

Final Projects for 5.72

Jianshu Cao

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- Select any two of the projects. You are advised but not required to choose projects relevant to your research. You are advised but not required to choose one from project 1–3 on reaction rate theory and one from project 4–6 on chemical kinetics.
- If you choose to work on more than two projects, please specify which projects you wish to be graded on.
- Complete the final exam independently without discussion with your classmates. You are encouraged to use references and lecture notes.
- Show all your steps, in a clear and orderly way. Justify your answers in detail to ensure full credits.
- Each project is 100 points, and the full score of the final exam is 200 points.

List of Projects

1. Barrier crossing and Kramers' turnover
2. Multi-dimensional transition state theory
3. Electron transfer and solvent dynamics
4. Single molecule kinetics and photon statistics
5. Self-consistent kinetic pathway analysis
6. Non-linear chemical kinetics

1 Barrier crossing and Kramers' turnover

The simple transition state rate theory predicts exponential dependence on the activation energy and linear dependence on the vibrational frequency in the reactant well. However, TST is essentially an equilibrium theory, and does not account for solvent dynamic effects. The Kramers theory uses the Fokker–Planck (FP) equation to describe the solvent effects on barrier crossing, and successfully predicts the dependence on the friction coefficient and a turnover in the reaction rate.

1.1

To help understand friction effects on chemical reactions, we first consider a dissipative harmonic oscillator described by the Markovian Langevin equation (LE):

$$m\ddot{x} + m\gamma\dot{x} + m\omega^2x = f(t) \quad (1)$$

where $\langle f(t)f(0) \rangle = 2\gamma mk_B T \delta(t)$. Solve LE for the correlation function $C(t) = \langle x(t)x(0) \rangle$ and discuss the under-damped limit, $\gamma \ll \omega$, and the over-damped limit, $\gamma \gg \omega$. (You may neglect the critical damping case.)

1.2

Using the solution for the over-damped oscillator, show the equivalence between the Langevin equation and the 1-D Fokker–Planck (FP) equation or the Smoluchowski equation:

$$\frac{\partial P(x, t)}{\partial t} = D \frac{\partial}{\partial x} \left[\frac{\partial}{\partial x} - \beta F(x) \right] P(x, t) \quad (2)$$

where $F(x)$ is the force, $F(x) = -dU(x)/dx = -m\omega^2x$.

1.3

We consider the 1-D potential $U(x)$ and solve for the reaction rate using the flux-over-population method. For the diffusive barrier crossing, we rewrite the Smoluchowski equation as

$$\frac{\partial P(x, t)}{\partial t} = -\frac{\partial J(x, t)}{\partial x} \quad (3)$$

where the flux is

$$J(x, t) = -D \left[\frac{\partial P(x, t)}{\partial x} - \beta F(x) P(x, t) \right]. \quad (4)$$

In the flux-over-population method, we set the flux constant, $J(x, t) = J_s$, and find the steady-state population distribution, $P_s(x)$. Following this set-up, derive the steady-state population in the reactant well

$$n_s = \int_{-\infty}^{x_B} P_s(x) dx = \frac{J_s}{D} \int_{-\infty}^{x_B} dx e^{-\beta U(x)} \int_x^{\infty} dx' e^{\beta U(x')}. \quad (5)$$

1.4

Next we approximate the 1-D potential as $U(x) = U_R + \frac{1}{2}m\omega_R^2(x - x_R)^2$ at the reactant well and as $U(x) = U_B - \frac{1}{2}m\omega_B^2(x - x_B)^2$ at the reaction barrier, [see Question 2.2] and assume $\beta E_a = \beta(U_B - U_R) \gg 1$. Derive the diffusive limit of the reaction rate

$$k_{strong} = \frac{J_s}{n_s} \approx \frac{D\beta m\omega_R\omega_B}{2\pi} e^{-\beta E_a} = \left(\frac{\omega_B}{\gamma} \right) \frac{\omega_R}{2\pi} e^{-\beta E_a} = \alpha k_{TST}. \quad (6)$$

Explain why the diffusive rate is always smaller than k_{TST} (i.e., $\alpha \ll 1$).

1.5

In the weak damping limit, $\gamma \ll \omega$, we can describe the under-damped motion as energy diffusion

$$\frac{\partial P(E, t)}{\partial t} = \gamma \omega(E) \frac{\partial}{\partial E} \left[I(E) \left(P(E, t) + k_B T \frac{\partial P(E, t)}{\partial E} \right) \right], \quad (7)$$

where $I(E)$ is the action and $\omega(E) = dE/dI$ is the energy-dependent frequency. Show the equivalence of this equation and the LE solution for the under-damped harmonic oscillator in Eq. (1).

1.6

Following the same steps as in Question 1.3, use the flux-over-population method to derive the steady-state population in the reactant well

$$n_s = \int_{U_R}^{U_B} dE P_s(E) = \frac{\beta J_s}{\gamma} \int_{U_R}^{U_B} dE \frac{e^{-\beta E}}{\omega(E)} \int_E^{U_B} dE' \frac{e^{\beta E'}}{I(E')}. \quad (8)$$

Hint. In this case an appropriate definition of flux is:

$$J(I, t) = -\gamma I(E) \left(P(E, t) + k_B T \frac{\partial P(E, t)}{\partial E} \right) \quad (9)$$

so that we have

$$\frac{\partial P(E, t)}{\partial t} = -\frac{\partial J(I, t)}{\partial I}. \quad (10)$$

1.7

Next we approximate the 1-D potential as $E = U_R + \delta E$ in the well region and $E = U_B + \delta E$ in the barrier region and assume $\beta E_A = \beta(U_B - U_R) \gg 1$. Derive the weak-damping limit of the reaction rate

$$k_{weak} = \frac{J_s}{n_s} \approx \gamma \omega_R I_B \beta e^{-\beta E_A} = \alpha k_{TST} \quad (11)$$

and explain why the energy diffusive rate is always smaller than k_{TST} (i.e., $\alpha \leq 1$).

1.8

When the dynamics are not diffusive, we need to consider the full Kramers problem, which is equivalent to solving LE for barrier crossing. Kramers solved this problem in 1940 and obtained the rate

$$k_{intermediate} = \frac{\lambda}{\omega_B} k_{TST} = \alpha k_{TST}, \quad (12)$$

where λ is the effective barrier frequency solved from the quadratic equation

$$\lambda^2 + \lambda\gamma - \omega_B^2 = 0. \quad (13)$$

Confirm $\alpha \leq 1$ and that the rate is consistent with the MDTST rate.

1.9

The weak and strong damping limits correspond to spatial diffusion and energy diffusion. Explain the different dependence on the friction coefficient γ in these two limits and predict a turnover in behavior as a function of γ .

1.10

An easy interpolation between the two limits is

$$\frac{1}{k} = \frac{1}{k_{weak}} + \frac{1}{k_{intermediate}} \quad (14)$$

Plot k_{weak} , k_{strong} , $k_{intermediate}$, and the above interpolated rate. Show the reaction rate is always smaller than k_{TST} and explain the turnover condition.

References

- P. Hänggi, P. Talkner, M. Borkovec. Reaction-rate theory: fifty years after Kramers. *Rev. Mod. Phys.* **62**, 251 (1990). doi:10.1103/RevModPhys.62.251.
- A. Nitzan. *Chemical dynamics in condensed phases* (Oxford University Press, Oxford, 2006), Chapter 16. ISBN 9780198529798.

2 Multi-dimensional Transition State Theory

Condensed phase chemical reactions are strongly influenced by the coupling of the reaction coordinate to the solvent dynamics. This dynamics effect can be captured using the multi-dimensional transition state theory (MDTST). The starting point of MDTST is Zwanzig's Gaussian bath Hamiltonian (GBH), which describes the solvent effect with deterministic multi-dimensional equations of motion. The Pollack paper employs this explicit description to derive the MDTST rate and recover the Grote-Hynes rate expression, a generalization of the Kramers rate from the Markovian limit to non-Markovian limit.

2.1

In class, we derived the transition state theory from response theory, giving,

$$k_{TST} = \frac{\langle \theta(v_x) v_x \delta(x_B - x) \rangle}{\langle \theta(x_B - x) \rangle} \quad (15)$$

where x_B is the barrier top. Explain when this rate expression is valid and show that the true rate is always lower than the TST rate, i.e.,

$$k_{true} \leq k_{TST}. \quad (16)$$

2.2

The 1-D reaction potential can be expanded as $U(x) = U_R + \frac{1}{2}m\omega_R^2(x - x_R)^2$ near the reactant well and as $U(x) = U_B - \frac{1}{2}m\omega_B^2(x - x_B)^2$ around the barrier top. Use the above potential form to derive the standard TST rate,

$$k = \frac{\omega_R}{2\pi} e^{-\beta E_a} \quad (17)$$

where $E_a = U_B - U_R$ is the activation energy. Explain the assumptions involved in deriving the above expression.

2.3

Let's generalize the above discussion to an $(N+1)$ -dimensional system defined by the Hamiltonian

$$H = \sum_{i=0}^N m_i \frac{v_i^2}{2} + U(x_0, x_1, \dots, x_N), \quad (18)$$

where U is the multi-dimensional potential surface. We introduce the reaction coordinate as $y = c_i x_i$, which is the linear combination of the $N + 1$ coordinates. Derive the following generalization of Eq. (15)

$$k = \frac{\langle \theta(v_y) v_y \delta(y - y_B) \rangle}{\langle \theta(y_B - y) \rangle} = \frac{\int dv_y \int dy e^{-\beta(m_y v_y^2/2 + W)} \theta(v_y) v_y \delta(y - y_B)}{\int dv_y \int dy e^{-\beta(m_y v_y^2/2 + W)}} \quad (19)$$

where m_y is the effective mass of the reaction coordinate. Here, y_B is the coordinate of the saddle point on the potential surface, and $W(y)$ is the potential of mean force,

$$e^{-\beta W(y)} = \left\langle \delta \left(y - \sum_{i=0}^N c_i x_i \right) \right\rangle. \quad (20)$$

2.4

We now consider a quadratic expansion of the potential surface near the reactant well as

$$U(x) = U_R + \frac{1}{2} m \omega_R^2 (x - x_{R0})^2 + \frac{1}{2} \sum_{i=1}^N m_i \omega_{Ri}^2 (x - x_{Ri})^2 \quad (21)$$

and around the saddle point as

$$U(x) = U_B - \frac{1}{2} m \omega_B^2 (x - x_{B0})^2 + \frac{1}{2} \sum_{i=1}^N m_i \omega_{Bi}^2 (x - x_{Bi})^2 \quad (22)$$

Use Eq. (19) to derive the rate

$$k = \frac{\omega_R}{2\pi} e^{-\beta F_a} \quad (23)$$

Here, $F_a = E_a - TS_a$ is the activation free energy, and S_a is the activation entropy.

2.5

To describe solvent effects explicitly, Zwanzig proposed the Gaussian bath Hamiltonian (GBH):

$$H = \frac{1}{2}mv_x^2 + U(x) + \sum_{i=1}^N \frac{m_i}{2} \left[v_i^2 + \omega_i^2 \left(q_i + \frac{c_i}{m_i\omega_i^2}x \right)^2 \right], \quad (24)$$

where x is the system coordinate and q_i are the bath coordinates. The harmonic bath Hamiltonian yields dissipative dynamics described by the generalized Langevin equation (GLE):

$$m\ddot{x} + m \int_0^t \gamma(t-\tau)\dot{x}(\tau)d\tau + \frac{dU}{dx} = f(t), \quad (25)$$

where $\gamma(t)$ is the friction kernel and $f(t)$ is the noise. Derive the relationship between GBH and GLE:

$$\gamma(t) = \frac{1}{m} \sum_i \frac{c_i^2}{m_i\omega_i^2} \cos(\omega_i t). \quad (26)$$

2.6

Let's expand the one-dimensional system potential $U(x)$ in quadratic form, as in Question 2.2. Transform the $N+1$ coupled modes to normal modes, and derive the MDTST rate,

$$k = \frac{\lambda_{R0}}{2\pi} \prod_{i=1}^N \frac{\lambda_{Ri}}{\lambda_{Bi}} e^{-\beta E_a} \quad (27)$$

where λ_{Bi} are a set of eigen-frequencies at the saddle point and λ_{Ri} are a set of eigen-frequencies in the reactant well.

2.7

Prove the following identities:

$$\lambda_{B0}^2 \prod_i \lambda_{Bi}^2 = \omega_B^2 \prod_i \omega_i^2 \lambda_{R0}^2 \prod_i \lambda_{Ri}^2 = \omega_R^2 \prod_i \omega_i^2$$

2.8

Using the above two identifies, derive the MDTST rate as:

$$k = \frac{\lambda}{\omega_B} \frac{\omega_R}{2\pi} e^{-\beta E_a} = \alpha k_{TST}, \quad (28)$$

which is known as the Grote–Hynes rate. Here $\lambda = \lambda_{B0}$ is the effective barrier frequency which satisfies

$$\lambda^2 + \hat{\gamma}(\lambda) - \omega_B^2 = 0 \quad (29)$$

with $\hat{\gamma}$ the Laplace transform of the memory kernel

$$\hat{\gamma}(z) = \frac{1}{m} \sum_i \frac{c_i^2}{m_i \omega_i^2} \frac{z}{z^2 + \omega_i^2}. \quad (30)$$

Show $\alpha \leq 1$ so that the MDTST rate is always smaller than the 1-D TST rate.

2.9

For a Debye solvent, the friction kernel is given by

$$\gamma(t) = \frac{\gamma_0}{\tau_D} e^{-t/\tau_D} \quad (31)$$

with τ_D the Debye relaxation time. Plot α as functions of γ_0 and τ_D , respectively, and discuss its various limits.

References

- P. Hänggi, P. Talkner, M. Borkovec. Reaction-rate theory: fifty years after Kramers. *Rev. Mod. Phys.* **62**, 251 (1990).
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- E. Pollak. Theory of activated rate processes: A new derivation of Kramers' expression. *J. Chem. Phys.* **85**, 865 (1986).
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3 Electron transfer and solvent dynamics

Electron transfer underlies many chemical processes, including photochemistry, solar energy conversion, electrochemistry, and molecular electronic devices, and plays a key role in important biological functions such as photosynthesis and vision. Simply put, electron transfer (ET) is a transition of electronic states, which changes the electronic charge distribution in a molecular system and which is induced by solvent fluctuations and accompanied by solvent reorganization. The basic physics of electron transfer is elucidated by the celebrated Marcus theory, which has inspired numerous experimental and theoretical studies.

3.1

The Marcus curves represent the free energy surfaces associated with the two electronic states, i.e., $U_1(x) = \frac{1}{2}k(x + x_0)^2$ for the donor and $U_2(x) = \frac{1}{2}k(x - x_0)^2$ for the acceptor. The coordinate represents the collective solvent polarization that couples to electron transfer. The energetics is characterized by two parameters, the free energy bias, Δ , and the solvent reorganization energy, E_r . Show that the activation energy is given by $E_a = (\Delta + E_r)^2/4E_r$ and the vertical transition energy is given by $E_v = \Delta + E_r$. Explain the physical meanings of E_r , E_a , and E_v . Why does the Marcus rate depend on E_a instead of E_r and E_v ?

3.2

The donor and acceptor states are coupled through the non-adiabatic coupling constant J . Then, the overall Hamiltonian becomes

$$H = \begin{bmatrix} U_1 & J \\ J & U_2 \end{bmatrix} \quad (32)$$

In the weak coupling limit, we use the golden-rule rate,

$$k = \frac{2\pi J^2}{\hbar^2} \langle \delta(U_1 - U_2) \rangle, \quad (33)$$

where the average is carried out over the equilibrium distribution of the donor. Derive the Marcus ET rate expression:

$$k_{ET} = \frac{2\pi}{\hbar\sqrt{4\pi k_B T E_r}} J^2 e^{-\beta E_a}. \quad (34)$$

Plot this rate as a function of the energy bias Δ , and discuss the inverted regime.

3.3

The Marcus rate describes non-adiabatic electron transfer in the limit of weak electronic coupling, $J\beta \ll 1$. As J increases, the nature of electron transfer changes. Diagonalize the ET Hamiltonian H at a fixed coordinate, write the adiabatic potentials, and draw the adiabatic surfaces. Determine the critical value of J when the barrier on the lower adiabatic surface disappears, and explain the consequence.

3.4

One interesting application of Marcus theory is to calculate proton-coupled electron transfer (PCET) rate. Here, we treat the solvent degree of freedom classically and the proton degree quantum mechanically. Apply the Fermi's golden-rule expression to derive the PCET rate

$$k_{PCET} = \sum_{if} \frac{2\pi |J_{if}|^2}{\hbar \sqrt{4\pi k_B T E_r}} e^{-\beta E_{a,if}}, \quad (35)$$

where the subscripts i and f refer to the proton state before and after electron transfer, respectively, E_i and E_f are the corresponding eigen-energies, and $J_{if} = \langle i|J|f \rangle$ is the effective coupling constant. The activation energy depends on the initial and final proton states as $E_{a,if} = (\Delta_{if} + E_r)^2/4E_r$, where $\Delta_{if} = \Delta + E_f - E_i$ (35)

3.5

The Debye model is often used to describe dielectric relaxation of the solvent, which is directly coupled to electron transfer. In general, the dielectric response is given by

$$\mathcal{D}(t) = \epsilon_e \mathcal{E}(t) + \int_{-\infty}^t \epsilon_n(t - \tau) \mathcal{E}(\tau) d\tau \quad (36)$$

where ϵ_e is the electronic part of the dielectric response function and ϵ_n is the nuclear part of the dielectric response function. In the Debye model,

the nuclear part of response is exponential: $\epsilon_n(t) = \epsilon_n e^{-t/\tau_D}/\tau_D$, with τ_D the Debye relaxation time. In electron transfer, the charge redistribution is described by a sudden change in the electric displacement: $\mathcal{D}(t) = \mathcal{D}\theta(t)$. Derive the corresponding electric field induced by charge redistribution:

$$\mathcal{E}(t) = \frac{1}{\epsilon_s} \mathcal{D} + \left(\frac{1}{\epsilon_e} - \frac{1}{\epsilon_s} \right) \mathcal{D} e^{t/\tau_L} \quad (37)$$

where $\epsilon_s = \epsilon_n + \epsilon_e$ and τ_L is the longitudinal relaxation time, $\tau_L = (\epsilon_e/\epsilon_s)\tau_D$.

3.6

The Marcus rate, derived from the golden-rule expression, is essentially an equilibrium theory, in the same spirit as TST. Non-adiabatic transitions occur when solvent fluctuations bring the polarization to resonance, so the overall rate of solvent-controlled electron transfer (SCET) is given by

$$k^{-1} = k_D^{-1} + k_{ET}^{-1} \quad (38)$$

where k_D is the solvent relaxation rate for ET and k_{ET} is the electron transfer rate. Justify the above rate expression, and discuss the limits of slow and fast solvent relaxation.

3.7

To derive the SCET rate expression, we consider diffusion on the Marcus curve with a sink at the transition state (i.e. the curve crossing point x_c), giving

$$\dot{P}(x, t) = \mathcal{L}P(x, t) - KP(x, t) \quad (39)$$

where $\mathcal{L}P = D\partial_x^2 P - \beta D\partial_x(FP)$ is the diffusion operator defined on the donor surface, and $K = (2\pi J^2/\hbar)\delta(x - x_c)$ is the transfer operator defined at the crossing point x_c . Explain this equation, and show that the SCET rate is given by the mean first passage time expression

$$\frac{1}{k} = \int_0^\infty P(x, t) dt = \text{Tr} \left[\frac{1}{K - \mathcal{L}} P_{eq} \right] \quad (40)$$

where $P_{eq} \propto e^{-\beta U_1(x)}$ is the equilibrium distribution of the donor state.

3.8

For the special case of symmetric ET (i.e., $\Delta = 0$), solve the SCET equation and derive the following expression

$$k_D^{-1} = \frac{1}{P_{eq}(x_c)} \int_0^\infty dt [G(x_c, t) - P_{eq}(x_c)] \quad (41)$$

where $G(t) = e^{\mathcal{L}t} \delta(x - x_c)$.

References

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4 Single molecule kinetics and photon statistics

Advanced spectroscopic techniques allow us to measure dynamics and reactions one molecule at a time, thus unraveling the static and dynamic disorder often difficult to resolve in ensemble experiments. The basic single molecule approach is fluorescence photon detection under constant illumination. Here we discuss the basic theoretical description for single molecule kinetics with application to photon emission sequences. Emphasis is placed on the distribution function of single molecule events, the Poisson indicator, and Mandel's Q parameter in photon statistics. For simplicity, we limit our discussion to renewal processes, which have no correlation between single molecule events.

4.1

Consider a sequence of single molecule events (e.g., fluorescence photons) detected at time t_1, t_2, \dots . The average moment of events in this sequence is

$$\langle N^l(t) \rangle = \left\langle \left[\int_0^t \sum_i \delta(\tau - t_i) d\tau \right]^l \right\rangle, \quad (42)$$

where the average is taken over stochastic realizations of the same single molecule process. Explain this expression and use it to show,

$$\langle N^2(t) \rangle - \langle N(t) \rangle^2 = \int_0^t \int_0^t \rho_2(\tau_1, \tau_2) d\tau_1 d\tau_2, \quad (43)$$

where ρ_2 is the two-event density given by

$$\rho_2(\tau_1, \tau_2) = \sum_{i \neq j} \langle \delta(\tau_1 - t_i) \delta(\tau_2 - t_j) \rangle. \quad (44)$$

4.2

One important measurement in single molecule experiments is the waiting time distribution function, $f(t) = \langle \sum_i \delta(t_i - t_{i+1} - t) \rangle$, which is the probability distribution function of two adjacent events. Derive the expression for the Laplace transform of $f(t)$,

$$\hat{f}(s) = \int e^{-st} f(t) dt = \sum_{l=0}^{\infty} \frac{(-1)^l s^l}{l!} \langle \tau^l \rangle, \quad (45)$$

where $\langle \tau^l \rangle = \int_0^\infty t^l f(t) dt$ is the moment of the waiting time. Show the relationship between the first two moments

$$\langle \tau^2 \rangle = 2\langle \tau \rangle^2 \quad (46)$$

for a Poisson process with $f(t) = ke^{-kt}$.

4.3

For a stationary Markovian process, the average number density becomes constant

$$\rho_1(t) = k = \frac{1}{\langle \tau \rangle}, \quad (47)$$

and the two-event density becomes time invariant,

$$\rho_2(t_1, t_2) = \rho_2(t_1 - t_2). \quad (48)$$

Explain these results and prove the following relationship

$$\hat{\rho}_2(s) = k \frac{\hat{f}(s)}{1 - \hat{f}(s)}, \quad (49)$$

where functions with s variables are Laplace transforms.

4.4

Instead of measuring the waiting time distribution function, we can also use counting statistics to probe the underlying kinetics. One such a measure is the Poisson indicator (i.e., the randomness parameter or Fano parameter), given by

$$Q_P(t) = \frac{\langle N^2(t) \rangle - \langle N(t) \rangle^2 - \langle N(t) \rangle}{\langle N(t) \rangle}. \quad (50)$$

Show that the Poisson indicator vanishes for a Poisson process and approaches a constant at long times.

4.5

The long time limit of the Poisson indicator is known as Mandel's Q parameter: $Q_M = \lim_{t \rightarrow \infty} Q_P(t)$. Combining the above equations, we have

$$Q_M = 2 \int_0^\infty \frac{\rho_2(\tau) - \rho_1^2}{k} d\tau = 2 \lim_{s \rightarrow 0} \left[\frac{\hat{f}}{1 - \hat{f}} - \frac{k}{s} \right] = \frac{\langle \tau^2 \rangle - 2\langle \tau \rangle^2}{\langle \tau \rangle^2}. \quad (51)$$

Derive this result step by step. With this expression, we can use the waiting time distribution function to calculate counting statistics including Mandel's Q parameter.

4.6

Consider a fluorescence emission process with excitation rate k_1 and fluorescence emission rate k_f . Find the waiting time distribution function, $f(t)$, and the first two moments $\langle \tau \rangle$ and $\langle \tau^2 \rangle$. Use these moments to derive Mandel's Q parameter.

4.7

Use the expression for $f(t)$ to obtain the photon density $\rho_2(t)$. Calculate the Poisson indicator and the Mandel parameter. Verify the result for Q_M is consistent with the moment calculation.

4.8

In addition to excitation and emission, we include the stimulated emission with rate k_2 . Repeat the above calculation of the waiting distribution function, the first two moments, and Mandel's Q parameter.

4.9

Calculate the Poisson indicator, plot it as a function of time, and explain the time-dependence, especially at short time and long time.

References

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5 Self-consistent kinetic pathway analysis

In class, we introduced the ‘pathway summation’ as an intuitive method to calculate the evolution of probability in a discrete Markov chain. We will now generalize the method to single-molecule reaction processes and predict the first-passage time distribution function of enzymatic turnover reactions. The basic idea is to calculate the joint probability of transitions along each pathway leading to the product state and sum up the probabilities of all possible pathways. The pathway summation method is intuitive and has recently been applied to single molecule reactions, molecular motors, and photon statistics.

5.1

A fundamental chemical reaction follows single exponential decay, $Q(t) = ke^{-kt}$, where $Q(t)$ is the probability distribution function (PDF) of decay. Evaluate the m -th moment of the first passage time $\langle t^m \rangle = \int Q(t)t^m dt$ and confirm

$$\langle t^m \rangle = (-1)^m \left. \frac{\partial^m \hat{Q}(s)}{\partial s^m} \right|_{s=0} \quad (52)$$

where $\hat{Q}(s) = \int_0^\infty e^{-st}Q(t)dt$ is the Laplace transform and s is the Laplace variable.

5.2

Consider a two-step sequential reaction, $A_1 \rightarrow A_2 \rightarrow A_3$, with rate constants k_{12} and k_{23} , respectively. (You may assume $k_{12} \neq k_{23}$.) The distribution of the first passage time from A_1 to A_3 is

$$Q_{13}(t) = \int_0^t Q_{12}(t-t')Q_{23}(t')dt' \quad (53)$$

or, in Laplace space, $\hat{Q}_{13}(s) = \hat{Q}_{12}(s)\hat{Q}_{23}(s)$. Write an explicit expression for $Q_{13}(t)$ and calculate the mean first passage time $\langle t \rangle$. Explain why the initial value of the calculated $Q_{13}(t)$ is zero, $Q_{13}(0) = 0$.

5.3

We now generalize the above argument to a chain reaction with multiple steps, $A_1 \rightarrow A_2 \cdots \rightarrow A_{n-1} \rightarrow A_n$. The PDF of the first passage time reads

$$Q_{1,n}(s) = Q_{12}(s)Q_{23}(s) \cdots Q_{n-1,n}(s) \quad (54)$$

where n is the final state. Use the above expression to obtain an expression for the mean first passage time $\langle t \rangle$.

5.4

A sequence of chemical reactions can achieve remarkable timing, giving rise to the notion of ‘biological clock.’ To demonstrate this effect, consider a sequence of n reactions with identical rate constant,

$$k_1 = k_2 = \cdots = k_n = nk. \quad (55)$$

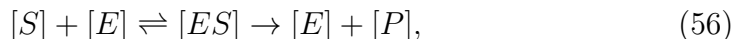
Calculate the distribution $Q_{1,n}(t)$, mean first passage time $\langle t \rangle$, and the variance $\langle \delta t^2 \rangle = \langle (t - \langle t \rangle)^2 \rangle$. Plot $Q_{1,n}(t)$ as a function of time for $n = 1, 2$, and 10, and explain the change in $Q(t)$ as n increases.

5.5

Consider decay from state 0 to state 1 with rate k_{01} and to state 2 with rate k_{02} . We assign the transition PDF’s of the branching reaction as $Q_{01}(t) = k_{01}e^{-k_0 t}$ and $Q_{02}(t) = k_{02}e^{-k_0 t}$ with $k_0 = k_{01} + k_{02}$ the depletion rate from state 0. Explain the above result and generalize it to decay from state 0 to n different states.

5.6

The Michaelis–Menten mechanism of enzymatic reactions is given by



which consists of three states: state 1, free substrate and enzyme; state 2, substrate–enzyme complex; and state 3, product. With the constant substrate concentration $[S]$, the stationary-state population of state 2 can be determined from

$$\frac{d[ES]}{dt} = k_1[E] - (k_2 + k_{-1})[ES] = 0, \quad (57)$$

where $k_1 = k_1^0[S]$ is the substrate binding rate, k_{-1} is the dissociation rate, and k_2 is the catalytic rate. For a single enzyme, its probability is conserved, giving $[E] + [ES] = 1$. Derive the stationary-state population

$$[ES] = \frac{k_1}{k_1 + k_{-1} + k_2} \quad (58)$$

and the Michaelis–Menten rate

$$k_{MM} = k_2[ES] = \frac{[S]k_2}{[S] + k_M} \quad (59)$$

with the Michaelis constant $k_M = (k_{-1} + k_2)/k_1^0$.

5.7

We now apply the pathway summation technique to the Michaelis–Menten scheme in Eq. (56). Starting from state 1, a substrate $[S]$ binds with the enzyme $[E]$ to form a substrate–enzyme complex $[ES]$, i.e., state 2, which can branch to form a product $[P]$ or return to the state 1. Following the pathway, we obtain the PDF of the turnover time by solving self-consistently

$$Q(s) = Q_{12}(s)[Q_{23}(s) + Q(s)Q_{21}(s)], \quad (60)$$

where the two terms in brackets represent the two decay channels from state 2. The solution to the self-consistent equation in Eq. (60) yields

$$Q(s) = \frac{Q_{12}(s)Q_{23}(s)}{1 - Q_{12}(s)Q_{21}(s)}. \quad (61)$$

Expand the denominator in the above expression, draw the pathway associated with each term in the expansion, and explain the self-consistent solution in Eq. (61).

5.8

The PDF's associated with the three reaction steps are specified by rate constants as $Q_{12}(t) = k_1 e^{-k_1 t}$, $Q_{21}(t) = k_{-1} e^{-(k_{-1} + k_2)t}$, and $Q_{23}(t) = k_2 e^{-(k_{-1} + k_2)t}$, with $k_1 = k_1^0[S]$. Use Eq. (61) to derive the mean first passage time and confirm the Michaelis–Menten expression in Eq. (59), derived earlier using the stationary-state approach.

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6 Nonlinear chemical kinetics

Single molecule experiments monitor one molecule at a time and is essentially linear kinetics. A chemical reaction generally involves many reactive components, and the concentration of each component changes with time. This time-dependence is described by a set of coupled non-linear rate equations, which is usually not solvable but can be analyzed for its asymptotic behavior. At long times, the concentration can reach a stationary solution, which is either constant or oscillatory. The solution can be either stable or unstable under external perturbations. The non-linear equations predict the average concentration in the thermodynamic limit, whereas the probability distribution of population evolution is described by master equations, which are generally not solvable except for special cases where the generating function method is applicable. Often, we measure the average populations and mean square fluctuations, which can be obtained approximately by expanding master equations.

6.1

The stability of non-linear chemical kinetics can be determined by the Jacobian matrix of its rate equations. Consider a two-component kinetics system:

$$\dot{x}_1 = k_1(x_1, x_2)\dot{x}_2 = k_2(x_1, x_2)$$

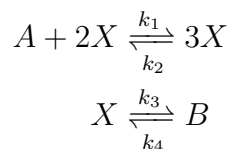
Write out the Jacobian matrix and solve for its eigen-values.

6.2

Use the above eigen-values to classify the different behaviors of the non-linear kinetics around the steady-state solution.

6.3

One of the well-studied non-linear chemical reactions is the Schlögl model:



Find the equilibrium concentrations $c_{eq,X}$, $c_{eq,A}$, and $c_{eq,B}$, and establish the detailed balance condition

$$R_{eq} = \frac{c_{eq,A}}{c_{eq,B}}. \quad (62)$$

6.4

Let's fix the concentrations c_A and c_B at constant values but away from the equilibrium values. Then the rate equation becomes

$$\dot{c}_X = k_1 c_A c_X^2 - k_2 c_X^3 - k_3 c_X + k_4 c_B. \quad (63)$$

Given the steady-state solution $c_{ss,X}$, find the corresponding Jacobian, and use the Jacobian to discuss the stability of the steady-state solution of the Schlögl model.

6.5

Consider a simple model for population dynamics. Let k_g be the generation influx which is independent of n and k_d the death rate linearly dependent on n . The master equation for the population distribution function $P(n, t)$ reads

$$\dot{P}(n, t) = k_g [P(n-1, t) - P(n, t)] + k_d [(n+1)P(n+1, t) - nP(n, t)]. \quad (64)$$

Solve for the average population $\langle n \rangle$ and the second moment $\langle n^2 \rangle$, and show the population distribution is Poisson.

6.6

This simple model is one of the few examples that can be solved exactly. To demonstrate this, we construct a generating function

$$F(z, t) = \sum_{n=0}^{\infty} P(n, t) z^n. \quad (65)$$

Derive the equation for $F(z, t)$

$$\frac{\partial F(z, t)}{\partial t} = k_g (z-1) F(z, t) + k_d (1-z) \frac{\partial F(z, t)}{\partial z} \quad (66)$$

and solve it with the characteristic function method.

6.7

Using the generating function, find the distribution function $P(n, t)$ and show the consistency with the first two moments obtained earlier. Here we assume the initial population is at m , i.e., $P(n, 0) = \delta_{n,m}$.

6.8

Now we generalize the simple model to the birth–death problem. In addition to the population influx and population decay, we introduce a birth rate of k_b . Then, the master equation for the birth–death problem reads

$$\begin{aligned} \dot{P}(n, t) = & k_g[P(n-1, t) - P(n, t)] + k_d[(n+1)P(n+1, t) - nP(n, t)] \\ & + k_b[(n-1)P(n-1, t) - nP(n, t)] \end{aligned} \quad (67)$$

Solve for the average population $\langle n \rangle$ and the second moment $\langle n^2 \rangle$, and discuss their behavior in different regimes.

6.9

If the number of molecules are large, $n \gg 1$, we can approximately take n to be a continuous variable, expand $P(n \pm 1, t)$ around $P(n, t)$, and obtain the Fokker–Planck equation. Following this procedure, derive the Fokker–Planck equation for the birth–death problem:

$$\begin{aligned} \dot{P}(n, t) = & -k_g \left[\partial_n - \frac{1}{2} \partial_n^2 \right] P(n, t) + k_d \left[\partial_n + \frac{1}{2} \partial_n^2 \right] nP(n, t) \\ & - k_b \left[\partial_n - \frac{1}{2} \partial_n^2 \right] nP(n, t). \end{aligned} \quad (68)$$

6.10

Solve the diffusion equation for its steady-state solution and relaxation rate. Find the first and second moments and compare with the exact solution obtained earlier.

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