

Exercise 4

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1 Dynamics of a chemical reaction

Consider a vessel with three chemical species A , B and AB . At time t , there are respectively $n_A(t)$, $n_B(t)$ and $n_{AB}(t)$ molecules of each species that can react according to the chemical reaction



where r_F is the forward rate at which A and B react to form the compound AB (dimerization), and r_B is the backward rate at which AB can split into the two species A and B (dissociation). Note that r_F and r_B are microscopical rates, in the sense that they do not depend on the number of molecules in the vessel or its volume.

To reduce the dimensionality, we assume that $n_A(t) = n_B(t) = n(t)$, and introduce the variable $n(t) + n_C(t) = N$. The variable N is not the total number of molecules, but it is a constant quantity that does not change over time and it is useful for characterizing the size of the system (see table 1). Thus, the time evolution of the system is fully described by the variable n (i.e. the number of molecules A and B) and N from which we can calculate $n_{AB} = N - n$.

time	$n = n_A$	$n = n_B$	n_{AB}	num. molecules	$N = n + n_{AB}$
t_1	10	10	12	32	22
t_2	9	9	13	31	22

Table 1: Example

Under these assumptions, the macroscopical rates, i.e. rates that take into account the number of molecules per species in the vessel at time t , are defined as

$$r_F n(t)^2, \quad (2)$$

for the forward reaction (dimerization) and

$$r_B (N - n(t))2, \quad (3)$$

for the backward reaction (dissociation).

Computational exercise Simulate the chemical reaction described in eq. 1 using the Gillespie's algorithm:

1. Estimate the total rate at time t using eqs. 2 and 3:

$$r(t) = r_B(t) + r_F(t).$$

2. To estimate the time at which the next reaction occurs, draw the timestep τ from the distribution

$$r(t) \exp(-r(t)\tau) d\tau,$$

that describes the probability to change the system state in the time interval $[t + \tau, t + \tau + d\tau]$, with $d\tau$ infinitesimal time step. Calculating the CDF and by exploiting the probability integral transform theorem, the time interval τ can be calculated as

$$\tau = -\frac{\log(u_1)}{r(t)},$$

with $u_1 \in \mathcal{U}(0, 1)$ random number from a uniform distribution.

3. After having calculated τ , we need to select which reaction occurs. Given that one of the two reactions will surely occur at time $t + \tau$, we estimate the probability of the forward reaction as

$$P_F(t) = r_F \frac{n(t)^2}{N} \frac{1}{r(t)}$$

, and the probability of the backward reaction as

$$P_B(t) = r_B(N - n(t)) \frac{1}{r(t)}$$

4. Then, we draw a second random number u_2 from a uniform distribution $\mathcal{U}(0, 1)$
5. If $u_2 < P_f$ the forward reaction occurs, otherwise the backward reaction occurs.

Using the Gillespie algorithm, generate a set of trajectories, then construct the probability distribution (the histogram) at different timesteps.

2 System size expansion

The *master equation* of the system described above is written as

$$\frac{\partial P(n, t)}{\partial t} = - \left(r_F \frac{n^2}{N} \right) P(n, t) \quad (4)$$

$$- r_B(N - n)P(n, t) \quad (5)$$

$$+ r_F \frac{(n+1)^2}{N} P(n+1, t) \quad (6)$$

$$+ r_B(N - n + 1)P(n-1, t). \quad (7)$$

Here, we solve the master equation via a linear noise approximation method called *system size expansion* [1]. The idea of the system size expansion is that the dynamics of the stochastic variable $n(t)$ can be decomposed into a deterministic dynamics of the concentration $\varphi(t)$ and a stochastic dynamics of the oscillations $x(t)$ according to the ansatz

$$n(t) = \Omega\varphi(t) + \sqrt{\Omega}x(t), \quad (8)$$

where Ω is a parameter that represents the size of the system, in this context $\Omega = N$. Under this assumption it is possible to derive an ordinary differential equation for φ :

$$\dot{\varphi} = r_B(1 - \varphi) - r_F\varphi^2, \quad (9)$$

and a partial differential equation (Fokker-Planck equation) for the probability distribution of the oscillations $\Pi(x, t)$:

$$\frac{\partial \Pi(x, t)}{\partial t} = - \frac{\partial}{\partial \varphi} [2r_F\varphi + r_B] \cdot \frac{\partial (x\Pi)}{\partial x} + \frac{1}{2} [r_F\varphi^2 + r_B - r_B\varphi] \cdot \frac{\partial^2 \Pi}{\partial x^2} \quad (10)$$

The solution of eq. 10 is

$$\Pi(x, t) = \frac{1}{\sqrt{2\pi \langle x(t)^2 \rangle}} \exp \left(- \frac{1}{2} \frac{(x - \langle x(t) \rangle)^2}{\langle x(t)^2 \rangle} \right), \quad (11)$$

where the mean of the fluctuations $\langle x(t) \rangle$ is solution of the ordinary equation

$$\frac{\partial \langle x \rangle}{\partial t} = (-2r_F\varphi - b) \langle x \rangle, \quad (12)$$

while the variance of the oscillations $\langle x^2 \rangle$ is

$$\frac{\partial \langle x^2 \rangle}{\partial t} = 2(-2r_F\varphi - b) \langle x^2 \rangle + \varphi^2 r_F + r_B - \varphi r_B. \quad (13)$$

Given a solution for eq. 9 and eq. 11, the solution of the master equation (eq. 7) is finally written as

$$P(n, t) = \frac{1}{\sqrt{N}} \Pi \left(\frac{n - N\varphi(t)}{\sqrt{N}}, t \right). \quad (14)$$

Computational exercise

1. Find $x(t)$, $\langle x(t) \rangle$ and $\langle x(t)^2 \rangle$ solving eqs. 9, 12 and 13 with a numerical method. For example using a Runge-Kutta method (RK45 with Python and scipy).
2. Use $\langle x(t) \rangle$ and $\langle x(t)^2 \rangle$ to estimate the probability distribution of the oscillations defined in eq. 11.
3. Use eq. 14 to find the distribution $P(n, t)$.
4. Compare $P(n, t)$ with the distribution estimated by Gillespie's algorithm.

References

- [1] van Kampen, N. G. (2007) *Stochastic Processes in Physics and Chemistry*, North-Holland Personal Library