# Open Markov processes and reaction networks

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# Compositional modeling of open systems

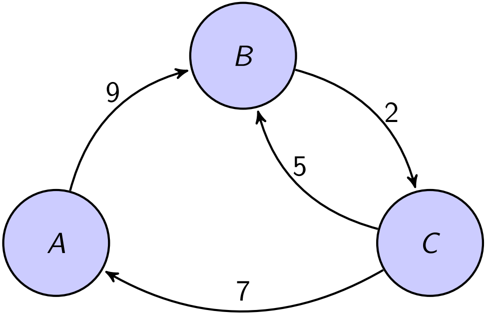
# Compositional modeling of open systems

Consider the set of coupled differential equations represented by the labelled graph:

$$\frac{dp}{dt} = Hp$$

$$H = \begin{pmatrix} -9 & 0 & 7 \\ 9 & -2 & 5 \\ 0 & 2 & -12 \end{pmatrix}$$

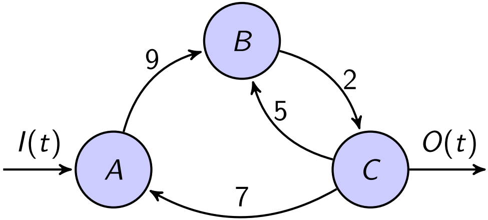
$$p(t) = \begin{pmatrix} A(t) \\ B(t) \\ C(t) \end{pmatrix}$$



# Compositional modeling of open systems

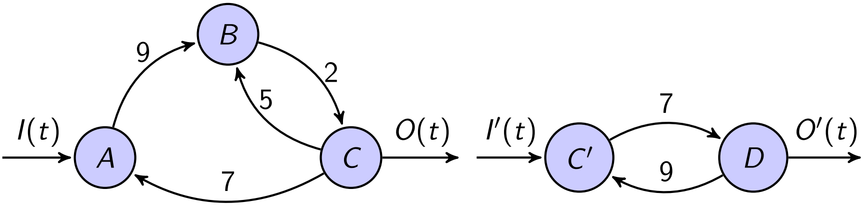
Given smooth functions of time $I(t) \in \mathbb{R}$ and $O(t) \in \mathbb{R}$, we can write down an open dynamical system:

$$
\begin{aligned}
\dot{A} &= -9A + 7C + I(t) \\
\dot{B} &= 9A - 2B + 5C \\
\dot{C} &= 2B - 12C - O(t)
\end{aligned}
$$



# Compositional modeling of open systems

Let's couple this system with another such open system:

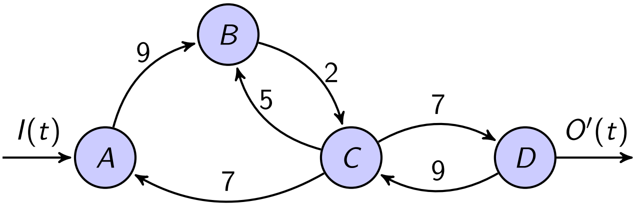



$$\begin{aligned}\dot{A} &= -9A + 7C + I(t)\\ \dot{B} &= 9A - 2B + 5C\\ \dot{C} &= 2B - 12C - O(t)\end{aligned}$$

$$\begin{aligned}\dot{C}' &= -7C' + 9D + I'(t)\\ \dot{D} &= 7C' - 9D - O'(t)\end{aligned}$$

# Compositional modeling of open systems

When the outflow $O(t)$ matches the inflow $I'(t)$, we can compose the systems by identifying $C(t)$ and $C'(t)$ and adding their time derivatives:




$$
\begin{aligned}
\dot{A} &= -9A + 7C + I(t) \\
\dot{B} &= 9A - 2B + 5C \\
\dot{C} &= 2B - 19C + 9D \\
\dot{D} &= 7C - 9D - O'(t)
\end{aligned}
$$

# Some Papers

Much of what I'll discuss can be found in:

- John C. Baez and Blake S. Pollard, A compositional framework for reaction networks, submitted.
- John C. Baez, Brendan Fong and Blake S. Pollard, A compositional framework for Markov processes, *Journal of Mathematical Physics*.
- Blake S. Pollard, Open Markov processes: A compositional perspective on non-equilibrium steady states in biology, *Entropy*.
- Blake S. Pollard, A Second Law for open Markov processes, *Open Systems and Information Dynamics*.

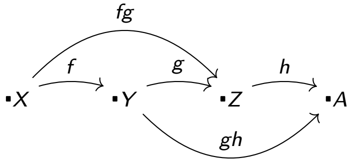
# Idea: View open systems as morphisms in categories

# Idea: View open systems as morphisms in categories

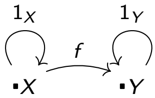
A category $\mathcal{C}$ consists of

- a collection of **objects** $X, Y \ldots$ and
- a collection of **morphisms** $f\colon X \to Y \ldots$

closed under an **associative composition** operation

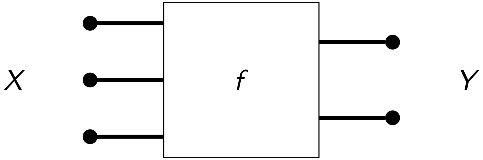



together with **identity morphisms** $1_X\colon X \to X$ satisfying the **left/right identity laws**

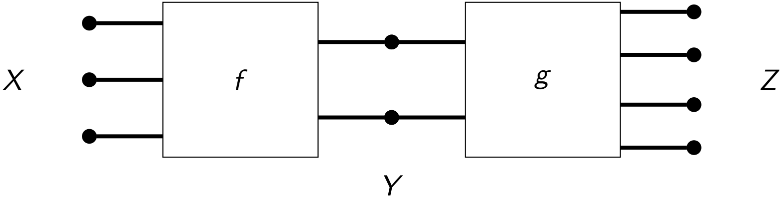


# Open systems as morphisms in a category

We can think of open systems as morphisms in a category.




Composition corresponds to connecting systems.



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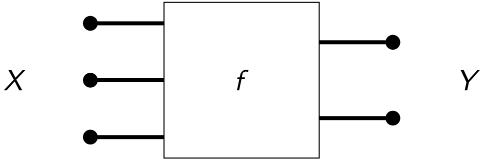
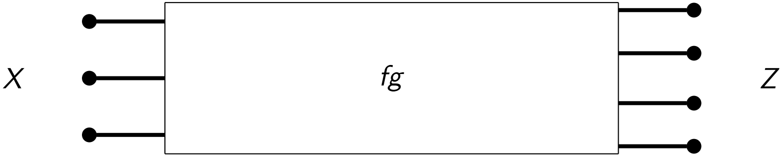



Composition corresponds to connecting systems.

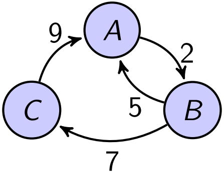


# What types of open systems do we consider?

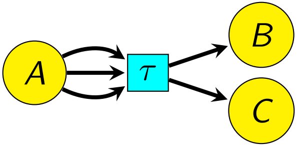
We study systems which admit a graphical syntax.

In my thesis, I focus on two classes of systems: *Markov processes* and *reaction networks*.

Markov processes specify systems of *linear* differential equations and can be represented using *directed, labelled graphs*.




Reaction networks specify systems of *polynomial* differential equations and can be represented by certain *bipartite graphs*, commonly known as Petri nets.



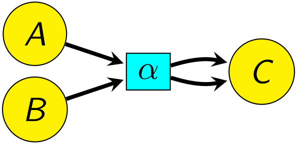
# Reaction networks

## Definition

*A* **reaction network with rates** $(S, T, s, t, r)$ *consists of:*

- *a finite set* $S$
- *a finite set* $T$
- *functions* $s, t \colon T \to \mathbb{N}^S$
- *a function* $r \colon T \to (0, \infty)$.

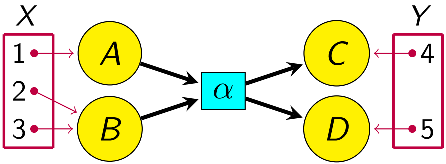
*We call the elements of* $S$ **species**, *those of* $\mathbb{N}^S$ **complexes**, *and those of* $T$ **transitions**. *Any transition* $\tau \in T$ *has a* **source** $s(\tau)$, *a* **target** $t(\tau)$, *and a* **rate constant** $r(\tau)$. *If* $s(\tau) = \kappa$ *and* $t(\tau) = \kappa'$ *we write* $\tau \colon \kappa \to \kappa'$.



# Open reaction networks

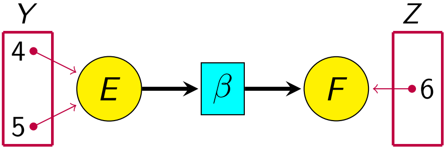
Open reaction networks are generalizations of reaction networks in which certain species are labelled as **input** and **output** species.

$$R\colon X \to Y$$



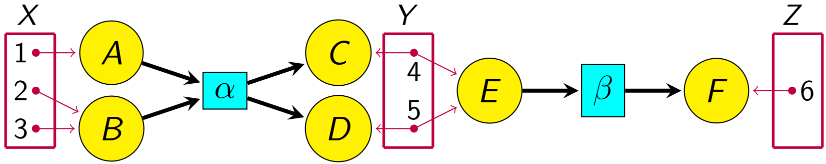
# Composition of open reaction networks

Consider another open reaction network $R' \colon Y \to Z$



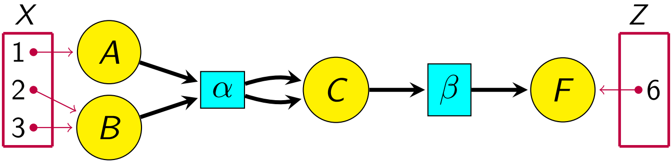
# Composition of open reaction networks

To compose $R\colon X \to Y$ and $R'\colon Y \to Z$ we first combine them



# Composition of open reaction networks

Then, we identify any species which are in the image of the same point in $Y$




This gives a new open reaction network $RR' \colon X \to Z$.

# Decorated cospan categories

We utilize an approach to the categorical modeling of open systems, due to Brendan Fong, called 'decorated cospans.'

A **cospan** in any category $\mathcal{C}$ is a diagram of the form

$$X \xrightarrow{\;i\;} S \xleftarrow{\;o\;} Y.$$

To 'open' a system built on some finite set $S$, we specify a pair of functions $i\colon X \to S$ and $o\colon Y \to S$ specifying the inputs and outputs of the system.

The apex $S$ of the cospan is 'decorated' by some additional data.

For `RxNet`, this data is that of a reaction network with rates on $S$.

# The category of open reaction networks

### Definition

*An* **open reaction network** $R\colon X \to Y$ *consists of a cospan of finite sets*

$$X \xrightarrow{\;i\;} S \xleftarrow{\;o\;} Y .$$

*together with a reaction network* $R = (S, T, s, t, r)$ *on* $S$.

### Theorem ( Baez, P. )

*There is a category* `RxNet` *whose objects are finite sets and whose morphisms are isomorphism classes of open reaction networks.*

# Functors

A functor is a map between categories which respects composition and preserves identities.

Given categories $\mathcal{C}$ and $\mathcal{D}$, a functor

$$F\colon \mathcal{C} \to \mathcal{D}$$

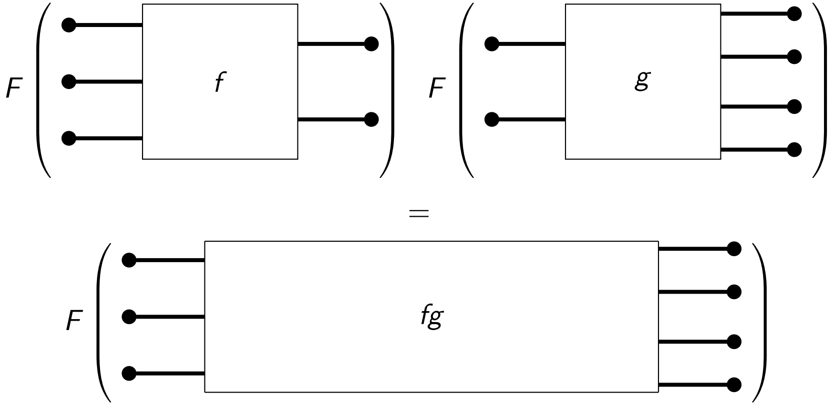
sends objects to objects and morphisms to morphisms such that:

$$F(fg) = F(f)F(g)$$

$$F(1_x) = 1_{F(x)}$$

# Functors for studying 'behaviors' of open systems

$$F\colon \texttt{OpenSys} \to \texttt{Behavior}$$



# What types of behaviors do we consider for these systems?

For my Oral, I discussed non-equilibrium steady states of open Markov processes using a variational principle.

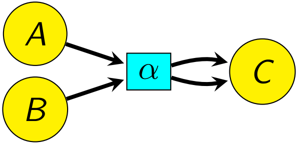
Not all non-equilibrium steady states of open Markov processes obey a variational principle.

Today I'll describe compositional approaches to capturing the dynamical and steady state behaviors of an arbitrary open reaction network without recourse to a variational principle.

# The rate equation

A reaction network with rates specifies a set of coupled, non-linear differential equations called its **rate equation**:

$$\begin{aligned} \frac{dA(t)}{dt} &= -r(\alpha)A(t)B(t) \\ \frac{dB(t)}{dt} &= -r(\alpha)A(t)B(t) \\ \frac{dC(t)}{dt} &= 2r(\alpha)A(t)B(t) \end{aligned}$$



# The rate equation

Given a reaction network with rates $R = (S, T, s, t, r)$, with species set $S = \{1, 2, \ldots, |S|\}$, let us denote a vector of **concentrations** of each species by $c = (c_1, c_2, \ldots, c_{|S|}) \in \mathbb{R}^S$. Concentrations are non-negative.

Introducing the notation

$$c^{s(\tau)} = \prod_{\sigma \in S} c_\sigma^{s_\sigma(\tau)},$$

we can write the rate equation of a general reaction network obeying mass-action kinetics as

$$\frac{dc}{dt} = \sum_{\tau \in T} r(\tau)\,(\ t(\tau) - s(\tau)\ )\, c^{s(\tau)}.$$

# The rate equation

Given a reaction network $R = (S, T, s, t, r)$, we can define a vector field

$$v(c) = \sum_{\tau \in T} r(\tau)\,(\ t(\tau) - s(\tau)\ )\,c^{s(\tau)}$$

generating the time evolution of the concentrations $c \in \mathbb{R}^S$ via

$$\frac{dc}{dt} = v(c).$$

For mass-action kinetics, the vector field $v \colon \mathbb{R}^S \to \mathbb{R}^S$ is polynomial in the concentrations.

# A category of open dynamical systems

## Definition

*An* **open dynamical system** $D \colon X \to Y$ *on* $S$ *consists of a cospan of finite sets*

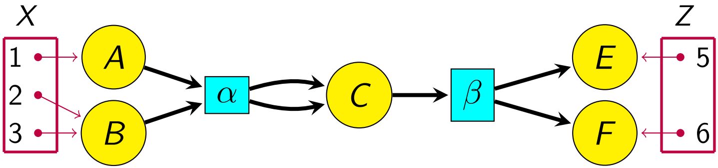
$$X \xrightarrow{i} S \xleftarrow{o} Y$$

*together with a polynomial vector field* $v$ *on* $\mathbb{R}^S$*.*

## Theorem (Baez, P.)

*There is a category* `Dynam` *where objects are finite sets and morphisms are isomorphism classes of open dynamical systems.*

# The gray-boxing functor

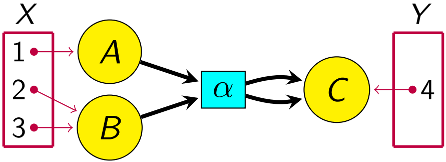



**Theorem (Baez, P.)**

*There is a functor* ■ : $\texttt{RxNet} \to \texttt{Dynam}$ *sending an open reaction network to its corresponding open dynamical system.*

# The gray-boxing functor

$\blacksquare(R\colon X \to Y)$



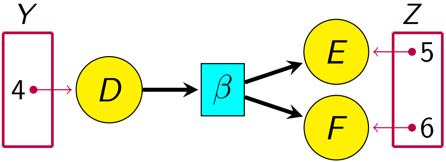

$$v_A = -r(\alpha)A(t)B(t)$$

$$v_B = -r(\alpha)A(t)B(t)$$

$$v_C = 2r(\alpha)A(t)B(t)$$

# The gray-boxing functor

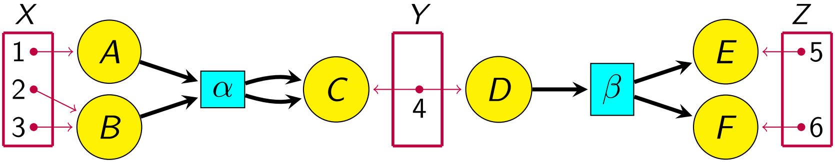
■$(R' \colon Y \to Z)$




$$
\begin{aligned}
v_D &= -r(\beta)D(t) \\
v_E &= r(\beta)D(t) \\
v_F &= r(\beta)D(t)
\end{aligned}
$$

# The gray-boxing functor

$\blacksquare(R\colon X \to Y)\blacksquare(R'\colon Y \to Z)$



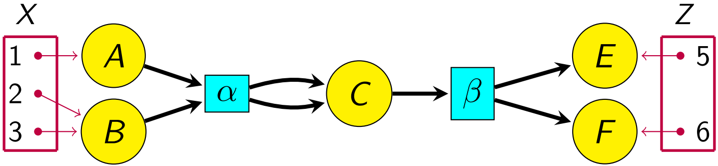

$$v_A = -r(\alpha)AB \qquad v_D = -r(\beta)D$$

$$v_B = -r(\alpha)AB \qquad v_E = r(\beta)D$$

$$v_C = 2r(\alpha)AB \qquad v_F = r(\beta)D$$

# The gray-boxing functor

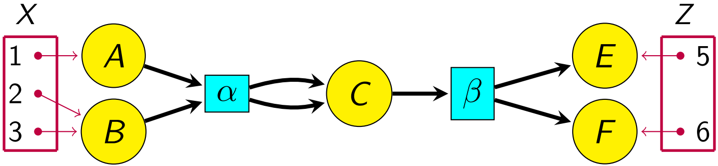
$\blacksquare(R\colon X \to Y)\blacksquare(R'\colon Y \to Z)$




$$
\begin{aligned}
v_A &= -r(\alpha)AB \\
v_B &= -r(\alpha)AB \\
v_C + v_D &= 2r(\alpha)AB - r(\beta)D \text{ and } C = D \\
v_E &= r(\beta)D \\
v_F &= r(\beta)D
\end{aligned}
$$

# The gray-boxing functor

$\blacksquare(RR' \colon X \to Z)$




$$v_A = -r(\alpha)AB$$

$$v_B = -r(\alpha)AB$$

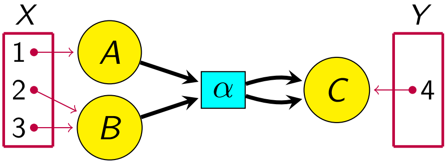
$$v_C = 2r(\alpha)AB - r(\beta)C$$

$$v_E = r(\beta)C$$

$$v_F = r(\beta)C$$

# The open rate equation

Let $I\colon \mathbb{R} \to \mathbb{R}^X$ and $O\colon \mathbb{R} \to \mathbb{R}^Y$ be arbitrary smooth functions of time specifying the **inflows** and **outflows**.




$$\frac{dA(t)}{dt} = -r(\alpha)A(t)B(t) + I_1(t)$$

$$\frac{dB(t)}{dt} = -r(\alpha)A(t)B(t) + I_2(t) + I_3(t)$$

$$\frac{dC(t)}{dt} = 2r(\alpha)A(t)B(t) - O_4(t)$$

# The open rate equation

Given an open dynamical system together with specified inflows $I \in \mathbb{R}^X$ and outflows $O \in \mathbb{R}^X$, we define the pushforward $i_* \colon \mathbb{R}^X \to \mathbb{R}^S$ by

$$i_*(I)_\sigma = \sum_{\{x : i(x) = \sigma\}} I_x$$

and define $o_* \colon \mathbb{R}^Y \to \mathbb{R}^S$ by

$$o_*(O)_\sigma = \sum_{\{y : o(y) = \sigma\}} O_y .$$

We can then write down the **open rate equation** as

$$\frac{dc(t)}{dt} = v(c(t)) + i_*(I(t)) - o_*(O(t)).$$

# Steady states

A **steady state** solution of the open rate equation is a concentration vector $c \in \mathbb{R}^S$ such that

$$\frac{dc}{dt} = 0.$$

From the open rate equation

$$\frac{dc}{dt} = v(c) + i_*(I) - o_*(O)$$

we see that this implies

$$v(c) = o_*(O) - i_*(I).$$

This imposes relations among the steady state concentrations and flows along the boundary.

# Semialgebraic relations

A **semialgebraic subspace** of a vector space is a one defined in terms of polynomials and inequalities.

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There is a category `SemiAlgRel` where objects are real vector spaces $V$ and morphisms are semialgebraic relations.

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There is a category `SemiAlgRel` where objects are real vector spaces $V$ and morphisms are semialgebraic relations.

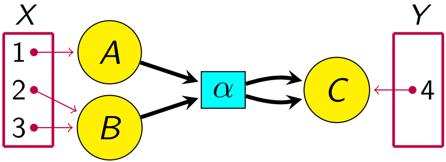
Composition of relations requires that they agree on their overlap.

Given semialgebraic relations $A\colon U \rightsquigarrow V$ and $B\colon V \rightsquigarrow W$, their composite $AB\colon U \rightsquigarrow W$ is given by

$$AB = \{(u, w)\colon \exists v \in V \text{ with } (u, v) \in A \text{ and } (v, w) \in B\}.$$

# Steady state behavior

We characterize the steady state behavior of an open reaction network in terms of the semialgebraic relation imposed between inputs and outputs.




$$\frac{dA(t)}{dt} = -r(\alpha)A(t)B(t) + I_1(t)$$

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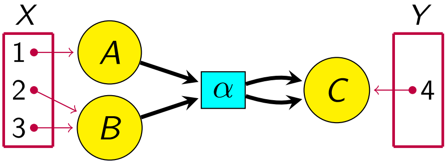
$$\frac{dC(t)}{dt} = 2r(\alpha)A(t)B(t) - O_4(t)$$

# Steady state behavior

$$c_X = (c_1, c_2, c_3) \in \mathbb{R}^3, \quad I_X = (I_1, I_2, I_3) \in \mathbb{R}^X$$

$$c_Y = c_4 \in \mathbb{R}^Y, \quad O_Y = O_4 \in \mathbb{R}^Y$$




$$(c_X, I_X, c_Y, O_Y) \subseteq \mathbb{R}^X \oplus \mathbb{R}^X \oplus \mathbb{R}^Y \oplus \mathbb{R}^Y$$

such that

$$I_1 = r(\alpha)AB$$

$$I_2 + I_3 = r(\alpha)AB$$

$$O_4 = 2r(\alpha)AB$$

# The black-box functor

**Theorem (Baez, P.)**

*There is a functor*

$$\blacksquare \colon \mathtt{Dynam} \to \mathtt{SemiAlgRel}$$

*sending an open dynamical system to the semialgebraic relation characterizing its steady state boundary concentrations and flows.*

# The black-box functor

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*sending an open dynamical system to the semialgebraic relation characterizing its steady state boundary concentrations and flows.*

## Theorem (Baez, P.)

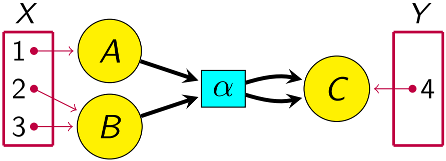
*Composing the gray-boxing and black-boxing functors gives a functor*

$$\mathtt{RxNet} \xrightarrow{\;{\color{gray}\blacksquare}\;} \mathtt{Dynam} \xrightarrow{\;\blacksquare\;} \mathtt{SemiAlgRel}$$

*sending an open reaction network to the subspace of possible steady state boundary concentrations and flows.*

# Black-boxing

$$\blacksquare(R \colon X \to Y)$$

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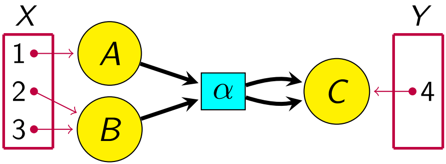
# Black-boxing

$$\blacksquare(\square(R))\colon \mathbb{R}^X \oplus \mathbb{R}^X \rightsquigarrow \mathbb{R}^Y \oplus \mathbb{R}^Y$$




$$(c_X, I_X, c_Y, O_Y)$$

such that

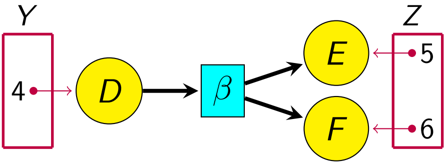
$$I_1 = r(\alpha)AB$$

$$I_2 + I_3 = r(\alpha)AB$$

$$O_4 = 2r(\alpha)AB$$

# The 'gray-boxing' functor

$\blacksquare(R' \colon Y \to Z)$



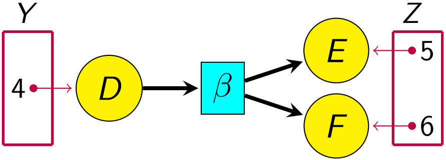

$$\frac{dD(t)}{dt} = -r(\beta)D(t) + I_4(t)$$

$$\frac{dE(t)}{dt} = r(\beta)D(t) - O_5(t)$$

$$\frac{dF(t)}{dt} = r(\beta)D(t) - O_6(t)$$

# Black-boxing

$$\blacksquare(\square(R')) \colon \mathbb{R}^Y \oplus \mathbb{R}^Y \rightsquigarrow \mathbb{R}^Z \oplus \mathbb{R}^Z$$




$$(c_Y, I_Y, c_Z, O_Z)$$

$$I_4 = r(\beta)D$$

$$O_5 = r(\beta)D$$

$$O_6 = r(\beta)D$$

# Composing relations

$$\blacksquare({\color{lightgray}\blacksquare}(R))\blacksquare({\color{lightgray}\blacksquare}(R'))$$

$$(c_X, I_X, c_Y, O_Y)(c_Y, I_Y, c_Z, O_Z)$$

$$\begin{array}{cc} I_1 = r(\alpha)AB & I_4 = r(\beta)D \\ I_2 + I_3 = r(\alpha)AB & O_5 = r(\beta)D \\ O_4 = 2r(\alpha)AB & O_6 = r(\beta)D \end{array}$$

# Composing relations

$$\blacksquare({\color{gray}\blacksquare}(R))\blacksquare({\color{gray}\blacksquare}(R'))$$

$$(c_X, I_X, c_Y, O_Y)(c_Y, I_Y, c_Z, O_Z)$$

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$$C = D$$

$$O_4 = I_4$$

# Composing relations

$$\blacksquare(\textcolor{gray}{\blacksquare}(R))\blacksquare(\textcolor{gray}{\blacksquare}(R'))$$

$$(c_X, I_X, c_Y, O_Y)(c_Y, I_Y, c_Z, O_Z)$$

$$\begin{array}{cc} I_1 = r(\alpha)AB & I_4 = r(\beta)D \\ I_2 + I_3 = r(\alpha)AB & O_5 = r(\beta)D \\ O_4 = 2r(\alpha)AB & O_6 = r(\beta)D \end{array}$$

$$C = D$$

$$2r(\alpha)AB = r(\beta)D$$

# Composing relations

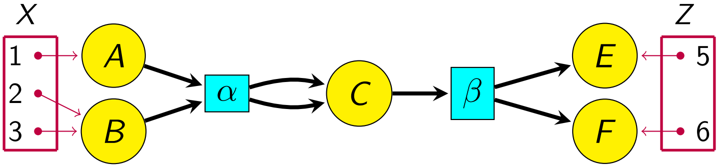
$$\blacksquare(\square(R))\blacksquare(\square(R')) \colon \mathbb{R}^X \oplus \mathbb{R}^X \rightsquigarrow \mathbb{R}^Z \oplus \mathbb{R}^Z$$

$$(c_X, I_X, c_Z, O_Z)$$

$$I_1 = r(\alpha)AB$$
$$I_2 + I_3 = r(\alpha)AB$$
$$2r(\alpha)AB = r(\beta)C$$
$$O_5 = r(\beta)C$$
$$O_6 = r(\beta)C.$$

# Black-boxing

$$\blacksquare(RR' \colon X \to Y)$$




$$\frac{dA}{dt} = -r(\alpha)AB + I_1$$

$$\frac{dB}{dt} = -r(\alpha)AB + I_2 + I_3$$

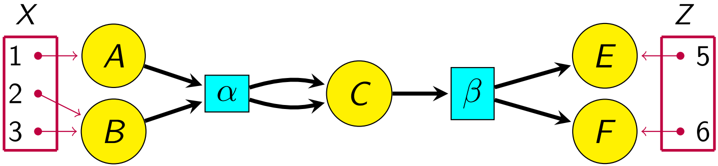
$$\frac{dC}{dt} = 2r(\alpha)AB - r(\beta)C$$

$$\frac{dE}{dt} = r(\beta)C - O_5$$

$$\frac{dF}{dt} = r(\beta)C - O_6$$

# Black-boxing

$$\blacksquare(\square(RR')) \colon \mathbb{R}^X \oplus \mathbb{R}^X \rightsquigarrow \mathbb{R}^Z \oplus \mathbb{R}^Z$$




$$I_1 = r(\alpha)AB$$

$$I_2 + I_3 = r(\alpha)AB$$

$$2r(\alpha)AB = r(\beta)C$$

$$O_5 = r(\beta)C$$

$$O_6 = r(\beta)C.$$

# Conclusions

The fact that black-boxing is accomplished via a functor means that one can compute the steady state behavior of a composite open reaction network by composing the semialgebraic relations characterizing the steady state behaviors of its constituent systems:

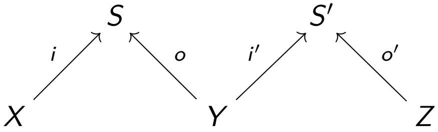
$$\blacksquare({\color{gray}\blacksquare}(R))\blacksquare({\color{gray}\blacksquare}(R')) = \blacksquare({\color{gray}\blacksquare}(RR'))$$

This provides a compositional approach to studying both the dynamical and steady state behaviors of open reaction networks.

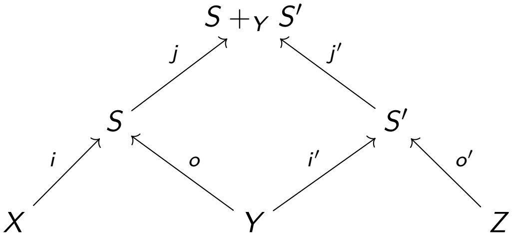
# Thank you!

# Composition in Dynam

Given open dynamical systems $D\colon X \to Y$ on $S$ and $D'\colon Y \to Z$ on $S'$




with vector fields $v\colon \mathbb{R}^S \to \mathbb{R}^S$ and $v'\colon \mathbb{R}^{S'} \to \mathbb{R}^{S'}$ to get an open dynamical system $DD'\colon X \to Z$ on $S +_Y S'$




we need to cook up a vector field $v''\colon \mathbb{R}^{S +_Y S'} \to \mathbb{R}^{S +_Y S'}$.

# Composition in $\mathtt{Dynam}$

To get a vector field $v'' \colon \mathbb{R}^{S+_Y S'} \to \mathbb{R}^{S+_Y S'}$, first take the inclusion map

$$[j, j'] \colon S + S' \to S +_Y S'$$

and define two maps, $[j, j']_* \colon \mathbb{R}^{S+S'} \to \mathbb{R}^{S+_Y S'}$ as

$$[j, j']_*(v + v')_\sigma = \sum_{\{\sigma' | [j,j'](\sigma') = \sigma\}} (v + v')_{\sigma'},$$

and $[j, j']^* \colon \mathbb{R}^{S+_Y S'} \to \mathbb{R}^{S+S'}$ as

$$[j, j']^*(c'') = c'' \circ [j, j']$$

with $c'' \in \mathbb{R}^{S+_Y S'}$. We can then define our vector field via the expression

$$v''(c'') = [j, j']_*(v + v')[j, j']^*(c'').$$