space with the volume V. The motion is following a LE, What is the mean first passage time? for exiting that volume V, starting from an initial position within V.

We give $P(a,t)$ as the probability density

$$\frac{\partial P}{\partial t} = -\frac{\partial}{\partial a}v(a)P + \frac{\partial}{\partial a}B\frac{\partial}{\partial a}P = \mathcal{D}P$$

where $\mathscr{D}\cdot$ is the diffusion operator

$$\mathscr{D}\cdot = -\frac{\partial}{\partial a}v(a) + \frac{\partial}{\partial a}B\frac{\partial}{\partial a}\cdot$$

We start from an initial position $a_0 \in V$, so $P(a,0) = \delta(a - a_0)$

$$\frac{\partial P}{\partial t} = \mathscr{D}P \qquad \Rightarrow \qquad P(a,t) = e^{\mathscr{D}t}P(a,0)$$

$$\boxed{P(a,t) = e^{\mathscr{D}t}\delta(a - a_0)}$$

$$\boxed{\mathscr{D}^\dagger \tau = -1}$$

To estimate the mfpt, we are observing boundary condition: at time $t \to \infty$, $P(a,t) \to 0$ for $a \in V$. The survival probability $S(a_0,t) =$ the number of points still in the volume at time t starting at a_0.

$$S(t,a_0) = \int_V da P(a,t)$$

$S(t,a_0) - S(t + dt,a_0) =$ number of systems in V at time t that escaped during $t \to t + dt$.

We can then define $\rho(a_0,t)dt$ the probability of leaving during that time interval

$$\rho(a_0,t) = -\frac{\partial S(t,a_0)}{\partial t}$$

$$\rho(a_0,t)dt = S(t,a_0) - S(t + dt,a_0) = -\frac{\partial S(t,a_0)}{\partial t}dt$$

The mfpt $\tau(a_0) = \int_0^\infty dt\, t \times \rho(a_0,t)$

$$\tau(a_0) = \int_0^\infty dt\, t \cdot \left[-\frac{\partial S(t,a_0)}{\partial t}\right] = \int_0^\infty S(t,a_0)dt - [t \cdot S(t,a_0)]\,|_0^\infty = \int_0^\infty S(t,a_0)dt$$

Remind that $S(t,a_0) = \int_V da P(a,t)$, $\tau(a_0) = \int_0^\infty dt \int_V da P(a,t)$, thus

$$\tau(a_0) = \int_0^\infty dt \int_V da\, e^{\mathscr{D}t}\delta(a - a_0) = \int_0^\infty dt \int_V da\, \delta(a - a_0) \cdot e^{\mathscr{D}^\dagger t} \cdot \mathbf{1}$$

$$\tau(a_0) = \int_0^\infty dt\, e^{\mathscr{D}^\dagger t} \cdot \mathbf{1}$$

$$\mathscr{D}^\dagger \tau(a_0) = \int_0^\infty dt\, \mathscr{D}^\dagger e^{\mathscr{D}^\dagger t} = \left[e^{\mathscr{D}^\dagger t}\right]\,|_0^\infty$$

if $t \to \infty$, then $P(a_0,t) \to 0$, and $e^{\mathscr{D}^\dagger t} \to 0$, finally we obtain $\boxed{\mathscr{D}^\dagger \tau(a_0) = -1}$

7.4.4 Kramers theory of crossing barrier

High friction limit ζ large $\to \gamma$ large. $t \gg 1/\gamma$, always in the diffusion region, no ballastic motion, we have Soluchowski equation.

$$\mathscr{D}\cdot = D\frac{\partial}{\partial x}e^{-\beta U(0)}\frac{\partial}{\partial x}e^{\beta U(0)}$$

$$\mathscr{D}^{\dagger}\cdot = De^{\beta U(0)}\frac{\partial}{\partial x}e^{-\beta U(0)}\frac{\partial}{\partial x}\cdot$$

$$De^{\beta U(0)}\frac{\partial}{\partial x}e^{-\beta U(0)}\frac{\partial}{\partial x}\tau(x) = -1$$

$$e^{\beta U(0)}\frac{\partial}{\partial x}e^{-\beta U(0)}\frac{\partial}{\partial x}\tau(x) = \frac{-1}{D}$$

integrate from $-\infty$ to y inside the volume

$$\frac{\partial}{\partial x}e^{-\beta U(0)}\frac{\partial}{\partial x}\tau(x) = -\frac{1}{D}e^{-\beta U(0)} \qquad \Rightarrow \qquad \left[e^{-\beta U(0)}\frac{\partial}{\partial x}\tau(x)\right]\Big|_{-\infty}^{y} = \int_{-\infty}^{y}-\frac{1}{D}e^{-\beta U(Z)}dZ$$

$$e^{-\beta U(y)}\frac{\partial}{\partial x}\tau(x)|_{y} = -\frac{1}{D}\int_{-\infty}^{y}e^{-\beta U(Z)}dZ$$

$$\frac{\partial}{\partial x}\tau(x)|_{y} = -\frac{1}{D}e^{\beta U(y)}\int_{-\infty}^{y}e^{-\beta U(Z)}dZ$$

then integrate from x_0 to x_{max}, note that $\tau(x_{max}) = 0$ since it's the transition state point

$$\tau(x_{max}) - \tau(x_0) = -\frac{1}{D}\int_{x_0}^{x_{max}}e^{\beta U(y)}dy\int_{-\infty}^{y}e^{-\beta U(Z)}dZ$$

$$\boxed{\tau(x_0) = \frac{1}{D}\int_{x_0}^{x_{max}}e^{\beta U(y)}dy\int_{-\infty}^{y}e^{-\beta U(Z)}dZ}$$

To go further, we assume harmonic potential next to the barrier top and in the reactant.

$$U(x) = U_{min} + \frac{1}{2}m\omega_{min}^2(x - x_{min})^2 \qquad U(x) = U_{max} - \frac{1}{2}m\omega_{max}^2(x - x_{max})^2$$

*** Limit at small $1/\beta = k_BT$

$$\tau(x_0) = \frac{1}{D}\int_{x_0}^{x_{max}}dye^{\beta U(y)}\int_{-\infty}^{y}e^{-\beta U(Z)}dZ$$

it is hard to calculate the second integration to y, thus we suppose $y \to +\infty$. For the Gaussian integration

$$\int_{-\infty}^{+\infty}e^{-ax^2}dx = \sqrt{\frac{\pi}{a}}$$

$$\int_{-\infty}^{y} e^{-\beta U(Z)} dZ \simeq \int_{-\infty}^{+\infty} e^{-\beta\left[U_{min}+\frac{1}{2}m\omega_{min}^2(x-x_{min})^2\right]} dZ = e^{-\beta U_{min}} \times \sqrt{\frac{2\pi}{\beta m\omega_{min}^2}}$$

similarly, we make approximations $\int_{x_0}^{x_{max}} \to \int_{-\infty}^{x_{max}} \to \frac{1}{2}\int_{-\infty}^{+\infty}$

$$\int_{x_0}^{x_{max}} dy\, e^{\beta U(y)} = \int_{x_0}^{x_{max}} dy\, e^{\beta\left[U_{max}-\frac{1}{2}m\omega_{max}^2(x-x_{max})^2\right]} \simeq \frac{1}{2}e^{\beta U_{max}}\sqrt{\frac{2\pi}{\beta m\omega_{max}^2}}$$

There would be little difference while integration due to these approximations. Finally we have

$$\tau(x_0) = \frac{1}{2D}e^{\beta U_{max}}\sqrt{\frac{2\pi}{\beta m\omega_{max}^2}} \cdot e^{-\beta U_{min}}\sqrt{\frac{2\pi}{\beta m\omega_{min}^2}} = \frac{\pi}{D\beta m\omega_{min}\omega_{max}}e^{\beta(U_{max}-U_{min})}$$

Since $D = \frac{k_B T}{\zeta}$ $\Rightarrow$ $\frac{k_B T}{D} = \gamma m$, as well as $k = \frac{1}{2\tau}$

$$k = \frac{\omega_{min}\omega_{max}}{2\pi\gamma}e^{-\beta(U_{max}-U_{min})}$$

at the barrier top. 50% probability to enter the opposite direction, thus we have the coefficient 2.

Low friction limit (See Zwanzig ch 4.5) We cannot apply Smoluchowski, very few impacts with solvent molecule $\Rightarrow$ the idea is to study diffusion in the energy space

- diffusion equation for $P(E,t)$,

$$\frac{\partial}{\partial t}P(E,t) = \frac{\partial}{\partial E}\frac{\zeta}{m}I(E)\left[1 + \frac{1}{\beta}\frac{\partial}{\partial E}\right]\frac{\omega(E)\cdot P(E,t)}{2\pi}$$

- mfpt
- expansion to min/max $\Rightarrow \tau \propto \frac{1}{\zeta}$ $\Rightarrow$ $k \propto \zeta$ (at low friction); for high γ, $k \to 0$

7.4.5 Experimental observations of Kramers theory

To change the friction in the solutions, it's hard to add other compounds inside the solvent to increase several numerical order. Thus, we have to add pressure, then change density, so change friction, which would change the barrier perhaps. Barrier lowed while increasing friction. (Fig. C) Fig. D shows curves in different solvents.