Open Markov processes and reaction networks

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Thesis Defense
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Compositional modeling of open systems

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

\[ \frac{dp}{dt} = Hp \]

\[ H = \begin{bmatrix} -9 & 0 & 7 \\ 9 & -2 & 5 \\ 0 & 2 & -12 \end{bmatrix} \]

\[ p(t) = \begin{bmatrix} A(t) \\ B(t) \\ C(t) \end{bmatrix} \]

\[ B \quad C \quad A \]

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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:

\[
\begin{align*}
\dot{A} &= -9A + 7C + I(t) \\
\dot{B} &= 9A - 2B + 5C \\
\dot{C} &= 2B - 12C - O(t)
\end{align*}
\]
Compositional modeling of open systems

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

\[
\begin{align*}
\dot{A} &= -9A + 7C + I(t) \\
\dot{B} &= 9A - 2B + 5C \\
\dot{C} &= 2B - 12C - O(t)
\end{align*}
\]

\[
\begin{align*}
\dot{C'} &= -7C' + 9D + I'(t) \\
\dot{D} &= 7C' - 9D - O'(t)
\end{align*}
\]
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:

\[
\begin{align*}
\dot{A} &= -9A + 7C + I(t) \\
\dot{B} &= 9A - 2B + 5C \\
\dot{C} &= 2B - 19C + 9D \\
\dot{D} &= 7C - 9D - O'(t)
\end{align*}
\]
Some Papers

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

- Blake S. Pollard, *Open Markov processes: A compositional perspective on non-equilibrium steady states in biology*, *Entropy*.
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 $f : X \to Y \ldots$

closed under an associative composition operation

\[
\begin{array}{ccc}
X & \xrightarrow{f} & Y \\
\downarrow{g} & & \downarrow{h} \\
Z & \xrightarrow{f \circ g} & A
\end{array}
\]

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

\[
\begin{array}{ccc}
X & \xrightarrow{1_X} & X \\
\downarrow{f} & & \downarrow{1_Y} \\
X & \xrightarrow{f} & Y
\end{array}
\]
Open systems as morphisms in a category

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

Composition corresponds to connecting systems.
Open systems as morphisms in a category

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

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 \(s, t : T \rightarrow \mathbb{N}^S\)
- A function \(r : T \rightarrow (0, \infty)\).

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 \(\tau : \kappa \rightarrow \kappa'\).
Open reaction networks are generalizations of reaction networks in which certain species are labelled as **input** and **output** species.

\[ R: X \rightarrow Y \]
Composition of open reaction networks

Consider another open reaction network $R'$: $Y \rightarrow Z$

![Diagram of the open reaction network $R'$: $Y \rightarrow Z$]
Composition of open reaction networks

To compose $R: X \rightarrow Y$ and $R': Y \rightarrow Z$ 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 $RR' : X \rightarrow Z$. 
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

\[
\begin{array}{ccc}
S & \xrightarrow{i} & X \\
\downarrow & & \downarrow \\
Y & \xleftarrow{o} & S
\end{array}
\]

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

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

For $\text{RxNet}$, this data is that of a reaction network with rates on $S$. 
The category of open reaction networks

Definition

An open reaction network $R : X \to Y$ consists of a cospan of finite sets $S$ together with a reaction network $R = (S, T, s, t, r)$ on $S$.

Theorem (Baez, P.)

There is a category $\text{RxNet}$ 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

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

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

\[ F : \text{OpenSys} \rightarrow \text{Behavior} \]

\[
\begin{pmatrix}
\begin{array}{ccc}
\text{\includegraphics{f.png}}
\end{array}
\end{pmatrix}
\]

\[
\begin{pmatrix}
\begin{array}{ccc}
\text{\includegraphics{g.png}}
\end{array}
\end{pmatrix}
\]

\[
= \begin{pmatrix}
\begin{array}{ccc}
\text{\includegraphics{fg.png}}
\end{array}
\end{pmatrix}
\]
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**:

\[
\frac{dA(t)}{dt} = -r(\alpha)A(t)B(t)
\]

\[
\frac{dB(t)}{dt} = -r(\alpha)A(t)B(t)
\]

\[
\frac{dC(t)}{dt} = 2r(\alpha)A(t)B(t)
\]
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

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

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

$$\frac{dc}{dt} = \sum_{\tau \in T} r(\tau) \left( t(\tau) - s(\tau) \right) c^s(\tau).$$
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 $v : \mathbb{R}^S \to \mathbb{R}^S$ is polynomial in the concentrations.
A category of open dynamical systems

**Definition**

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

\[ \begin{array}{ccc}
& S & \\
& i & \leftarrow & o & \\
X & & & Y
\end{array} \]

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

**Theorem (Baez, P.)**

*There is a category $\text{Dynam}$ 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 \( \Box : \text{RxNet} \rightarrow \text{Dynam} \) sending an open reaction network to its corresponding open dynamical system.
The gray-boxing functor

\( R : X \to Y \)

\[
\begin{align*}
v_A &= -r(\alpha)A(t)B(t) \\
v_B &= -r(\alpha)A(t)B(t) \\
v_C &= 2r(\alpha)A(t)B(t)
\end{align*}
\]
The gray-boxing functor

\[ (R': Y \rightarrow Z) \]

\[
\begin{align*}
  v_D &= -r(\beta)D(t) \\
  v_E &= r(\beta)D(t) \\
  v_F &= r(\beta)D(t)
\end{align*}
\]
The gray-boxing functor

\((R: X \rightarrow Y)(R': Y \rightarrow Z)\)

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

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

\(v_C = 2r(\alpha)AB\)

\(v_D = -r(\beta)D\)

\(v_E = r(\beta)D\)

\(v_F = r(\beta)D\)
The gray-boxing functor

\((R: X \to Y) \circ (R': Y \to Z)\)

\[ v_A = -r(\alpha)AB \]

\[ v_B = -r(\alpha)AB \]

\[ v_C + v_D = 2r(\alpha)AB - r(\beta)D \text{ and } C = D \]

\[ v_E = r(\beta)D \]

\[ v_F = r(\beta)D \]
The gray-boxing functor

\( (RR' : X \to Z) \)

\[\begin{align*}
\nu_A &= -r(\alpha)AB \\
\nu_B &= -r(\alpha)AB \\
\nu_C &= 2r(\alpha)AB - r(\beta)C \\
\nu_E &= r(\beta)C \\
\nu_F &= r(\beta)C
\end{align*}\]
The open rate equation

Let $I: \mathbb{R} \to \mathbb{R}^X$ and $O: \mathbb{R} \to \mathbb{R}^Y$ 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 $i_* : \mathbb{R}^X \to \mathbb{R}^S$ by

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

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

\[
\frac{dc}{dt} = v(c) + i_\ast(I) - o_\ast(O)
\]

we see that this implies

\[
v(c) = o_\ast(O) - i_\ast(I).
\]

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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A semialgebraic relation $A: U \rightsquigarrow V$ is a semialgebraic subspace $A \subseteq U \oplus V$. 
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There is a category $\text{SemiAlgRel}$ where objects are real vector spaces $V$ and morphisms are semialgebraic relations.
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Composition of relations requires that they agree on their overlap.
Semialgebraic relations

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A semialgebraic relation $A: U \leadsto V$ is a semialgebraic subspace $A \subseteq U \oplus V$.

There is a category $\text{SemiAlgRel}$ 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 $A: U \leadsto V$ and $B: V \leadsto W$, their composite $AB: U \leadsto W$ is given by

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

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

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

\[
\frac{dC(t)}{dt} = 2r(\alpha)A(t)B(t) - O_4(t)
\]
Steady state behavior

\[ c_X = (c_1, c_2, c_3) \in \mathbb{R}^3, \quad l_X = (l_1, l_2, l_3) \in \mathbb{R}^X \]

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

\[ (c_X, l_X, c_Y, O_Y) \subseteq \mathbb{R}^X \oplus \mathbb{R}^X \oplus \mathbb{R}^Y \oplus \mathbb{R}^Y \]

such that

\[ l_1 = r(\alpha)AB \]

\[ l_2 + l_3 = r(\alpha)AB \]

\[ O_4 = 2r(\alpha)AB \]
The black-box functor

Theorem (Baez, P.)

There is a functor

\[ \mathbb{B} : \text{Dynam} \rightarrow \text{SemiAlgRel} \]

sending an open dynamical system to the semialgebraic relation characterizing its steady state boundary concentrations and flows.
The black-box functor

**Theorem (Baez, P.)**

There is a functor

\[
\begin{array}{c}
\text{■} : \text{Dynam} \rightarrow \text{SemiAlgRel}
\end{array}
\]

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

\[
\begin{array}{c}
\text{RxNet} \rightarrow \text{Dynam} \rightarrow \text{SemiAlgRel}
\end{array}
\]

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

\[(R : X \rightarrow Y)\]

\[
\frac{dA(t)}{dt} = -r(\alpha)A(t)B(t) + l_1(t)
\]

\[
\frac{dB(t)}{dt} = -r(\alpha)A(t)B(t) + l_2(t) + l_3(t)
\]

\[
\frac{dC(t)}{dt} = 2r(\alpha)A(t)B(t) - O_4(t)
\]
Black-boxing

\[ \mathbb{B}(\mathbb{R}(R)) : R^X \oplus R^X \sim R^Y \oplus R^Y \]

![Diagram showing black-boxing concept]

such that

\[ (c_X, l_X, c_Y, O_Y) \]

\[ l_1 = r(\alpha)AB \]

\[ l_2 + l_3 = r(\alpha)AB \]

\[ O_4 = 2r(\alpha)AB \]
The ‘gray-boxing’ functor

\((R': Y \rightarrow Z)\)

\[
\frac{dD(t)}{dt} = -r(\beta)D(t) + l_4(t)
\]

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

\[
\frac{dF(t)}{dt} = r(\beta)D(t) - O_6(t)
\]
Black-boxing

\[ \mathbf{\mathcal{M}(\mathcal{M}(R'))}: \mathbb{R}^Y \oplus \mathbb{R}^Y \leadsto \mathbb{R}^Z \oplus \mathbb{R}^Z \]

\[ I_4 = r(\beta)D \]

\[ O_5 = r(\beta)D \]

\[ O_6 = r(\beta)D \]
Composing relations

\[ \square((R)) \square((R')) \]

\[(c_X, l_X, c_Y, O_Y)(c_Y, l_Y, c_Z, O_Z)\]

\[ l_1 = r(\alpha)AB \quad l_4 = r(\beta)D \]
\[ l_2 + l_3 = r(\alpha)AB \quad O_5 = r(\beta)D \]
\[ O_4 = 2r(\alpha)AB \quad O_6 = r(\beta)D \]
Composing relations

\[ \text{■}(\text{■}(R))\text{■}(\text{■}(R')) \]

\[(c_X, l_X, c_Y, O_Y)(c_Y, l_Y, c_Z, O_Z)\]

\[l_1 = r(\alpha)AB \quad l_4 = r(\beta)D\]

\[l_2 + l_3 = r(\alpha)AB \quad O_5 = r(\beta)D\]

\[O_4 = 2r(\alpha)AB \quad O_6 = r(\beta)D\]

\[C = D\]

\[O_4 = l_4\]
Composing relations

\[ (c_X, l_X, c_Y, O_Y)(c_Y, l_Y, c_Z, O_Z) \]

\[ l_1 = r(\alpha)AB \quad l_4 = r(\beta)D \]
\[ l_2 + l_3 = r(\alpha)AB \quad O_5 = r(\beta)D \]
\[ O_4 = 2r(\alpha)AB \quad O_6 = r(\beta)D \]

\[ C = D \]
\[ 2r(\alpha)AB = r(\beta)D \]
Composing relations

\[ \mathbf{R} \oplus \mathbf{R} \Rightarrow \mathbf{R} \oplus \mathbf{R} \]

\[ (c_x, l_x, c_z, O_Z) \]

\[ l_1 = r(\alpha)AB \]
\[ l_2 + l_3 = r(\alpha)AB \]
\[ 2r(\alpha)AB = r(\beta)C \]
\[ O_5 = r(\beta)C \]
\[ O_6 = r(\beta)C. \]
Black-boxing

\[(RR': X \rightarrow Y)\]

\[
\begin{align*}
\frac{dA}{dt} &= -r(\alpha)AB + l_1 \\
\frac{dB}{dt} &= -r(\alpha)AB + l_2 + l_3 \\
\frac{dC}{dt} &= 2r(\alpha)AB - r(\beta)C \\
\frac{dE}{dt} &= r(\beta)C - O_5 \\
\frac{dF}{dt} &= r(\beta)C - O_6
\end{align*}
\]
\[ (R R') : \mathbb{R}^X \oplus \mathbb{R}^X \sim \mathbb{R}^Z \oplus \mathbb{R}^Z \]

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

\[ \Box(\Box(R))\Box(\Box(R')) = \Box(\Box(RR')) \]

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 $D: X \rightarrow Y$ on $S$ and $D': Y \rightarrow Z$ on $S'$

\[
\begin{array}{c}
S \\
\uparrow i \\
X \\
| \\
\uparrow o \\
Y \\
| \\
\uparrow i' \\
S' \\
\downarrow o' \\
Z
\end{array}
\]

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

\[
\begin{array}{c}
S +_Y S' \\
\uparrow j \\
S \\
| \\
\uparrow o \\
Y \\
| \\
\uparrow i' \\
S' \\
\downarrow o' \\
Z
\end{array}
\]

we need to cook up a vector field $v'': \mathbb{R}^{S+_YS'} \rightarrow \mathbb{R}^{S+_YS'}$. 
Composition in Dynam

To get a vector field $v'' : \mathbb{R}^{S+\gamma S'} \rightarrow \mathbb{R}^{S+\gamma S'}$, first take the inclusion map

$$[j, j'] : S + S' \rightarrow S + \gamma S'$$

and define two maps, $[j, j']_* : \mathbb{R}^{S+S'} \rightarrow \mathbb{R}^{S+\gamma S'}$ as

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

and $[j, j']^* : \mathbb{R}^{S+\gamma S'} \rightarrow \mathbb{R}^{S+S'}$ as

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

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

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