



Aalto University

Deterministic formulation of reaction networks

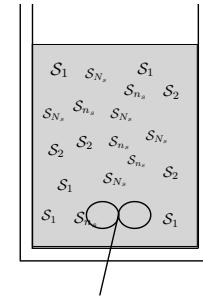
Stochastic analysis and simulation of reactive and diffusive systems

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A general reaction network

We will consider the molecules of N_s **chemical species** homogeneously distributed in a volume V , at thermal equilibrium, and interacting through N_r **reaction channels**



- Typically, more reactions than species, $N_r > N_s$
- The reaction channels are all irreversible

We symbolise the n_s -th species with S_{n_s} and its abundance in the compartment at time t with the **copy number** $N_{n_s}(t)$, while the reaction channels are denoted by \mathcal{R}_{n_r}

The **total copy number** $N_{\text{tot}}(t)$ of all species indicates how large the system is

$$N_{\text{tot}}(t) = \sum_{n_s=1}^{N_s} N_{n_s}(t)$$

A general reaction network (cont.)

Large total copy numbers $N_{\text{tot}}(t)$ usually imply a system with large size or volume V

- Quantities/parameters Ω other than V can be used to indicate size, too

Copy numbers $N_{n_s}(t)$ can be divided by the **size of the system** Ω , to get concentrations

$$X_{n_s}(t) = \frac{N_{n_s}(t)}{\Omega}$$

The choice of the system size Ω depends on the type of **concentration** we want to define

- (Not unusual to use $[S_{n_s}(t)]$ to denote concentrations, instead of $X_{n_s}(t)$)

A general reaction network (cont.)

Molar concentrations are obtained by choosing $\Omega = N_A V$, N_A is Avogadro's constant

- The Avogadro's constant is the number of molecules in a mole

$$N_A \approx 6.022 \times 10^{23} \text{ moles}^{-1}$$

For the molar concentrations (units $\text{M} = \text{moles litre}^{-1}$), we have

$$X_{n_s}(t) = \frac{N_{n_s}(t)}{N_A V}$$

Relative concentrations can be obtained by choosing $\Omega = N_{\text{tot}}$

- Relative concentrations are dimensionless quantities

$$X_{n_s}(t) = \frac{N_{n_s}(t)}{N_{\text{tot}}(t)}$$

In principle, it may be possible to use a different scaling factor Ω_{n_s} for each species

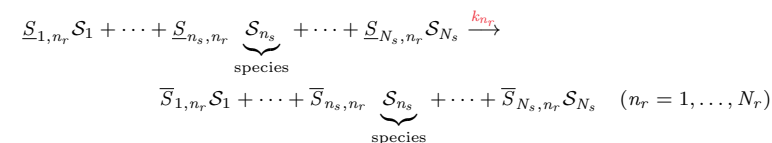
- This practice is commonplace when copy-numbers N_{n_s} differ in magnitude

Reactions and stoichiometries

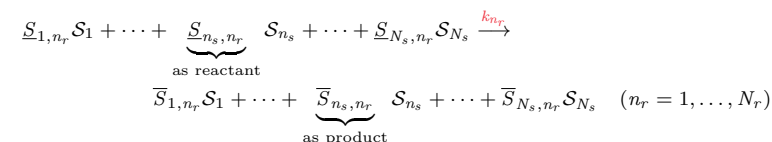
Reaction networks

A general reaction network | Reactions

For a \mathcal{R}_{n_r} -th reaction channel, we use the general reaction form based on all N_s species



The participation of the n_s -th species to the n_r -th reaction is indicated by coefficients



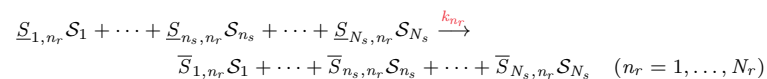
The **stoichiometric coefficients**, or **stoichiometries**

$\rightsquigarrow \underline{\mathcal{S}}_{n_s,n_r}$ when species \mathcal{S}_{n_s} is a reactant

$\rightsquigarrow \bar{\mathcal{S}}_{n_s,n_r}$ when species \mathcal{S}_{n_s} is a product

The **rate constant** k_{n_r} tells us about the assumed **reaction kinetics**

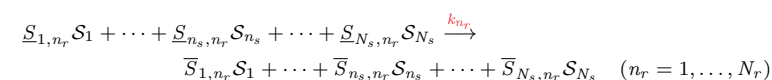
A general reaction network | Reactions (cont.)



If we have that $\underline{\mathcal{S}}_{n_s,n_r} = \bar{\mathcal{S}}_{n_s,n_r} \neq 0$, then species \mathcal{S}_{n_s} is a catalyst

If we have that $\bar{\mathcal{S}}_{n_s,n_r} > \underline{\mathcal{S}}_{n_s,n_r} > 0$, then species \mathcal{S}_{n_s} is a auto-catalyst

A general reaction network | Reactions (cont.)



We did not specify any restriction on the stoichiometric coefficients $\underline{\mathcal{S}}_{n_s,n_r}$ and $\bar{\mathcal{S}}_{n_s,n_r}$

We may take for $\underline{\mathcal{S}}_{n_s,n_r}$ the actual number of molecules needed for a reactive event

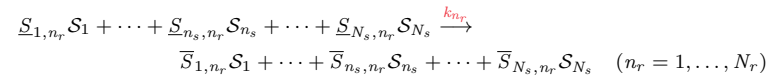
- What about reactions that proceed through intermediate steps (chain reactions)
- They will have be written as a sequence of single-collision reactions
- (The intermediate products will appear as separate items as \mathcal{S})

As three-body collisions are rare evenets, we will consider mainly reactions such that

$$\sum_{n_s=1}^{N_s} \underline{\mathcal{S}}_{n_s,n_r} = 0 \text{ or } 1 \text{ or } 2 \quad (\text{or possibly } 3 \text{ if a catalyst is involved})$$

Importantly, the theoretical derivations are not subject to these restriction

A general reaction network | Reactions (cont.)



One occurrence of the n_r -th reaction changes the copy-number of the species involved

For species \mathcal{S}_{n_s} , the **change in copy-number** after the occurrence of one reaction \mathcal{R}_{n_r}

$$\underbrace{S_{n_s,n_r}}_{\text{change}} = \underbrace{\overline{S}_{n_s,n_r}}_{\text{after reaction}} - \underbrace{S_{n_s,n_r}}_{\text{before reaction}} \quad (n_r = 1, \dots, N_r)$$

If the copy-number of species \mathcal{S}_{n_s} is N_{n_s} (before reaction), after reaction \mathcal{R}_{n_r} we have

$$N_{n_s}(\text{after reaction}) = N_{n_s}(\text{before reaction}) + S_{n_s,n_r} \quad (n_r = 1, \dots, N_r)$$

Quantity $S_{n_s,n_r} = \overline{S}_{n_s,n_r} - \underline{S}_{n_s,n_r}$, the (n_s, n_r) -th element of **stoichiometric matrix** S

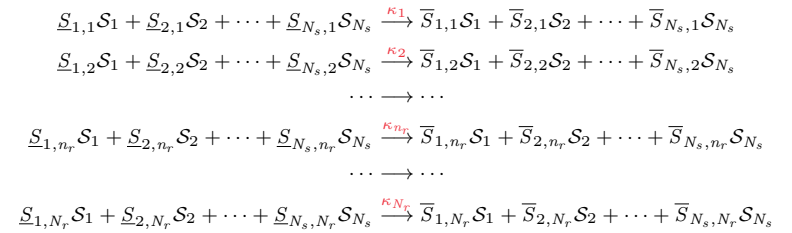
A general reaction network | Stoichiometries (cont.)

$$\underline{S} = \underbrace{\begin{bmatrix} \underline{S}_{1,1} & \underline{S}_{2,1} & \cdots & \underline{S}_{N_s,1} \\ \underline{S}_{1,2} & \underline{S}_{2,2} & \cdots & \underline{S}_{N_s,2} \\ \vdots & \vdots & \ddots & \vdots \\ \underline{S}_{1,n_r} & \underline{S}_{2,n_r} & \cdots & \underline{S}_{N_s,n_r} \\ \vdots & \vdots & \ddots & \vdots \\ \underline{S}_{1,N_r} & \underline{S}_{2,N_r} & \cdots & \underline{S}_{N_s,N_r} \end{bmatrix}}_{N_r \times N_s}$$

$$\overline{S} = \underbrace{\begin{bmatrix} \overline{S}_{1,1} & \overline{S}_{2,1} & \cdots & \overline{S}_{N_s,1} \\ \overline{S}_{1,2} & \overline{S}_{2,2} & \cdots & \overline{S}_{N_s,2} \\ \vdots & \vdots & \ddots & \vdots \\ \overline{S}_{1,n_r} & \overline{S}_{2,n_r} & \cdots & \overline{S}_{N_s,n_r} \\ \vdots & \vdots & \ddots & \vdots \\ \overline{S}_{1,N_r} & \overline{S}_{2,N_r} & \cdots & \overline{S}_{N_s,N_r} \end{bmatrix}}_{N_r \times N_s}$$

A general reaction network | Stoichiometries

An expanded view of all the N_r reaction channels, including all the N_s species involved



We collect the two sets of stoichiometric coefficients in two matrices, matrix \underline{S} and \overline{S}

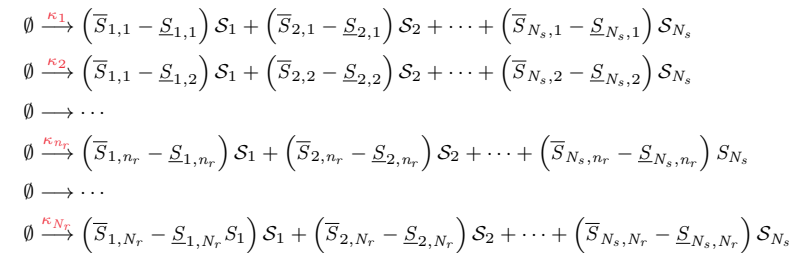
↪ Matrix \underline{S} for the reactants being consumed

↪ Matrix \overline{S} for the products being generated

The two matrices have size $N_r \times N_s$

A general reaction network | Stoichiometries (cont.)

After moving the reactants to the right hand side of the associated chemical equation



A general reaction network | Stoichiometries (cont.)

The (differences between) coefficients are arranged to form the stoichiometric matrix,

$$S = \underbrace{\begin{bmatrix} \left(\bar{S}_{1,1} - \underline{S}_{1,1} \right) & \left(\bar{S}_{2,1} - \underline{S}_{2,1} \right) & \cdots & \left(\bar{S}_{N_s,1} - \underline{S}_{N_s,1} \right) \\ \left(\bar{S}_{1,2} - \underline{S}_{1,2} \right) & \left(\bar{S}_{2,2} - \underline{S}_{2,2} \right) & \cdots & \left(\bar{S}_{N_s,2} - \underline{S}_{N_s,2} \right) \\ \vdots & \vdots & \vdots & \vdots \\ \left(\bar{S}_{1,n_r} - \underline{S}_{1,n_r} \right) & \left(\bar{S}_{2,n_r} - \underline{S}_{2,n_r} \right) & \cdots & \left(\bar{S}_{N_s,n_r} - \underline{S}_{N_s,n_r} \right) \\ \vdots & \vdots & \vdots & \vdots \\ \left(\bar{S}_{1,N_r} - \underline{S}_{1,N_r} \right) & \left(\bar{S}_{2,N_r} - \underline{S}_{2,N_r} \right) & \cdots & \left(\bar{S}_{N_s,N_r} - \underline{S}_{N_s,N_r} \right) \end{bmatrix}}_{N_r \times N_s}$$

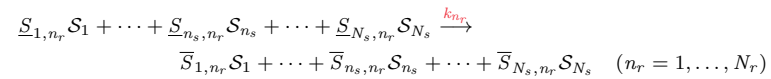
$$= \bar{S} - \underline{S}$$

The (n_s, n_r) element of the stoichiometric matrix encodes the net-change in copy number of the species n_s due to the occurrence of a single reaction event of the n_r -type

$$S_{n_s, n_r} = \bar{S}_{n_s, n_r} - \underline{S}_{n_s, n_r}$$

Time evolution
Reaction networks

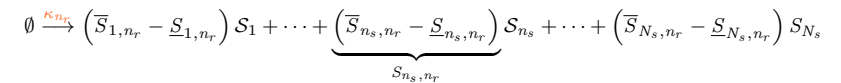
A general reaction network | Time evolution



We use $Z_{n_r}(t)$ to denote the **reaction count** of reaction \mathcal{R}_{n_r} at time t , since time $t = 0$

$\rightsquigarrow Z_{n_r}(t)$ can be used to denote the progress of the reaction channel

A general reaction network | Time evolution (cont.)



Let $Z_{n_r}(t)$ be the total number of reaction event of type \mathcal{R}_{n_r} that occurred since $t = 0$

- Each \mathcal{R}_{n_r} reaction contributes a change S_{n_s, n_r} to the copy-number of \mathcal{S}_{n_s}

The contribution of the n_r -th channel to the total change in copy-number of \mathcal{S}_{n_s}

$$\underbrace{S_{n_s, n_r} \times Z_{n_r}(t)}_{\text{one channel, over time}}$$

A general reaction network | Time evolution (cont.)

$$\underbrace{S_{n_s, n_r} \times Z_{n_r}(t)}_{\text{one channel, over time}}$$

Over $[0, t)$, over all N_r channels, the total change of copy-number of species S_{n_s}

$$\begin{aligned} N_{n_s}(t) - N_{n_s}(t=0) &= S_{n_s,1}Z_1(t) + S_{n_s,2}Z_2(t) + \dots + S_{n_s,N_r}Z_{N_r}(t) \\ &= \underbrace{\sum_{n_r=1}^{N_r} S_{n_s, n_r} Z_{n_r}(t)}_{\text{all channels, over time}} \end{aligned}$$

Reordering, we have an expression for the evolution of the copy-number $N_{n_s}(t)$

$$N_{n_s}(t) = N_{n_s}(t=0) + \sum_{n_r=1}^{N_r} S_{n_s, n_r} Z_{n_r}(t)$$

A general reaction network | Time evolution (cont.)

Further developing the expression, we get

$$\begin{aligned} \begin{bmatrix} N_1(t) \\ \vdots \\ N_{n_s}(t) \\ \vdots \\ N_{N_s}(t) \end{bmatrix} &= \begin{bmatrix} N_1(0) \\ \vdots \\ N_{n_s}(0) \\ \vdots \\ N_{N_s}(0) \end{bmatrix} + \begin{bmatrix} S_{1,1}Z_1(t) + S_{1,2}Z_2(t) + \dots + S_{1,N_r}Z_{N_r}(t) \\ \vdots \\ S_{n_s,1}Z_1(t) + S_{n_s,2}Z_2(t) + \dots + S_{n_s,N_r}Z_{N_r}(t) \\ \vdots \\ S_{N_s,1}Z_1(t) + S_{N_s,2}Z_2(t) + \dots + S_{N_s,N_r}Z_{N_r}(t) \end{bmatrix} \\ &= \begin{bmatrix} N_1(0) \\ \vdots \\ N_{n_s}(0) \\ \vdots \\ N_{N_s}(0) \end{bmatrix} + \begin{bmatrix} S_{1,1} & S_{1,2} & \dots & S_{1,N_r} \\ \vdots & \vdots & \vdots & \vdots \\ S_{n_s,1} & S_{n_s,2} & \dots & S_{n_s,N_r} \\ \vdots & \vdots & \vdots & \vdots \\ S_{N_s,1} & S_{N_s,2} & \dots & S_{N_s,N_r} \end{bmatrix} \begin{bmatrix} Z_1(t) \\ \vdots \\ Z_{n_r}(t) \\ \vdots \\ Z_{N_r}(t) \end{bmatrix} \end{aligned}$$

A general reaction network | Time evolution (cont.)

$$N_{n_s}(t) = N_{n_s}(t=0) + \sum_{n_r=1}^{N_r} S_{n_s, n_r} Z_{n_r}(t) \quad (n_s = 1, \dots, N_s)$$

Stacking up, for all the N_s species across all the N_r reaction channels

$$\begin{aligned} \begin{bmatrix} N_1(t) \\ N_2(t) \\ \vdots \\ N_{n_s}(t) \\ \vdots \\ N_{N_s}(t) \end{bmatrix} &= \begin{bmatrix} N_1(t=0) + \sum_{n_r=1}^{N_r} S_{1, n_r} Z_{n_r}(t) \\ N_2(t=0) + \sum_{n_r=1}^{N_r} S_{2, n_r} Z_{n_r}(t) \\ \vdots \\ N_{n_s}(t=0) + \sum_{n_r=1}^{N_r} S_{n_s, n_r} Z_{n_r}(t) \\ \vdots \\ N_{N_s}(t=0) + \sum_{n_r=1}^{N_r} S_{N_s, n_r} Z_{n_r}(t) \end{bmatrix} \\ &= \begin{bmatrix} N_1(0) \\ N_2(0) \\ \vdots \\ N_{n_s}(0) \\ \vdots \\ N_{N_s}(0) \end{bmatrix} + \begin{bmatrix} \sum_{n_r=1}^{N_r} S_{1, n_r} Z_{n_r}(t) \\ \sum_{n_r=1}^{N_r} S_{2, n_r} Z_{n_r}(t) \\ \vdots \\ \sum_{n_r=1}^{N_r} S_{n_s, n_r} Z_{n_r}(t) \\ \vdots \\ \sum_{n_r=1}^{N_r} S_{N_s, n_r} Z_{n_r}(t) \end{bmatrix} \end{aligned}$$

A general reaction network | Time evolution (cont.)

$$\begin{bmatrix} N_1(t) \\ \vdots \\ N_{n_s}(t) \\ \vdots \\ N_{N_s}(t) \end{bmatrix} = \begin{bmatrix} N_1(0) \\ \vdots \\ N_{n_s}(0) \\ \vdots \\ N_{N_s}(0) \end{bmatrix} + \begin{bmatrix} S_{1,1} & S_{1,2} & \dots & S_{1,N_r} \\ \vdots & \vdots & \vdots & \vdots \\ S_{n_s,1} & S_{n_s,2} & \dots & S_{n_s,N_r} \\ \vdots & \vdots & \vdots & \vdots \\ S_{N_s,1} & S_{N_s,2} & \dots & S_{N_s,N_r} \end{bmatrix} \begin{bmatrix} Z_1(t) \\ \vdots \\ Z_{n_r}(t) \\ \vdots \\ Z_{N_r}(t) \end{bmatrix}$$

Then, we can define the vectors of copy-numbers and reaction-counts

$$\begin{aligned} N(t) &= (N_1(t), \dots, N_{N_s}(t)) \\ Z(t) &= (Z_1(t), \dots, Z_{N_r}(t)) \end{aligned}$$

The resulting conservation relation

$$N(t) = N(t=0) + SZ(t)$$

A general reaction network | Time evolution (cont.)

The vector N_t of copy-numbers, at time t , is a vector in a N_s -dimensional state space

$$N(t) = \begin{bmatrix} N_1(t) \\ \vdots \\ N_{n_s}(t) \\ \vdots \\ N_{N_s}(t) \end{bmatrix} \quad \begin{array}{l} \text{The integral values } N_{n_s}(t) \text{ of copy-numbers constitute a lattice} \\ \text{Each point of the lattice belonging to the octant of nonnegative} \\ \text{values corresponds to a state of the system, ... and vice versa} \end{array}$$

An event of reaction \mathcal{R}_{n_r} changes the state of the system from N_s to $N_s + \bar{S}_{n_s, n_r} - \underline{S}_{n_s, n_r}$

This is equivalent to change $N(t)$ by adding a vector corresponding to row n_r -th of S

$$\begin{bmatrix} \bar{S}_{1, n_r} - \underline{S}_{1, n_r} \\ \bar{S}_{2, n_r} - \underline{S}_{2, n_r} \\ \dots \\ \bar{S}_{N_s, n_r} - \underline{S}_{3, n_r} \end{bmatrix}$$

A general reaction network | Time evolution (cont.)

An event of reaction $\mathcal{R}_{n'_r}$ changes the state of the system from N_s to $N_s + \bar{S}_{n_s, n'_r} - \underline{S}_{n_s, n'_r}$

This is equivalent to change $N(t)$ by adding a vector corresponding to row n'_r -th of S

$$\begin{bmatrix} \bar{S}_{1, n'_r} - \underline{S}_{1, n'_r} \\ \bar{S}_{2, n'_r} - \underline{S}_{2, n'_r} \\ \dots \\ \bar{S}_{N_s, n'_r} - \underline{S}_{3, n'_r} \end{bmatrix}$$

A second sequence of lattice points becomes accessible

$$\underbrace{\begin{bmatrix} N_1(0) \\ \vdots \\ N_{n_s}(0) \\ \vdots \\ N_{N_s}(0) \end{bmatrix}}_{N(1)} + \underbrace{\begin{bmatrix} \bar{S}_{1, n'_r} - \underline{S}_{1, n'_r} \\ \vdots \\ \bar{S}_{2, n'_r} - \underline{S}_{2, n'_r} \\ \vdots \\ \bar{S}_{N_s, n'_r} - \underline{S}_{3, n'_r} \end{bmatrix}}_{N(2)} + \dots + \underbrace{\begin{bmatrix} \bar{S}_{1, n'_r} - \underline{S}_{1, n'_r} \\ \vdots \\ \bar{S}_{2, n'_r} - \underline{S}_{2, n'_r} \\ \vdots \\ \bar{S}_{N_s, n'_r} - \underline{S}_{3, n'_r} \end{bmatrix}}_{N(Z_{n'_r})}$$

A general reaction network | Time evolution (cont.)

Reaction \mathcal{R}_{n_r} proceeds, state moves along a sequence of lattice points lying on a line

$$\underbrace{\begin{bmatrix} N_1(0) \\ \vdots \\ N_{n_s}(0) \\ \vdots \\ N_{N_s}(0) \end{bmatrix}}_{N(1)} + \underbrace{\begin{bmatrix} \bar{S}_{1, n_r} - \underline{S}_{1, n_r} \\ \vdots \\ \bar{S}_{2, n_r} - \underline{S}_{2, n_r} \\ \vdots \\ \bar{S}_{N_s, n_r} - \underline{S}_{3, n_r} \end{bmatrix}}_{N(2)} + \dots + \underbrace{\begin{bmatrix} \bar{S}_{1, n_r} - \underline{S}_{1, n_r} \\ \vdots \\ \bar{S}_{2, n_r} - \underline{S}_{2, n_r} \\ \vdots \\ \bar{S}_{N_s, n_r} - \underline{S}_{3, n_r} \end{bmatrix}}_{N(Z_{n_r})}$$

A general reaction network | Time evolution (cont.)

Reactions \mathcal{R}_{n_r} and $\mathcal{R}_{n'_r}$ together, at time t after $Z_{n_r}(t)$ and $Z_{n'_r}(t)$ reaction events

$$\underbrace{\begin{bmatrix} N_1(0) \\ \vdots \\ N_{n_s}(0) \\ \vdots \\ N_{N_s}(0) \end{bmatrix}}_{N(t)} + Z_{n_r}(t) \underbrace{\begin{bmatrix} S_{1, n_r} \\ \vdots \\ S_{2, n_r} \\ \vdots \\ S_{N_s, n_r} \end{bmatrix}}_{N(1)} + Z_{n'_r}(t) \underbrace{\begin{bmatrix} S_{1, n'_r} \\ \vdots \\ S_{2, n'_r} \\ \vdots \\ S_{N_s, n'_r} \end{bmatrix}}_{N(2)}, \quad Z_{n_r}(t), Z_{n'_r}(t) = 0, 1 \dots$$

A sub-lattice is generated of points accessible from the initial state $N(0)$

- For closed systems, we have that $\sum_{n_s=1}^{N_s} N_{n_s}(t) < \infty$
- The sub-lattice does not cover the entire octant

When all reactions are taken into account, we have the relation encountered earlier

$$N(t) = N(0) + \sum_{n_r=1}^{N_r} Z_{n_r}(t) \begin{bmatrix} S_{1, n_r} \\ \vdots \\ S_{2, n_r} \\ \vdots \\ S_{N_s, n_r} \end{bmatrix}$$

A general reaction network | Time evolution (cont.)

For reactions in a closed vessel, the sub-lattice is a bounded set of all accessible states

↪ By construction, the system is confined to the sub-lattice containing $N(0)$

$$N(t) = N(0) + \underbrace{\sum_{n_r=1}^{N_r} Z_{n_r}(t)}_{\text{States accessible from } N(0)} \begin{bmatrix} S_{1,n_r} \\ \vdots \\ S_{2,n_r} \\ \vdots \\ S_{N_s,n_r} \end{bmatrix}$$

If this representation were unique (for a given $N(0)$, each accessible point $N(t)$ associates to a single set of reaction counts $Z(t)$), then we could map N -space onto Z -space

- One reaction would be a unit step along the associated coordinate Z_{n_r}

It would be nice, but there is no reason why such a representation should be unique

A general reaction network | Time evolution (cont.)

We think of $N(t)$, $X(t)$, and $Z(t)$ as alternative ways of describing the reaction system

- Variables $N(t)$, $X(t)$, and $Z(t)$ are macroscopic descriptors

We hope they would approximately satisfy a set of differential or difference equations

Reactions are discrete events, should be preferably described by difference equations

↪ Reactions are discrete events in time

↪ Copy-numbers do not vary continuously in time

The precise **time of occurrence** of reaction events is not predictable by these variables

- As it is the result of many (un-modelled) microscopic factors

The precise **type of reaction** is also not predictable by macroscopic variables

Instead of treating the macroscopic variables as deterministic quantities, we formulate them as stochastic variables and define a **mesoscopic description** of the reaction system

A general reaction network | Time evolution (cont.)

Similarly, we can define $X(t) = (X_1(t), \dots, X_{N_s}(t))$ with each $X_{n_s}(t) = \Omega^{-1} N_{n_s}(t)$

We get the expression for the evolution of concentrations

$$X(t) = X(t=0) + S \frac{Z(t)}{\Omega}$$

In vector form, we get

$$\begin{bmatrix} X_1(t) \\ X_2(t) \\ \vdots \\ X_{n_s}(t) \\ \vdots \\ X_{N_s}(t) \end{bmatrix} = \begin{bmatrix} X_1(0) \\ X_2(0) \\ \vdots \\ X_{n_s}(0) \\ \vdots \\ X_{N_s}(0) \end{bmatrix} + \frac{1}{\Omega} \begin{bmatrix} S_{1,1} & S_{2,1} & \cdots & S_{N_s,1} \\ S_{1,2} & S_{2,2} & \cdots & S_{N_s,2} \\ \vdots & \vdots & \ddots & \vdots \\ S_{1,n_r} & S_{2,n_r} & \cdots & S_{N_s,n_r} \\ \vdots & \vdots & \ddots & \vdots \\ S_{1,N_r} & S_{2,N_r} & \cdots & S_{N_s,N_r} \end{bmatrix} \begin{bmatrix} Z_1(t) \\ Z_2(t) \\ \vdots \\ Z_{n_r}(t) \\ \vdots \\ Z_{N_r}(t) \end{bmatrix}$$

A general reaction network | Time evolution (cont.)

Suppose that because of the large number of molecules, reaction counts change quickly

- Each quantity $Z_{n_r}(t)$ can be approximated by a continuous quantity $Z_{n_r}^c(t)$

Under these circumstances, changes in copy-number due to a single reaction are small

- Also copy-numbers $N_{n_s}(t)$ can be approximated by a continuous quantity $N_{n_s}^c(t)$
- (Similarly, concentrations $X_{n_s}(t)$ can be approximated by $X_{n_s}^c(t)$)

We derived the relations based on copy-numbers and reaction counts

$$N(t) = N(t=0) + SZ(t)$$

$$X(t) = X(t=0) + S \frac{Z(t)}{\Omega}$$

These relations can be re-written for the continuous quantities,

$$N^c(t) = N^c(0) + SZ^c(t)$$

$$X^c(t) = X^c(0) + S \frac{X^c(t)}{\Omega}$$

A general reaction network | Time evolution (cont.)

$$N^c(t) = N^c(0) + SZ^c(t)$$

$$X^c(t) = X^c(0) + S \frac{X^c(t)}{\Omega}$$

The relations for the continuous counterparts re-written and expanded

$$\begin{bmatrix} N_1^c(t) \\ \vdots \\ N_{n_s}^c(t) \\ \vdots \\ N_{N_s}^c(t) \end{bmatrix} = \begin{bmatrix} N_1^c(0) \\ \vdots \\ N_{n_s}^c(0) \\ \vdots \\ N_{N_s}^c(0) \end{bmatrix} + \begin{bmatrix} S_{1,1} & \cdots & S_{N_s,1} \\ \vdots & \ddots & \vdots \\ S_{1,n_r} & \cdots & S_{N_s,n_r} \\ \vdots & \ddots & \vdots \\ S_{1,N_r} & \cdots & S_{N_s,N_r} \end{bmatrix} \begin{bmatrix} Z_1^c(t) \\ \vdots \\ Z_{n_r}^c(t) \\ \vdots \\ Z_{N_r}^c(t) \end{bmatrix}$$

$$\begin{bmatrix} X_1^c(t) \\ \vdots \\ X_{n_s}^c(t) \\ \vdots \\ X_{N_s}^c(t) \end{bmatrix} = \begin{bmatrix} X_1^c(0) \\ \vdots \\ X_{n_s}^c(0) \\ \vdots \\ X_{N_s}^c(0) \end{bmatrix} + \frac{1}{\Omega} \begin{bmatrix} S_{1,1} & \cdots & S_{N_s,1} \\ \vdots & \ddots & \vdots \\ S_{1,n_r} & \cdots & S_{N_s,n_r} \\ \vdots & \ddots & \vdots \\ S_{1,N_r} & \cdots & S_{N_s,N_r} \end{bmatrix} \begin{bmatrix} Z_1^c(t) \\ \vdots \\ Z_{n_r}^c(t) \\ \vdots \\ Z_{N_r}^c(t) \end{bmatrix}$$

Kinetics

Reaction networks

A general reaction network | Kinetics

$$N^c(t) = N^c(0) + SZ^c(t)$$

$$X^c(t) = X^c(0) + S \frac{X^c(t)}{\Omega}$$

Taking time derivatives, we get the instantaneous rates of change in the copy-numbers

$$\dot{N}^c(t) = 0 + S\dot{Z}^c(t)$$

$$\dot{X}^c(t) = 0 + S \frac{\dot{X}^c(t)}{\Omega}$$

Derivatives $\dot{N}^c(t)$ and $\dot{X}^c(t)$ give the net copy-number and concentrations rates (fluxes)

$$\dot{N}^c(t) = S\dot{Z}^c(t)$$

Useful expression, as long as a relation between derivative $\dot{N}^c(t)$ and $N^c(t)$ is available

- (Similarly, for a relation between $\dot{X}^c(t)$ and $X^c(t)$)

Everything else being a constant, the relation must be encoded by the derivative $\dot{Z}^c(t)$

A general reaction network | Kinetics (cont.)

For the sake of reasoning, suppose that such a relationship is available in some form

$$\dot{Z}^c(t) = \hat{v}(N^c(t))$$

$$= \Omega \times v(X^c(t))$$

The function $v(X^c(t)) = (v_1(X^c(t)), \dots, v_{N_r}(X^c(t)))$ is the **reaction rate**

↪ Reaction count per unit time, per unit of system size

- For a specific concentration $X^c(t)$ and time t

Function $\hat{v}(N^c(t)) = (\hat{v}_1(N^c(t)), \dots, \hat{v}_{N_r}(N^c(t)))$ is the **conversion rate**

↪ Reaction count per unit time

- At a specific t and $N^c(t)$

A general reaction network | Kinetics (cont.)

$$\dot{Z}^c(t) = \underbrace{\Omega v(X^c(t))}_{\hat{v}(N^c(t))}$$

The reaction rate v is the reaction count per unit time, \dot{Z}^c , divided by system's size Ω

$$v(X^c(t)) = \begin{bmatrix} v_1(X_1^c(t), \dots, X_{n_s}^c(t), \dots, X_{N_r}^c(t)) \\ \vdots \\ v_{n_r}(X_1^c(t), \dots, X_{n_s}^c(t), \dots, X_{N_r}^c(t)) \\ \vdots \\ v_{N_r}(X_1^c(t), \dots, X_{n_s}^c(t), \dots, X_{N_r}^c(t)) \end{bmatrix} \\ = \frac{\dot{Z}^c(t)}{\Omega}$$

The temperature is assumed to be constant, no other dependences other than $X^c(t)$

- The assumption is realistic, otherwise we could have had $v(X^c(t), T(t))$

A general reaction network | Kinetics (cont.)

For a large class of reactions, we have **rate laws with definite orders**, in which the rate $\Omega v(X^c(t))$ is proportional to the concentration of each reactant raised to some power

$$v_{n_r}(X^c(t)) = k_{n_r} [X_1^c(t)^{g_{1,n_r}} \times X_2^c(t)^{g_{2,n_r}} \times \dots \times X_{N_s}^c(t)^{g_{N_s,n_r}}] \\ = k_{n_r} \prod_{n_s=1}^{N_s} X_{n_s}^c(t)^{g_{n_s,n_r}}, \quad n_r = 1, \dots, N_r$$

Rate constants k_{n_r} summarise factors like activation energy and molecular orientation

Exponents g_{n_s,n_r} define the order of reaction \mathcal{R}_{n_r} with respect to reactant species \mathcal{S}_{n_s}

↪ (For elementary reactions, exponents g_{n_s,n_r} equal the stoichiometries \underline{S}_{n_s,n_r})

The sum of exponents $\sum_{n_s=1}^{N_s} g_{n_s,n_r}$ over a channel is the actual order of the reaction

A general reaction network | Kinetics (cont.)

The specific form of the reaction rate $v_{n_r}(X^c(t))$ of the n_r -th reaction is its **rate law**

We obtain the deterministic kinetic equations, by incorporating the rate law

$$\dot{N}^c(t) = S \dot{Z}^c(t) \\ = S [\Omega v(X^c(t))] \\ = S \hat{v}(N^c(t))$$

Similarly,

$$\dot{X}^c(t) = S \frac{\dot{Z}^c(t)}{\Omega} \\ = S \frac{\cancel{\Omega} v(X^c(t))}{\cancel{\Omega}} \\ = S v(X^c(t))$$

A general reaction network | Kinetics (cont.)

$$v_{n_r}(X^c(t)) = k_{n_r} \prod_{n_s=1}^{N_s} X_{n_s}^c(t)^{g_{n_s,n_r}}, \quad n_r = 1, \dots, N_r$$

This is the **law of mass-action kinetics**, justified by collision and transition state theory

$$v(X^c(t)) = \begin{bmatrix} k_1 \prod_{n_s=1}^{N_s} X_{n_s}^c(t)^{g_{n_s,1}} \\ k_2 \prod_{n_s=1}^{N_s} X_{n_s}^c(t)^{g_{n_s,2}} \\ \dots \\ k_{N_r} \prod_{n_s=1}^{N_s} X_{n_s}^c(t)^{g_{n_s,N_r}} \end{bmatrix}$$

Reactions not described by rate laws of this form have no definite reaction order

↪ Michaelis-Menten kinetics, Hill kinetics, competitive inhibition, ...