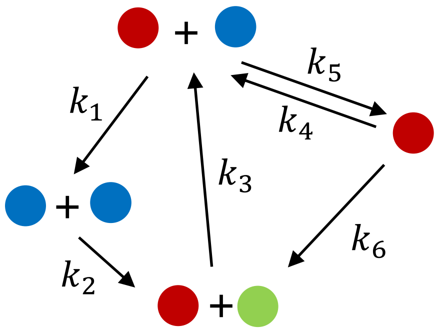
Studying infection disease models with chemical reaction network theory



Jinsu Kim

Department of Mathematics, POSTECH

Value Creating University POSTECH POHANG UNIVERSITY OF SCIENCE AND TECHNOLOGY

June 13th, 2022

Preparing for the next pandemic, BIRS 2022

Network representation for biochemical systems

Biochemical system

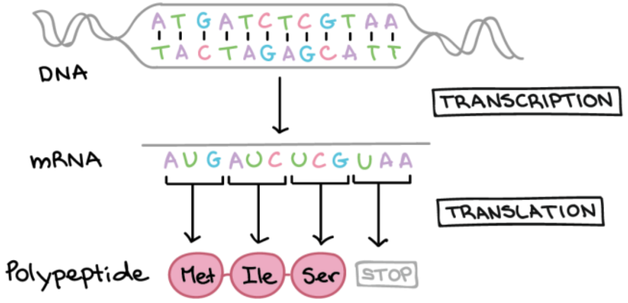


Image: https://www.khanacademy.org

Network representation for biochemical systems

Biochemical system

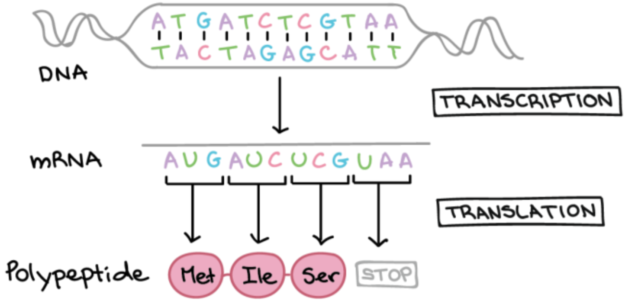


Image: https://www.khanacademy.org

Boolean Network

Reaction network

Petri-Net

Gene regulatory network

…

Network representation for biochemical systems

Biochemical system

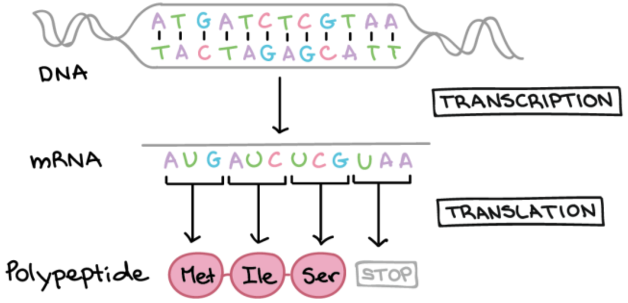


Image: https://www.khanacademy.org

Boolean Network

Reaction network

$$P \xrightarrow{\kappa_1} \emptyset \underset{\kappa_3}{\overset{\kappa_2}{\rightleftharpoons}} m \xrightarrow{\kappa_4} m + P$$

Petri-Net

Gene regulatory network

…

Network representation for biochemical systems

Biochemical system

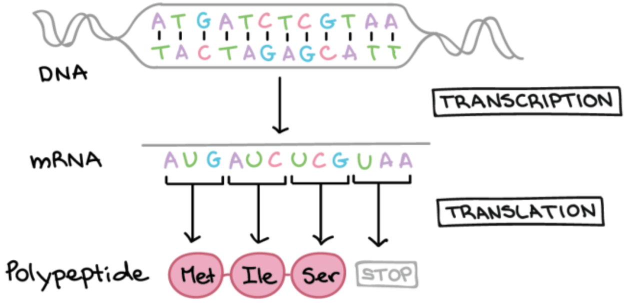


Image: https://www.khanacademy.org

Boolean Network

Reaction network

$$P \xrightarrow{\kappa_1} \emptyset \underset{\kappa_3}{\overset{\kappa_2}{\rightleftharpoons}} m \xrightarrow{\kappa_4} m + P$$

Petri-Net

Gene regulatory network

…

Network representation for biochemical systems

Biochemical system

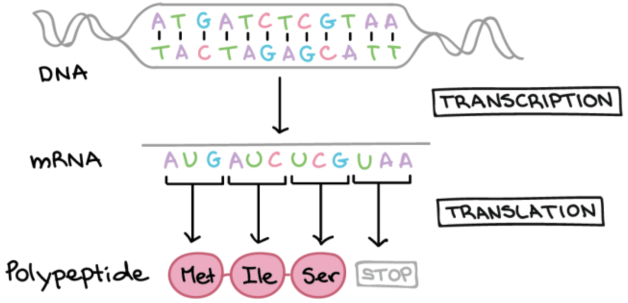


Image: https://www.khanacademy.org

Boolean Network

Reaction network

$$P \xrightarrow{\kappa_1} \emptyset \underset{\kappa_3}{\overset{\kappa_2}{\rightleftharpoons}} m \xrightarrow{\kappa_4} m + P$$

Petri-Net

Gene regulatory network

…

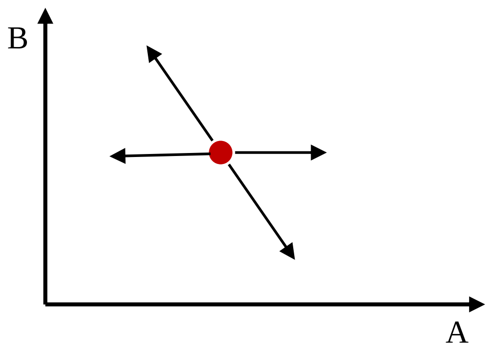
Deterministic model
- ODE
- PDE

Stochastic model
- Markov chain
- SPDE

Hybrid model

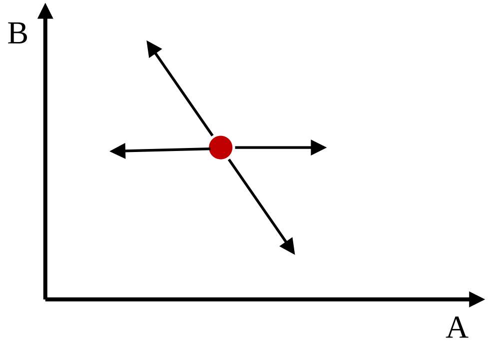
Deterministic modeling for reaction networks

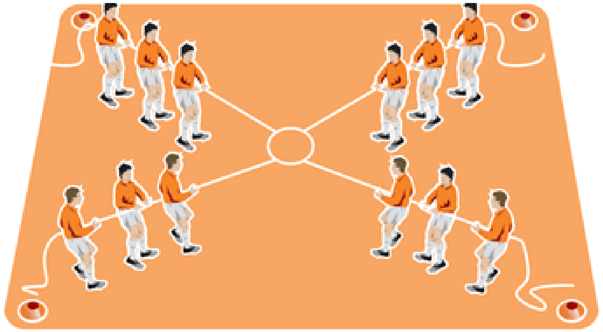
$$B \rightleftharpoons A, \quad A \rightleftharpoons \emptyset$$



Deterministic modeling for reaction networks

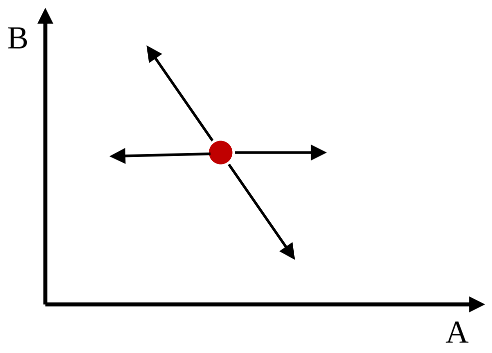
$$B \rightleftharpoons A, \quad A \rightleftharpoons \emptyset$$

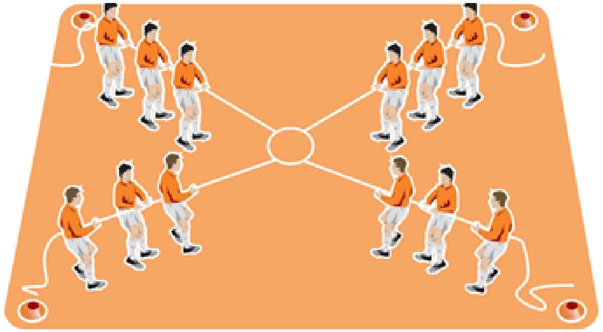




Deterministic modeling for reaction networks

$$B \rightleftharpoons A, \quad A \rightleftharpoons \emptyset$$

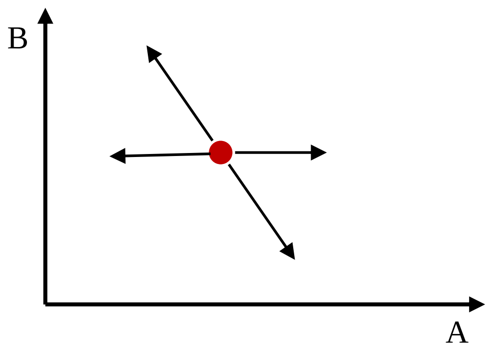


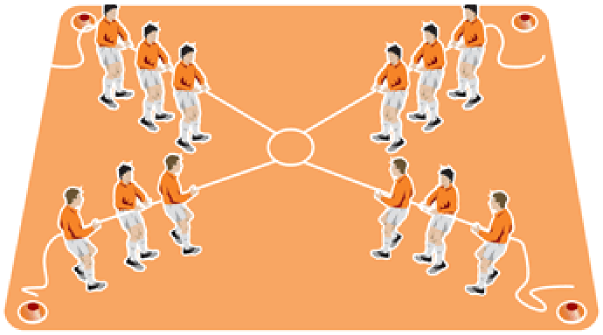


$x(t) = (x_A(t), x_B(t))$: Concentration of A and B

Deterministic modeling for reaction networks

$$B \rightleftharpoons A, \quad A \rightleftharpoons \emptyset$$

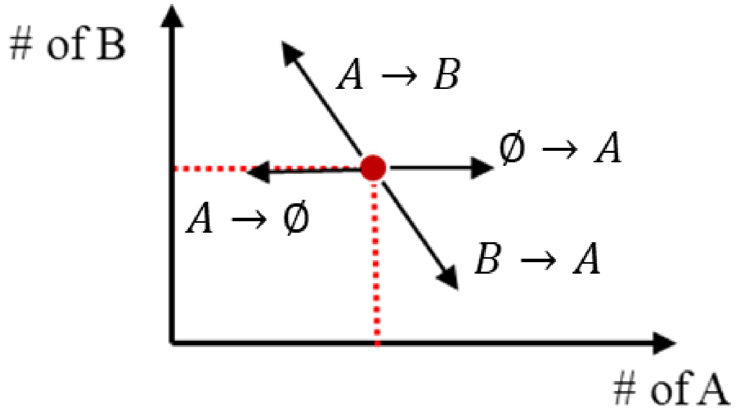




$x(t) = (x_A(t), x_B(t))$: Concentration of A and B

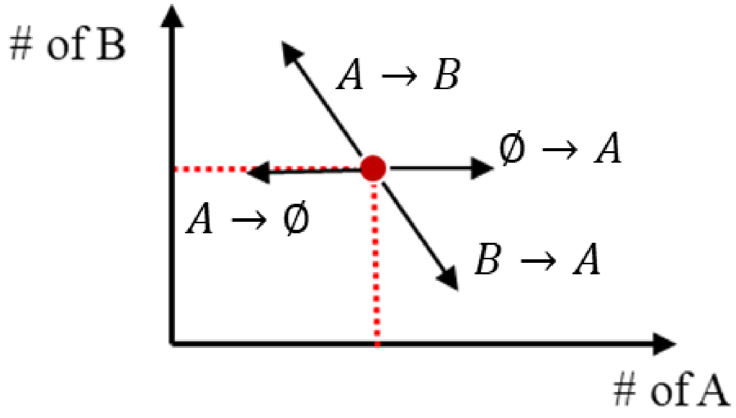
$$\dot{x}(t) = \sum_{y \to y'} \mathscr{K}_{y \to y'}(x(t))(y' - y).$$

Stochastic modeling for reaction networks

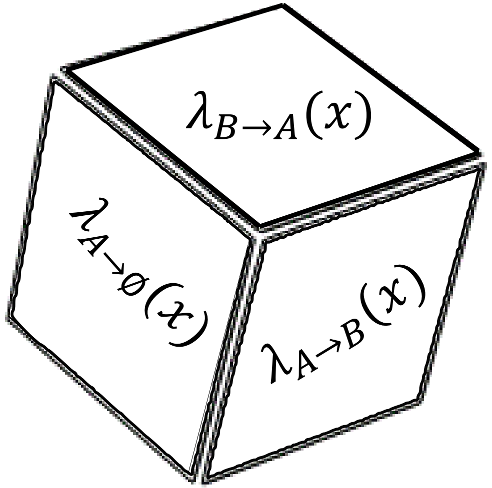


$$B \underset{\kappa_2}{\overset{\kappa_1}{\rightleftharpoons}} A, \quad A \underset{\kappa_4}{\overset{\kappa_3}{\rightleftharpoons}} \emptyset$$

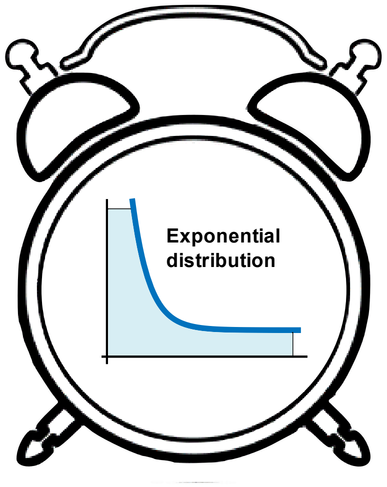
Stochastic modeling for reaction networks



$$B \underset{\kappa_2}{\overset{\kappa_1}{\rightleftharpoons}} A, \quad A \underset{\kappa_4}{\overset{\kappa_3}{\rightleftharpoons}} \emptyset$$

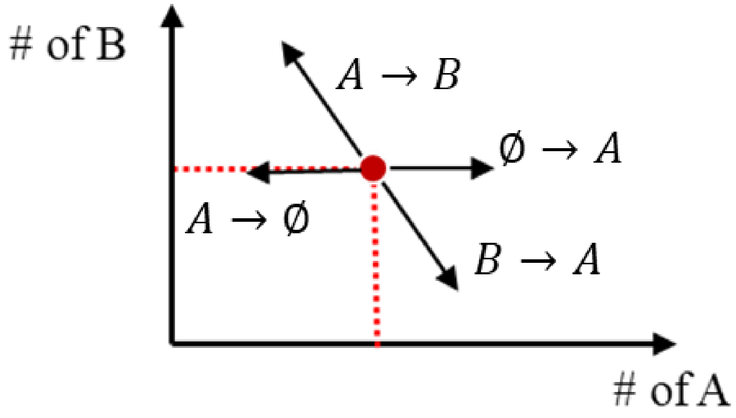


Where to go



When to go

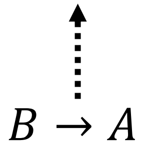
Stochastic modeling for reaction networks



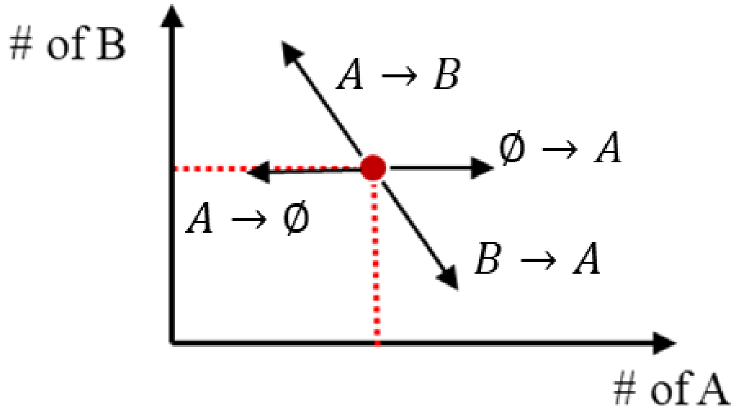
$$B \underset{\kappa_2}{\overset{\kappa_1}{\rightleftharpoons}} A, \quad A \underset{\kappa_4}{\overset{\kappa_3}{\rightleftharpoons}} \emptyset$$

$X(t) = (X_A(t), X_B(t))$: Copy numbers of A and B , Continuous time Markov chain

$$P(X(t+\Delta t) = x + (1,-1)^\top | X(t) = x) = \lambda_{B\to A}(x)\Delta t + o(\Delta t)$$



Stochastic modeling for reaction networks



$$B \underset{\kappa_2}{\overset{\kappa_1}{\rightleftharpoons}} A, \quad A \underset{\kappa_4}{\overset{\kappa_3}{\rightleftharpoons}} \emptyset$$

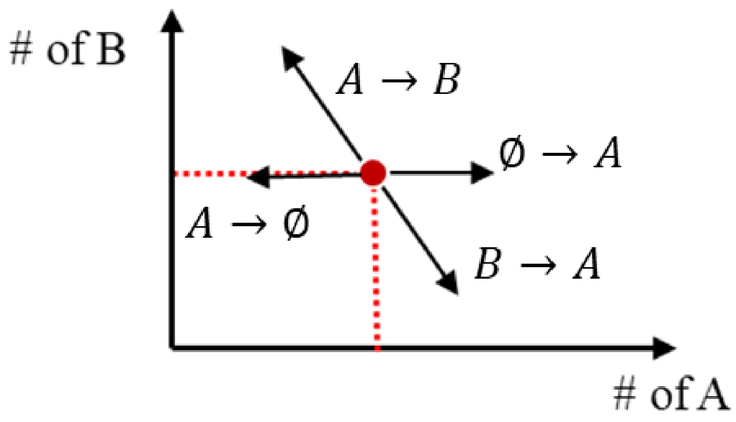
$X(t) = (X_A(t), X_B(t))$: Copy numbers of A and B , Continuous time Markov chain

$$P(X(t+\Delta t) = x + (1,-1)^\top | X(t) = x) = \boxed{\lambda_{B\to A}(x)} \Delta t + o(\Delta t)$$

$B \to A$

Reaction Intensity

Stochastic modeling for reaction networks



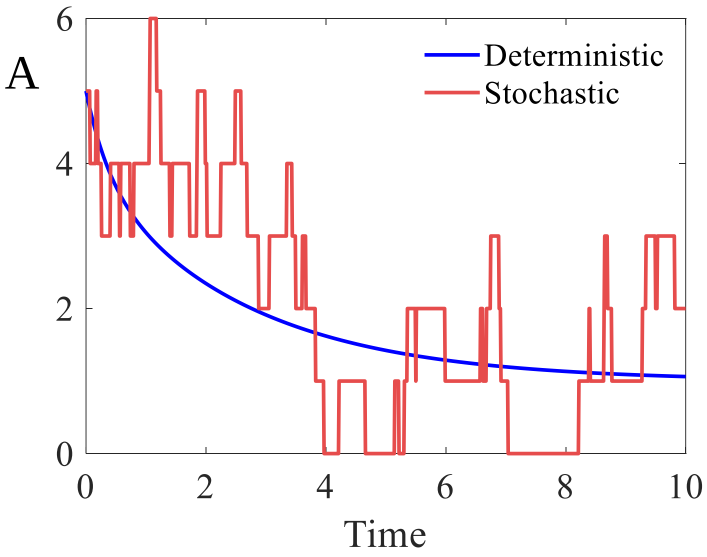
$$B \underset{\kappa_2}{\overset{\kappa_1}{\rightleftharpoons}} A, \quad A \underset{\kappa_4}{\overset{\kappa_3}{\rightleftharpoons}} \emptyset$$

$X(t) = (X_A(t), X_B(t))$: Copy numbers of A and B , Continuous time Markov chain

$$P(X(t+\Delta t) = x + (1,-1)^\top | X(t) = x) = \lambda_{B\to A}(x)\Delta t + o(\Delta t)$$

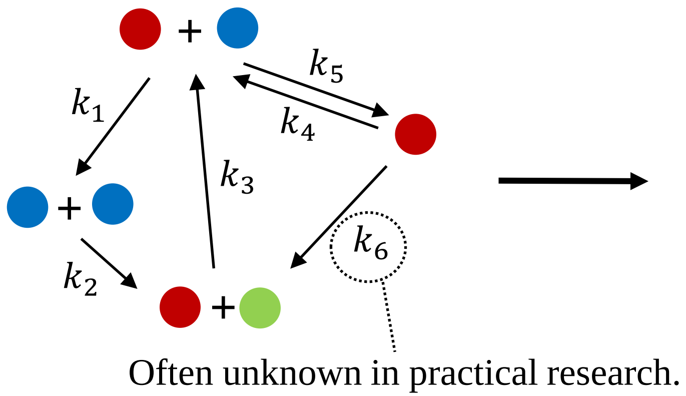
$B \to A$

Reaction Intensity



Network structural conditions ⇒ Dynamical Properties

Biological interaction systems



Derive qualitative behaviors of the associated dynamics by solely using graph topological conditions, regardless of the parameters $\kappa_i's$.

Theorem [Horn and Jackson(1972), Feinberg (1972)] :
If # nodes-# connected components-dim{reaction vectors} = 0 and weakly reversible network

⇒ The associated ODE under mass action admits a unique locally stable steady state on each compatibility class.

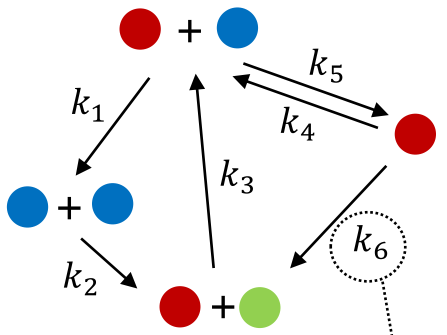
Ex) $2A \xrightarrow{\kappa_1} B$, $B \xrightarrow{\kappa_2} \emptyset$, $\emptyset \xrightarrow{\kappa_3} 2A$

# of complexes = 3
# of connected component = 1
dim(reaction vectors) = dim{ (-2,1), (0,-1), (2,0) } = 2

3-2-1=0

Network structural conditions ⇒ Dynamical Properties

Biological interaction systems ⟶



Often unknown in practical research.

⟶ Derive qualitative behaviors of the associated dynamics by solely using graph topological conditions, regardless of the parameters $\kappa_i' s$.

> Theorem [Anderson, Craciun and Kurtz (2010)] :
> If # nodes-# connected components-dim{reaction vectors} = 0 and weakly reversible network
> ⇒ For the associated Markov chain under mass action,
>
> $\lim_{t\to\infty} p(A,t) = \pi(A)$ for any $A \subset \mathbb{Z}^d_{\geq 0}$ and [illegible] is a product form of Poissons.

Stationary distribution

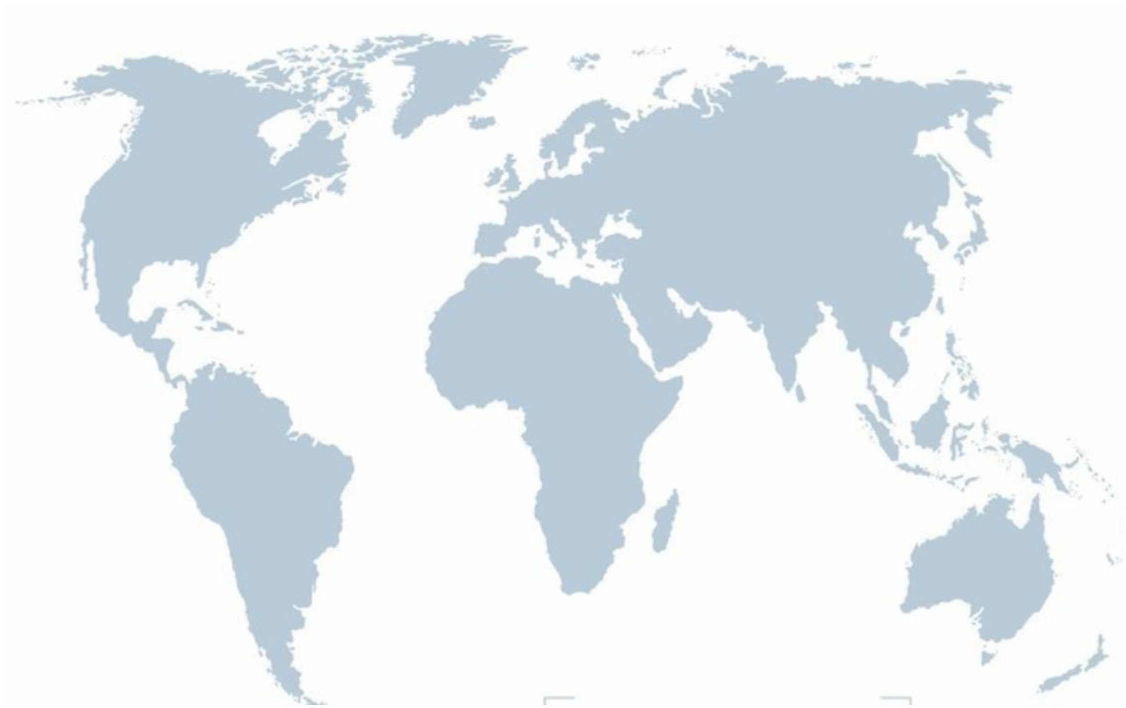
Ex)

$$\begin{array}{ccc} 2A & \xrightarrow{\kappa_1} & B \\ \kappa_3 \nwarrow & & \swarrow \kappa_2 \\ & \emptyset & \end{array}$$

# of complexes = 3
# of connected component = 1
dim(reaction vectors) = dim{ (-2,1), (0,-1), (2,0) } = 2

3-2-1=0

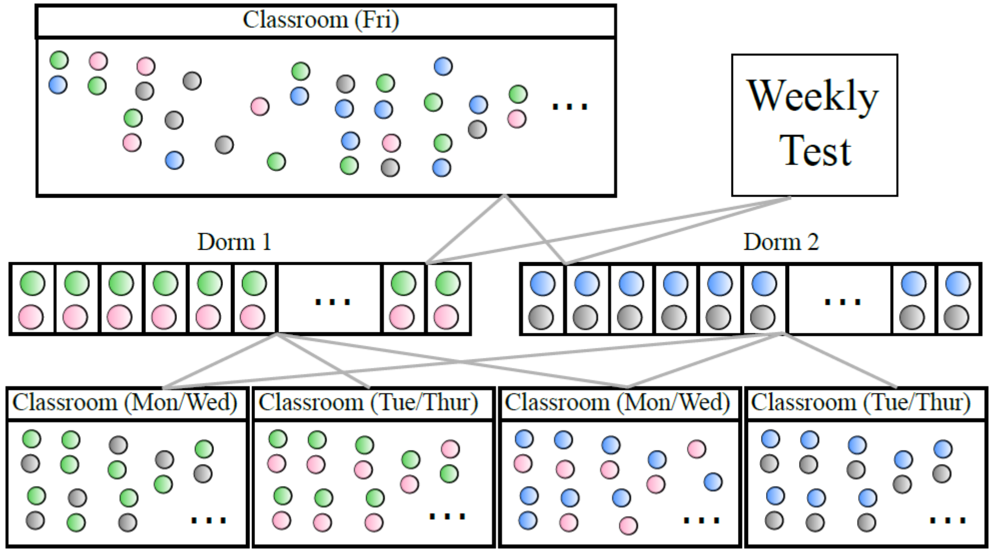
When the network structural conditions can be used for studying infection-disease models?



SIR
SEIR
SIRSS
…

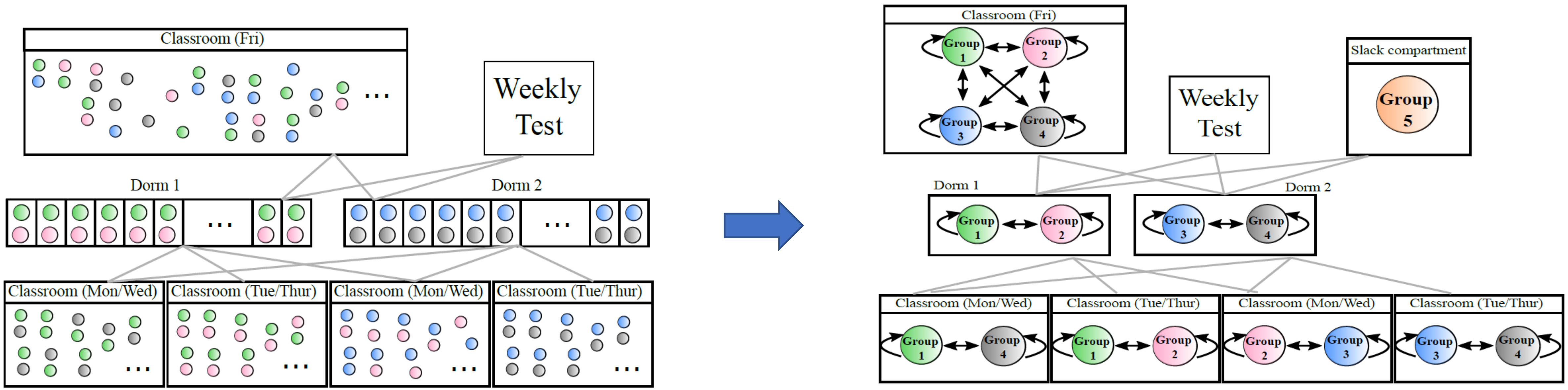
In macroscale, each model may have the same structure, but have different parameters.

Infection-disease models of small communities



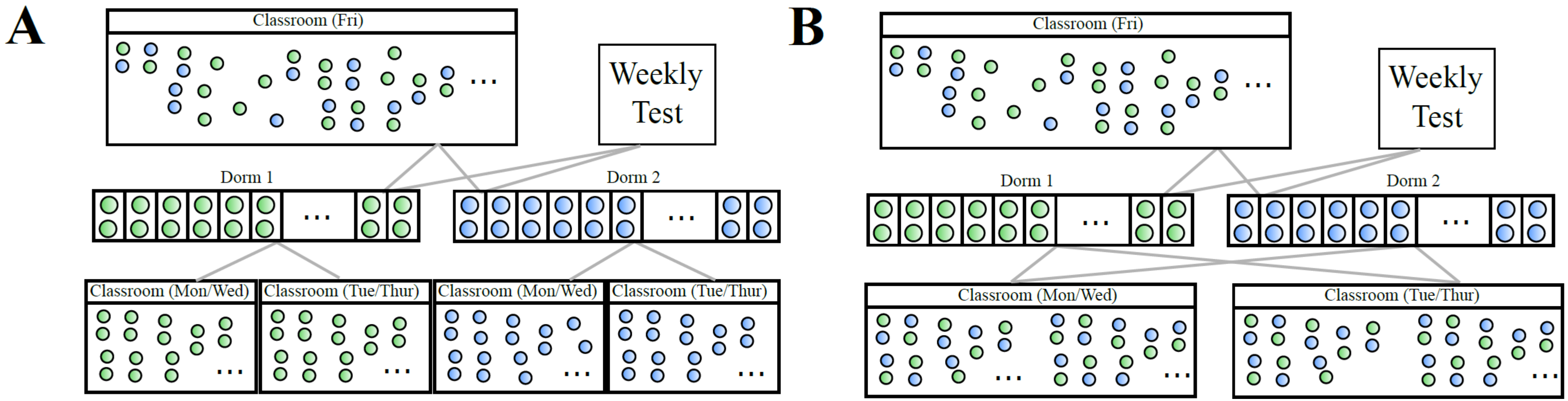
Joint work with German Enciso (UC Irvine) and Suzanne Sindi (UC Merced)

Infection-disease models of small communities



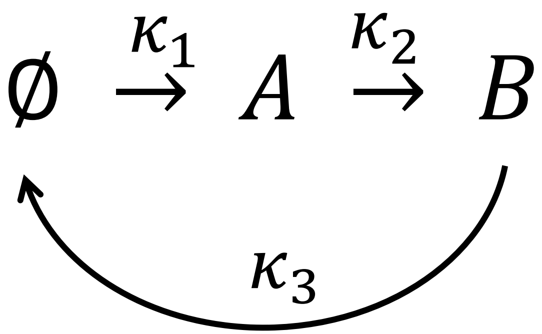
Joint work with German Enciso (UC Irvine) and Suzanne Sindi (UC Merced)

Infection-disease models of small communities



Joint work with German Enciso (UC Irvine) and Suzanne Sindi (UC Merced)

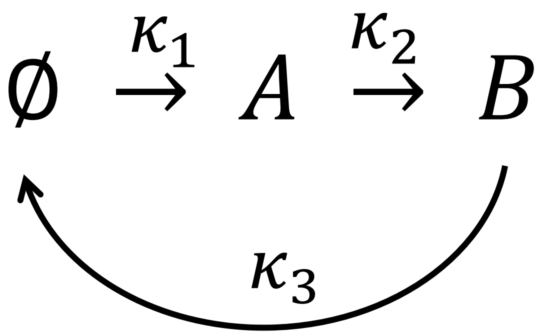
Toy examples



Yuji Hirono, Takashi Okada, Hiroyasu Miyazaki, Yoshimasa Hidaka, "Structural reduction of chemical reaction networks based on topology", Phys. Rev. Research 3, 043123 (2021).

Structural reduction for steady states

Toy examples

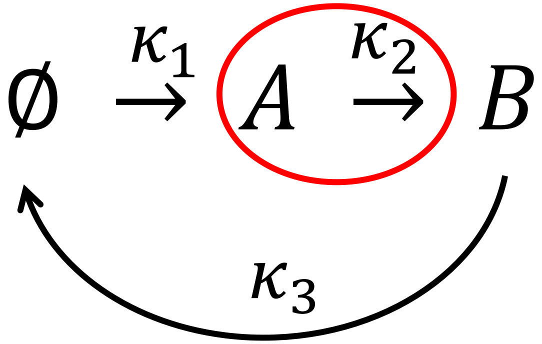


$$a^* = \frac{\kappa_1}{\kappa_2}, \qquad b^* = \frac{\kappa_2 a^*}{\kappa_3} = \frac{\kappa_1}{\kappa_3}.$$

Yuji Hirono, Takashi Okada, Hiroyasu Miyazaki, Yoshimasa Hidaka, "Structural reduction of chemical reaction networks based on topology", Phys. Rev. Research 3, 043123 (2021).

Structural reduction for steady states

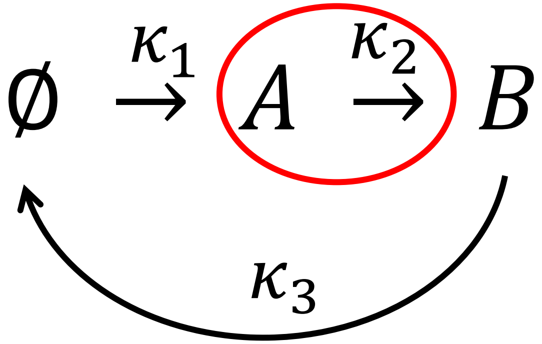
Toy examples



$$a^* = \frac{\kappa_1}{\kappa_2}, \qquad b^* = \frac{\kappa_2 a^*}{\kappa_3} = \frac{\kappa_1}{\kappa_3}.$$

Yuji Hirono, Takashi Okada, Hiroyasu Miyazaki, Yoshimasa Hidaka, "Structural reduction of chemical reaction networks based on topology", Phys. Rev. Research 3, 043123 (2021).

Toy examples

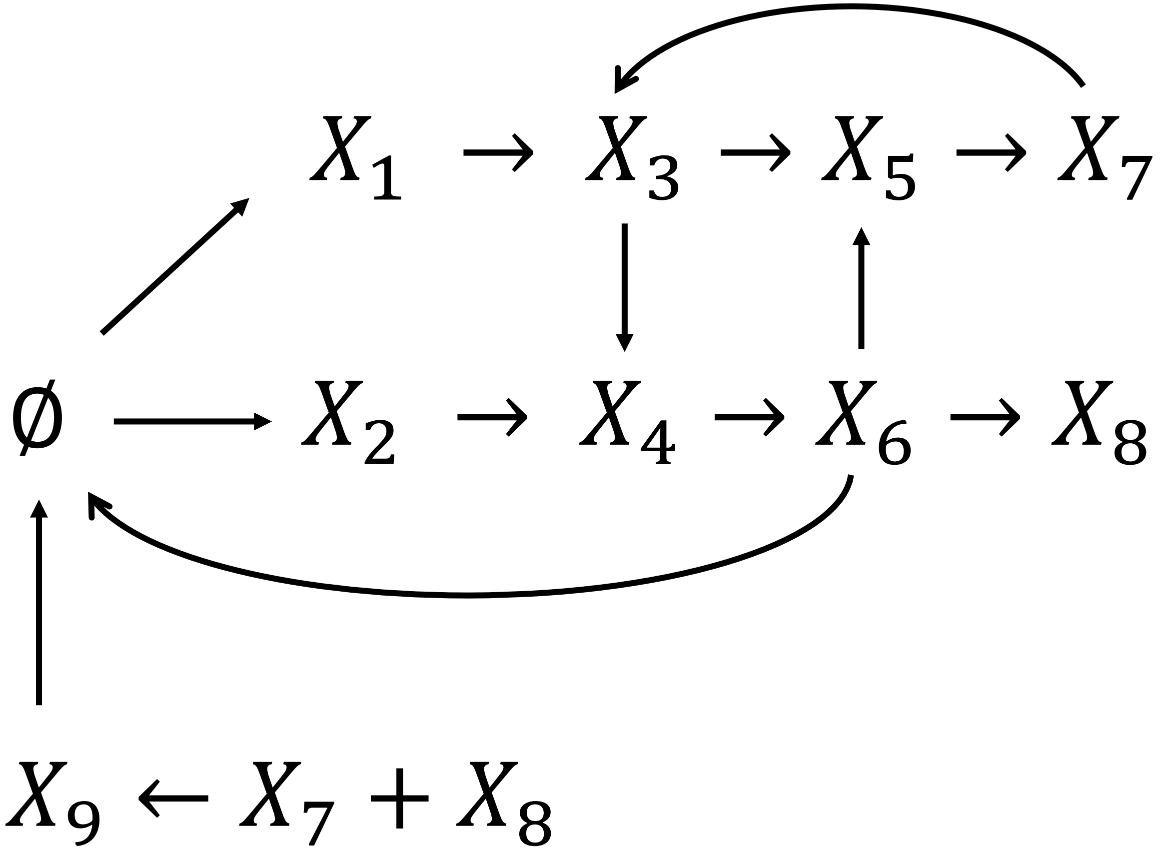


$$a^* = \frac{\kappa_1}{\kappa_2}, \qquad b^* = \frac{\kappa_2 a^*}{\kappa_3} = \frac{\kappa_1}{\kappa_3}.$$

$$\emptyset \underset{\kappa_3}{\overset{\kappa_1}{\rightleftharpoons}} B$$

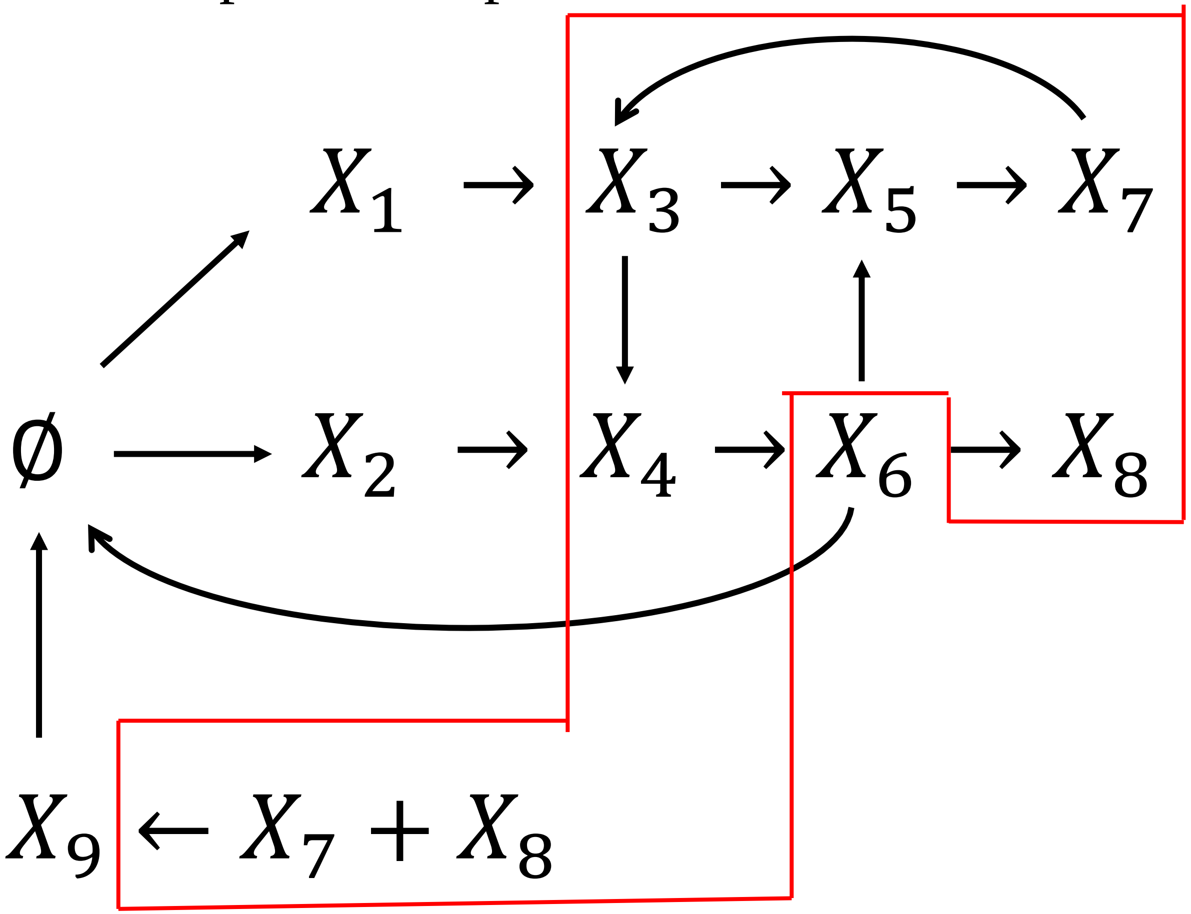
Yuji Hirono, Takashi Okada, Hiroyasu Miyazaki, Yoshimasa Hidaka, "Structural reduction of chemical reaction networks based on topology", Phys. Rev. Research 3, 043123 (2021).

More complex example



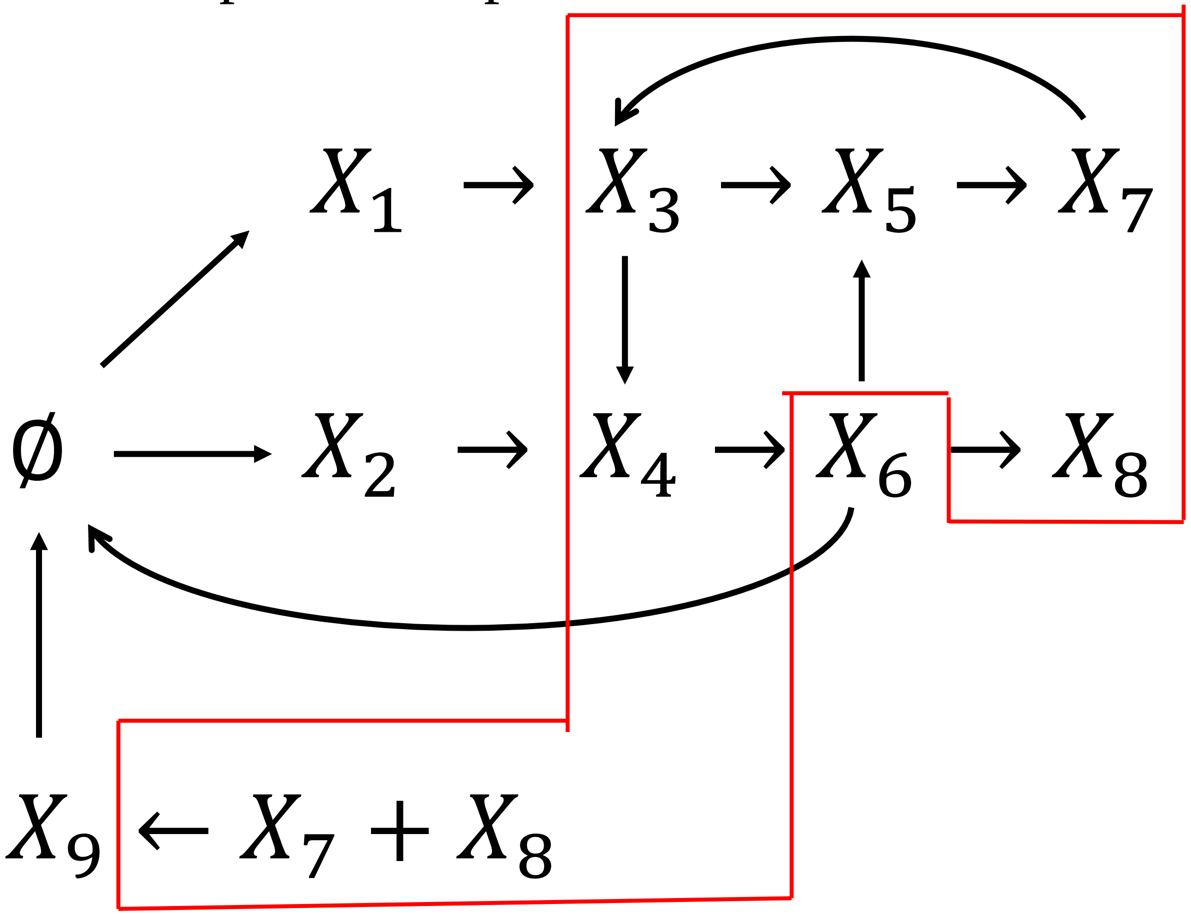
Yuji Hirono, Takashi Okada, Hiroyasu Miyazaki, Yoshimasa Hidaka, "Structural reduction of chemical reaction networks based on topology", Phys. Rev. Research 3, 043123 (2021).

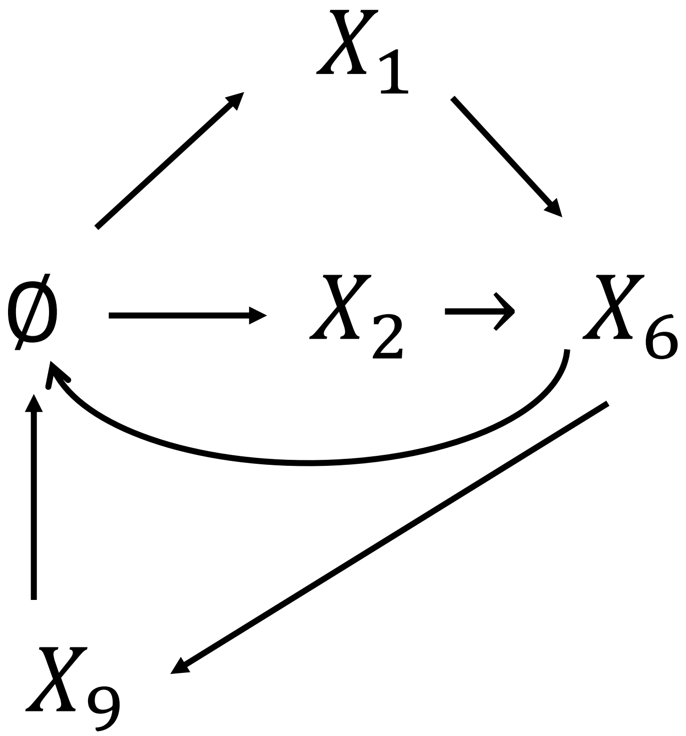
More complex example



Yuji Hirono, Takashi Okada, Hiroyasu Miyazaki, Yoshimasa Hidaka, "Structural reduction of chemical reaction networks based on topology", Phys. Rev. Research 3, 043123 (2021).

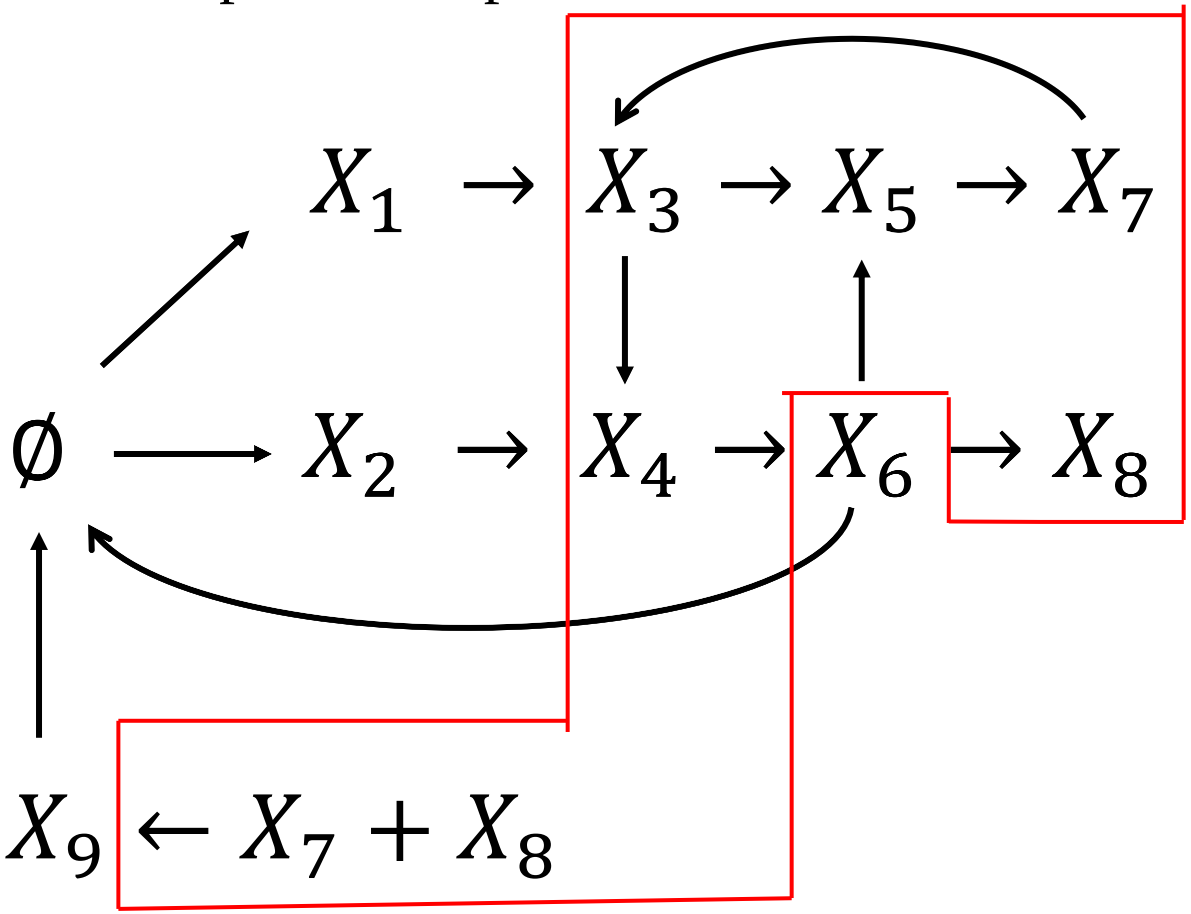
More complex example

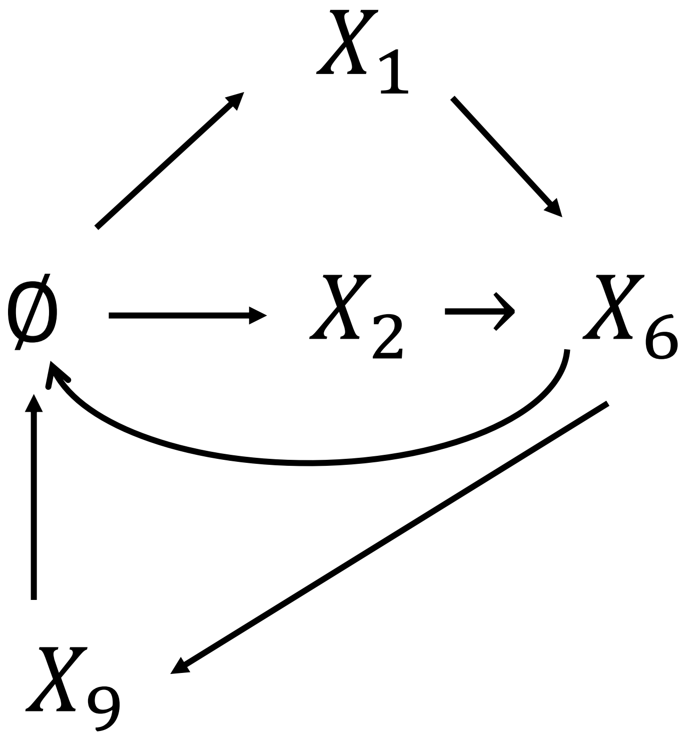




Yuji Hirono, Takashi Okada, Hiroyasu Miyazaki, Yoshimasa Hidaka, "Structural reduction of chemical reaction networks based on topology", Phys. Rev. Research 3, 043123 (2021).

More complex example





Relate the algebraic structure of the deterministic system to homology and cohomology.

Yuji Hirono, Takashi Okada, Hiroyasu Miyazaki, Yoshimasa Hidaka, "Structural reduction of chemical reaction networks based on topology", Phys. Rev. Research 3, 043123 (2021).

Extending to the stochastic model