Aalto University

# Degradation $\mathcal{A} \to \emptyset$ and production $\emptyset \to \mathcal{A}$

## Stochastic analysis and simulation of reactive and diffusive systems

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CHEM-LV03
2022

$\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$
Chemical master equation
Statistics
Stationary distribution

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

Stochastic simulation

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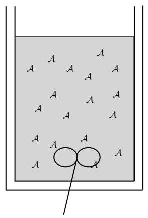
## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Simulation

We extend our analysis to consider a system with a single species and two reactions



We consider the degradation of some chemical species $\mathcal{A}$ to some uninteresting form $\emptyset$

$$\mathcal{A} \xrightarrow{\kappa_1} \emptyset$$

We also consider the production of the same species $\mathcal{A}$ from an uninteresting form $\emptyset$

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

The degradation reaction does not state that $\mathcal{A}$ is degraded into nothing, but that it is degraded into unmoddeled species, or that there is an outflux to another compartment

The production reaction does not state that $\mathcal{A}$ is created from nothing, but that it is produced from unmodelled species, or that there is an influx from another compartment

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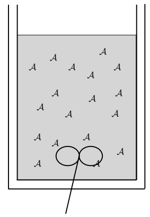
## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Simulation (cont.)



$$\mathcal{A} \xrightarrow{\kappa_1} \emptyset$$
$$\emptyset \xrightarrow{\kappa_2} \mathcal{A}$$

The reactions occur in a vessel of volume $V$

- ⇝ The content of the vessel is well mixed
- ⇝ The system is in thermal equilibrium

The rate constant $\kappa_1$ is defined in such a way that the quantity $(\kappa_1 \, \mathrm{d}t)$ corresponds to the probability that a molecule of $\mathcal{A}$ is degraded in the infinitesimally small interval

$$[t, t + \mathrm{d}t)$$

The rate constant $\kappa_2$ is defined in such a way that quantity $(V \, \kappa_2 \, \mathrm{d}t)$ is the probability that a molecule of $\mathcal{A}$ is produced, in the infinitesimal interval and in the unit volume

$$[t, t + \mathrm{d}t) \text{ and } V$$

## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Simulation (cont.)

Rate constants $\kappa_1$ for degradation and $\kappa_2$ for production have different physical units

- ⇝ $\kappa_1$ is expressed in $[\text{sec}^{-1}]$
- ⇝ $\kappa_2$ is expressed in $[\text{sec}^{-1}\text{m}^{-3}]$

The probability of the degradation reaction depends on the state of the system

- ⇝ (It grows with the number of molecules available)

The probability of the production reaction depends on the size of the system

- ⇝ (It is constant, but proportional to volume)

To understand the reasoning behind the scaling of $\kappa_2$ by volume, think of dividing the container in two equally large parts, the production rate in each is also divided by two



## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Simulation (cont.)

To model and simulate this system of two reactions, we consider again reaction events

For the first reaction, over the infinitesimal time d$t$, we had

$$\begin{aligned}
\mathbb{P}(\text{one degradation}) &= \mathbb{P}(\text{EITHER molecule } \mathcal{A}_1 \text{ OR } \cdots \text{ OR } \mathcal{A}_{N_\mathcal{A}(t)} \text{ degrades}) && \text{(1a)}\\
&= \mathbb{P}(\mathcal{A}_1 \text{ degrades} \cup \cdots \cup \mathcal{A}_{N_\mathcal{A}(t)} \text{ degrades}) && \text{(1b)}\\
&= \mathbb{P}(\mathcal{A}_1 \text{ degrades}) + \cdots + \mathbb{P}(\mathcal{A}_{N_\mathcal{A}(t)} \text{ degrades}) && \text{(1c)}\\
&= N_\mathcal{A}(t) \times \mathbb{P}(\text{a molecule of } \mathcal{A} \text{ degrades}) && \text{(1d)}\\
&= N_\mathcal{A}(t) \times \kappa_1 \mathrm{d}t && \text{(1e)}
\end{aligned}$$

Again, the molecules of $\mathcal{A}$ were assumed to be indistinguishable and act independently

For the second reaction, over the infinitesimal time d$t$, we have

$$\mathbb{P}(\text{one production}) = V\kappa_2 \mathrm{d}t \qquad (2)$$



## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Simulation (cont.)

We can start our reasoning about the system in terms of time until the next reaction

$$\mathcal{A} \xrightarrow{\kappa_1} \emptyset$$
$$\emptyset \xrightarrow{\kappa_2} \mathcal{A}$$

The state changes EITHER when one degradation OR one production reaction occurs

The probability that an event occurs in $[t, t + \mathrm{d}t)$ equals the probability $N_\mathcal{A}(t)\kappa_1\mathrm{d}t$ that the first reaction occurs PLUS the probability $V\kappa_2\mathrm{d}t$ that the second one occurs

$$\mathbb{P}(\text{one degradation}) = \underbrace{N_\mathcal{A}(t) \times \kappa_1}\,\mathrm{d}t$$
$$\mathbb{P}(\text{one production}) = \underbrace{V\kappa_2}\,\mathrm{d}t$$

Let $(\alpha(t)\ \mathrm{d}t)$ be the probability that EITHER the first OR the second reaction occurs

$$\alpha(t) = \underbrace{N_\mathcal{A}(t)\kappa_1 + V\kappa_2}_{\text{Probability per unit time}}$$

We think of $\alpha(t)$ as the propensity of the system to react at time $t$, given its state $N_\mathcal{A}$



## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Simulation (cont.)

$$\alpha(t) = N_\mathcal{A}(t)\kappa_1 + V\kappa_2$$

We use this combined information to determine the time $s$ until the next reaction event

- ⇝ The time $s$ is an exponentially distributed number
  - (Regardless of what reaction it will be)
  - (Give the state of the system at $t$)

That is,

$$s \sim \text{Exp}\,(\alpha(t))$$

Formally, time $t+s$ is to be understood as the exit time of the system from state $N_\mathcal{A}(t)$

- ⇝ The expected (the mean) exit time is the reciprocal of $\alpha(t)$

As $\alpha(t) = N_\mathcal{A}(t)\kappa_1 + V\kappa_2$ increases/decreases with the increase/decrease in copy numbers (other things being constant), also the mean exit time will change accordingly

- ⇝ A large/small copy numbers of reactants indicates frequent/rare reactions

# $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Simulation (cont.)

The next reaction occurs at some time $t + s$, we need to determine which one it will be

⇝ The index of the next reaction is a discrete random variable

Based on their relative probability of occurrence, we have

⇝ For the first reaction

$$\mathbb{P}(\text{degradation occurs}) = \frac{N_{\mathcal{A}}(t)\kappa_1}{\alpha(t)}$$

⇝ For the second reaction

$$\mathbb{P}(\text{production occurs}) = \frac{\kappa_2 V}{\alpha(t)}$$

The next reaction type is a random variable $M$ with a generalised Bernoulli distribution

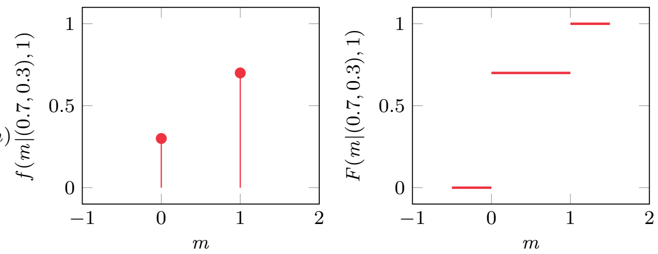
- (A variable with multinomial distribution with two events, and one trial)
- (If one trial and whatever the number of events, a binomial distribution)



# $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Simulation (cont.)

## Definition (Multinomial/Binomial distribution)

$m \sim \text{Mult}(p, n)$




The probability mass function

$$f(m \mid p, n) = \begin{cases} \dfrac{n!}{\prod x_k!} \prod p_k^{x_k}, & \sum x_k = 1 \\ 0, & \text{elsewhere} \end{cases}$$



**Algorithm 1** Degradation + production | Stochastic simulation algorithm

**procedure** DEGRADATION + PRODUCTION | SSA, EXPONENTIAL + MULTINOMIAL
**Input:** $n_{\mathcal{A}}(t = 0) = n_{\mathcal{A}}(0)$, V, $\kappa_1$ and $\kappa_2$
**Output:** $(n_{\mathcal{A}}(t + s_z))_{z=1,2,\ldots}$
Set $t = 0$, $r = 0$ and $s_z = 0$
Compute $\alpha_1(t) = n_{\mathcal{A}}(t + s_z)\kappa_1$, $\alpha_2(t + s_z) = V\kappa_2$, and $\alpha(t) = \sum \alpha_{n_r}(t)$
Compute $p = (p_1, p_2)$, with $p_{n_r} = \alpha_{n_r}/\alpha(t)$ for $n_r = 1, 2$
Compute the time $s_{z+1}$ until next reaction

$$s_{z+1} \sim \text{Exp}(\alpha(t))$$

Compute the type $m_{z+1}$ of next reaction

$$m_{z+1} \sim \text{Mult}(p, n = 1)$$

Set

$$n_A(t + s_{z+1}) = \begin{cases} n_A(t + s_z) + 1, & \text{if } m = 1 \\ n_A(t + s_z) - 1, & \text{if } m = 0 \end{cases}$$

Set $z \rightsquigarrow z + 1$
Set $t \rightsquigarrow t + s_{z+1}$
Repeat
**end procedure**

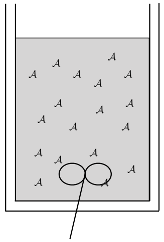


# $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Simulation (cont.)

## Example

The evolution of $n_{\mathcal{A}}(t)$ is obtained by stochastic simulation for given parameter values

$$\mathcal{A} \xrightarrow{\kappa_1} \emptyset$$
$$\emptyset \xrightarrow{\kappa_2} \mathcal{A}$$



Kinetic parameters

$$\kappa_1 = 0.1\text{sec}^{-1}$$
$$\kappa_2 V = 1.0\text{sec}^{-1}$$

Initial conditions

$$n_{\mathcal{A}}(0) = 0$$

Each time the simulation is repeated, a different realisation of $(N_{\mathcal{A}}(t))_{t>0}$ is obtained

$$\{n_{\mathcal{A}}^{(r)}(t_k)\}_{k=1}^{K} \qquad (r = 1, 2, \ldots, R)$$

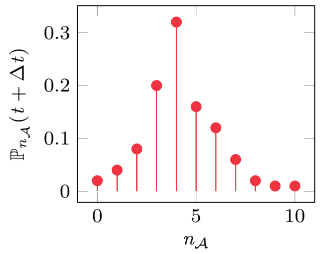
# $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$

## Chemical master equation



## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Master equation

Let $\mathbb{P}_{n_\mathcal{A}}(t+\Delta t)$ be the probability that there are $n_\mathcal{A}$ molecules of $\mathcal{A}$ at time $(t+\Delta t)$




$$\mathcal{A} \xrightarrow{\kappa_1} \emptyset$$
$$\emptyset \xrightarrow{\kappa_2} \mathcal{A}$$



## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Master equation (cont.)

$$\mathcal{A} \xrightarrow{\kappa_1} \emptyset$$
$$\emptyset \xrightarrow{\kappa_2} \mathcal{A}$$

There are only three ways that lead to have $n_\mathcal{A}(t+\Delta t)$ molecules of $\mathcal{A}$, given $n_\mathcal{A}(t)$

- ⇝ $n_\mathcal{A}(t+\Delta t)$ was $n_\mathcal{A}(t)+1$ and one degradation occurred in $[t, t+\Delta t)$

$$(n_\mathcal{A}+1)\kappa_1\Delta t$$

- ⇝ $n_\mathcal{A}(t+\Delta t)$ was $n_\mathcal{A}(t)-1$ and one production occurred in $[t, t+\Delta t)$

$$V\kappa_2\Delta t$$

- ⇝ $n_\mathcal{A}(t+\Delta t)$ was $n_\mathcal{A}(t)$ and no reactions occurred in $[t, t+\Delta t)$

$$1-[(n_\mathcal{A}+1)\kappa_1\Delta t + V\kappa_2\Delta t]$$



## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Master equation

$$\begin{aligned}\mathbb{P}_{n_\mathcal{A}}(t+\Delta t) = &\underbrace{\mathbb{P}_{n_\mathcal{A}(t)}(t) \times \underbrace{[1-(n_\mathcal{A}+1)\kappa_1\Delta t - V\kappa_2\Delta t]}}_{\text{No reactions occur}} \\ &+ \underbrace{\mathbb{P}_{n_\mathcal{A}(t)+1}(t) \times \underbrace{(n_\mathcal{A}+1)\kappa_1\Delta t}}_{\text{Degradation occurs}} \\ &+ \underbrace{\mathbb{P}_{n_\mathcal{A}(t)-1}(t) \times \underbrace{V\kappa_2\Delta t}}_{\text{Production occurs}}\end{aligned}$$

After rearranging and for $\Delta t \to 0$, we get the ordinary differential difference equation

$$\frac{\mathrm{d}\mathbb{P}_{n_\mathcal{A}}(t)}{\mathrm{d}t} = \kappa_1(n_\mathcal{A}+1)\mathbb{P}_{n_\mathcal{A}+1}(t) - \kappa_1 n_\mathcal{A}\mathbb{P}_{n_\mathcal{A}}(t) + \kappa_2 V\mathbb{P}_{n_\mathcal{A}-1}(t) - \kappa_2 V\mathbb{P}_{n_\mathcal{A}}(t)$$

## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Master equation (cont.)

$$\frac{d\mathbb{P}_{n_\mathcal{A}}(t)}{dt} = \underbrace{\underbrace{\kappa_1(n_\mathcal{A}+1)\mathbb{P}_{n_\mathcal{A}+1}(t)}_{\text{Gain}} - \underbrace{\kappa_1 n_\mathcal{A}\mathbb{P}_{n_\mathcal{A}}(t)}_{\text{Loss}}}_{\text{Degradation}} + \underbrace{\underbrace{\kappa_2 V\mathbb{P}_{n_\mathcal{A}-1}(t)}_{\text{Gain}} - \underbrace{\kappa_2 V\mathbb{P}_{n_\mathcal{A}}(t)}_{\text{Loss}}}_{\text{Production}}$$
$$= \kappa_1\left[(n_\mathcal{A}+1)\mathbb{P}_{n_\mathcal{A}+1}(t) - n_\mathcal{A}\mathbb{P}_{n_\mathcal{A}}(t)\right] + \kappa_2 V\left[\mathbb{P}_{n_\mathcal{A}-1}(t) - \mathbb{P}_{n_\mathcal{A}}(t)\right]$$

Each reaction contributes to the rate of change of $\mathbb{P}_{n_\mathcal{A}}$ with one gain and one loss term

$$\frac{d\mathbb{P}_{n_\mathcal{A}}(t)}{dt} = \underbrace{\underbrace{\kappa_1(n_\mathcal{A}+1)\mathbb{P}_{n_\mathcal{A}+1}(t)}_{\text{Degradation}} + \underbrace{\kappa_2 V\mathbb{P}_{n_\mathcal{A}-1}(t)}_{\text{Production}}}_{\text{Gain}} - \underbrace{\underbrace{\kappa_1 n_\mathcal{A}\mathbb{P}_{n_\mathcal{A}}(t)}_{\text{Degradation}} - \underbrace{\kappa_2 V\mathbb{P}_{n_\mathcal{A}}(t)}_{\text{Production}}}_{\text{Loss}}$$
$$= \left[\kappa_1(n_\mathcal{A}+1)\mathbb{P}_{n_\mathcal{A}+1}(t) + \kappa_2 V\mathbb{P}_{n_\mathcal{A}-1}(t)\right] - \left[\kappa_1 n_\mathcal{A} + \kappa_2 V\right]\mathbb{P}_{n_\mathcal{A}}(t)$$



## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Master equation (cont.)

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

For each copy-number $n_\mathcal{A}$ and at each time $t$, the rate at which the probability of that number changes depends on an outgoing flow and on an incoming flow of probability

Whenever gains and losses are equal, the rate of change in probability is equal to zero

- We say that the system, from the viewpoint of $\mathbb{P}_{n_\mathcal{A}}(t)$, is at steady-state



## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Master equation (cont.)

$$\frac{d\mathbb{P}_{n_\mathcal{A}}(t)}{dt} = \kappa_1(n_\mathcal{A}+1)\mathbb{P}_{n_\mathcal{A}+1}(t) - \kappa_1 n_\mathcal{A}\mathbb{P}_{n_\mathcal{A}}(t) + \kappa_2 V\mathbb{P}_{n_\mathcal{A}-1}(t) - \kappa_2 V\mathbb{P}_{n_\mathcal{A}}(t)$$

We know that chemical master equations (CME) are defined for all $n_\mathcal{A} \in \{0, 1, \dots, \infty\}$

- In a degradation + production systems, there is no maximum number $n_\mathcal{A}$

$$\mathcal{A} \xrightarrow{\kappa_1} \emptyset$$
$$\emptyset \xrightarrow{\kappa_2} \mathcal{A}$$

This master equation consists of a set of infinitely many ordinary differential equations

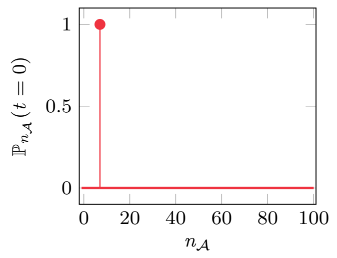
⇝ The initial condition is the set $\{\mathbb{P}_{n_\mathcal{A}}(t=0)\}_{n_\mathcal{A}=0}^{\infty}$ of initial probabilities



## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Master equation (cont.)

$$\frac{d\mathbb{P}_{n_\mathcal{A}}(t)}{dt} = \kappa_1(n_\mathcal{A}+1)\mathbb{P}_{n_\mathcal{A}+1}(t) - \kappa_1 n_\mathcal{A}\mathbb{P}_{n_\mathcal{A}}(t) + \kappa_2 V\mathbb{P}_{n_\mathcal{A}-1}(t) - \kappa_2 V\mathbb{P}_{n_\mathcal{A}}(t)$$
$$(\text{with } n_\mathcal{A} = 0, 1, \dots, \infty)$$

Assume to known the initial number of molecule of $\mathcal{A}$ and use it as initial condition




$$\mathbb{P}_{n_\mathcal{A}}(t=0) = \begin{cases} 1, & \text{for } n_\mathcal{A} = \overline{n_\mathcal{A}} \\ 0, & \text{elsewhere} \end{cases}$$

## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Master equation (cont.)

$$\frac{d\mathbb{P}_{n_{\mathcal{A}}}(t)}{dt} = \kappa_1 (n_{\mathcal{A}} + 1)\mathbb{P}_{n_{\mathcal{A}}+1}(t) - \kappa_1 n_{\mathcal{A}} \mathbb{P}_{n_{\mathcal{A}}}(t) + \kappa_2 V \mathbb{P}_{n_{\mathcal{A}}-1}(t) - \kappa_2 V \mathbb{P}_{n_{\mathcal{A}}}(t)$$
$$(\text{with } n_{\mathcal{A}} = 0, 1, \dots, \infty)$$

We can inspect the component equations for a first two values of the copy number $n_{\mathcal{A}}$

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

$$\begin{aligned}\frac{d\mathbb{P}_0(t)}{dt} &= \kappa_1 (0 + 1)\mathbb{P}_{0+1}(t) - \kappa_1 (0) \mathbb{P}_0(t) + \kappa_2 V \mathbb{P}_{0-1}(t) - \kappa_2 V \mathbb{P}_0(t) \\ &= \kappa_1 \mathbb{P}_1(t) - \kappa_2 V \mathbb{P}_0(t)\end{aligned}$$

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

$$\begin{aligned}\frac{d\mathbb{P}_1(t)}{dt} &= \kappa_1 (1 + 1)\mathbb{P}_{1+1}(t) - \kappa_1 (1) \mathbb{P}_1(t) + \kappa_2 V \mathbb{P}_{1-1}(t) - \kappa_2 V \mathbb{P}_1(t) \\ &= 2\kappa_1 \mathbb{P}_2(t) - \kappa_1 \mathbb{P}_1(t) + \kappa_2 V \mathbb{P}_0(t) - \kappa_2 V \mathbb{P}_1(t) \\ &= 2\kappa_1 \mathbb{P}_2(t) - (\kappa_1 + \kappa_2 V)\mathbb{P}_1(t) + \kappa_2 V \mathbb{P}_0(t)\end{aligned}$$



## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Master equation (cont.)

$$\frac{d\mathbb{P}_{n_{\mathcal{A}}}(t)}{dt} = \kappa_1 (n_{\mathcal{A}} + 1)\mathbb{P}_{n_{\mathcal{A}}+1}(t) - \kappa_1 n_{\mathcal{A}} \mathbb{P}_{n_{\mathcal{A}}}(t) + \kappa_2 V \mathbb{P}_{n_{\mathcal{A}}-1}(t) - \kappa_2 V \mathbb{P}_{n_{\mathcal{A}}}(t)$$
$$(\text{with } n_{\mathcal{A}} = 0, 1, \dots, \infty)$$

We can inspect the component equations for a last two values of the copy numbers $n_{\mathcal{A}}$

For $n_{\mathcal{A}} = \overline{n_{\mathcal{A}}}$, we have

$$\begin{aligned}\frac{d\mathbb{P}_{\overline{n_{\mathcal{A}}}}(t)}{dt} &= \kappa_1 (\overline{n_{\mathcal{A}}} + 1)\mathbb{P}_{\overline{n_{\mathcal{A}}}+1}(t) - \kappa_1 (\overline{n_{\mathcal{A}}}) \mathbb{P}_{\overline{n_{\mathcal{A}}}}(t) + \kappa_2 V \mathbb{P}_{\overline{n_{\mathcal{A}}}-1}(t) - \kappa_2 V \mathbb{P}_{\overline{n_{\mathcal{A}}}}(t) \\ &= \kappa_2 V \mathbb{P}_{\overline{n_{\mathcal{A}}}-1}(t) - (\kappa_1 \overline{n_{\mathcal{A}}} + \kappa_2 V)\mathbb{P}_{\overline{n_{\mathcal{A}}}}(t)\end{aligned}$$

For $n_{\mathcal{A}} = \overline{n_{\mathcal{A}}} - 1$, we have

$$\begin{aligned}\frac{d\mathbb{P}_{\overline{n_{\mathcal{A}}}-1}(t)}{dt} &= \kappa_1 (\overline{n_{\mathcal{A}}} - 1 + 1)\mathbb{P}_{\overline{n_{\mathcal{A}}}-1+1}(t) - \kappa_1 (\overline{n_{\mathcal{A}}} - 1) \mathbb{P}_{\overline{n_{\mathcal{A}}}-1}(t) \\ &\quad + \kappa_2 V \mathbb{P}_{\overline{n_{\mathcal{A}}}-1-1}(t) - \kappa_2 V \mathbb{P}_{\overline{n_{\mathcal{A}}}-1}(t) \\ &= \kappa_1 \overline{n_{\mathcal{A}}} \mathbb{P}_{\overline{n_{\mathcal{A}}}}(t) - \kappa_1 (\overline{n_{\mathcal{A}}} - 1)\mathbb{P}_{\overline{n_{\mathcal{A}}}-1}(t) + \kappa_2 V \mathbb{P}_{\overline{n_{\mathcal{A}}}-2}(t) - \kappa_2 V \mathbb{P}_{\overline{n_{\mathcal{A}}}-1}(t) \\ &= \kappa_1 \overline{n_{\mathcal{A}}} \mathbb{P}_{\overline{n_{\mathcal{A}}}}(t) - [\kappa_1 (\overline{n_{\mathcal{A}}} - 1) + \kappa_2 V]\mathbb{P}_{\overline{n_{\mathcal{A}}}-1}(t) + \kappa_2 V \mathbb{P}_{\overline{n_{\mathcal{A}}}-2}(t)\end{aligned}$$



## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Master equation (cont.)

$$\frac{d\mathbb{P}_{n_{\mathcal{A}}}(t)}{dt} = \kappa_1 (n_{\mathcal{A}} + 1)\mathbb{P}_{n_{\mathcal{A}}+1}(t) - \kappa_1 n_{\mathcal{A}} \mathbb{P}_{n_{\mathcal{A}}}(t) + \kappa_2 V \mathbb{P}_{n_{\mathcal{A}}-1}(t) - \kappa_2 V \mathbb{P}_{n_{\mathcal{A}}}(t)$$
$$(\text{with } n_{\mathcal{A}} = 0, 1, \dots, \infty)$$

To solve this master equation in practice, a truncation at some $n_{\mathcal{A}} \gg \overline{n_{\mathcal{A}}}$ can be used

⇝ The approximation is acceptable, because $\mathbb{P}_{n_{\mathcal{A}}} \to 0$ as $n_{\mathcal{A}} \to \infty$, whatever $t$



## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Master equation (cont.)

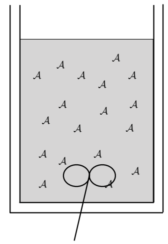
### Example

The solution to the chemical master equation

$$\mathcal{A} \xrightarrow{\kappa_1} \emptyset$$
$$\emptyset \xrightarrow{\kappa_2} \mathcal{A}$$

Kinetic parameters and initial conditions

$$\kappa_1 = 0.1\text{sec}^{-1}$$
$$\kappa_2 V = 1.0\text{sec}^{-1}$$
$$n_{\mathcal{A}}(0) = 0$$



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

Statistics



## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Statistics

We can use the master equation to determine the expected evolution $(\mathrm{E}[N_{\mathcal{A}}(t)])_{t \geq 0}$

In general, we have

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

We can also use the master equation to determine the spread around $(\mathrm{E}[N_{\mathcal{A}}(t)])_{t \geq 0}$

In general, we have

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



## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Statistics (cont.)

In addition, we have derived the chemical master equation for all values $n_{\mathcal{A}} = 0, 1, \ldots, \infty$

$$\frac{\mathrm{d}\mathbb{P}_{n_{\mathcal{A}}}(t)}{\mathrm{d}t} = \kappa_1 (n_{\mathcal{A}} + 1) \mathbb{P}_{n_{\mathcal{A}}+1}(t) - \kappa_1 n_{\mathcal{A}} \mathbb{P}_{n_{\mathcal{A}}}(t) + \kappa_2 V \mathbb{P}_{n_{\mathcal{A}}-1}(t) - \kappa_2 V \mathbb{P}_{n_{\mathcal{A}}}(t)$$

That is,

$$\begin{aligned} \frac{\mathrm{d}\mathbb{P}_0(t)}{\mathrm{d}t} &= \kappa_1 \mathbb{P}_1(t) - \kappa_2 V \mathbb{P}_0(t) \\ \frac{\mathrm{d}\mathbb{P}_1(t)}{\mathrm{d}t} &= 2\kappa_1 \mathbb{P}_2(t) - (\kappa_1 + \kappa_2 V) \mathbb{P}_1(t) + \kappa_2 V \mathbb{P}_0(t) \\ \frac{\mathrm{d}\mathbb{P}_2(t)}{\mathrm{d}t} &= 3\kappa_1 \mathbb{P}_3(t) - (2\kappa_1 + \kappa_2 V) \mathbb{P}_2(t) + \kappa_2 V \mathbb{P}_1(t) \\ \cdots &= \cdots \\ \frac{\mathrm{d}\mathbb{P}_{\overline{n_{\mathcal{A}}}-1}(t)}{\mathrm{d}t} &= \kappa_1 \overline{n_{\mathcal{A}}} \mathbb{P}_{\overline{n_{\mathcal{A}}}}(t) - [\kappa_1 (\overline{n_{\mathcal{A}}} - 1) + \kappa_2 V] \, \mathbb{P}_{\overline{n_{\mathcal{A}}}-1}(t) + \kappa_2 V \mathbb{P}_{\overline{n_{\mathcal{A}}}-2}(t) \\ \frac{\mathrm{d}\mathbb{P}_{\overline{n_{\mathcal{A}}}}(t)}{\mathrm{d}t} &= \kappa_2 V \mathbb{P}_{\overline{n_{\mathcal{A}}}-1}(t) - (\kappa_1 \overline{n_{\mathcal{A}}} + \kappa_2 V) \, \mathbb{P}_{\overline{n_{\mathcal{A}}}}(t) \end{aligned}$$



## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Statistics (cont.)

By multiplying each component equation of the master equation by $n_{\mathcal{A}}$, we obtain

$$\begin{aligned} n_{\mathcal{A}} \frac{\mathrm{d}\mathbb{P}_{n_{\mathcal{A}}}(t)}{\mathrm{d}t} = {} & \kappa_1 n_{\mathcal{A}} (n_{\mathcal{A}} + 1) \mathbb{P}_{n_{\mathcal{A}}+1}(t) - \kappa_1 {n_{\mathcal{A}}}^2 \mathbb{P}_{n_{\mathcal{A}}}(t) \\ & + \kappa_2 n_{\mathcal{A}} V \mathbb{P}_{n_{\mathcal{A}}-1}(t) - \kappa_2 n_{\mathcal{A}} V \mathbb{P}_{n_{\mathcal{A}}}(t) \quad (\text{for all } n_{\mathcal{A}} = 0, 1, \ldots, \infty) \end{aligned}$$

That is,

$$\begin{aligned} n_{\mathcal{A}} \frac{\mathrm{d}\mathbb{P}_0(t)}{\mathrm{d}t} &= \kappa_1 n_{\mathcal{A}} \mathbb{P}_1(t) - \kappa_2 n_{\mathcal{A}} V \mathbb{P}_0(t) \\ n_{\mathcal{A}} \frac{\mathrm{d}\mathbb{P}_1(t)}{\mathrm{d}t} &= 2\kappa_1 n_{\mathcal{A}} \mathbb{P}_2(t) - (\kappa_1 + \kappa_2 V) \, n_{\mathcal{A}} \mathbb{P}_1(t) + \kappa_2 n_{\mathcal{A}} V \mathbb{P}_0(t) \\ n_{\mathcal{A}} \frac{\mathrm{d}\mathbb{P}_2(t)}{\mathrm{d}t} &= 3\kappa_1 n_{\mathcal{A}} \mathbb{P}_3(t) - (2\kappa_1 + \kappa_2 V) \, n_{\mathcal{A}} \mathbb{P}_2(t) + \kappa_2 n_{\mathcal{A}} V \mathbb{P}_1(t) \\ \cdots &= \cdots \end{aligned}$$

Summing over all the values of $n_{\mathcal{A}}$, we get

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

## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Statistics (cont.)

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

Rearranging terms, we get

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



## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Statistics (cont.)

We can write the ordinary differential equation for the evolution of the process' mean

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



## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Statistics (cont.)

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

Changing the indexes $(n_\mathcal{A}+1) \rightsquigarrow n_\mathcal{A}$ and $n_\mathcal{A} \rightsquigarrow (n_\mathcal{A}-1)$ in the first term, we write

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



## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Statistics (cont.)

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

Changing the indexes $(n_\mathcal{A}-1) \rightsquigarrow n_\mathcal{A}$ and $n_\mathcal{A} \rightsquigarrow (n_\mathcal{A}+1)$ in the third term, we write

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

## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Statistics (cont.)

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

Combining the first and second term (gain and loss due to degradation), we get

$$\begin{aligned} \frac{\mathrm{d}M_{\mathcal{A}}(t)}{\mathrm{d}t} &= \kappa_1 \sum_{n_{\mathcal{A}}=0}^{\infty} \underbrace{\left[(n_{\mathcal{A}}-1) n_{\mathcal{A}} - {n_{\mathcal{A}}}^2\right]}_{-n_{\mathcal{A}}} \mathbb{P}_{n_{\mathcal{A}}}(t) \\ &+ \kappa_2 V \sum_{n_{\mathcal{A}}=0}^{\infty} (n_{\mathcal{A}}+1) \mathbb{P}_{n_{\mathcal{A}}}(t) - \kappa_2 V \sum_{n_{\mathcal{A}}=0}^{\infty} n_{\mathcal{A}} \mathbb{P}_{n_{\mathcal{A}}}(t) \\ &= -\kappa_1 \sum_{n_{\mathcal{A}}=0}^{\infty} n_{\mathcal{A}} \mathbb{P}_{n_{\mathcal{A}}}(t) + \kappa_2 V \sum_{n_{\mathcal{A}}=0}^{\infty} (n_{\mathcal{A}}+1) \mathbb{P}_{n_{\mathcal{A}}}(t) - \kappa_2 V \sum_{n_{\mathcal{A}}=0}^{\infty} n_{\mathcal{A}} \mathbb{P}_{n_{\mathcal{A}}}(t) \end{aligned}$$



## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Statistics (cont.)

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

Combining the third and fourth terms (gain and loss from production), we get

$$\begin{aligned} \frac{\mathrm{d}M_{\mathcal{A}}(t)}{\mathrm{d}t} &= -\kappa_1 \sum_{n_{\mathcal{A}}=0}^{\infty} n_{\mathcal{A}} \mathbb{P}_{n_{\mathcal{A}}}(t) \\ &+ \kappa_2 V \sum_{n_{\mathcal{A}}=0}^{\infty} (n_{\mathcal{A}}+1) \mathbb{P}_{n_{\mathcal{A}}}(t) - \kappa_2 V \sum_{n_{\mathcal{A}}=0}^{\infty} n_{\mathcal{A}} \mathbb{P}_{n_{\mathcal{A}}}(t) \\ &= -\kappa_1 \sum_{n_{\mathcal{A}}=0}^{\infty} n_{\mathcal{A}} \mathbb{P}_{n_{\mathcal{A}}}(t) + \kappa_2 V \sum_{n_{\mathcal{A}}=0}^{\infty} \underbrace{\left[(n_{\mathcal{A}}+1) - n_{\mathcal{A}}\right]}_{1} \mathbb{P}_{n_{\mathcal{A}}}(t) \\ &= -\kappa_1 \sum_{n_{\mathcal{A}}=0}^{\infty} n_{\mathcal{A}} \mathbb{P}_{n_{\mathcal{A}}}(t) + \kappa_2 V \sum_{n_{\mathcal{A}}=0}^{\infty} \mathbb{P}_{n_{\mathcal{A}}}(t) \end{aligned}$$



## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Statistics (cont.)

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

Because we have that $\sum n_{\mathcal{A}} \mathbb{P}_{n_{\mathcal{A}}}(t) = M_{\mathcal{A}}(t)$ and $\sum \mathbb{P}_{n_{\mathcal{A}}}(t) = 1$, we have

$$\frac{\mathrm{d}M_{\mathcal{A}}(t)}{\mathrm{d}t} = -\kappa_1 M_{\mathcal{A}}(t) + \kappa_2 V$$

The equation of motion for the expected value of $(N_{\mathcal{A}}(t))_{t \geq 0}$

To integrate it, we need to specify the initial condition,

$$M_{\mathcal{A}}(t=0) = M_{\mathcal{A}}(0)$$

The solution can be written in closed form,

$$M_{\mathcal{A}}(t) = \frac{\kappa_2}{\kappa_1} V + \left( M_{\mathcal{A}}(0) - \frac{\kappa_2}{\kappa_1} V \right) \exp\left(-\kappa_1 t\right)$$



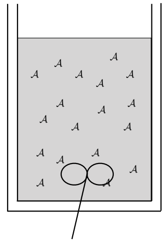
## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Statistics (cont.)

### Example

We consider the evolution of the mean process from an initial condition $M_{\mathcal{A}}(0) = 0$

$$\mathcal{A} \xrightarrow{\kappa_1} \emptyset$$

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



Kinetic parameters and initial conditions

$$\begin{aligned} \kappa_1 &= 0.1 \mathrm{sec}^{-1} \\ \kappa_2 V &= 1.0 \mathrm{sec}^{-1} \\ n_{\mathcal{A}}(0) &= 0 \end{aligned}$$

We have,

$$\begin{aligned} M_{\mathcal{A}}(t) &= \frac{\kappa_2}{\kappa_1} V + \left(M_{\mathcal{A}}(0) - \frac{\kappa_2}{\kappa_1} V\right) \exp\left(-\kappa_1 t\right) \\ &= \frac{\kappa_2}{\kappa_1} V - \frac{\kappa_2}{\kappa_1} V \exp\left(-\kappa_1 t\right) \\ &= \frac{\kappa_2}{\kappa_1} V \left(1 - \exp\left(-\kappa_1 t\right)\right) \end{aligned}$$

## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Statistics (cont.)

We can derive an ordinary differential equation for the evolution of the process' variance

We start by considering the definition of variance of the process at time $t$

$$\begin{aligned}
\mathrm{E}\left[(N_{\mathcal{A}}(t) - M_{\mathcal{A}}(t))^2\right] &= \sum_{n_{\mathcal{A}}=0}^{\infty} [n_{\mathcal{A}} - M_{\mathcal{A}}(t)]^2 \, \mathbb{P}_{n_{\mathcal{A}}}(t) \\
&= \sum_{n_{\mathcal{A}}=0}^{\infty} \left[{n_{\mathcal{A}}}^2 - 2n_{\mathcal{A}} M_{\mathcal{A}}(t) + M_{\mathcal{A}}(t)^2\right] \mathbb{P}_{n_{\mathcal{A}}}(t) \\
&= \sum_{n_{\mathcal{A}}=0}^{\infty} {n_{\mathcal{A}}}^2 \mathbb{P}_{n_{\mathcal{A}}}(t) - 2M_{\mathcal{A}}(t) \underbrace{\sum_{n_{\mathcal{A}}=0}^{\infty} n_{\mathcal{A}} \mathbb{P}_{n_{\mathcal{A}}}(t)}_{M_{\mathcal{A}}(t)} \\
&\quad + M_{\mathcal{A}}(t)^2 \underbrace{\sum_{n_{\mathcal{A}}=0}^{\infty} \mathbb{P}_{n_{\mathcal{A}}}(t)}_{=1} \\
&= \sum_{n_{\mathcal{A}}=0}^{\infty} {n_{\mathcal{A}}}^2 \mathbb{P}_{n_{\mathcal{A}}}(t) - M_{\mathcal{A}}(t)^2 \\
&= V_{\mathcal{A}}(t)
\end{aligned}$$

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Chemical master equation
Statistics
Stationary distribution

## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Statistics (cont.)

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

That is, we have quickly found a relationship between the process' mean and variance
$\rightsquigarrow$ (This relation is general, not system specific, it will be used later on)

By taking the derivative of both sides with respect to time, we get

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

Rearranging, we have

$$\frac{\mathrm{d}V_{\mathcal{A}}(t)}{\mathrm{d}t} = \underbrace{\frac{\mathrm{d}}{\mathrm{d}t} \underbrace{\sum_{n_{\mathcal{A}}=0}^{\infty} {n_{\mathcal{A}}}^2 \mathbb{P}_{n_{\mathcal{A}}}(t)}_{!}}_{?} - 2 \underbrace{M_{\mathcal{A}}(t)}_{!}$$

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Statistics
Stationary distribution

## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Statistics (cont.)

In addition, for all values $n_{\mathcal{A}} = 0, 1, \dots, \infty$, we derived the chemical master equation

$$\frac{\mathrm{d}\mathbb{P}_{n_{\mathcal{A}}}(t)}{\mathrm{d}t} = \kappa_1 (n_{\mathcal{A}} + 1)\mathbb{P}_{n_{\mathcal{A}}+1}(t) - \kappa_1 n_{\mathcal{A}} \mathbb{P}_{n_{\mathcal{A}}}(t) + \kappa_2 V \mathbb{P}_{n_{\mathcal{A}}-1}(t) - \kappa_2 V \mathbb{P}_{n_{\mathcal{A}}}(t)$$

By multiplying each component ($n_{\mathcal{A}} = 0, 1, \dots, \infty$) of the master equation by ${n_{\mathcal{A}}}^2$

$$\begin{aligned}
{n_{\mathcal{A}}}^2 \frac{\mathrm{d}\mathbb{P}_{n_{\mathcal{A}}}(t)}{\mathrm{d}t} &= \kappa_1 {n_{\mathcal{A}}}^2 (n_{\mathcal{A}} + 1)\mathbb{P}_{n_{\mathcal{A}}+1}(t) - \kappa_1 {n_{\mathcal{A}}}^3 \mathbb{P}_{n_{\mathcal{A}}}(t) \\
&\quad + \kappa_2 {n_{\mathcal{A}}}^2 V \mathbb{P}_{n_{\mathcal{A}}-1}(t) - \kappa_2 {n_{\mathcal{A}}}^2 V \mathbb{P}_{n_{\mathcal{A}}}(t)
\end{aligned}$$

After summing over $n_{\mathcal{A}}$ and rearranging the terms, we get

$$\begin{aligned}
\frac{\mathrm{d}}{\mathrm{d}t} \sum_{n_{\mathcal{A}}=0}^{\infty} {n_{\mathcal{A}}}^2 \mathbb{P}_{n_{\mathcal{A}}}(t) &= \kappa_1 \sum_{n_{\mathcal{A}}=0}^{\infty} {n_{\mathcal{A}}}^2 (n_{\mathcal{A}} + 1)\mathbb{P}_{n_{\mathcal{A}}+1}(t) - \kappa_1 \sum_{n_{\mathcal{A}}=0}^{\infty} n_{\mathcal{A}}^3 \mathbb{P}_{n_{\mathcal{A}}}(t) \\
&\quad + \kappa_2 V \sum_{n_{\mathcal{A}}=1}^{\infty} {n_{\mathcal{A}}}^2 \mathbb{P}_{n_{\mathcal{A}}-1}(t) - \kappa_2 V \sum_{n_{\mathcal{A}}=0}^{\infty} {n_{\mathcal{A}}}^2 \mathbb{P}_{n_{\mathcal{A}}}(t)
\end{aligned}$$

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$\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$
Chemical master equation
Statistics
Stationary distribution

## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Statistics (cont.)

$$\begin{aligned}
\frac{\mathrm{d}}{\mathrm{d}t} \sum_{n_{\mathcal{A}}=0}^{\infty} {n_{\mathcal{A}}}^2 \mathbb{P}_{n_{\mathcal{A}}}(t) &= \kappa_1 \underbrace{\sum_{n_{\mathcal{A}}=0}^{\infty} {n_{\mathcal{A}}}^2 (n_{\mathcal{A}} + 1)\mathbb{P}_{n_{\mathcal{A}}+1}(t)} - \kappa_1 \sum_{n_{\mathcal{A}}=0}^{\infty} {n_{\mathcal{A}}}^3 \mathbb{P}_{n_{\mathcal{A}}}(t) \\
&\quad + \kappa_2 V \sum_{n_{\mathcal{A}}=1}^{\infty} {n_{\mathcal{A}}}^2 \mathbb{P}_{n_{\mathcal{A}}-1}(t) - \kappa_2 V \sum_{n_{\mathcal{A}}=0}^{\infty} {n_{\mathcal{A}}}^2 \mathbb{P}_{n_{\mathcal{A}}}(t)
\end{aligned}$$

Changing indexes $(n_{\mathcal{A}} + 1) \rightsquigarrow n_{\mathcal{A}}$ and $n_{\mathcal{A}} \rightsquigarrow (n_{\mathcal{A}} - 1)$ in the first sum, we get

$$\begin{aligned}
\frac{\mathrm{d}}{\mathrm{d}t} \sum_{n_{\mathcal{A}}=0}^{\infty} n_{\mathcal{A}}^2 \mathbb{P}_{n_{\mathcal{A}}}(t) &= \kappa_1 \underbrace{\sum_{n_{\mathcal{A}}-1=0}^{\infty} (n_{\mathcal{A}} - 1)^2 n_{\mathcal{A}} \mathbb{P}_{n_{\mathcal{A}}}(t)} - \kappa_1 \sum_{n_{\mathcal{A}}=0}^{\infty} n_{\mathcal{A}}^3 \mathbb{P}_{n_{\mathcal{A}}}(t) \\
&\quad + \kappa_2 V \sum_{n_{\mathcal{A}}=1}^{\infty} n_{\mathcal{A}}^2 \mathbb{P}_{n_{\mathcal{A}}-1}(t) - \kappa_2 V \sum_{n_{\mathcal{A}}=0}^{\infty} n_{\mathcal{A}}^2 \mathbb{P}_{n_{\mathcal{A}}}(t) \\
&= \kappa_1 \sum_{\underbrace{n_{\mathcal{A}} = 1}_{n_{\mathcal{A}}=0}}^{\infty} (n_{\mathcal{A}} - 1)^2 n_{\mathcal{A}} \mathbb{P}_{n_{\mathcal{A}}}(t) - \kappa_1 \sum_{n_{\mathcal{A}}=0}^{\infty} n_{\mathcal{A}}^3 \mathbb{P}_{n_{\mathcal{A}}}(t) \\
&\quad + \kappa_2 V \sum_{n_{\mathcal{A}}=1}^{\infty} n_{\mathcal{A}}^2 \mathbb{P}_{n_{\mathcal{A}}-1}(t) - \kappa_2 V \sum_{n_{\mathcal{A}}=0}^{\infty} n_{\mathcal{A}}^2 \mathbb{P}_{n_{\mathcal{A}}}(t)
\end{aligned}$$

## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Statistics (cont.)

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}t}\sum_{n_\mathcal{A}=0}^{\infty} n_\mathcal{A}^2\mathbb{P}_{n_\mathcal{A}}(t) &= \kappa_1 \sum_{n_\mathcal{A}=0}^{\infty}(n_\mathcal{A}-1)^2 n_\mathcal{A}\mathbb{P}_{n_\mathcal{A}}(t) - \kappa_1\sum_{n_\mathcal{A}=0}^{\infty} n_\mathcal{A}^3\mathbb{P}_{n_\mathcal{A}}(t)\\ &+ \kappa_2 V \underbrace{\sum_{n_\mathcal{A}=1}^{\infty} n_\mathcal{A}^2\mathbb{P}_{n_\mathcal{A}-1}(t)} - \kappa_2 V\sum_{n_\mathcal{A}=0}^{\infty} n_\mathcal{A}^2\mathbb{P}_{n_\mathcal{A}}(t)\end{aligned}$$

Changing indexes $(n_\mathcal{A}-1) \rightsquigarrow n_\mathcal{A}$ and $n_\mathcal{A} \rightsquigarrow (n_\mathcal{A}+1)$ in the third sum, we get

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}t}\sum_{n_\mathcal{A}=0}^{\infty} n_\mathcal{A}^2\mathbb{P}_{n_\mathcal{A}}(t) &= \kappa_1 \sum_{n_\mathcal{A}=0}^{\infty}(n_\mathcal{A}-1)^2 n_\mathcal{A}\mathbb{P}_{n_\mathcal{A}}(t) - \kappa_1\sum_{n_\mathcal{A}=0}^{\infty} n_\mathcal{A}^3\mathbb{P}_{n_\mathcal{A}}(t)\\ &+ \kappa_2 V \underbrace{\sum_{n_\mathcal{A}+1=1}^{\infty} (n_\mathcal{A}+1)^2\mathbb{P}_{n_\mathcal{A}}(t)} - \kappa_2 V\sum_{n_\mathcal{A}=0}^{\infty} n_\mathcal{A}^2\mathbb{P}_{n_\mathcal{A}}(t)\\ &= \kappa_1 \sum_{n_\mathcal{A}=0}^{\infty}(n_\mathcal{A}-1)^2 n_\mathcal{A}\mathbb{P}_{n_\mathcal{A}}(t) - \kappa_1\sum_{n_\mathcal{A}=0}^{\infty} n_\mathcal{A}^3\mathbb{P}_{n_\mathcal{A}}(t)\\ &+ \kappa_2 V \sum_{n_\mathcal{A}=0}^{\infty} (n_\mathcal{A}+1)^2\mathbb{P}_{n_\mathcal{A}}(t) - \kappa_2 V\sum_{n_\mathcal{A}=0}^{\infty} n_\mathcal{A}^2\mathbb{P}_{n_\mathcal{A}}(t)\end{aligned}$$



## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Statistics (cont.)

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}t}\sum_{n_\mathcal{A}=0}^{\infty} n_\mathcal{A}^2\mathbb{P}_{n_\mathcal{A}}(t) &= \underbrace{\kappa_1 \sum_{n_\mathcal{A}=0}^{\infty}(n_\mathcal{A}-1)^2 n_\mathcal{A}\mathbb{P}_{n_\mathcal{A}}(t) - \kappa_1\sum_{n_\mathcal{A}=0}^{\infty} n_\mathcal{A}^3\mathbb{P}_{n_\mathcal{A}}(t)}\\ &+ \kappa_2 V \sum_{n_\mathcal{A}=0}^{\infty} (n_\mathcal{A}+1)^2\mathbb{P}_{n_\mathcal{A}}(t) - \kappa_2 V\sum_{n_\mathcal{A}=0}^{\infty} n_\mathcal{A}^2\mathbb{P}_{n_\mathcal{A}}(t)\end{aligned}$$

Combining the first and second sum, we get

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}t}\sum_{n_\mathcal{A}=0}^{\infty} n_\mathcal{A}^2\mathbb{P}_{n_\mathcal{A}}(t) &= \kappa_1 \sum_{n_\mathcal{A}=0}^{\infty}\underbrace{\left[(n_\mathcal{A}-1)^2 n_\mathcal{A} - n_\mathcal{A}^3\right]}_{-2n_\mathcal{A}^2+n_\mathcal{A}}\mathbb{P}_{n_\mathcal{A}}(t)\\ &+ \kappa_2 V \sum_{n_\mathcal{A}=0}^{\infty} (n_\mathcal{A}+1)^2\mathbb{P}_{n_\mathcal{A}}(t) - \kappa_2 V\sum_{n_\mathcal{A}=0}^{\infty} n_\mathcal{A}^2\mathbb{P}_{n_\mathcal{A}}(t)\\ &= \kappa_1 \sum_{n_\mathcal{A}=0}^{\infty}(-2n_\mathcal{A}^2+n_\mathcal{A})\mathbb{P}_{n_\mathcal{A}}(t)\\ &+ \kappa_2 V \sum_{n_\mathcal{A}=0}^{\infty} (n_\mathcal{A}+1)^2\mathbb{P}_{n_\mathcal{A}}(t) - \kappa_2 V\sum_{n_\mathcal{A}=0}^{\infty} n_\mathcal{A}^2\mathbb{P}_{n_\mathcal{A}}(t)\end{aligned}$$



## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Statistics (cont.)

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

Combining the third and fourth sum, we get

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}t}\sum_{n_\mathcal{A}=0}^{\infty} n_\mathcal{A}^2\mathbb{P}_{n_\mathcal{A}}(t) &= \kappa_1 \sum_{n_\mathcal{A}=0}^{\infty}(-2n_\mathcal{A}^2+n_\mathcal{A})\mathbb{P}_{n_\mathcal{A}}(t)\\ &+ \kappa_2 V \sum_{n_\mathcal{A}=0}^{\infty}\underbrace{\left[(n_\mathcal{A}+1)^2 - n_\mathcal{A}^2\right]}_{2n_\mathcal{A}+1}\mathbb{P}_{n_\mathcal{A}}(t)\\ &= \kappa_1 \sum_{n_\mathcal{A}=0}^{\infty}(-2n_\mathcal{A}^2+n_\mathcal{A})\mathbb{P}_{n_\mathcal{A}}(t) + \kappa_2 V\sum_{n_\mathcal{A}=0}^{\infty}(2n_\mathcal{A}+1)\mathbb{P}_{n_\mathcal{A}}(t)\,T\end{aligned}$$



## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Statistics (cont.)

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

We can use some of the identities introduced earlier to get

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}t}\underbrace{\sum_{n_\mathcal{A}=0}^{\infty} n_\mathcal{A}^2\mathbb{P}_{n_\mathcal{A}}(t)}_{V_\mathcal{A}(t)+M_\mathcal{A}(t)^2} &= \kappa_1 \sum_{n_\mathcal{A}=0}^{\infty}(-2n_\mathcal{A}^2+n_\mathcal{A})\mathbb{P}_{n_\mathcal{A}}(t) + \kappa_2 V\sum_{n_\mathcal{A}=0}^{\infty}(2n_\mathcal{A}+1)\mathbb{P}_{n_\mathcal{A}}(t)\\ &= -2\kappa_1\underbrace{\sum_{n_\mathcal{A}=0}^{\infty} n_\mathcal{A}^2\mathbb{P}_{n_\mathcal{A}}(t)}_{V_\mathcal{A}(t)+M_\mathcal{A}(t)^2} + \kappa_1\underbrace{\sum_{n_\mathcal{A}=0}^{\infty} n_\mathcal{A}\mathbb{P}_{n_\mathcal{A}}(t)}_{M_\mathcal{A}(t)}\\ &+ 2\kappa_2 V\underbrace{\sum_{n_\mathcal{A}=0}^{\infty} n_\mathcal{A}\mathbb{P}_{n_\mathcal{A}}(t)}_{M_\mathcal{A}(t)} + \kappa_2 V\underbrace{\sum_{n_\mathcal{A}=0}^{\infty}\mathbb{P}_{n_\mathcal{A}}(t)}_{1}\end{aligned}$$

## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Statistics (cont.)

$$\frac{\mathrm{d}}{\mathrm{d}t}\big[V_{\mathcal{A}}(t) + M_{\mathcal{A}}(t)^2\big] = -2\kappa_1 \left[V_{\mathcal{A}}(t) + M_{\mathcal{A}}(t)^2\right] + \kappa_1 M_{\mathcal{A}}(t) + 2\kappa_2 V M_{\mathcal{A}}(t) + \kappa_2 V$$

Taking the derivative with respect to time, we obtain

$$\begin{aligned}\frac{\mathrm{d}\,V_{\mathcal{A}}(t)}{\mathrm{d}t} + 2M_{\mathcal{A}}(t)\frac{\mathrm{d}M_{\mathcal{A}}(t)}{\mathrm{d}t} \\ = -2\kappa_1 \left[V_{\mathcal{A}}(t) + M_{\mathcal{A}}(t)^2\right] + \kappa_1 M_{\mathcal{A}}(t) + 2\kappa_2 V M_{\mathcal{A}}(t) + \kappa_2 V\end{aligned}$$

Rearranging, we get

$$\begin{aligned}\frac{\mathrm{d}\,V_{\mathcal{A}}(t)}{\mathrm{d}t} &= -2M_{\mathcal{A}}(t) \underbrace{\frac{\mathrm{d}M_{\mathcal{A}}(t)}{\mathrm{d}t}}_{-\kappa_1 M_{\mathcal{A}}(t) + \kappa_2 V} -2\kappa_1 \left[V_{\mathcal{A}}(t) + M_{\mathcal{A}}(t)^2\right] \\ &\quad + \kappa_1 M_{\mathcal{A}}(t) + 2\kappa_2 V M_{\mathcal{A}}(t) + \kappa_2 V \\ &= -2\kappa_1 V_{\mathcal{A}}(t) + \kappa_1 M_{\mathcal{A}}(t) + \kappa_2 V\end{aligned}$$



## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Statistics (cont.)

$$\begin{aligned}\frac{\mathrm{d}M_{\mathcal{A}}(t)}{\mathrm{d}t} &= -\kappa_1 M_{\mathcal{A}}(t) + \kappa_2 V \\ \frac{\mathrm{d}\,V_{\mathcal{A}}(t)}{\mathrm{d}t} &= -2\kappa_1 V_{\mathcal{A}}(t) + \kappa_1 M_{\mathcal{A}}(t) + \kappa_2 V\end{aligned}$$

The equations of motion for the mean and variance process can be integrated in time

- Initial conditions must be provided
- That is, $M_{\mathcal{A}}(0)$ and $V_{\mathcal{A}}(0)$



## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Statistics (cont.)

$$\begin{aligned}\frac{\mathrm{d}M_{\mathcal{A}}(t)}{\mathrm{d}t} &= -\kappa_1 M_{\mathcal{A}}(t) + \kappa_2 V \\ \frac{\mathrm{d}\,V_{\mathcal{A}}(t)}{\mathrm{d}t} &= -2\kappa_1 V_{\mathcal{A}}(t) + \kappa_1 M_{\mathcal{A}}(t) + \kappa_2 V\end{aligned}$$

We are interested in the expected value and spread of the process after an infinite time

Both the expected value and the spread of the process approach steady-state

$$\begin{aligned}M_{\mathcal{A}}^{\mathrm{ss}} &= \lim_{t\to\infty} M_{\mathcal{A}}(t) \\ V_{\mathcal{A}}^{\mathrm{ss}} &= \lim_{t\to\infty} V_{\mathcal{A}}(t)\end{aligned}$$

By letting the derivatives to be equal to zero, we get

$$\begin{aligned}0 &= -\kappa_1 M_{\mathcal{A}}^{\mathrm{ss}} + \kappa_2 V \\ 0 &= -2\kappa_1 V_{\mathcal{A}}^{\mathrm{ss}} + \kappa_1 M_{\mathcal{A}}^{\mathrm{ss}} + \kappa_2 V\end{aligned}$$

After solving the set of equations, we get

$$M_{\mathcal{A}}^{\mathrm{ss}} = V_{\mathcal{A}}^{\mathrm{ss}} = \frac{\kappa_2}{\kappa_1} V$$



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

## Stationary distribution

## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Stationary distribution

It is interesting to understand what is the limit probability distribution $\mathbb{P}_{n_{\mathcal{A}}}(t \to \infty)$

$$\pi_{n_{\mathcal{A}}} = \lim_{t\to\infty} \mathbb{P}_{n_{\mathcal{A}}}(t) \qquad (\text{for all } n_{\mathcal{A}} = 0, 1, \dots)$$

One way to determine this limit distribution is by running many stochastic simulations for a sufficiently long time, then build an empirical approximation of the distribution

Alternatively, we can consider the steady-state form of the chemical master equation

- For all $n_{\mathcal{A}} = 0, 1, \dots,$, we have

$$\underbrace{\frac{d\mathbb{P}_{n_{\mathcal{A}}}(t)}{dt}}_{0} = \kappa_1 (n_{\mathcal{A}} + 1)\mathbb{P}_{n_{\mathcal{A}}+1}(t) - \kappa_1 n_{\mathcal{A}} \mathbb{P}_{n_{\mathcal{A}}}(t) + \kappa_2 V \mathbb{P}_{n_{\mathcal{A}}-1}(t) - \kappa_2 V \mathbb{P}_{n_{\mathcal{A}}}(t)$$



## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Stationary distribution (cont.)

$$\frac{d\mathbb{P}_{n_{\mathcal{A}}}(t)}{dt} = \kappa_1 (n_{\mathcal{A}} + 1)\mathbb{P}_{n_{\mathcal{A}}+1}(t) - \kappa_1 n_{\mathcal{A}} \mathbb{P}_{n_{\mathcal{A}}}(t) + \kappa_2 V \mathbb{P}_{n_{\mathcal{A}}-1}(t) - \kappa_2 V \mathbb{P}_{n_{\mathcal{A}}}(t)$$

For the case of $n_{\mathcal{A}} = 0$ molecules, at $t = \infty$ we get

$$\begin{aligned}
0 &= \kappa_1 (n_{\mathcal{A}} + 1)\mathbb{P}_{n_{\mathcal{A}}+1}(t) - \kappa_1 n_{\mathcal{A}} \mathbb{P}_{n_{\mathcal{A}}}(t) + \kappa_2 V \mathbb{P}_{n_{\mathcal{A}}-1}(t) - \kappa_2 V \mathbb{P}_{n_{\mathcal{A}}}(t) \\
&= \kappa_1 (n_{\mathcal{A}} + 1)\mathbb{P}_{n_{\mathcal{A}}+1}(\infty) - \kappa_1 n_{\mathcal{A}} \mathbb{P}_{n_{\mathcal{A}}}(\infty) + \kappa_2 V \mathbb{P}_{n_{\mathcal{A}}-1}(\infty) - \kappa_2 V \mathbb{P}_{n_{\mathcal{A}}}(\infty) \\
&= \kappa_1 (n_{\mathcal{A}} + 1)\pi_{n_{\mathcal{A}}+1} - \kappa_1 n_{\mathcal{A}} \pi_{n_{\mathcal{A}}} + \kappa_2 V \pi_{n_{\mathcal{A}}-1} - \kappa_2 V \pi_{n_{\mathcal{A}}} \\
&= \kappa_1 (1)\pi_{n_{\mathcal{A}}=1} - \kappa_1 (0)\pi_{n_{\mathcal{A}}=0} + \kappa_2 V \pi_{n_{\mathcal{A}}=-1} - \kappa_2 V \pi_{n_{\mathcal{A}}=0} \\
&= \kappa_1 \pi_{n_{\mathcal{A}}=1} - \kappa_2 V \pi_{n_{\mathcal{A}}=0}
\end{aligned}$$

This yields the relationship between the long-term probabilities of $n_{\mathcal{A}} = 0$ and $n_{\mathcal{A}} = 1$

$$\pi_{n_{\mathcal{A}}=1} = \left(\frac{\kappa_2}{\kappa_1} V\right) \pi_{n_{\mathcal{A}}=0},$$



## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Stationary distribution (cont.)

$$\frac{d\mathbb{P}_{n_{\mathcal{A}}}(t)}{dt} = \kappa_1 (n_{\mathcal{A}} + 1)\mathbb{P}_{n_{\mathcal{A}}+1}(t) - \kappa_1 n_{\mathcal{A}} \mathbb{P}_{n_{\mathcal{A}}}(t) + \kappa_2 V \mathbb{P}_{n_{\mathcal{A}}-1}(t) - \kappa_2 V \mathbb{P}_{n_{\mathcal{A}}}(t)$$

Similarly, for $n_{\mathcal{A}} = 1$ molecules

$$\begin{aligned}
0 &= \kappa_1 (n_{\mathcal{A}} + 1)\pi_{n_{\mathcal{A}}+1} - \kappa_1 n_{\mathcal{A}} \pi_{n_{\mathcal{A}}} + \kappa_2 V \pi_{n_{\mathcal{A}}-1} - \kappa_2 V \pi_{n_{\mathcal{A}}} \\
&= \kappa_1 (2)\pi_{n_{\mathcal{A}}=2} - \kappa_1 (1)\pi_{n_{\mathcal{A}}=1} + \kappa_2 V \pi_{n_{\mathcal{A}}=0} - \kappa_2 V \pi_{n_{\mathcal{A}}=1} \\
&= 2\kappa_1 \pi_{n_{\mathcal{A}}=2} - \kappa_1 \pi_{n_{\mathcal{A}}=1} + \kappa_2 V \pi_{n_{\mathcal{A}}=0} - \kappa_2 V \pi_{n_{\mathcal{A}}=1} \\
&= 2\kappa_1 \pi_{n_{\mathcal{A}}=2} - (\kappa_1 + \kappa_2 V)\pi_{n_{\mathcal{A}}=1} + \kappa_2 V \pi_{n_{\mathcal{A}}=0}
\end{aligned}$$

This yields the relation between the long-term probabilities of $n_{\mathcal{A}} = 0, 1$ and $n_{\mathcal{A}} = 2$

$$\pi_{n_{\mathcal{A}}=2} = \frac{1}{2}\left(\frac{\kappa_1 + \kappa_2 V}{\kappa_1}\right) \pi_{n_{\mathcal{A}}=1} - \frac{1}{2}\left(\frac{\kappa_2}{\kappa_1} V\right) \pi_{n_{\mathcal{A}}=0}$$



## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Stationary distribution (cont.)

$$\frac{d\mathbb{P}_{n_{\mathcal{A}}}(t)}{dt} = \kappa_1 (n_{\mathcal{A}} + 1)\mathbb{P}_{n_{\mathcal{A}}+1}(t) - \kappa_1 n_{\mathcal{A}} \mathbb{P}_{n_{\mathcal{A}}}(t) + \kappa_2 V \mathbb{P}_{n_{\mathcal{A}}-1}(t) - \kappa_2 V \mathbb{P}_{n_{\mathcal{A}}}(t)$$

Then, for $n_{\mathcal{A}} = 2$ molecules

$$\begin{aligned}
0 &= \kappa_1 (n_{\mathcal{A}} + 1)\pi_{n_{\mathcal{A}}+1} - \kappa_1 n_{\mathcal{A}} \pi_{n_{\mathcal{A}}} + \kappa_2 V \pi_{n_{\mathcal{A}}-1} - \kappa_2 V \pi_{n_{\mathcal{A}}} \\
&= \kappa_1 (3)\pi_{n_{\mathcal{A}}=3} - \kappa_1 (2)\pi_{n_{\mathcal{A}}=2} + \kappa_2 V \pi_{n_{\mathcal{A}}=1} - \kappa_2 V \pi_{n_{\mathcal{A}}=2} \\
&= 3\kappa_1 \pi_{n_{\mathcal{A}}=3} - 2\kappa_1 \pi_{n_{\mathcal{A}}=2} + \kappa_2 V \pi_{n_{\mathcal{A}}=1} - \kappa_2 V \pi_{n_{\mathcal{A}}=2} \\
&= 3\kappa_1 \pi_{n_{\mathcal{A}}=3} - 2(\kappa_1 + \kappa_2 V)\pi_{n_{\mathcal{A}}=2} + \kappa_2 V \pi_{n_{\mathcal{A}}=1}
\end{aligned}$$

This yields the relation between the long-term probabilities of $n_{\mathcal{A}} = 1, 2$ and $n_{\mathcal{A}} = 3$

$$\pi_{n_{\mathcal{A}}=3} = \frac{1}{2}\left[\frac{2(\kappa_1 + \kappa_2 V)}{\kappa_1}\right] \pi_{n_{\mathcal{A}}=2} - \frac{1}{3}\left(\frac{\kappa_2 V}{\kappa_1}\right) \pi_{n_{\mathcal{A}}=1}$$

## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Stationary distribution (cont.)

$$\frac{\mathrm{d}\mathbb{P}_{n_\mathcal{A}}(t)}{\mathrm{d}t} = \kappa_1(n_\mathcal{A}+1)\mathbb{P}_{n_\mathcal{A}+1}(t) - \kappa_1 n_\mathcal{A}\mathbb{P}_{n_\mathcal{A}}(t) + \kappa_2 V\mathbb{P}_{n_\mathcal{A}-1}(t) - \kappa_2 V\mathbb{P}_{n_\mathcal{A}}(t)$$

For the general case, the steady-state chemical master equation for $n_\mathcal{A} = 1, 2, \dots$

$$0 = \kappa_1(n_\mathcal{A}+1)\pi_{n_\mathcal{A}+1} - \kappa_1 n_\mathcal{A}\pi_{n_\mathcal{A}} + \kappa_2 V\pi_{n_\mathcal{A}-1} - \kappa_2 V\pi_{n_\mathcal{A}}$$

This yields the relation between the long-term probabilities of $n_\mathcal{A}-1, n_\mathcal{A}$ and $n_\mathcal{A}+1$

$$\pi_{n_\mathcal{A}+1} = \frac{1}{\kappa_1(n_\mathcal{A}+1)}\left[(\kappa_1 n_\mathcal{A} + \kappa_2 V)\,\pi_{n_\mathcal{A}} - \kappa_2 V\pi_{n_\mathcal{A}-1}\right]$$



## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Stationary distribution (cont.)

We can iteratively obtain $\pi_{n_\mathcal{A}}$ for all values of $n_\mathcal{A} = 1, 2, \dots, \infty$, from a known $\pi_{n_\mathcal{A}=0}$

$$\pi_{n_\mathcal{A}+1} = \frac{1}{\kappa_1(n_\mathcal{A}+1)}\left[(\kappa_1 n_\mathcal{A} + \kappa_2 V)\,\pi_{n_\mathcal{A}} - \kappa_2 V\pi_{n_\mathcal{A}-1}\right]$$

After computing $\{\pi_{n_\mathcal{A}}\}_{n_\mathcal{A}=0}^{\overline{n_\mathcal{A}}\gg 0}$, we re-normalise to satisfy the usual closure constraint

$$\sum_{n_\mathcal{A}=0}^{\infty} \pi_{n_\mathcal{A}} = 1$$

That is, for all $n_\mathcal{A}$ we re-compute all the $\pi_{n_\mathcal{A}}$

$$\pi_{n_\mathcal{A}} = \frac{\pi_{n_\mathcal{A}}}{\sum_{n_\mathcal{A}=0}^{\overline{n_\mathcal{A}}} \pi_{n_\mathcal{A}}} \qquad (n_\mathcal{A} = 1, 2, \dots, \infty)$$



## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Stationary distribution (cont.)

The recursion from the steady-state master equation has also a closed-form solution

$$\pi_{n_\mathcal{A}} = \frac{C}{n_\mathcal{A}!}\left(\frac{\kappa_2 V}{\kappa_1}\right)^{n_\mathcal{A}} \qquad (\text{for all } n_\mathcal{A} = 0, 1, \dots \text{ and } C \in \mathbb{R})$$

To determine constant $C$, substitute $\pi_{n_\mathcal{A}}$ in the normalisation constraint

$$\begin{aligned} 1 &= \sum_{n_\mathcal{A}=0}^{\infty} \underbrace{\frac{C}{n_\mathcal{A}!}\left(\frac{\kappa_2 V}{\kappa_1}\right)^{n_\mathcal{A}}}_{\pi_{n_\mathcal{A}}} \\ &= C\sum_{n_\mathcal{A}=0}^{\infty} \frac{1}{n_\mathcal{A}!}\left(\frac{\kappa_2 V}{\kappa_1}\right)^{n_\mathcal{A}} \\ &= C\exp\left(\frac{\kappa_2 V}{\kappa_1}\right) \end{aligned}$$

Rearranging, we get

$$C = \exp\left(-\frac{\kappa_2 V}{\kappa_1}\right)$$



## $\mathcal{A} \to \emptyset$ and $\emptyset \to \mathcal{A}$ | Stationary distribution (cont.)

The resulting stationary distribution $\pi_{n_\mathcal{A}}$ of copy numbers is the Poisson distribution

$$\pi_{n_\mathcal{A}} = \frac{1}{n_\mathcal{A}!}\left(\frac{\kappa_2 V}{\kappa_1}\right)^{n_\mathcal{A}} \exp\left(-\frac{\kappa_2 V}{\kappa_1}\right)$$

Transient distributions are also Poisson, with mean $M_\mathcal{A}(t)$, if $n_\mathcal{A}(0) = 0$