LECTURE #12

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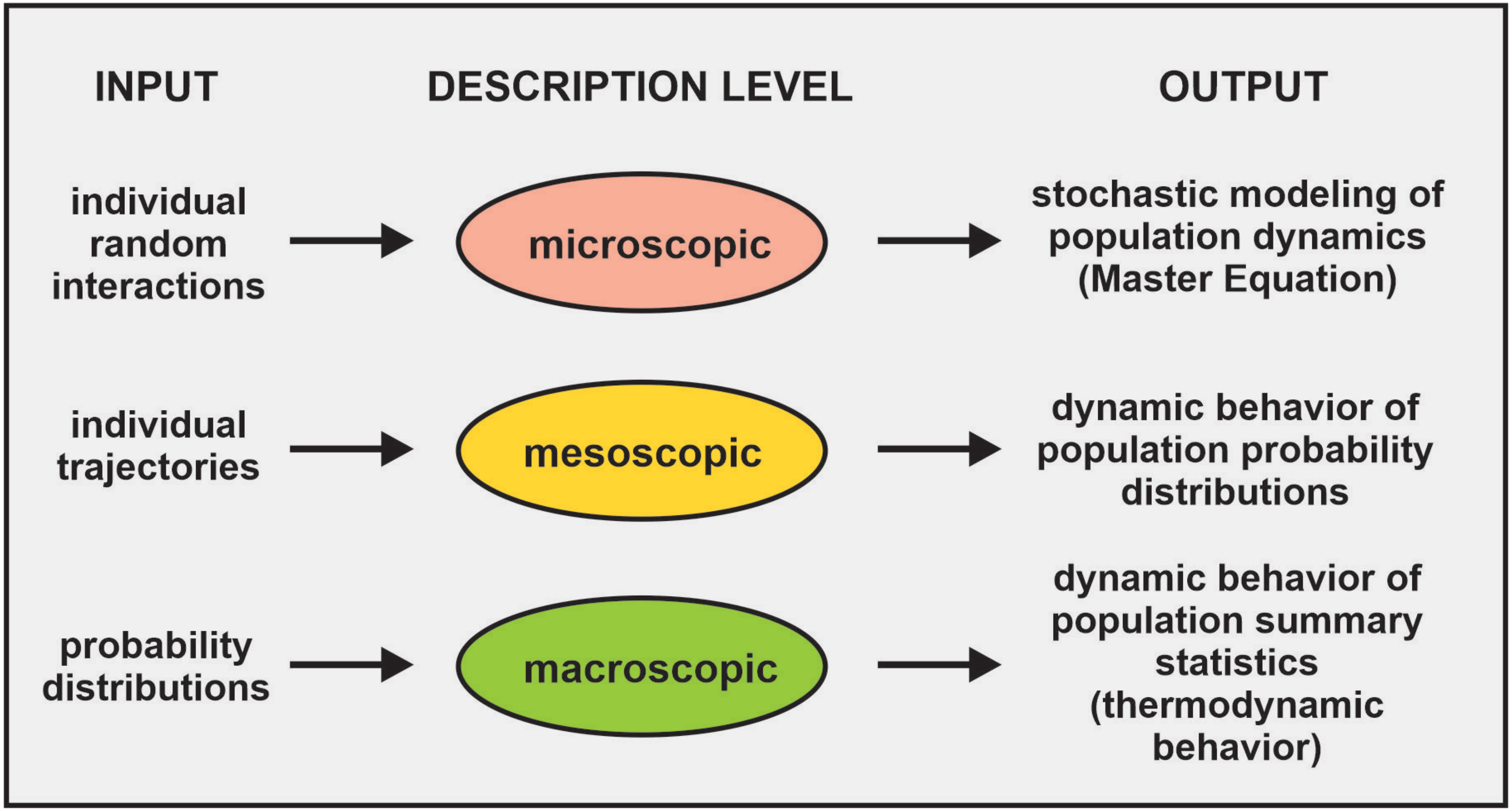
MESOSCOPIC DESCRIPTION

Description Levels of Complex Systems



Mesoscopic Behavior

- We would now like to derive mathematical properties of the dynamic behavior of the probability distribution of the system state and investigate the
  - **existence**
  - **uniqueness**
  - **stability**

  of the (stationary) solution to the ME at steady state; i.e., when

$$\frac{d\mathbf{p}(t)}{dt} = \mathbf{P}\mathbf{p} = 0$$

- This can be done by using a mesoscopic description of the network in terms of the population probabilities.

Existence of Stationary Solution

- To derive a stationary solution to the ME, we must solve the system of K linear equations:

$$\boxed{\mathbf{P}\mathbf{p} = 0}$$

- Since the elements of each column of matrix $\mathbf{P}$ add to zero, its rows are linearly dependent.
- Therefore, the rank of $\mathbf{P}$ will be less than K.
- Consequently, the system of equations will have at least one nontrivial solution.
- Unfortunately, this result does not say how many nontrivial solutions exist and which ones are valid probability distributions.

Irreducible Markovian Reaction Networks

- We first consider the dynamic behavior of an irreducible Markovian reaction network.

- This type of network is defined by the property that, for any pair $(\mathbf{x}, \mathbf{x}')$ of population states, there exists at least one sequence of reactions that takes the system from state $\mathbf{x}$ to state $\mathbf{x}'$.

- These states are said to be communicating.

Existence & Uniqueness of Stationary Solution

- It can be shown that an irreducible Markovian reaction network converges to a unique probability distribution $\bar{\mathbf{p}}$ at steady-state, which does not depend on the initial probability distribution such that $\mathbf{0} < \bar{\mathbf{p}} < \mathbf{1}$.

- Consequently, in an irreducible Markovian reaction network, the population process can take any value at steady-state with nonzero probability.

Existence & Uniqueness of Stationary Solution

- On the other hand, the theory of systems of ordinary differential equations with constant coefficients implies that, for a given initial probability distribution $\mathbf{p}(0)$, the equation

$$\frac{d\mathbf{p}(t)}{dt} = \mathbf{P}\mathbf{p}(t), \;\; t > 0$$

  is satisfied by a unique probability distribution $\mathbf{p}(t)$, which is analytic for all $0 \leq t < \infty$.

- As a matter of fact,

$$\boxed{\mathbf{p}(t) = \exp(t\mathbf{P})\mathbf{p}(0)}$$

Existence & Uniqueness of Stationary Solution

- Since the elements of each column of matrix $\mathbf{P}$ add to zero,

$$\frac{d[\mathbf{1}^T \mathbf{p}(t)]}{dt} = \mathbf{1}^T \frac{d\mathbf{p}(t)}{dt} = \mathbf{1}^T \mathbf{P}\mathbf{p}(t) = 0$$

- This result, together with the fact that $\mathbf{1}^T \mathbf{p}(0) = 1$, implies that $\mathbf{1}^T \mathbf{p}(t) = 1$, for all $t > 0$.
- Unfortunately, it is not clear whether $\mathbf{0} \leq \mathbf{p}(t) \leq \mathbf{1}$, for every $t > 0$.
- It turns out however that, for an <u>irreducible</u> Markovian reaction network, $\mathbf{0} < \mathbf{p}(t) < \mathbf{1}$, for every $t > 0$.

Eigenvalue Representation

- If $\lambda_k, k = 1, 2, \ldots, K$, are the eigenvalues of matrix $\mathbf{P}$, with corresponding right and left eigenvectors $\mathbf{r}_k, \mathbf{l}_k, k = 1, 2, \ldots, K$, then the solution of

$$\frac{d\mathbf{p}(t)}{dt} = \mathbf{P}\mathbf{p}(t), \;\; t > 0$$

is given by

$$\boxed{\mathbf{p}(t) = \exp\big(\mathbf{P}t\big)\mathbf{p}(0) = \sum_{k=1}^{K} c_k \mathbf{r}_k \, e^{\lambda_k t}, \;\; 0 \leq t \leq \infty}$$

- We assume here that the eigenvalues of $\mathbf{P}$ have the same algebraic and geometric multiplicity, an assumption satisfied by many Markovian reaction networks.

multiplicity of the corresponding root of the characteristic polynomial

number of linearly independent eigenvectors associated with the eigenvalue

https://en.wikipedia.org/wiki/Eigenvalues_and_eigenvectors

Eigenvalue Representation

$$\mathbf{p}(t) = \sum_{k=1}^{K} c_k \mathbf{r}_k \, e^{\lambda_k t}, \;\; 0 \leq t \leq \infty$$

- In this case, the right and left eigenvectors are biorthogonal, which implies that the constants c_k are given by

$$c_k = \frac{\mathbf{l}_k^T \mathbf{p}(0)}{\mathbf{l}_k^T \; \mathbf{r}_k}$$

- Consequently, we can use the eigenvalues and eigenvectors of $\mathbf{P}$ to analytically specify the entire mesoscopic behavior of a Markovian reaction network.

Eigenvalue Representation

$$\mathbf{p}(t) = \sum_{k=1}^{K} c_k \mathbf{r}_k \, e^{\lambda_k t}, \;\; 0 \le t \le \infty$$

- For an irreducible Markovian reaction network, matrix $\mathbf{P}$ has only one zero eigenvalue, with the remaining $K-1$ eigenvalues having negative real parts.
- If we therefore assume that $\lambda_1 = 0$, then the stationary distribution will be given by

$$\overline{\mathbf{p}} = \frac{\mathbf{r}_1}{\mathbf{1}^T \mathbf{r}_1}$$

- $\mathbf{r}_1$ is the right eigenvector corresponding to the zero eigenvalue.

Stability of ME Solution

- It turns out that the solution $\mathbf{p}(t),\ t \geq 0$ of the ME is asymptotically stable with respect to $\overline{\mathbf{p}}$, in the sense that

$$\lim_{t \to \infty} D[\mathbf{p}(t), \overline{\mathbf{p}}] = 0$$

  where

$$D[\mathbf{p}, \mathbf{q}] = \sum_{k=1}^{K} p_k \ln \frac{p_k}{q_k} \geq 0$$

  is the Kullback-Leibler divergence between the two probability distributions $\mathbf{p}$ and $\mathbf{q}$.

- As a matter of fact, it can be shown that

$$\frac{dD[\mathbf{p}(t), \overline{\mathbf{p}}]}{dt} \leq 0$$

  where equality is achieved <u>only</u> at steady-state.

https://en.wikipedia.org/wiki/Kullback-Leibler_divergence

Summary

- For a given initial probability vector $\mathbf{p}(0)$, the ME associated with an irreducible Markovian reaction network has a unique and strictly positive solution $\mathbf{0} < \mathbf{p}(t) < \mathbf{1}, \; 0 \leq t \leq \infty$.

- This solution:
  - Is analytic for all $0 \leq t < \infty$.
  - Converges to a stationary distribution $\mathbf{0} < \overline{\mathbf{p}} < \mathbf{1}$ that does not depend on the initial probability distribution $\mathbf{p}(0)$.
  - Is asymptotically stable with respect to $\overline{\mathbf{p}}$.

Remarks

- It is not in general easy to check whether a Markovian reaction network is irreducible.
- We often assume that a given Markovian reaction network is comprised of only reversible reactions (reactions which can occur in both directions with nonzero probability).
- This is a plausible assumption since, in principle, a transition between two physical states can occur in the reverse direction as well.
- In this case, we are dealing with completely reducible networks, which are discussed next.

Remarks

- From the equation

$$\frac{d\mathbf{p}(t)}{dt} = \mathbf{P}\mathbf{p}(t)$$

we have that (by approximating the derivative)

$$\mathbf{p}(t+dt) \simeq (\mathbf{I} + \mathbf{P}dt)\mathbf{p}(t) = \mathbf{Q}\mathbf{p}(t)$$

- The matrix $\mathbf{Q} = \mathbf{I} + \mathbf{P}dt$ is known as the <u>transition probability</u> matrix.
- We therefore have

$$p_j(t+dt) = \sum_i q_{ji} p_i(t)$$

$$q_{ji} = \Pr[\text{state at time } t+dt \text{ is } j \,|\, \text{state at time } t \text{ is } i]$$

$$= \begin{cases} p_{ji}dt, & \text{if } j \neq i \\ 1 + p_{ii}dt, & \text{if } j = i \end{cases}$$

Remarks

$$p_j(t+dt) = \sum_i q_{ji} p_i(t)$$

$$\begin{aligned} &\Pr[\text{state at time } t+dt \text{ is } j] \\ &\quad = \sum_i \Pr[\text{state at time } t+dt \text{ is } j \mid \text{state at time } t \text{ is } i] \\ &\qquad \times \Pr[\text{state at time } t \text{ is } i] \end{aligned}$$

- The new probability $p_j(t+dt)$ of the j-th state is determined by summing the state probabilities at time t weighted with the elements of the j-th row of $\mathbf{Q} = \mathbf{I} + \mathbf{P}dt$.
- This implies that the j-th state can be reached only from those states for which the corresponding elements of the j-th row of matrix $\mathbf{Q} = \mathbf{I} + \mathbf{P}dt$ are nonzero.

Completely Reducible Networks

- After appropriately ordering the states, we may be able to cast matrix $\mathbf{P}$ into a block diagonal form with diagonal elements $\mathbf{P}_1, \mathbf{P}_2, \ldots, \mathbf{P}_K$ where each submatrix $\mathbf{P}_k$ is irreducible.

- The resulting Markovian reaction network is said to be completely reducible.

- In this case, the original Markovian reaction network can be decomposed into K non-interacting subnetworks with non-overlapping state-spaces, which can be treated independently of each other.

Completely Reducible Networks

- Let $\mathbf{p}_1(t)$ and $\mathbf{p}_2(t)$ be the probability distributions of the state vectors at time t, determined by the partition of the state-space suggested by a matrix $\mathbf{P}$ with two irreducible diagonal blocks.
- In this case, note that

$$\begin{bmatrix} \mathbf{p}_1(t+dt) \\ \mathbf{p}_2(t+dt) \end{bmatrix} \simeq \begin{bmatrix} \mathbf{I}_1 + \mathbf{P}_1 dt & \mathbf{O} \\ \mathbf{O} & \mathbf{I}_2 + \mathbf{P}_2 dt \end{bmatrix} \begin{bmatrix} \mathbf{p}_1(t) \\ \mathbf{p}_2(t) \end{bmatrix}$$

- This shows that the states in the first group can only be reached from states within this group.
- The same is true from the states in the second group.
- Therefore, the system will be operating within two different groups of states independently from each other.

Completely Reducible Networks

- Each reaction subnetwork is characterized by <u>unique</u> dynamic and stationary solutions $\mathbf{p}_k(t),\ \overline{\mathbf{p}}_k,\ k = 1, 2, \ldots, K$, which satisfy the properties discussed in the case of irreducible networks.

- However, the dynamic and stationary solutions of the original ME are determined by the initial condition.

Completely Reducible Networks

- If the ME is initialized with a population vector in the state-space of the k-th subnetwork, then its dynamic and stationary solutions will be given by

$$\begin{bmatrix} \mathbf{0} \\ \vdots \\ \mathbf{p}_k(t) \\ \vdots \\ \mathbf{0} \end{bmatrix} \quad \text{and} \quad \begin{bmatrix} \mathbf{0} \\ \vdots \\ \overline{\mathbf{p}}_k \\ \vdots \\ \mathbf{0} \end{bmatrix}$$

does not depend on the initial condition

Incompletely Reducible Networks

- What happens when the Markovian reaction network contains irreversible reactions and matrix $\mathbf{P}$ is not irreducible?
- Let us assume that, after appropriately ordering the states, we have that

$$\mathbf{P} = \begin{bmatrix} \mathbf{P}_1 & \mathbf{T}_1 \\ \mathbf{O} & \mathbf{T}_2 \end{bmatrix}$$

  where $\mathbf{P}_1$ and $\mathbf{T}_2$ are square matrices, $\mathbf{P}_1$ is irreducible, and at least one element of $\mathbf{T}_1$ is strictly positive.
- The associated Markovian reaction network is said to be incompletely reducible.

Incompletely Reducible Networks

- Let $\mathbf{p}_1(t)$ and $\mathbf{p}_2(t)$ be the probability distributions of the state vectors at time t, determined by the partition of the state-space suggested by the previous matrix $\mathbf{P}$.
- Note that, in this case

$$\begin{bmatrix} \mathbf{p}_1(t+dt) \\ \mathbf{p}_2(t+dt) \end{bmatrix} \simeq \begin{bmatrix} \mathbf{I}_1 + \mathbf{P}_1 dt & \mathbf{T}_1 dt \\ \mathbf{O} & \mathbf{I}_2 + \mathbf{T}_2 dt \end{bmatrix} \begin{bmatrix} \mathbf{p}_1(t) \\ \mathbf{p}_2(t) \end{bmatrix}$$

- Therefore, the states in the first group can be reached either from the states within this group or from states in the second group.
- On the other hand, the states in the second group can only be reached from the states within this group.

Incompletely Reducible Networks

- Note that, in this case, the ME results in the following two differential equations:

$$\frac{d\mathbf{p}_1(t)}{dt} = \mathbf{P}_1\mathbf{p}_1(t) + \mathbf{T}_1\mathbf{p}_2(t)$$

$$\frac{d\mathbf{p}_2(t)}{dt} = \mathbf{T}_2\mathbf{p}_2(t)$$

Incompletely Reducible Networks

$$\frac{d\mathbf{p}_1(t)}{dt} = \mathbf{P}_1\mathbf{p}_1(t) + \mathbf{T}_1\mathbf{p}_2(t)$$
$$\frac{d\mathbf{p}_2(t)}{dt} = \mathbf{T}_2\mathbf{p}_2(t)$$

- From the <u>second</u> equation, we have that

$$\mathbf{p}_2(t) = \exp\{\mathbf{T}_2 t\}\mathbf{p}_2(0)$$

- On the other hand, the dynamic behavior of $\mathbf{p}_1$ is driven by both $\mathbf{p}_1(t)$ and $\mathbf{p}_2(t)$.

Incompletely Reducible Networks

$$\frac{d\mathbf{p}_1(t)}{dt} = \mathbf{P}_1\mathbf{p}_1(t) + \mathbf{T}_1\mathbf{p}_2(t)$$
$$\frac{d\mathbf{p}_2(t)}{dt} = \mathbf{T}_2\mathbf{p}_2(t)$$

- Since

$$\mathbf{p}_2(t) = \exp\{\mathbf{T}_2 t\}\mathbf{p}_2(0)$$

then, if $\mathbf{p}_2(0) = \mathbf{0}$, we have

$$\mathbf{p}_1(t) = \exp\{\mathbf{P}_1 t\}\mathbf{p}_1(0)$$
$$\mathbf{p}_2(t) = \mathbf{0}$$

Incompletely Reducible Networks

- In this case, and since matrix $\mathbf{P}_1$ is <u>irreducible</u>, the stationary solution of the ME governing an incompletely reducible Markovian reaction network will be <u>unique</u> and given by the probability vector

$$\bar{\mathbf{p}} = \begin{bmatrix} \bar{\mathbf{p}}_1 \\ \mathbf{0} \end{bmatrix}$$

where $\bar{\mathbf{p}}_1$ is the (unique) solution of the linear system of equations $\mathbf{P}_1\mathbf{p} = \mathbf{0}$.

Incompletely Reducible Networks

- When $\mathbf{p}_2(0) \neq \mathbf{0}$, we have that

$$\frac{d[\mathbf{1}^T \mathbf{p}_2(t)]}{dt} = \mathbf{1}^T \frac{d\mathbf{p}_2(t)}{dt} = \mathbf{1}^T \mathbf{T}_2 \mathbf{p}_2(t) = -\mathbf{1}^T \mathbf{T}_1 \mathbf{p}_2(t) < 0$$

  provided that $\mathbf{p}_2(t) \neq \mathbf{0}$, since the elements of each column of matrix $\mathbf{P}$ add to zero and we have assumed that at least one element of matrix $\mathbf{T}_1$ is strictly positive.
- Therefore, $\mathbf{p}_2(t)$ asymptotically becomes zero as $t \to \infty$.
- As a matter of fact, $\mathbf{p}_2(t)$ assigns probability mass over the <u>transient</u> states of the Markovian reaction network, as opposed to $\mathbf{p}_1(t)$ that assigns probability mass over the <u>persistent</u> states.

Incompletely Reducible Networks

- In this case, and since matrix $\mathbf{P}_1$ is <u>irreducible</u>, the stationary solution of the ME governing an incompletely reducible Markovian reaction network will be <u>unique</u> and given by the probability vector

$$\overline{\mathbf{p}} = \begin{bmatrix} \overline{\mathbf{p}}_1 \\ \mathbf{0} \end{bmatrix}$$

where $\overline{\mathbf{p}}_1$ is the (unique) solution of the linear system of equations

$$\mathbf{P}_1 \mathbf{p} = \mathbf{0}$$

- This result is the same as when $\mathbf{p}_2(0) = \mathbf{0}$.

Example

- Consider a Markovian reaction network comprised of five species and the following five reactions:

$$X_1 + X_2 \xrightarrow{\kappa_1} X_3$$
$$X_3 \xrightarrow{\kappa_2} X_1 + X_2$$
$$X_4 \xrightarrow{\kappa_3} X_3$$
$$X_4 \xrightarrow{\kappa_4} X_5$$
$$X_5 \xrightarrow{\kappa_5} X_4$$

- We assume (for simplicity) that the system is always initialized with state

$$X_1(0) = X_2(0) = X_3(0) = X_4(0) = 0$$
$$X_5(0) = 1$$

- Then, the state space is given by

$$\mathbb{S} = \left\{ \mathbf{x}_1 = \begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 1 \end{bmatrix}, \mathbf{x}_2 = \begin{bmatrix} 0 \\ 0 \\ 0 \\ 1 \\ 0 \end{bmatrix}, \mathbf{x}_3 = \begin{bmatrix} 0 \\ 0 \\ 1 \\ 0 \\ 0 \end{bmatrix}, \mathbf{x}_4 = \begin{bmatrix} 1 \\ 1 \\ 0 \\ 0 \\ 0 \end{bmatrix} \right\}$$

Example

- In this case, the ME becomes

$$\frac{d\mathbf{p}(t)}{dt} = \mathbf{P}\mathbf{p}(t), \quad \mathbf{p}(0) = \begin{bmatrix} 1 \\ 0 \\ 0 \\ 0 \end{bmatrix} \qquad \mathbb{S} = \left\{ \mathbf{x}_1 = \begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 1 \end{bmatrix}, \mathbf{x}_2 = \begin{bmatrix} 0 \\ 0 \\ 0 \\ 1 \\ 0 \end{bmatrix}, \mathbf{x}_3 = \begin{bmatrix} 0 \\ 0 \\ 1 \\ 0 \\ 0 \end{bmatrix}, \mathbf{x}_4 = \begin{bmatrix} 1 \\ 1 \\ 0 \\ 0 \\ 0 \end{bmatrix} \right\}$$

where

$$\mathbf{P} = \begin{bmatrix} -\kappa_5 & \kappa_4 & 0 & 0 \\ \kappa_5 & -(\kappa_3 + \kappa_4) & 0 & 0 \\ 0 & \kappa_3 & -\kappa_2 & \kappa_1 \\ 0 & 0 & \kappa_2 & -\kappa_1 \end{bmatrix} \qquad \mathbf{p}(t) = \begin{bmatrix} p(\mathbf{x}_1;t) \\ p(\mathbf{x}_2;t) \\ p(\mathbf{x}_3;t) \\ p(\mathbf{x}_4;t) \end{bmatrix}$$

$$X_1 + X_2 \xrightarrow{\kappa_1} X_3$$
$$X_3 \xrightarrow{\kappa_2} X_1 + X_2$$
$$X_4 \xrightarrow{\kappa_3} X_3$$
$$X_4 \xrightarrow{\kappa_4} X_5$$
$$X_5 \xrightarrow{\kappa_5} X_4$$

Example

- Relabeling the state-space in reverse order, so that

$$\mathbb{S} = \left\{ \mathbf{x}_1 = \begin{bmatrix} 1 \\ 1 \\ 0 \\ 0 \\ 0 \end{bmatrix}, \mathbf{x}_2 = \begin{bmatrix} 0 \\ 0 \\ 1 \\ 0 \\ 0 \end{bmatrix}, \mathbf{x}_3 = \begin{bmatrix} 0 \\ 0 \\ 0 \\ 1 \\ 0 \end{bmatrix}, \mathbf{x}_4 = \begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 1 \end{bmatrix} \right\}$$

results in

$$\mathbf{P} = \begin{bmatrix} -\kappa_5 & \kappa_4 & 0 & 0 \\ \kappa_5 & -(\kappa_3+\kappa_4) & 0 & 0 \\ 0 & \kappa_3 & -\kappa_2 & \kappa_1 \\ 0 & 0 & \kappa_2 & -\kappa_1 \end{bmatrix} \rightarrow \left[\begin{array}{cc|cc} -\kappa_1 & \kappa_2 & 0 & 0 \\ \kappa_1 & -\kappa_2 & \kappa_3 & 0 \\ \hline 0 & 0 & -(\kappa_3+\kappa_4) & \kappa_5 \\ 0 & 0 & \kappa_4 & -\kappa_5 \end{array}\right]$$

Example

$$\mathbf{P} = \left[\begin{array}{cc|cc} -\kappa_1 & \kappa_2 & 0 & 0 \\ \kappa_1 & -\kappa_2 & \kappa_3 & 0 \\ \hline 0 & 0 & -(\kappa_3+\kappa_4) & \kappa_5 \\ 0 & 0 & \kappa_4 & -\kappa_5 \end{array}\right] \qquad \mathbb{S} = \left\{ \mathbf{x}_1 = \begin{bmatrix} 1 \\ 1 \\ 0 \\ 0 \\ 0 \end{bmatrix}, \mathbf{x}_2 = \begin{bmatrix} 0 \\ 0 \\ 1 \\ 0 \\ 0 \end{bmatrix}, \mathbf{x}_3 = \begin{bmatrix} 0 \\ 0 \\ 0 \\ 1 \\ 0 \end{bmatrix}, \mathbf{x}_4 = \begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 1 \end{bmatrix} \right\}$$

- This implies that the <u>persistent</u> and <u>transient</u> states are

$$\mathcal{P} = \left\{ \mathbf{x}_1 = \begin{bmatrix} 1 \\ 1 \\ 0 \\ 0 \\ 0 \end{bmatrix}, \mathbf{x}_2 = \begin{bmatrix} 0 \\ 0 \\ 1 \\ 0 \\ 0 \end{bmatrix} \right\} \qquad \mathcal{T} = \left\{ \mathbf{x}_3 = \begin{bmatrix} 0 \\ 0 \\ 0 \\ 1 \\ 0 \end{bmatrix}, \mathbf{x}_4 = \begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 1 \end{bmatrix} \right\}$$

Example

- If $\kappa_3 = 0$, then

$$\mathbf{P} = \left[\begin{array}{cc|cc} -\kappa_1 & \kappa_2 & 0 & 0 \\ \kappa_1 & -\kappa_2 & \kappa_3 & 0 \\ \hline 0 & 0 & -(\kappa_3+\kappa_4) & \kappa_5 \\ 0 & 0 & \kappa_4 & -\kappa_5 \end{array}\right] \to \left[\begin{array}{cc|cc} -\kappa_1 & \kappa_2 & 0 & 0 \\ \kappa_1 & -\kappa_2 & 0 & 0 \\ \hline 0 & 0 & -\kappa_4 & \kappa_5 \\ 0 & 0 & \kappa_4 & -\kappa_5 \end{array}\right]$$

$$X_1 + X_2 \xrightarrow{\kappa_1} X_3$$
$$X_3 \xrightarrow{\kappa_2} X_1 + X_2$$
$$X_4 \xrightarrow{\kappa_3} X_3$$
$$X_4 \xrightarrow{\kappa_4} X_5$$
$$X_5 \xrightarrow{\kappa_5} X_4$$

$\Rightarrow$

$$\boxed{\begin{array}{l} X_1 + X_2 \xrightarrow{\kappa_1} X_3 \\ X_3 \xrightarrow{\kappa_2} X_1 + X_2 \end{array}}$$

$$\boxed{\begin{array}{l} X_4 \xrightarrow{\kappa_4} X_5 \\ X_5 \xrightarrow{\kappa_5} X_4 \end{array}}$$

two irreducible and independent Markovian networks

Example

- If

$$X_1 + X_2 \xrightarrow{\kappa_1} X_3$$
$$X_3 \xrightarrow{\kappa_2} X_1 + X_2$$
$$X_4 \xrightarrow{\kappa_3} X_3$$
$$X_4 \xrightarrow{\kappa_4} X_5$$
$$X_5 \xrightarrow{\kappa_5} X_4$$

$\Rightarrow$

$$X_1 + X_2 \xrightarrow{\kappa_1} X_3$$
$$X_3 \xrightarrow{\kappa_2} X_1 + X_2$$
$$X_4 \xrightarrow{\kappa_3} X_3$$
$$\boxed{X_3 \xrightarrow{\kappa_6} X_4}$$
NEW REACTION
$$X_4 \xrightarrow{\kappa_4} X_5$$
$$X_5 \xrightarrow{\kappa_5} X_4$$

then

$$\mathbf{P} = \begin{bmatrix} -\kappa_1 & \kappa_2 & 0 & 0 \\ \kappa_1 & -(\kappa_2 + \kappa_6) & \kappa_3 & 0 \\ 0 & \kappa_6 & -(\kappa_3 + \kappa_4) & \kappa_5 \\ 0 & 0 & \kappa_4 & -\kappa_5 \end{bmatrix}$$

one <u>irreducible</u>
Markovian network

General Markovian Reaction Networks

- In general, the population states in a Markovian reaction network can be classified into two distinct groups:
  - **transient**
  - **persistent**
- These states can be <u>uniquely</u> partitioned into non-overlapping sets $\mathcal{P}_k, k = 1, 2, \ldots, K$ and $\mathcal{T}_{K+1}$.
  - $\mathcal{P}_k, k = 1, 2, \ldots, K$, are <u>irreducible</u> sets containing <u>persistent states</u> with the additional property that, for every $k \neq k'$, each state in $\mathcal{P}_k$ does not communicate with any state in $\mathcal{P}_{k'}$.
  - $\mathcal{T}_{K+1}$ contains the <u>transient states</u>.

General Markovian Reaction Networks

- By appropriately ordering the states, we can write matrix $\mathbf{P}$ in the form

$$\mathbf{P} = \begin{bmatrix} \mathbf{P}_1 & \mathbf{O} & \dots & \mathbf{O} & \mathbf{T}_1 \\ \mathbf{O} & \mathbf{P}_2 & \dots & \mathbf{O} & \mathbf{T}_2 \\ \vdots & \vdots & & \vdots & \vdots \\ \mathbf{O} & \mathbf{O} & \dots & \mathbf{P}_K & \mathbf{T}_K \\ \mathbf{O} & \mathbf{O} & \dots & \mathbf{O} & \mathbf{T}_{K+1} \end{bmatrix}$$

- $\mathbf{P}_k$ is a <u>square irreducible</u> matrix that characterizes how probability mass is dynamically distributed among the <u>persistent</u> states in $\mathscr{P}_k$.
- For $k = 1, 2, \dots, K$, $\mathbf{T}_k$ is a matrix that tells how probability mass is transferred from the <u>transient</u> states in $\mathscr{T}_{K+1}$ to the <u>persistent</u> states in $\mathscr{P}_k$.
- $\mathbf{T}_{K+1}$ is a square matrix that characterizes how probability mass is dynamically distributed among the <u>transient</u> states in $\mathscr{T}_{K+1}$.