Causal models for dynamical systems

Jonas Peters
University of Copenhagen, Denmark
jonas.peters@math.ku.dk

Stefan Bauer
MPI Tübingen, Germany
stefan.bauer@tuebingen.mpg.de

Niklas Pfister
University of Copenhagen, Denmark
np@math.ku.dk

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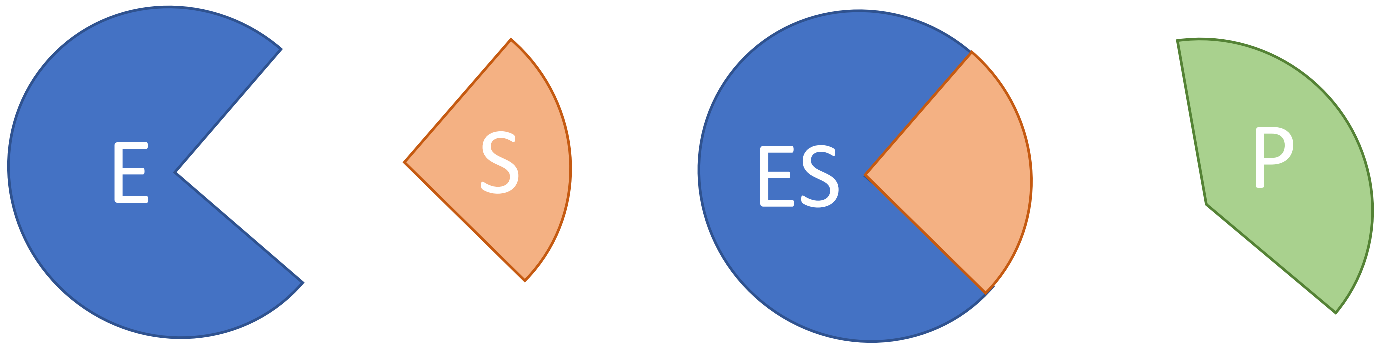
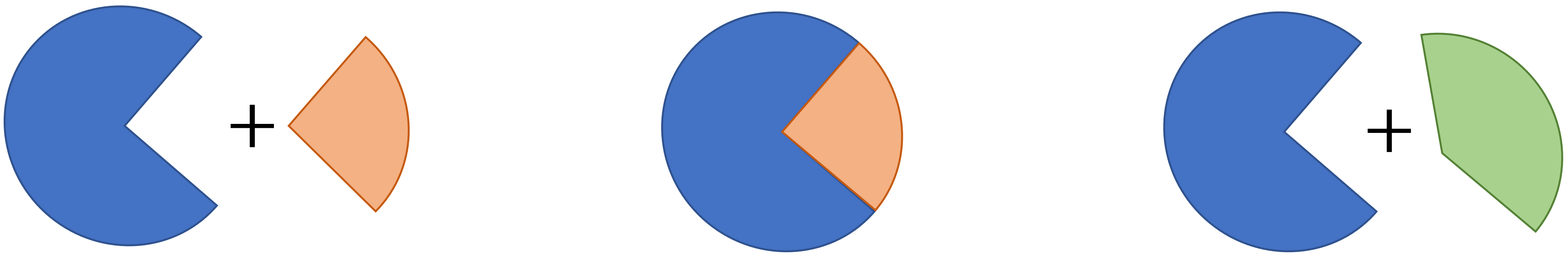
Presented by Vincent Hu

Dynamical Systems

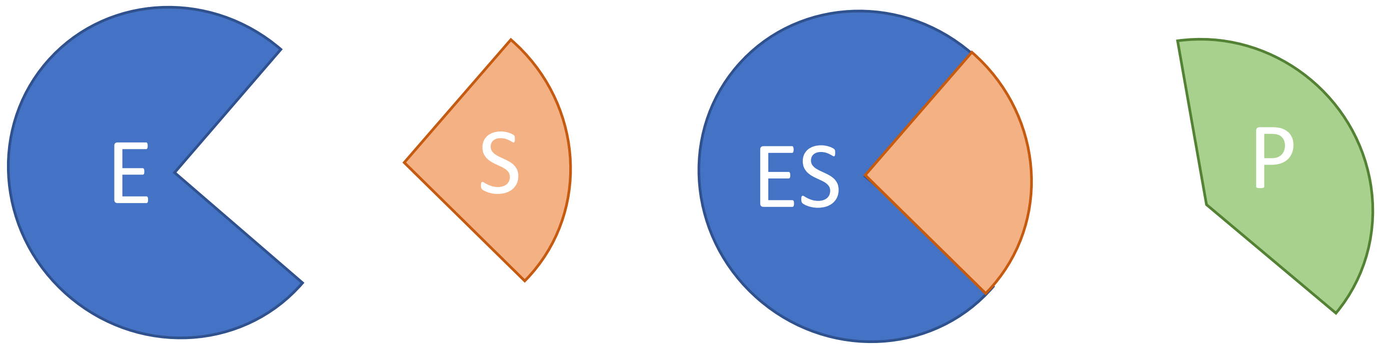
Say we want to model protein activity

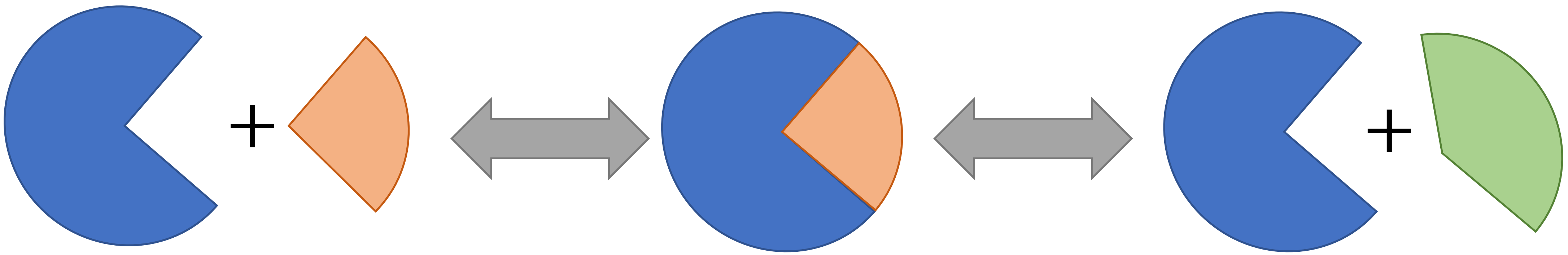




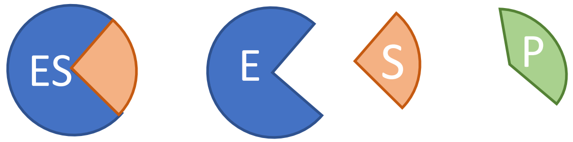
Dynamical Systems

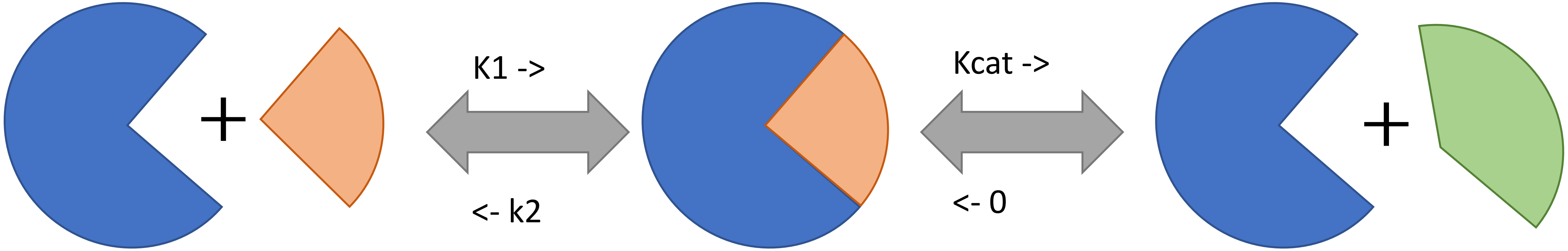
Say we want to model protein activity





Dynamical Systems





From this, we could try to derive a model as follows:

$$E + S \xrightarrow{k_1} ES$$

$$ES \xrightarrow{k_2} E + S$$

$$ES \xrightarrow{k_3} E + P$$

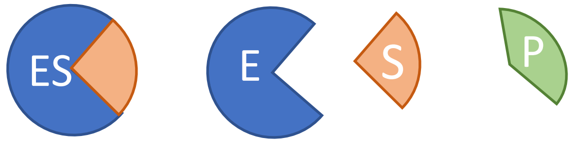
$$\frac{d}{dt}[S] = -k_1[S][E] + k_2[ES]$$

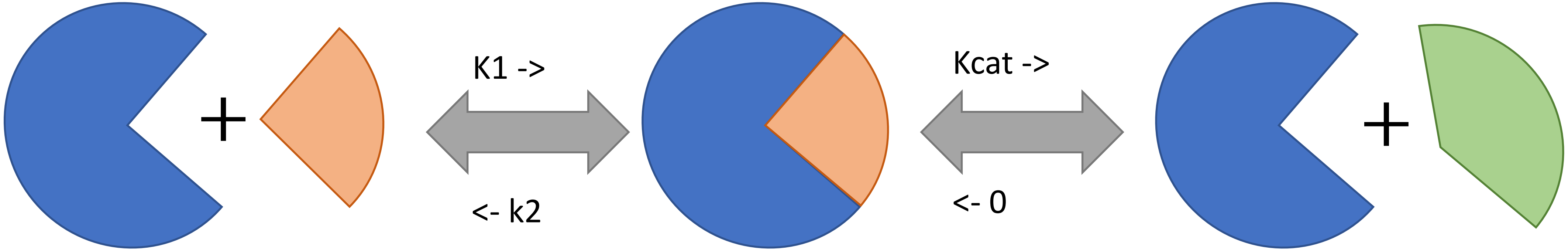
$$\frac{d}{dt}[E] = -k_1[S][E] + k_2[ES] + k_3[ES]$$

$$\frac{d}{dt}[P] = k_3[ES]$$

$$\frac{d}{dt}[ES] = k_1[S][E] - k_2[ES] - k_3[ES]$$

Dynamical Systems



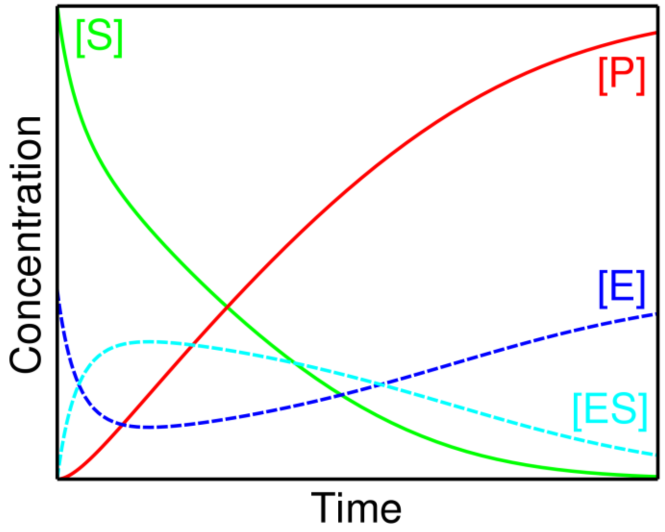


From this model, we can derive from initial conditions a continuous time prediction of the evolution of the system:

$$\frac{d}{dt}[S] = -k_1[S][E] + k_2[ES]$$
$$\frac{d}{dt}[E] = -k_1[S][E] + k_2[ES] + k_3[ES]$$
$$\frac{d}{dt}[P] = k_3[ES]$$
$$\frac{d}{dt}[ES] = k_1[S][E] - k_2[ES] - k_3[ES]$$

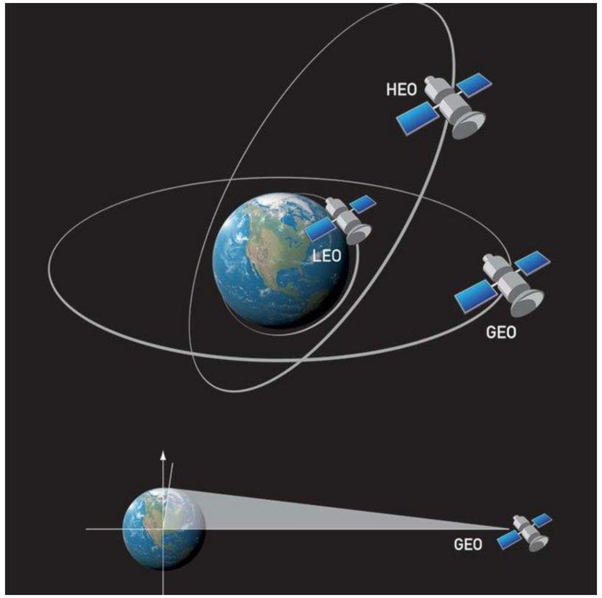
+

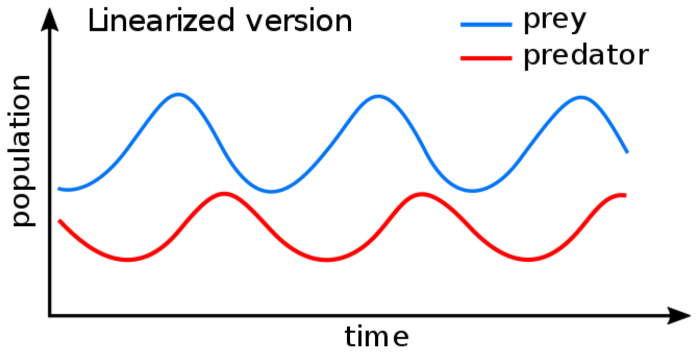
$$[S](t=0) = 10mM$$
$$[E](t=0) = 1\,nM$$
$$[P](t=0) = 0mM$$
$$[ES](t=0) = 0mM$$



Dynamical Systems

- A dynamical system is a model of an evolving system over some value





Deterministic Causal Kinetic Models

- A deterministic causal kinetic model is a tuple (X_t, G, F) where
  - X_t is a set of objects $\{x_t^1, \dots x_t^d\}$
  - G is a graph with nodes of elements of X_t
  - F is a collection of d ODEs and initial value assignments

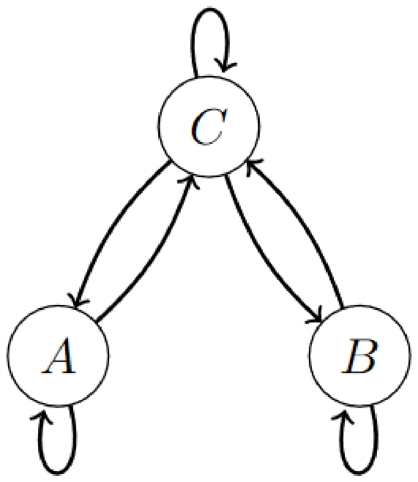
$$
\begin{aligned}
\frac{\mathrm{d}}{\mathrm{d}t} x_t^1 &:= f^1(x_t^{\mathbf{PA}_1}), & x_0^1 &:= \xi_0^1, \\
\frac{\mathrm{d}}{\mathrm{d}t} x_t^2 &:= f^2(x_t^{\mathbf{PA}_2}), & x_0^2 &:= \xi_0^2, \\
&\vdots \\
\frac{\mathrm{d}}{\mathrm{d}t} x_t^d &:= f^d(x_t^{\mathbf{PA}_d}), & x_0^d &:= \xi_0^d.
\end{aligned}
$$

Deterministic Causal Kinetic Models

ODE representations

$$A \xrightarrow{k_1} 2A$$
$$B \xrightarrow{k_2} 2B$$
$$A + C \xrightarrow{k_3} 2C$$
$$B + C \xrightarrow{k_4} 2C$$
$$C \xrightarrow{k_5} \varnothing$$

$$\frac{\mathrm{d}}{\mathrm{dt}}[A] = k_1[A] - k_3[A][C]$$
$$\frac{\mathrm{d}}{\mathrm{dt}}[B] = k_2[B] - k_4[B][C]$$
$$\frac{\mathrm{d}}{\mathrm{dt}}[C] = k_3[A][C] + k_4[B][C] - k_5[C]$$



- Given a deterministic causal kinetic model, we can model the observation of the causal model as noisy observations
  - $X_t = x_t + \epsilon_t$

Stochastic Causal Kinetic Models

- What if the evolution of objects is stochastic in nature?
  - Use Stochastic differential equation

$$\mathrm{d}X_t^k := f^k(X_t^{\mathbf{PA}_k})\mathrm{d}t + h^k(X_t^{\mathbf{PA}_k})\mathrm{d}W_t^k, \qquad X_0^k := \xi_0^k,$$

- W_t is a Wiener process which has the following properties
  - $W_0 = 0$
  - $W_{t+u} - W_t \perp W_s \; for \; s < t$
  - $W_{t+u} - W_t \sim N(0, u)$
  - W_t is continuous in t

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Interventions on Causal Kinetic Models

- What do interventions look like?

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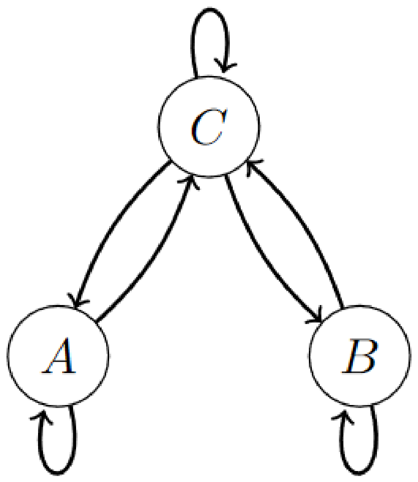

Interventions on Causal Kinetic Models

- We can replace initial values, or dynamics $x_0^k := \xi$ or $\frac{\mathrm{d}}{\mathrm{d}t} x_t^k := g(x_t^{\mathbf{PA}})$,

ODE representations

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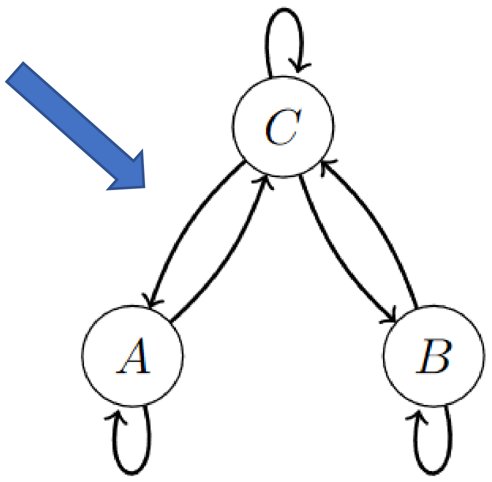


Interventions on Causal Kinetic Models

- We can change initial values, or dynamics

$$x_0^k := \xi \quad \text{or} \quad \frac{\mathrm{d}}{\mathrm{d}t} x_t^k := g(x_t^{\mathbf{PA}}),$$

- An intervention on initial conditions: $do\left(x_0^k \ := c\right)$
- An intervention on dynamics: $do\left(\frac{d}{dt} x_t^k \ := g^k\left(x_t^{PA_k}\right)\right)$

Interventions example - Lotka-Volterra model

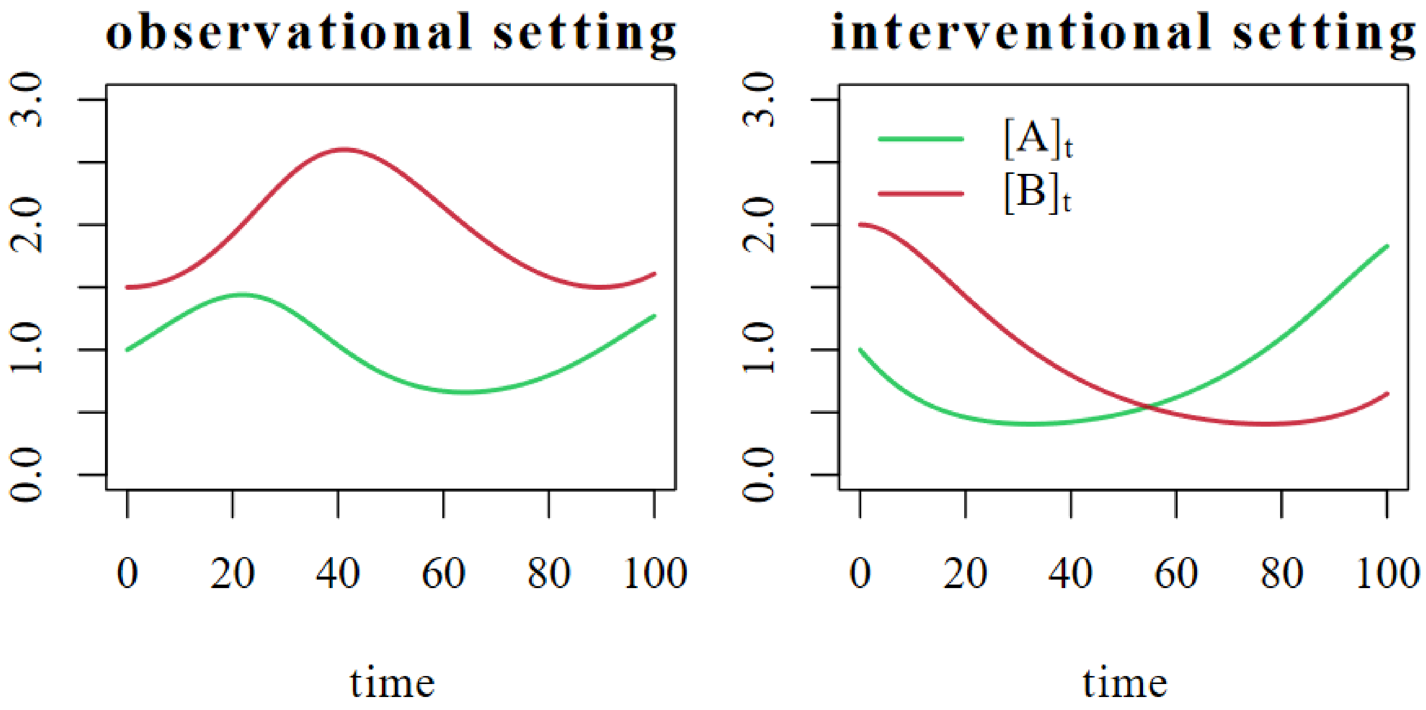
$$A \xrightarrow{k_1} 2A$$

$$A + B \xrightarrow{k_2} 2B$$

$$B \xrightarrow{k_3} \emptyset,$$

$$\frac{\mathrm{d}}{\mathrm{d}t}[A] = k_1[A] - k_2[A][B]$$

$$\frac{\mathrm{d}}{\mathrm{d}t}[B] = k_2[A][B] - k_3[B].$$



Intervention $k_1 = 1, [B]_0 = 2$

Challenges of Causal Kinetic Models

- Adjustments, do-calculus, effect of hidden variables, casual discovery are all open questions
- Systems of ODEs are harder to solve than simple algebraic equations
- Regression/Fitting on kinetic models is more involved
- It is unclear if conditional independence is the right notion for exploring graph properties

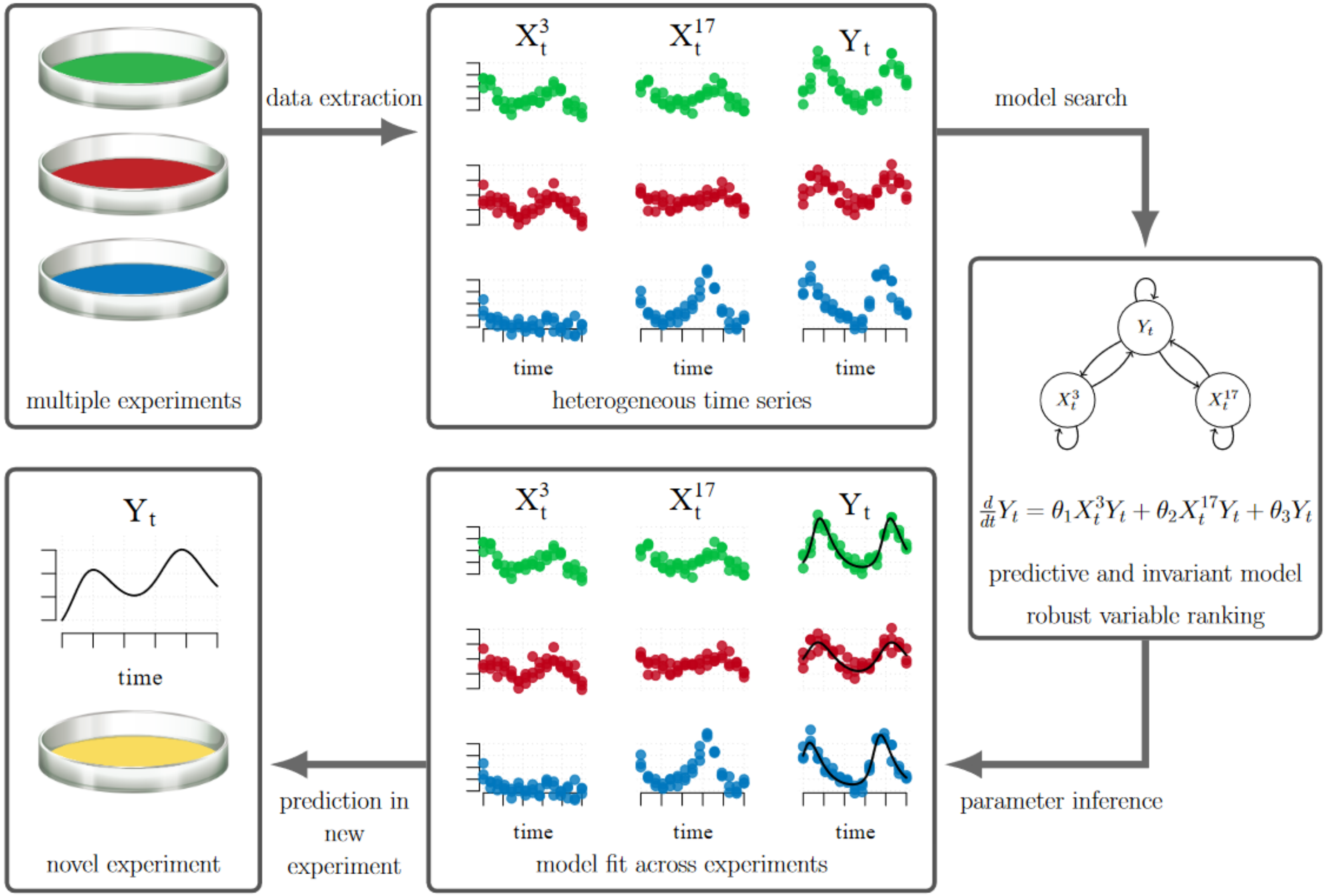
Structure Leaning on kinetic systems

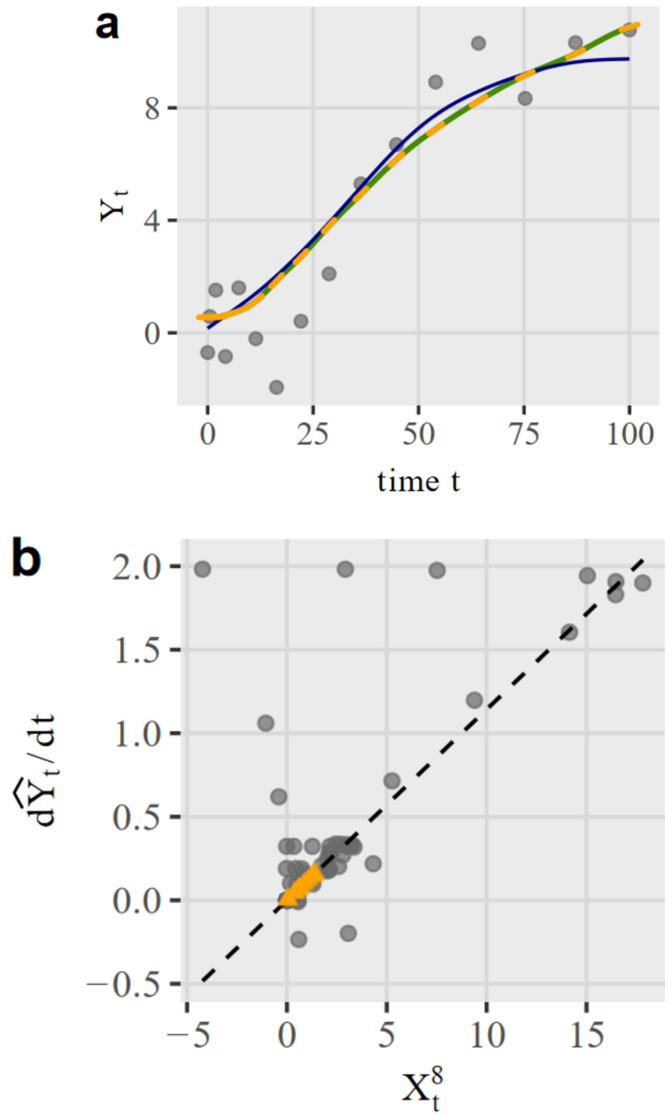
- Detailed in another publication

Learning stable and predictive structures in kinetic systems: Benefits of a causal approach

- Two concepts: Predictability and stability
  - Stability: How do parameters vary throughout the experiments?
  - Predictability: How well can you predict the data you have?

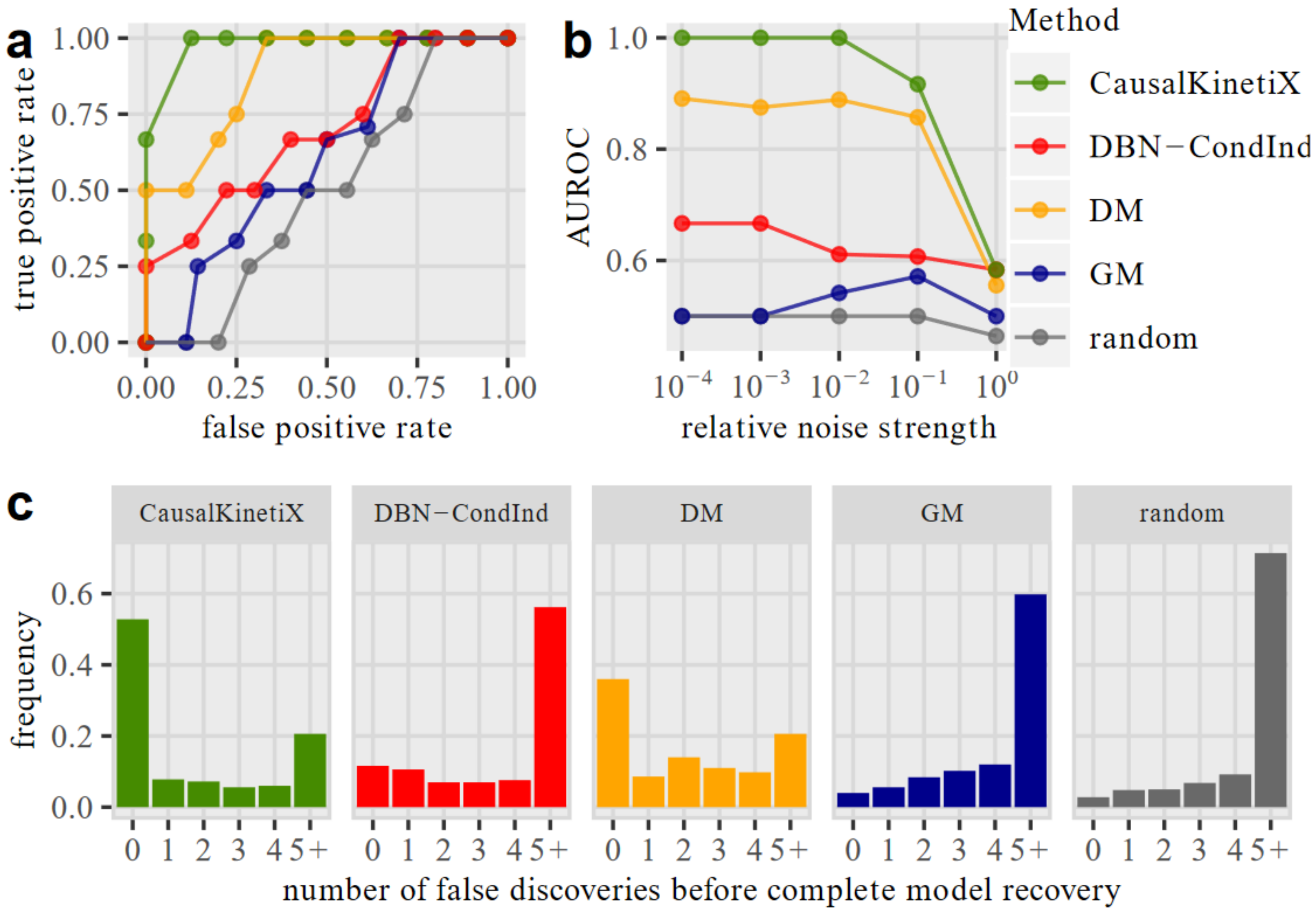
Structure Leaning on kinetic systems





Structure Leaning on kinetic systems

$$\dot{Y}_t = \theta_1 Z_t X_t^j X_t^k + \theta_2 Z_t X_t^p X_t^q - \theta_3 Y_t X_t^r X_t^s$$
$$\dot{Z}_t = -\theta_1 Z_t X_t^j X_t^k - \theta_2 Z_t X_t^p X_t^q + \theta_3 Y_t X_t^r X_t^s,$$



Conclusions

- Authors extend the formulation of causal models to kinetic models
- Open questions exist on many parts of causal inference
- Structure learning has some preliminary work and algorithms