Aalto University

Dimerisation, with production

Stochastic analysis and simulation of reactive and diffusive systems

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$2\mathcal{A} \rightarrow \emptyset$ and $\emptyset \rightarrow \mathcal{A}$

Probabilistic formulation

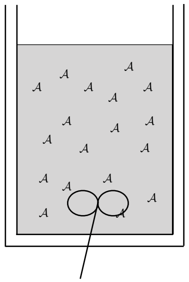
Dimerization, with production

We consider a certain chemical species $\mathcal{A}$ in a container of volume V and two reactions

- The dimerisation of species $\mathcal{A}$ coupled by the production of the same species

$$2\mathcal{A} \xrightarrow{\kappa_1/V} \emptyset$$

$$\emptyset \xrightarrow{\kappa_2} \mathcal{A}$$



The propensity function for dimerisation

$$\nu_1 \left(N_{\mathcal{A}}(t) \mid \kappa_1\right) = \frac{\kappa_1}{V}\left[N_{\mathcal{A}}(t) \times \left(N_{\mathcal{A}}(t) - 1\right)\right]$$

The propensity function for production

$$\nu_2 \left(N_{\mathcal{A}}(t) \mid \kappa_2\right) = \kappa_2 V$$

The dimerisation reaction is second order and the production reaction is zeroth-order

- Overall, the system is second-order

The combined propensity function

$$\nu \left(N_{\mathcal{A}}(t) \mid \kappa_1, \kappa_2\right) = \nu_1 \left(N_{\mathcal{A}}(t) \mid \kappa_1\right) + \nu_2 \left(N_{\mathcal{A}}(t) \mid \kappa_2\right)$$

$2\mathcal{A} \rightarrow \emptyset$ and $\emptyset \rightarrow \mathcal{A}$

Master equation

Dimerization | Master equation

Let $\mathbb{P}_{n_\mathcal{A}}(t)$ denote the probability that $n_\mathcal{A}$ molecules of $\mathcal{A}$ are in the system at time t

- Let Δt be a small interval such that in $[t, t + \Delta t)$ only one reaction occurs

$$2\mathcal{A} \xrightarrow{\kappa_1 / V} \emptyset$$
$$\emptyset \xrightarrow{\kappa_2} \mathcal{A}$$

There are three way that may lead to have $n_\mathcal{A}(t + \Delta t)$ molecules of $\mathcal{A}$

- One dimerisation reaction $\mathcal{A} + \mathcal{A} \rightarrow \emptyset$ occurred in $[t, t + \Delta t)$

$$n_\mathcal{A}(t + \Delta t) \text{ was } n_\mathcal{A}(t + \Delta t) + 2$$

  This occurs with probability $\kappa_1 / V \, [(n_\mathcal{A} + 2)(n_\mathcal{A} + 1)]$
- One production reaction $\emptyset \rightarrow \mathcal{A}$ occurred in $[t, t + \Delta t)$ occurred

$$n_\mathcal{A}(t + \Delta t) \text{ was } n_\mathcal{A}(t + \Delta t) - 1$$

  This occurs with probability $\kappa_2 V$
- No reaction occurred in $[t, t + \Delta t)$

$$n_\mathcal{A}(t + \Delta t) \text{ was } n_\mathcal{A}(t + \Delta t)$$

  This occurs with probability $1 - [\kappa_1 / V \, [(n_\mathcal{A} + 2)(n_\mathcal{A} + 1)] + \kappa_2 V]$

Dimerisation, with production | Master equation (cont.)

After combining the probabilities for all possible reaction events, we get the balance

$$\mathbb{P}_{n_\mathcal{A}}(t + \Delta t) = \underbrace{\mathbb{P}_{n_\mathcal{A}}(t) \times \left[1 - \frac{\kappa_1}{V} n_\mathcal{A}(n_\mathcal{A} - 1)\Delta t - \kappa_2 V \Delta t\right]}_{\text{No reaction}} + \underbrace{\mathbb{P}_{n_\mathcal{A}+2}(t) \times \frac{\kappa_1}{V}(n_\mathcal{A} + 2)(n_\mathcal{A} + 1)\Delta t}_{\text{Dimerisation}} + \underbrace{\mathbb{P}_{n_\mathcal{A}-1}(t) \times \kappa_2 V \Delta t}_{\text{Production}} \quad (1)$$

Manipulating terms, we get the change $\Delta \mathbb{P}_{n_\mathcal{A}}(t)$ in probability over the interval Δt

$$\frac{\mathbb{P}_{n_\mathcal{A}}(t + \Delta t) - \mathbb{P}_{n_\mathcal{A}}(t)}{\Delta t} = \frac{\kappa_1}{V}(n_\mathcal{A} + 2)(n_\mathcal{A} + 1)\mathbb{P}_{n_\mathcal{A}+2}(t) \pm 0 \times \mathbb{P}_{n_\mathcal{A}+1}(t) - \left[\frac{\kappa_1 V}{n_\mathcal{A}}(n_\mathcal{A} + 1) - \kappa_2 V\right]\mathbb{P}_{n_\mathcal{A}}(t) + \kappa_2 V \mathbb{P}_{n_\mathcal{A}-1}(t) \quad (2)$$

Dimerisation, with production | Master equation (cont.)

In the limit of a vanishing Δt, we get the chemical master equation for $n_\mathcal{A} = 1, 2, \dots$

$$\frac{\mathrm{d}\mathbb{P}_{n_\mathcal{A}}(t)}{\mathrm{d}t} = \frac{\kappa_1}{V}(n_\mathcal{A} + 2)(n_\mathcal{A} + 1)\mathbb{P}_{n_\mathcal{A}+2}(t) \pm 0 \times \mathbb{P}_{n_\mathcal{A}+1}(t) - \left[\frac{\kappa_1 V}{n_\mathcal{A}}(n_\mathcal{A} + 1) - \kappa_2 V\right]\mathbb{P}_{n_\mathcal{A}}(t) + \kappa_2 V \mathbb{P}_{n_\mathcal{A}-1}(t) \quad (3)$$

For $n_\mathcal{A} = 0$, we get

$$\frac{\mathrm{d}\mathbb{P}_0(t)}{\mathrm{d}t} = \frac{\kappa_1}{V}(2)(1)\mathbb{P}_2(t) \pm 0 \times \mathbb{P}_1(t) - \left[\frac{\kappa_1}{V} \times 0 \times (1) - \kappa_2 V\right]\mathbb{P}_0(t) + \kappa_2 V \mathbb{P}_{-1}(t)$$
$$= 2\frac{\kappa_1}{V}\mathbb{P}_2(t) + \kappa_2 V \mathbb{P}_0(t)$$

For $n_\mathcal{A} = 1$, we get

$$\frac{\mathrm{d}\mathbb{P}_1(t)}{\mathrm{d}t} = \frac{\kappa_1}{V}(3)(2)\mathbb{P}_3(t) \pm 0 \times \mathbb{P}_2(t) - \left[\frac{\kappa_1}{V} \times 1 \times (2) - \kappa_2 V\right]\mathbb{P}_1(t) + \kappa_2 V \mathbb{P}_0(t)$$
$$= 6\frac{\kappa_1}{V}\mathbb{P}_3(t) - \left[2\frac{\kappa_1}{V} - \kappa_2 V\right]\mathbb{P}_1(t) + \kappa_2 V \mathbb{P}_0(t)$$

Dimerisation, with production | Master equation (cont.)

$$\frac{\mathrm{d}\mathbb{P}_{n_\mathcal{A}}(t)}{\mathrm{d}t} = \frac{\kappa_1}{V}(n_\mathcal{A} + 2)(n_\mathcal{A} + 1)\mathbb{P}_{n_\mathcal{A}+2}(t) \pm 0 \times \mathbb{P}_{n_\mathcal{A}+1}(t) - \left[\frac{\kappa_1}{V} n_\mathcal{A}(n_\mathcal{A} + 1) - \kappa_2 V\right]\mathbb{P}_{n_\mathcal{A}}(t) + \kappa_2 V \mathbb{P}_{n_\mathcal{A}-1}(t) \quad (4)$$

One more component equations of the chemical master equation

For $n_\mathcal{A} = 2$, we get

$$\frac{\mathrm{d}\mathbb{P}_2(t)}{\mathrm{d}t} = \frac{\kappa_1}{V}(4)(3)\mathbb{P}_4(t) \pm 0 \times \mathbb{P}_3(t) - \left[\frac{\kappa_1}{V} \times 2 \times (3) - \kappa_2 V\right]\mathbb{P}_2(t) + \kappa_2 V \mathbb{P}_1(t)$$
$$= 12\frac{\kappa_1}{V}\mathbb{P}_4(t) - \left[6\frac{\kappa_1}{V} - \kappa_2 V\right]\mathbb{P}_2(t) + \kappa_2 V \mathbb{P}_1(t)$$

$2\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$

Statistics

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$2\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$
Master equation
Statistics

Dimerisation, with production | Statistics

We can use the master equation to determine the statistics of the process $(N_{\mathcal{A}}(t))_{t\geq 0}$

At a point t in time, we can determine the expected value of the process

$$\begin{aligned} \mathrm{E}\left[N_{\mathcal{A}}(t)\right] &= \sum_{n_{\mathcal{A}}=0}^{\infty} n_{\mathcal{A}} \mathbb{P}_{n_{\mathcal{A}}}(t) \\ &= M_{\mathcal{A}}(t) \end{aligned}$$

The expected mismatch with the expected value of the process at time t

$$\begin{aligned} \mathrm{E}\left[\left(n_{\mathcal{A}}(t) - M_{\mathcal{A}}(t)\right)^2\right] &= \sum_{n_{\mathcal{A}}=0}^{\infty} \left[n_{\mathcal{A}} - M_{\mathcal{A}}(t)\right]^2 \mathbb{P}_{n_{\mathcal{A}}}(t) \\ &= V_{\mathcal{A}}(t) \end{aligned}$$

For this system, these statistics can only be determined as numerical approximations

- Infinite sums and only empirical $\mathbb{P}_{n_{\mathcal{A}}}(t)$ from simulations

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$2\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$
Master equation
Statistics

Dimerisation, with production | Statistics (cont.)

We discus an approach based on generating functions used to determine $\mathbb{P}_{n_{\mathcal{A}}}(\infty) = \pi_{n_{\mathcal{A}}}$

- Probability generating functions are also known as discrete Laplace transforms

We use generating functions to determine steady-state statistics $M_{\mathcal{A}}(\infty)$ and $V_{\mathcal{A}}(\infty)$

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$2\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$
Master equation
Statistics

Dimerisation, with production | Statistics (cont.)

A probability generating function (PGF) is a function $G : [-1, 1] \times (0, \infty) \to \mathbb{R}$

$$G(x,t) = \sum_{n=0}^{\infty} x^n \mathbb{P}_n(t)$$

Variable t only indexes functions and variables

For the specific reaction system, we consider random variable $N = N_{\mathcal{A}}(t)$ at time t

$$G(x,t) = \sum_{n_{\mathcal{A}}=0}^{\infty} x^{n_{\mathcal{A}}} \mathbb{P}_{n_{\mathcal{A}}}(t)$$

Take the first derivative of the probability generating function with respect to x,

$$\begin{aligned} \frac{\partial G(x,t)}{\partial x} &= \frac{\partial}{\partial x}\left[\sum_{n_{\mathcal{A}}=0}^{\infty} x^{n_{\mathcal{A}}} \mathbb{P}_{n_{\mathcal{A}}}(t)\right] \\ &= \sum_{n_{\mathcal{A}}=0}^{\infty} \frac{\partial}{\partial x}\left[\underbrace{x^{n_{\mathcal{A}}}} \mathbb{P}_{n_{\mathcal{A}}}(t)\right] \\ &= \sum_{n_{\mathcal{A}}=0}^{\infty} \underbrace{n_{\mathcal{A}} x^{n_{\mathcal{A}}-1}} \mathbb{P}_{n_{\mathcal{A}}}(t) \end{aligned}$$

Dimerisation, with production | Statistics (cont.)

$$
\begin{aligned}
\frac{\partial G(x,t)}{\partial x} &= \sum_{n_\mathcal{A}=0}^{\infty} n_\mathcal{A} x^{n_\mathcal{A}-1} \mathbb{P}_{n_\mathcal{A}}(t) \\
&= \underbrace{(0) \times x^{0-1} \times \mathbb{P}_{n_\mathcal{A}=0}(t)}_{n_\mathcal{A}=0} + \sum_{n_\mathcal{A}=1}^{\infty} n_\mathcal{A} x^{n_\mathcal{A}-1} \mathbb{P}_{n_\mathcal{A}}(t) \\
&= \sum_{n_\mathcal{A}=1}^{\infty} n_\mathcal{A} x^{n_\mathcal{A}-1} \mathbb{P}_{n_\mathcal{A}}(t)
\end{aligned}
$$

After substituting $x = 1$, we get the expected value $M_\mathcal{A}(t)$ of the copy number $N_\mathcal{A}(t)$

$$
\begin{aligned}
\frac{\partial G(x,t)}{\partial x}\Big|_{x=1} &= \sum_{n_\mathcal{A}=1}^{\infty} n_\mathcal{A} \underbrace{(x=1)^{n_\mathcal{A}-1}}_{=1} \mathbb{P}_{n_\mathcal{A}}(t) \\
&= \sum_{n_\mathcal{A}=1}^{\infty} n_\mathcal{A} \mathbb{P}_{n_\mathcal{A}}(t) \\
&= \underbrace{\sum_{n_\mathcal{A}=0}^{\infty} n_\mathcal{A} \mathbb{P}_{n_\mathcal{A}}(t)}_{M_\mathcal{A}(t)}
\end{aligned}
$$

Dimerisation, with production | Statistics (cont.)

Take the second derivative of the probability generating function with respect to x,

$$
\begin{aligned}
\frac{\partial^2 G(x,t)}{\partial x^2} &= \frac{\partial}{\partial x}\left[\frac{\partial G(x,t)}{\partial x}\right] \\
&= \frac{\partial}{\partial x}\left[\sum_{n_\mathcal{A}=1}^{\infty} n_\mathcal{A} x^{n_\mathcal{A}-1} \mathbb{P}_{n_\mathcal{A}}(t)\right] \\
&= \sum_{n_\mathcal{A}=1}^{\infty} \frac{\partial}{\partial x}\left[n_\mathcal{A} \underbrace{x^{n_\mathcal{A}-1}} \mathbb{P}_{n_\mathcal{A}}(t)\right] \\
&= \sum_{n_\mathcal{A}=1}^{\infty} n_\mathcal{A} \underbrace{(n_\mathcal{A}-1)\, x^{n_\mathcal{A}-2}} \mathbb{P}_{n_\mathcal{A}}(t)
\end{aligned}
$$

Dimerisation, with production | Statistics (cont.)

$$
\begin{aligned}
\frac{\partial^2 G(x,t)}{\partial x^2} &= \sum_{n_\mathcal{A}=1}^{\infty} n_\mathcal{A}(n_\mathcal{A}-1)\, x^{n_\mathcal{A}-2} \mathbb{P}_{n_\mathcal{A}}(t) \\
&= \underbrace{(1)(1-1)\, x^{1-2} \mathbb{P}_{n_\mathcal{A}=1}(t)}_{n_\mathcal{A}=1} + \sum_{n_\mathcal{A}=2}^{\infty} n_\mathcal{A}(n_\mathcal{A}-1)\, x^{n_\mathcal{A}-2} \mathbb{P}_{n_\mathcal{A}}(t) \\
&= \sum_{n_\mathcal{A}=2}^{\infty} n_\mathcal{A}(n_\mathcal{A}-1)\, x^{n_\mathcal{A}-2} \mathbb{P}_{n_\mathcal{A}}(t)
\end{aligned}
$$

After substituting $x = 1$, we get the expected value of the quantity $[N_\mathcal{A}(t) - M_\mathcal{A}(t)]^2$

$$
\begin{aligned}
\frac{\partial^2 G(x,t)}{\partial x^2}\Big|_{x=1} &= \sum_{n_\mathcal{A}=2}^{\infty} n_\mathcal{A}(n_\mathcal{A}-1) \underbrace{(x=1)^{n_\mathcal{A}-2}}_{=1} \mathbb{P}_{n_\mathcal{A}}(t) \\
&= \sum_{n_\mathcal{A}=2}^{\infty} n_\mathcal{A}(n_\mathcal{A}-1)\, \mathbb{P}_{n_\mathcal{A}}(t) \\
&= \sum_{n_\mathcal{A}=0}^{\infty} n_\mathcal{A}(n_\mathcal{A}-1)\, \mathbb{P}_{n_\mathcal{A}}(t)
\end{aligned}
$$

Dimerisation, with production | Statistics (cont.)

$$
V_\mathcal{A}(t) = \sum_{n_\mathcal{A}=0}^{\infty} n_\mathcal{A}^2 \mathbb{P}_{n_\mathcal{A}}(t) - M_\mathcal{A}(t)^2
$$

We derived earlier the general equation for the evolution of the process' variance $V_\mathcal{A}(t)$

After some algebraic manipulations, we get

$$
\begin{aligned}
V_\mathcal{A}(t) &= \sum_{n_\mathcal{A}=0}^{\infty} n_\mathcal{A}^2 \mathbb{P}_{n_\mathcal{A}}(t) - M_\mathcal{A}(t)^2 \\
&= \underbrace{\sum_{n_\mathcal{A}=0}^{\infty} n_\mathcal{A}(n_\mathcal{A}-1)\, \mathbb{P}_{n_\mathcal{A}}(t)}_{\frac{\partial^2 G(x,t)}{\partial x^2}\big|_{x=1}} + \underbrace{M_\mathcal{A}(t)}_{\frac{\partial G(x,t)}{\partial x}\big|_{x=1}} - \underbrace{M_\mathcal{A}(t)^2}_{\left(\frac{\partial G(x,t)}{\partial x}\big|_{x=1}\right)^2}
\end{aligned}
$$

Mean and variance processes can be determined from the derivatives of $G(x,t)$ at $x = 1$

Dimerisation, with production | Statistics (cont.)

We can also use the generating function at $x = 0$ to determine probabilities $\mathbb{P}_{n_\mathcal{A}}(t)$

$$G(x,t) = \sum_{n_\mathcal{A}=0}^{\infty} x^{n_\mathcal{A}} \mathbb{P}_{n_\mathcal{A}}(t)$$

After substituting $x = 0$ in $G(x,t)$, we get

$$\begin{aligned} G(x=0,t) &= \sum_{n_\mathcal{A}=0}^{\infty} (0)^{n_\mathcal{A}} \mathbb{P}_{n_\mathcal{A}}(t) \\ &= (0)^0 \mathbb{P}_0(t) + \sum_{n_\mathcal{A}=1}^{\infty} \underbrace{(0)^{n_\mathcal{A}}}_{=0} \mathbb{P}_{n_\mathcal{A}}(t) \\ &= 1 \times \mathbb{P}_0(t) \end{aligned}$$

That is,

$$\mathbb{P}_0(t) = G(x,t)\Big|_{x=0}$$

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$2\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$
Master equation
Statistics

Dimerisation, with production | Statistics (cont.)

$$\frac{\partial G(x,t)}{\partial x} = \sum_{n_\mathcal{A}=1}^{\infty} n_\mathcal{A} x^{n_\mathcal{A}-1} \mathbb{P}_{n_\mathcal{A}}(t)$$

After substituting $x = 0$ in $\dfrac{\partial G(x,t)}{\partial x}$, we get

$$\begin{aligned} \frac{\partial G(x,t)}{\partial x}\Big|_{x=0} &= \sum_{n_\mathcal{A}=1}^{\infty} n_\mathcal{A} (0)^{n_\mathcal{A}-1} \mathbb{P}_{n_\mathcal{A}}(t) \\ &= (1)(0)^{1-1} \mathbb{P}_1(t) + \sum_{n_\mathcal{A}=2}^{\infty} n_\mathcal{A} \underbrace{(0)^{n_\mathcal{A}-1}}_{=0} \mathbb{P}_{n_\mathcal{A}}(t) \\ &= 1 \times 1 \times \mathbb{P}_1(t) \end{aligned}$$

That is,

$$\mathbb{P}_1(t) = \frac{\partial G(x,t)}{\partial x}\Big|_{x=0}$$

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$2\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$
Master equation
Statistics

Dimerisation, with production | Statistics (cont.)

$$\frac{\partial^2 G(x,t)}{\partial x^2} = \sum_{n_\mathcal{A}=2}^{\infty} n_\mathcal{A} \left(n_\mathcal{A} - 1\right) x^{n_\mathcal{A}-2} \mathbb{P}_{n_\mathcal{A}}(t)$$

After substituting $x = 0$ in $\dfrac{\partial^2 G(x,t)}{\partial x^2}$, we get

$$\begin{aligned} \frac{\partial^2 G(x,t)}{\partial x^2}\Big|_{x=0} &= \sum_{n_\mathcal{A}=2}^{\infty} n_\mathcal{A} \left(n_\mathcal{A} - 1\right) (0)^{n_\mathcal{A}-2} \mathbb{P}_{n_\mathcal{A}}(t) \\ &= (2)\,(2-1)\,(0)^{2-2} \mathbb{P}_2(t) + \sum_{n_\mathcal{A}=3}^{\infty} n_\mathcal{A} \left(n_\mathcal{A} - 1\right) \underbrace{(0)^{n_\mathcal{A}-2}}_{=0} \mathbb{P}_{n_\mathcal{A}}(t) \\ &= 2 \times 1 \times 1 \times \mathbb{P}_2(t) \end{aligned}$$

That is,

$$\mathbb{P}_2(t) = \frac{1}{2} \frac{\partial^2 G(x,t)}{\partial x^2}\Big|_{x=0}$$

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$2\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$
Master equation
Statistics

Dimerisation, with production | Statistics (cont.)

For higher-order derivatives, we get

$$\begin{aligned} \mathbb{P}_0(t) &= \frac{1}{0!} G(x,t)\Big|_{x=0} \\ \mathbb{P}_1(t) &= \frac{1}{1!} \frac{\partial G(x,t)}{\partial x}\Big|_{x=0} \\ \mathbb{P}_2(t) &= \frac{1}{2!} \frac{\partial^2 G(x,t)}{\partial x^2}\Big|_{x=0} \\ \mathbb{P}_3(t) &= \frac{1}{3!} \frac{\partial^3 G(x,t)}{\partial x^3}\Big|_{x=0} \\ \cdots &= \cdots \end{aligned}$$

By induction, we can write

$$\mathbb{P}_{n_\mathcal{A}}(t) = \frac{1}{n_\mathcal{A}!} \frac{\partial^{n_\mathcal{A}} G(x,t)}{\partial x^{n_\mathcal{A}}}\Big|_{x=0}$$

Dimerization | Probability generating function

In order to proceed, we have to determine the probability generating function $G(x,t)$

We start by multiplying the individual components of the master equation by $x^{n_\mathcal{A}}$

$$\frac{\mathrm{d}\mathbb{P}_{n_\mathcal{A}}(t)}{\mathrm{d}t} = \frac{\kappa_1}{V}(n_\mathcal{A}+2)(n_\mathcal{A}+1)\mathbb{P}_{n_\mathcal{A}+2}(t) \pm 0 \times \mathbb{P}_{n_\mathcal{A}+1}(t) - \left[\frac{\kappa_1}{V} n_\mathcal{A}(n_\mathcal{A}+1) - \kappa_2 V\right]\mathbb{P}_{n_\mathcal{A}}(t) + \kappa_2 V \mathbb{P}_{n_\mathcal{A}-1}(t)$$

That is, for all $n_\mathcal{A} = 0, 1, \ldots$ we write

$$x^{n_\mathcal{A}}\frac{\mathrm{d}\mathbb{P}_{n_\mathcal{A}}(t)}{\mathrm{d}t} = x^{n_\mathcal{A}}\frac{\kappa_1}{V}(n_\mathcal{A}+2)(n_\mathcal{A}+1)\mathbb{P}_{n_\mathcal{A}+2}(t) \pm x^{n_\mathcal{A}} \times 0 \times \mathbb{P}_{n_\mathcal{A}+1}(t) - x^{n_\mathcal{A}}\left[\frac{\kappa_1}{V} n_\mathcal{A}(n_\mathcal{A}+1) - \kappa_2 V\right]\mathbb{P}_{n_\mathcal{A}}(t) + x^{n_\mathcal{A}}\kappa_2 V \mathbb{P}_{n_\mathcal{A}-1}(t)$$

Dimerization | Probability generating function (cont.)

$$x^{n_\mathcal{A}}\frac{\mathrm{d}\mathbb{P}_{n_\mathcal{A}}(t)}{\mathrm{d}t} = x^{n_\mathcal{A}}\frac{\kappa_1}{V}(n_\mathcal{A}+2)(n_\mathcal{A}+1)\mathbb{P}_{n_\mathcal{A}+2}(t) \pm x^{n_\mathcal{A}} \times 0 \times \mathbb{P}_{n_\mathcal{A}+1}(t) - x^{n_\mathcal{A}}\left[\frac{\kappa_1}{V} n_\mathcal{A}(n_\mathcal{A}+1) - \kappa_2 V\right]\mathbb{P}_{n_\mathcal{A}}(t) + x^{n_\mathcal{A}}\kappa_2 V \mathbb{P}_{n_\mathcal{A}-1}(t)$$

Summing over $n_\mathcal{A}$ and rearranging terms, we get

$$\frac{\mathrm{d}}{\mathrm{d}t}\sum_{n_\mathcal{A}=0}^{\infty} x^{n_\mathcal{A}}\mathbb{P}_{n_\mathcal{A}}(t) = \frac{\kappa_1}{V}\sum_{n_\mathcal{A}=0}^{\infty} x^{n_\mathcal{A}}(n_\mathcal{A}+2)(n_\mathcal{A}+1)\mathbb{P}_{n_\mathcal{A}+2}(t) - \frac{\kappa_1}{V}\sum_{n_\mathcal{A}=0}^{\infty} x^{n_\mathcal{A}} n_\mathcal{A}(n_\mathcal{A}-1)\mathbb{P}_{n_\mathcal{A}}(t) - \kappa_2 V\sum_{n_\mathcal{A}=0}^{\infty} x^{n_\mathcal{A}}\mathbb{P}_{n_\mathcal{A}}(t) + \kappa_2 V\sum_{n_\mathcal{A}=0}^{\infty} x^{n_\mathcal{A}}\mathbb{P}_{n_\mathcal{A}-1}(t)$$

Dimerization | Probability generating function (cont.)

$$\frac{\partial}{\partial t}\underbrace{\sum_{n_\mathcal{A}=0}^{\infty} x^{n_\mathcal{A}}\mathbb{P}_{n_\mathcal{A}}(t)}_{G(x,t)} = \frac{\kappa_1}{V}\underbrace{\sum_{n_\mathcal{A}=2}^{\infty} x^{n_\mathcal{A}-2}(n_\mathcal{A})(n_\mathcal{A}-1)\mathbb{P}_{n_\mathcal{A}+2}(t)}_{\frac{\partial^2 G(x,t)}{\partial x^2}} - \frac{\kappa_1}{V}x^2\underbrace{\sum_{n_\mathcal{A}=2}^{\infty} x^{n_\mathcal{A}-2} n_\mathcal{A}(n_\mathcal{A}-1)\mathbb{P}_{n_\mathcal{A}}(t)}_{\frac{\partial^2 G(x,t)}{\partial x^2}} - \kappa_2 V\underbrace{\sum_{n_\mathcal{A}=0}^{\infty} x^{n_\mathcal{A}}\mathbb{P}_{n_\mathcal{A}}(t)}_{G(x,t)} + \kappa_2 V x\underbrace{\sum_{n_\mathcal{A}=0}^{\infty} x^{n_\mathcal{A}}\mathbb{P}_{n_\mathcal{A}}(t)}_{G(x,t)}$$

That is,

$$\frac{\partial G(x,t)}{\partial t} = \frac{\kappa_1}{V}\left(1-x^2\right)\frac{\partial^2 G(x,t)}{\partial x^2} + \kappa_2 V (x-1)\, G(x,t)$$

Dimerization | Probability generating function (cont.)

$$\frac{\partial G(x,t)}{\partial t} = \frac{\kappa_1}{V}\left(1-x^2\right)\frac{\partial^2 G(x,t)}{\partial x^2} + \kappa_2 V (x-1)\, G(x,t)$$

This yields a partial differential equation for the probability generating function $G(x,t)$

$\rightsquigarrow$ To solve it, we need to specify initial and boundary conditions

The initial condition $G(x, t=0)$ can be obtained by using $\mathbb{P}_{n_\mathcal{A}}(t=0)$, to get

$$G(x, t=0) = \sum_{n_\mathcal{A}=0}^{\infty} x^{n_\mathcal{A}}\mathbb{P}_{n_\mathcal{A}}(t=0)$$

For the first $G(x=1,t)$ of the two boundary conditions, we have

$$G(1,t) = \underbrace{\sum_{n_\mathcal{A}=0}^{\infty}\mathbb{P}_{n_\mathcal{A}}(t)}_{=1}$$

For the second boundary condition $G(x=-1,t)$, we have

$$G(-1,t) = G(-1,0)\exp\left(-2\kappa_2 V t\right)$$

Dimerization | Statistics (cont.)

We can use the stationary probability distribution function $G_{\text{SS}} : [-1, 1] \to \mathbb{R}$ to determine the stationary probability distribution $\pi_{n_\mathcal{A}}$ and statistics $M_\mathcal{A}(\infty)$ and $V_\mathcal{A}(\infty)$

For the stationary probability generating function, we can use the definition

$$\begin{aligned} G(x, t = \infty) &= \lim_{t \to \infty} G(x, t) \\ &= \lim_{t \to \infty} \left[\sum_{n_\mathcal{A}=0}^{\infty} x^{n_\mathcal{A}} \mathbb{P}_{n_\mathcal{A}}(t) \right] \\ &= \sum_{n_\mathcal{A}=0}^{\infty} \lim_{t \to \infty} \left[x^{n_\mathcal{A}} \mathbb{P}_{n_\mathcal{A}}(\infty) \right] \\ &= \sum_{n_\mathcal{A}=0}^{\infty} x^{n_\mathcal{A}} \pi_{n_\mathcal{A}} \\ &= G_{\text{SS}}(x) \end{aligned}$$

Dimerization | Statistics (cont.)

We can use the identities derived earlier to determine the statistics at steady-state

$$\begin{aligned} M_\mathcal{A}(\infty) &= \frac{\partial G_{\text{SS}}(x = 1)}{\partial x} \\ V_\mathcal{A}(\infty) &= \frac{\partial^2 G_{\text{SS}}(x = 1)}{\partial x^2} + M_\mathcal{A}(\infty) - M_\mathcal{A}^2(\infty) \end{aligned}$$

For the stationary distribution, for all $n_\mathcal{A} = 0, 1, \dots,$ we have the PDE

$$\pi_{n_\mathcal{A}} = \frac{1}{n_\mathcal{A}!} \frac{\partial^{n_\mathcal{A}} G_{\text{SS}}(x = 0)}{\partial x^{n_\mathcal{A}}}$$

Dimerization | Probability generating function (cont.)

To determine the stationary probability generating function $G_{\text{SS}}(x)$, we have

$$\begin{aligned} \frac{\partial G(x, t)}{\partial t} &= \frac{\kappa_1}{V} (1 - x^2) \frac{\partial^2 G(x, t)}{\partial x^2} + \kappa_2 V (x - 1) G(x, t) \\ &= 0 \end{aligned}$$

By algebraic manipulation, we get the ordinary differential equation

$$\frac{\partial G_{\text{SS}}(x)}{\partial x^2} = \frac{\kappa_2 V^2}{\kappa_1} \frac{1}{1 + x} G_{\text{SS}}(x)$$

Using modified Bessel functions $I_1(\cdot)$ and $K_1(\cdot)$ and integration constants C_1 and C_2,

$$G_{\text{SS}}(x) = C_1 \sqrt{1 + x}\, \underbrace{I_1 \left(2 \sqrt{\frac{\kappa_2 V^2 (1 + x)}{\kappa_1}} \right)}_{I_1(\cdot)} + C_2 \sqrt{1 + x}\, \underbrace{K_1 \left(2 \sqrt{\frac{\kappa_2 V^2 (1 + x)}{\kappa_1}} \right)}_{K_1(\cdot)}$$

Dimerization | Statistics (cont.)

Coefficients C_1 and C_2 can be determined from boundary conditions on G_{SS} at $x = \pm 1$

$$\begin{aligned} C_1 &= \left[\sqrt{2}\, \underbrace{I_1 \left(2 \sqrt{\frac{2 k_2 V^2}{k_1}} \right)}_{I_1(\cdot)} \right] \\ C_2 &= 0 \end{aligned}$$

Substituting, we get

$$\begin{aligned} G_{\text{SS}}(x) = {} & \underbrace{\left[\sqrt{2}\, \underbrace{I_1 \left(2 \sqrt{\frac{2 k_2 V^2}{k_1}} \right)}_{I_1(\cdot)} \right]}_{C_1} \sqrt{1 + x}\, \underbrace{I_1 \left(2 \sqrt{\frac{\kappa_2 V^2 (1 + x)}{\kappa_1}} \right)}_{I_1(\cdot)} \\ & + \underbrace{0}_{C_2} \sqrt{1 + x}\, \underbrace{K_1 \left(2 \sqrt{\frac{\kappa_2 V^2 (1 + x)}{\kappa_1}} \right)}_{K_1(\cdot)} \end{aligned}$$

Dimerization | Statistics (cont.)

$$G_{\text{SS}}(x) = \left[\sqrt{2}\,\underbrace{I_1\left(2\sqrt{\frac{2k_2 V^2}{k_1}}\right)}_{I_1(\cdot)}\right]\sqrt{1+x}\,\underbrace{I_1\left(2\sqrt{\frac{\kappa_2 V^2(1+x)}{\kappa_1}}\right)}_{I_1(\cdot)}$$

Taking the first derivative with respect to x to obtain $M_{\mathcal{A}}(\infty)$, we get

$$M_{\mathcal{A}}(\infty) = \underbrace{\frac{1}{4} + \sqrt{\frac{\kappa_2 V^2}{2\kappa_1}}\,\underbrace{I_1'\left(2\sqrt{\frac{2\kappa_2 V^2}{\kappa_1}}\right)}_{\frac{\partial I_1(\cdot)}{\partial x}}\left[\underbrace{I_1\left(2\sqrt{\frac{2\kappa_2 V^2}{\kappa_1}}\right)}_{I_1(\cdot)}\right]^{-1}}_{\frac{\partial G_{\text{SS}}(x=1)}{\partial x}}$$

Dimerization | Statistics (cont.)

Taking the second derivative with respect to x, we get

$$\frac{\partial^2 G_{\text{SS}}(x=1)}{\partial x^2} = \frac{\kappa_2}{2\kappa}V^2$$

After substituting to obtain $V_{\mathcal{A}}(\infty)$, we get

$$V_{\mathcal{A}}(\infty) = \underbrace{\frac{\kappa_2}{2\kappa_1}V^2}_{\frac{\partial^2 G_{\text{SS}}(x=1)}{\partial x^2}} + M_{\mathcal{A}}(\infty) - M_{\mathcal{A}}(\infty)^2$$

Dimerization | Statistics (cont.)

Let $X_{\mathcal{A}}(t) = N_{\mathcal{A}}(t)/V$ be the concentration of species $\mathcal{A}$ in the system at some time t

The deterministic reaction rate

$$\frac{\mathrm{d}X_{\mathcal{A}}(t)}{\mathrm{d}t} = -2k_1 X_{\mathcal{A}}(t)^2 + k_2$$

Multiplying by V, we get

$$\frac{\mathrm{d}N_{\mathcal{A}}(t)}{\mathrm{d}t} = -2\frac{k_1}{V}N_{\mathcal{A}}(t)^2 + k_2 V$$

The deterministic solution $(N_{\mathcal{A}}(t))_{t\geq 0}$ from $X_{\mathcal{A}}(0) = 0$ is not equal to $(\mathrm{E}\,[M_{\mathcal{A}}(t)])_{t\geq 0}$

For $k_1/V = 0.005\text{sec}^{-1}$ and $k_2 V = 1\text{sec}^{-1}$, the steady state concentration

$$\overline{A}_{\text{ss}} = \underbrace{V\sqrt{\frac{k_2}{2k_1}}}_{10} \neq \underbrace{M_{\mathcal{A}}(\infty)}_{10.13}$$

The result can be verified also by simulation using the empirical mean of the process

Dimerization | Statistics (cont.)

Deterministic differential equations are not necessarily solved by the stochastic mean

⇝ Deterministic solutions do not provide information about fluctuations