# Filtered Markovian Projection: Dimensionality Reduction in Filtering for Stochastic Reaction Networks

**Chiheb Ben Hammouda**

Utrecht University

Maksim Chupin

King Abdullah University of Science and Technology

Sophia Münker

UQ | RWTH AACHEN UNIVERSITY

Raúl Tempone

King Abdullah University of Science and Technology

UQ | RWTH AACHEN UNIVERSITY

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# Stochastic Reaction Networks (SRNs): Motivation

**Aim**: Model the time evolution of populations (molecules, species, agents, cells, ...) connected through reaction networks.

**Illustration**:

Reaction Network involving molecules/Species/Agents: A and B

$$A \xrightarrow{\theta_1} B$$

$$B \xrightarrow{\theta_2} A$$

$$A \xrightarrow{\theta_3} \emptyset$$

$$\begin{pmatrix} x_1 \\ x_2 \end{pmatrix} \begin{matrix} \#\ \textit{type } A \\ \#\ \textit{type } B \end{matrix}$$

$$\begin{matrix} \begin{pmatrix} 0 \\ 0 \end{pmatrix} & \begin{pmatrix} 1 \\ 0 \end{pmatrix} & \begin{pmatrix} 2 \\ 0 \end{pmatrix} & \cdots \\ \begin{pmatrix} 0 \\ 1 \end{pmatrix} & \begin{pmatrix} 1 \\ 1 \end{pmatrix} & \begin{pmatrix} 2 \\ 1 \end{pmatrix} & \cdots \\ \begin{pmatrix} 0 \\ 2 \end{pmatrix} & \begin{pmatrix} 1 \\ 2 \end{pmatrix} & \begin{pmatrix} 2 \\ 2 \end{pmatrix} & \cdots \\ \vdots & \vdots & \vdots & \ddots \end{matrix}$$

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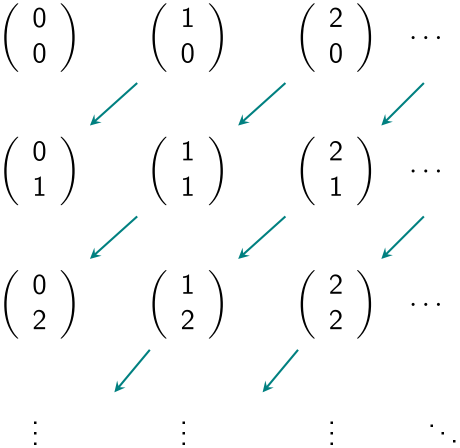

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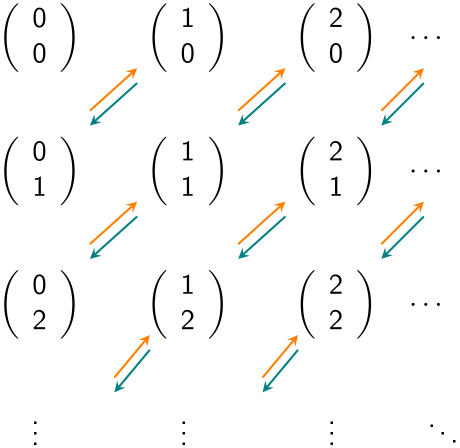

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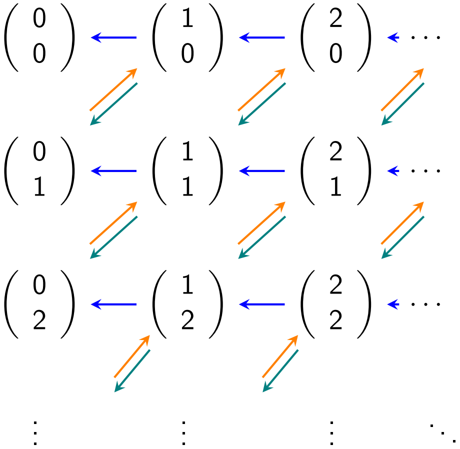

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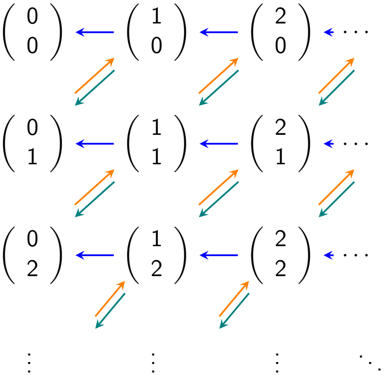


⚠ For $d$ number of molecule types/species/agents $\Rightarrow$ **state space: $\mathbb{N}^{\mathbf{d}}$**

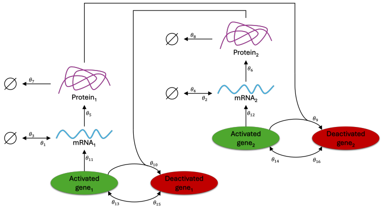
# Motivation: Dimensionality Reduction

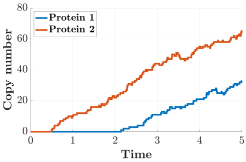
- **Challenge**: Numerical solutions for problems modeled by Stochastic Reaction Networks (SRNs) (particular type of Markov chains) often suffer from the curse of dimensionality
  - Forward Kolmogorov / Chemical Master Equations (time evolution of the joint (full) probability distribution over the possible states of the system).
  - Stochastic Filtering (i.e., estimate the conditional probability distribution of unobserved states for partially observed systems).
  - Stochastic Optimal Control.

# Motivation: Dimensionality Reduction

- **Challenge**: Numerical solutions for problems (e.g., Chemical Master Equations, Stochastic Filtering, Stochastic Optimal Control) modeled by SRNs often suffer from the curse of dimensionality.
- **Observation**: Quantities of interest often do not depend on the full-dimensional state (e.g., $\mathbb{E}[g(\mathbf{X}(\mathbf{t}))]$ with $g(\boldsymbol{x}) = \mathbb{1}_{\{x_i > \gamma\}}$).

Example: Bistable Gene Switch Network




Observed trajectory of Protein$_1$ and Protein$_2$.

We are interested in the distribution of the (hidden) mRNA$_2$ copy number.

# Motivation: Dimensionality Reduction

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- ⚠ Quantities of interest often do not depend on the full-dimensional state

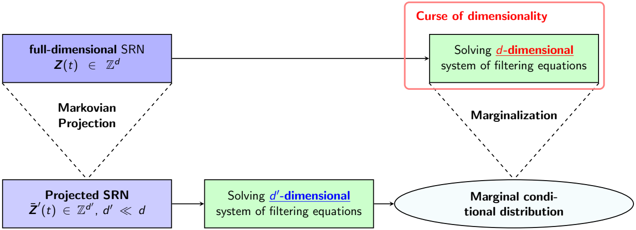
  $\Rightarrow$ **Solution**:

  1. construct a low dimensional Markovian process that mimics the evolution of the projected process (preserve the marginal distribution of the original process)
  2. $\Rightarrow$ Solve the resulting reduced-dimensional problem.

# Related Work

C. Ben Hammouda, M. Chupin, S Münker, and R Tempone. "Filtered Markovian Projection: Dimensionality Reduction in Filtering for Stochastic Reaction Networks". In: *arXiv preprint arXiv:2502.07918* (2025)

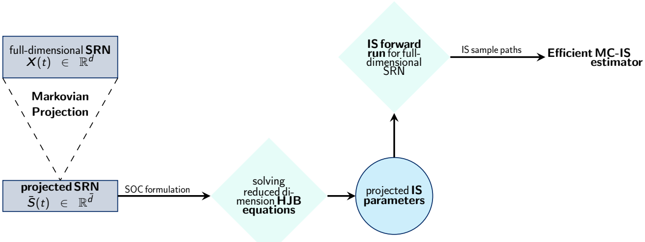
1. **Inverse Problem**: Design efficient finite-dimensional stochastic filters to estimate the conditional probability distribution of unobserved (hidden) state variables given partial observation trajectories.
   - Approach based on solving the system of filtering equations (an infinite-dimensional system of coupled ODEs with jumps) in a projected low-dimensional space via Markovian projection.



# Related Work

C. Ben Hammouda, N. Ben Rached, R. Tempone, and S. Wiechert. "Automated importance sampling via optimal control for stochastic reaction networks: A Markovian projection–based approach". In: *Journal of Computational and Applied Mathematics* 446 (2024), p. 115853

2. **Forward Problem**: Design efficient Monte Carlo (MC) estimators for rare event probabilities via a generic path dependent measure change (importance sampling).

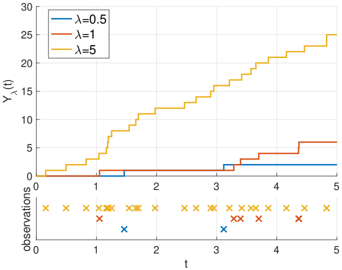


# Stochastic Reaction Networks (SRNs): Motivation

**Aim**: Model the evolution of populations connected through networks.

- Deterministic models (based on ODEs) capture the macroscopic behavior and are only valid for large populations.
- Presence of species/agents with small population sizes introduces stochastic effects (Elowitz et al. 2002; Raj et al. 2006; Erban et al. 2020)

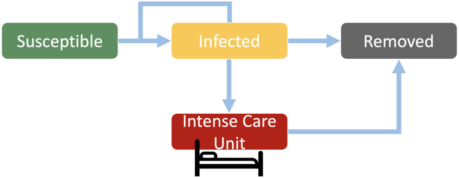
$\Rightarrow$ SRNs: continuous-time, discrete-space Markov chains driven by Poisson processes.

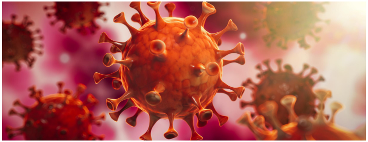



- Realizations of $Y_\lambda(t) \sim \text{Poisson}(\lambda t)$.
- For $0 < s < t$: $\mathbb{P}(Y_\lambda(t) - Y_\lambda(s) = k) = \frac{(\lambda(t-s))^k}{k!} e^{-\lambda(t-s)}$
- Observations given as crosses (correspond to a jump).
- Inter arrival time of $Y_\lambda$ is exponentially distributed with parameter $\lambda > 0$.

# Stochastic Reaction Networks (SRNs): Applications

1. Epidemiological networks (Brauer et al. 2012; Anderson et al. 2015).



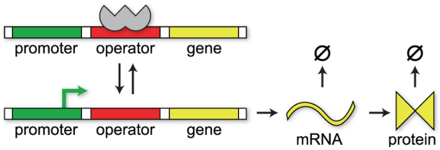



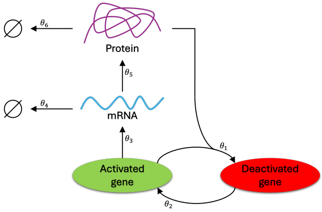
Example: SIR Model for epidemics. Removed means either recovered or dead

$$S + I \xrightarrow{k_1} I; \quad I \xrightarrow{k_2} R; \quad I \xrightarrow{k_3} IC; \quad IC \xrightarrow{k_4} R$$

# Stochastic Reaction Networks (SRNs): Applications

1. Epidemiological networks (Brauer et al. 2012; Anderson et al. 2015).
2. Transcription and translation in genomics and virus Kinetics (Peccoud et al. 1995; Hensel et al. 2009; Roberts et al. 2011)

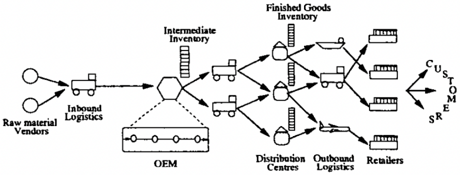



Example: Simple genetic switch (regulation)

# Stochastic Reaction Networks (SRNs): Applications

1. Epidemiological networks (Brauer et al. 2012; Anderson et al. 2015).
2. Transcription and translation in genomics and virus Kinetics (Peccoud et al. 1995; Hensel et al. 2009; Roberts et al. 2011)
3. Manufacturing supply chain, logistic/social/ecological networks, (Raghavan et al. 2002; Goutsias et al. 2013; Chiang et al. 2020)




Example:
Supply chain network

# Stochastic Reaction Networks (SRNs): Applications

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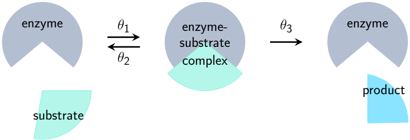
3. Manufacturing supply chain, logistic/social/ecological networks, (Raghavan et al. 2002; Goutsias et al. 2013; Chiang et al. 2020)
4. (Bio)chemical reactions (Rao et al. 2003; Briat et al. 2015),...




Example: Michaelis-Menten enzym kinetics

# Stochastic Reaction Networks: Mathematical Formulation

Consider a reaction network consisting of $d$ species/agents $S_1, \ldots, S_d$ and $J$ reaction channels:

$$\nu_{1j}^{-} S_1 + \cdots + \nu_{dj}^{-} S_d \xrightarrow{\theta_j} \nu_{1j}^{+} S_1 + \cdots + \nu_{dj}^{+} S_d, \quad \text{for } j = 1, \ldots, J.$$

- A stochastic reaction network is a continuous-time discrete-space Markov chain, $\mathbf{X}(t)$, defined on a probability space $(\Omega, \mathcal{F}, \mathbb{P})$

$$\mathbf{X}(t) = (X^{(1)}(t), \ldots, X^{(d)}(t)) : [0, T] \times \Omega \to \mathbb{N}^d$$

  - $X^{(i)}(t)$ models the counting number of the $i$-th agent/species at time $t$.
  - The dynamics of $\mathbf{X}$ is characterized by $(\boldsymbol{\nu}_j, a_j)_{j=1}^{J}$, where
    - $\boldsymbol{\nu}_j := \left(\nu_{1j}^{+} - \nu_{1j}^{-}, \ldots, \nu_{dj}^{+} - \nu_{dj}^{-}\right)^{\top} \in \mathbb{Z}^d$: stoichiometric (state change) vector.
    - $a_j : \mathbb{N}^d \to \mathbb{R}_+$: propensity (jump intensity) function

$$\mathbb{P}\left(\mathbf{X}(t + \Delta t) = \mathbf{x} + \boldsymbol{\nu}_j \,\middle|\, \mathbf{X}(t) = \mathbf{x}\right) = a_j(\mathbf{x})\Delta t + o\left(\Delta t\right)$$

# Stochastic Reaction Networks (SRNs): Mathematical Formulation

A reaction network consisting of $d$ species/agents $S_1, \dots, S_d$ and $J$ reaction channels:

$$\nu_{1j}^- S_1 + \cdots + \nu_{dj}^- S_d \xrightarrow{\theta_j} \nu_{1j}^+ S_1 + \cdots + \nu_{dj}^+ S_d, \quad \text{for } j = 1, \dots, J.$$

- From the *mass-action kinetic principle*:

$$a_j(\boldsymbol{x}) := \theta_j \underbrace{\prod_{i=1}^{d} \frac{x_i!}{(x_i - \nu_{ij}^-)!} 1_{\{x_i \geq \nu_{ij}^-\}}}_{\substack{\#\text{combinations of molecules} \\ \text{required for reaction } j}},$$

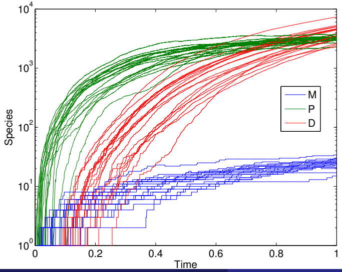
with $\theta_j$: reaction rate of the $j$th reaction.

# Dynamics of SRNs

- Kurtz's random time-change representation (Ethier et al. 2009)

$$\mathbf{X}(t) = \mathbf{X}(0) + \sum_{j=1}^{J} \underbrace{Y_j\left(\int_0^t a_j(\mathbf{X}(s))ds\right)}_{:=R_j(t)} \cdot \boldsymbol{\nu}_j, \qquad (1)$$

  - $\boldsymbol{X}(0) \sim \mu$ is the initial state
  - $\{Y_j\}_{1\leq j\leq J}$: independent unit-rate Poisson processes.
  - $R_j(t)$: number of occurrences of the $j$th reaction up to time $t$.




20 exact i.i.d. paths of $X = (M, P, D)$: counts the number of particles of each species in a problem from genomics.

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  - $\boldsymbol{X}(0) \sim \mu$ is the initial state.
  - $\{Y_j\}_{1\leq j\leq J}$: independent unit-rate Poisson processes.
  - $R_j(t)$: number of occurrences of the $j$th reaction up to time $t$.

- **Non-explosivity Assumption**: Condition (A.1) ensures that the system state will almost surely not grow to infinity in a finite time interval $[0, T]$.

$$\sup_{s\in[0,T]} \sum_{j=1}^{J} \mathbb{E}\left[a_j^2(\boldsymbol{X}(s))\right] < \infty, \quad \forall T > 0 \qquad (A.1)$$

# Motivation

A typical challenge arising in practical problems modeled by SRNs: a few state variables can be dynamically observed $\Rightarrow$ Partially observed SRNs.

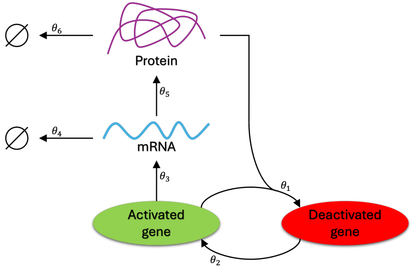



Figure: Gene Switch Network Example (Duso et al. 2018)

- In a real experiment, one can only measure the amount of fluorescent protein.
- All other hidden dynamic states of pivotal interest remain unknown, e.g.,
  - the number of mRNA molecules
  - the state of the gene (on/ off)

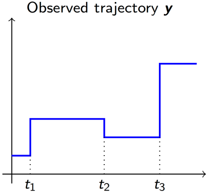
**Problem of Interest**: Given partial measurement trajectories, how to efficiently estimate the conditional probability distribution of unobserved (hidden) state-variables, i.e. efficiently solve the related stochastic filtering problem?

# Filtering Problem

For $t \in [0, T]$ and initial distribution $\mathbf{Z}(0) \sim \mu$

$$\boldsymbol{Z}(t) = \begin{pmatrix} \boldsymbol{X}(t) \\ \boldsymbol{Y}(t) \end{pmatrix}$$

hidden part
observed part




- **Hidden process:**
  $\boldsymbol{X}(t) = \boldsymbol{X}(0) + \sum_{j=1}^{J} R_j \left( \int_0^t a_j \left( \boldsymbol{X}(s), \boldsymbol{Y}(s) \right) ds \right) \boldsymbol{\nu}_{\boldsymbol{x},j}$, where
  - $\boldsymbol{\nu}_{\boldsymbol{x},j}$ is the stoichiometric vector corresponding to $\boldsymbol{X}(t)$
  - $R_j$ are independent unit-rate Poisson processes
- **Observed process:**
  $\boldsymbol{Y}(t) = \boldsymbol{Y}(0) + \sum_{j=1}^{J} R_j \left( \int_0^t a_j \left( \boldsymbol{X}(s), \boldsymbol{Y}(s) \right) ds \right) \boldsymbol{\nu}_{\boldsymbol{y},j}$, where
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# Filtering Problem

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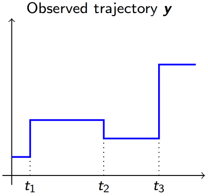


- **Hidden process:**
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**Goal:** Estimate conditional distribution of the hidden species/agents

$$\pi^{\boldsymbol{y}}(\boldsymbol{x}, t) := \mathbb{P}_{\mu}\left(\boldsymbol{X}(t) = \boldsymbol{x} \mid \boldsymbol{Y}(s) = \boldsymbol{y}(s), 0 \leq s \leq t\right).$$ [1]

[1] The well-posedness of $\pi^{\boldsymbol{y}}(\boldsymbol{x}, t)$ is guaranteed by Theorem 2.24 in (Bain et al. 2009)

# Filtering Problem: Setting

- We consider the case of noise-free and continuous in time observations.
- We assume that the trajectory $\boldsymbol{y}([0,T])$ can be observed with exact jump times $t_1, t_2, \ldots, t_n$.

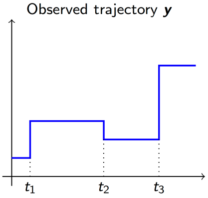
- The observed reactions

$$\mathcal{O}_k := \{j \in \{1, ..., J\} : \boldsymbol{\nu}_{\boldsymbol{y},j} = \boldsymbol{y}(t_k) - \boldsymbol{y}(t_k^-)\}$$

can only occur at $t = t_k$.

- Between jump times there could only occur unobserved reactions

$$\mathcal{U} := \{j \in \{1, ..., J\} : \boldsymbol{\nu}_{\boldsymbol{y},j} = \boldsymbol{0}\}$$



# Filtering Equations (Zechner et al. 2014)[2]

$$\pi^{\boldsymbol{y}}(\boldsymbol{x}, t) := \mathbb{P}_\mu\left(\boldsymbol{X}(t) = \boldsymbol{x} \mid \boldsymbol{Y}(s) = \boldsymbol{y}(s), 0 \leq s \leq t\right).$$

The unnormalized conditional pmf $\rho^{\boldsymbol{y}}(\boldsymbol{x}, t) \propto \pi^{\boldsymbol{y}}(\boldsymbol{x}, t)$ satisfies

- **between jump times** for $t \in (t_k, t_{k+1})$,

$$\frac{\mathrm{d}}{\mathrm{d}t}\rho^{\boldsymbol{y}}(\boldsymbol{x}, t) = \sum_{j \in \mathcal{U}} a_j(\boldsymbol{x} - \boldsymbol{\nu}_{\boldsymbol{x},j}, \boldsymbol{y}(t_k))\rho^{\boldsymbol{y}}(\boldsymbol{x} - \boldsymbol{\nu}_{\boldsymbol{x},j}, t) - \sum_{j=1}^{J} a_j(\boldsymbol{x}, \boldsymbol{y}(t_k))\rho^{\boldsymbol{y}}(\boldsymbol{x}, t)$$

- and **at jump times** $t_k$

$$\rho^{\boldsymbol{y}}(\boldsymbol{x}, t_k) = \frac{1}{|\mathcal{O}_k|}\sum_{j \in \mathcal{O}_k} a_j(\boldsymbol{x} - \boldsymbol{\nu}_{\boldsymbol{x},j}, \boldsymbol{y}(t_{k-1}))\rho^{\boldsymbol{y}}(\boldsymbol{x} - \boldsymbol{\nu}_{\boldsymbol{x},j}, t_k^-).$$

[2] Existence and uniqueness of the filtering equation are shown in (D'Ambrosio et al. 2022).

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The normalized pmf can be attained by

$$\pi^{\mathbf{y}}(\mathbf{x}, t) = \frac{\rho^{\mathbf{y}}(\mathbf{x}, t)}{\sum_{\hat{\mathbf{x}} \in X} \rho^{\mathbf{y}}(\hat{\mathbf{x}}, t)}.$$

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Let $\rho^{\mathbf{y}}(t) := \left(\rho^{\mathbf{y}}(\mathbf{x}_1,t), \rho^{\mathbf{y}}(\mathbf{x}_2,t),\dots\right)^\top$, then the filtering equations can be written as (**A** and **B** are infinite-dimensional matrices)

$$\frac{\mathrm{d}}{\mathrm{d}t}\boldsymbol{\rho}^{\mathbf{y}(t)} = \mathbf{A}\,\boldsymbol{\rho}^{\mathbf{y}}(t) \quad t\in(t_k,t_{k+1})$$

$$\boldsymbol{\rho}^{\mathbf{y}}(t_k) = \mathbf{B}\,\boldsymbol{\rho}^{\mathbf{y}}(t_k^-),$$

# Filtered Finite State Projection (FFSP)

- Extension of Finite State Projection (Munsky et al. 2006) originally introduced for efficiently solving the chemical master equation.
- **Idea** (D'Ambrosio et al. 2022):
  - Consider only for a finite subset of states $\{\boldsymbol{x}_1, \ldots, \boldsymbol{x}_N\} \subseteq \mathbb{N}^{\dim(\mathbf{X})}$.
  - Truncate the filtering equations $\Rightarrow$ system of (finite-dimensional) $N$ linear ODEs:

$$\frac{\mathrm{d}}{\mathrm{d}t}\boldsymbol{\rho}_N^{\boldsymbol{y}}(t) = \mathbf{A}_N \, \boldsymbol{\rho}_N^{\boldsymbol{y}}(t) \quad t \in (t_k, t_{k+1})$$
$$\boldsymbol{\rho}_N^{\boldsymbol{y}}(t_k) = \mathbf{B}_N \, \boldsymbol{\rho}_N^{\boldsymbol{y}}(t_k^-),$$

  - Control the approximation error $\mathcal{E}_{FFSP}$ by extending the truncated state space based on a posteriori estimates.

# Filtered Finite State Projection (FFSP)

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  - Control the approximation error $\mathcal{E}_{FFSP}$ by extending the truncated state space based on a posteriori estimates.

**Curse of Dimensionality**

If each hidden species takes $n$ possible states
$\rightarrow$ the truncated system contains $N = n^{dim(X)}$ equations

# Particle Filter (Rathinam et al. 2021)

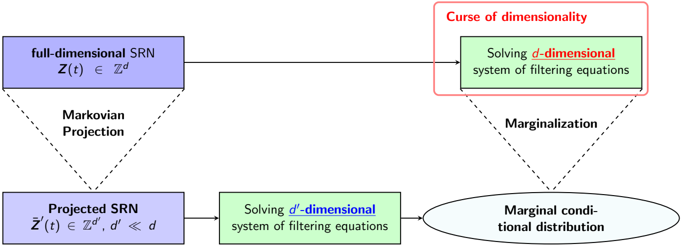
- It can be shown that: $\pi^{\boldsymbol{y}}(\boldsymbol{x}, t) \propto \mathbb{E}_{\mu}\left[1_{\{\boldsymbol{V}(t)=\boldsymbol{x}\}} w(t)\right]$, where
  - $\boldsymbol{V}$ is a modification of $\boldsymbol{X}$ in which reactions are consistent with the observed trajectory $\boldsymbol{y}$,
  - $w$ is a weight that represents the importance of trajectory $\boldsymbol{V}(t)$.
- Based on $M$ particles $\left\{\hat{\boldsymbol{V}}_k, \hat{w}_k\right\}_{k=1,..,M}$, one can use the estimator

$$\pi^{\boldsymbol{y}}(\boldsymbol{x}, t) \approx \frac{1}{\sum_{k=1}^{M} \hat{w}_k(t)} \sum_{k=1}^{M} 1_{\{\hat{\boldsymbol{V}}_k(t)=\boldsymbol{x}\}} \hat{w}_k(t).$$

## Challenges

- **Sample Degeneracy Issue**: When the number of hidden species is large ($\dim(\boldsymbol{X}) \gg 1$), most importance weights $\hat{w}_k$ collapse to near-zero values, resulting in unreliable posterior estimates.
- **Inaccurate estimation of tail probabilities**.

# Our approach in (Ben Hammouda et al. 2025): Motivation




1. employs a reduced variance particle filter for estimating the jump intensities of the projected process (obatined with Markovian Projection), and
2. solves the filtering equations in a low-dimensional space.

# Revisiting the Filtering Problem

**Setting**: we are only interested in a subset of the hidden process

$$Z = \begin{pmatrix} \boldsymbol{X}' \\ \boldsymbol{X}'' \\ \boldsymbol{Y} \end{pmatrix}$$

hidden species of interest
remaining hidden species
observed species

**Task**: estimate the marginal conditional distribution of $\boldsymbol{X}'$:

$$\pi'^{\boldsymbol{y}}(\boldsymbol{x}', t) := \mathbb{P}_\mu\left(\boldsymbol{X}'(t) = \boldsymbol{x}' \mid \boldsymbol{Y}(s) = \boldsymbol{y}(s), 0 \leq s \leq t\right).$$

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**1. Marginalization of the distribution**:
Solve the filtering problem for <u>$d$-dimensional</u> process $\boldsymbol{Z}$ and compute

$$\pi'^{\boldsymbol{y}}(\boldsymbol{x}', t) = \sum_{\boldsymbol{x}''} \pi^{\boldsymbol{y}}(\boldsymbol{x}', \boldsymbol{x}'', t).$$

$\Longrightarrow$ **curse of dimensionality**

# Revisiting the Filtering Problem

**Setting**: we are only interested in a subset of the hidden process

$$Z = \begin{pmatrix} \boldsymbol{X}' \\ \boldsymbol{X}'' \\ \boldsymbol{Y} \end{pmatrix}$$

hidden species of interest
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**2. Marginalization of the process**:
Try to solve the filtering problem for $d'$-dimensional process

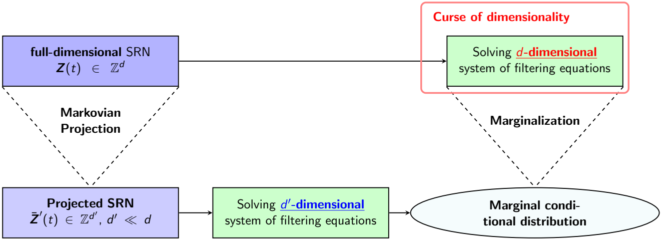
$$\boldsymbol{Z}' := \begin{pmatrix} \boldsymbol{X}' \\ \boldsymbol{Y} \end{pmatrix}.$$

**Challenge**: $\boldsymbol{Z}'$ is not a Markov process.

# Markovian Projection for Filtering

**Challenge**: $\boldsymbol{Z}'$ is a non-Markovian process.
**Solution**: construct a Markov process $\bar{\boldsymbol{Z}}'$ that mimics the distribution of $\boldsymbol{Z}'$.

$$\boldsymbol{Z} = \begin{bmatrix} \boldsymbol{X}' \\ \boldsymbol{X}'' \\ \boldsymbol{Y} \end{bmatrix} \longrightarrow \begin{bmatrix} \boldsymbol{X}' \\ \boldsymbol{Y} \end{bmatrix} = \boldsymbol{Z}', \qquad \longrightarrow \begin{bmatrix} \boldsymbol{X}'' \end{bmatrix} = \boldsymbol{Z}''$$



# Standard Markovian Projection for Filtering

- Recall: $\boldsymbol{Z}(t) = \boldsymbol{Z}_0 + \sum_{j=1}^{J} Y_j \left( \int_0^t a_j(\boldsymbol{Z}(\tau)) d\tau \right) \cdot \boldsymbol{\nu}_j$
- **Challenge**: $\boldsymbol{Z}'$ is not a Markov process.
- **Solution**: construct a Markov process $\bar{\boldsymbol{Z}}'$ that mimics the distribution of $\boldsymbol{Z}'$.

## Theorem (Ben Hammouda et al. 2024)

*Let $\boldsymbol{Z}(t) = \left(\boldsymbol{Z}'(t), \boldsymbol{Z}''(t)\right)^T$ be a non-explosive SRN (Assumption A.1). Define a $d'$-dimensional stochastic process $\bar{\boldsymbol{Z}}'$ via independent Poisson processes $\bar{R}_1, \ldots, \bar{R}_J$ as*

$$\bar{\boldsymbol{Z}}'(t) = \bar{\boldsymbol{Z}}'(0) + \sum_{j=1}^{J} \bar{R}_j \left( \int_0^t \bar{a}_j \left( \bar{\boldsymbol{Z}}'(s), s \right) \mathrm{d}s \right) \boldsymbol{\nu}_j' \quad t \in [0, T],$$

*where $\boldsymbol{\nu}_j'$ are stochiometric vectors of $\boldsymbol{Z}'$, $\bar{\boldsymbol{Z}}'(0) \stackrel{d}{=} \boldsymbol{Z}'(0)$, and*

$$\bar{a}_j(\bar{\boldsymbol{z}}', t) := \mathbb{E}\left[ a_j(\boldsymbol{Z}(t)) \mid \boldsymbol{Z}'(t) = \bar{\boldsymbol{z}}' \right], \quad \bar{\boldsymbol{z}}' \in \mathbb{Z}_{\geq 0}^{d'}$$

*Then $\bar{\boldsymbol{Z}}'(t)$ has the same distribution as $\boldsymbol{Z}'(t)$ for all $t \in [0, T]$.*

# Markovian Projection: Example

Goutsias's model of regulated transcription (d=6, J=10) (Goutsias 2005)

$\boldsymbol{Z} := (M, D, RNA, DNA, DNA \cdot D(0), DNA \cdot 2D)$ with projection $\boldsymbol{Z}' = \boldsymbol{Z}_2$ (projection to molecule type $D$)

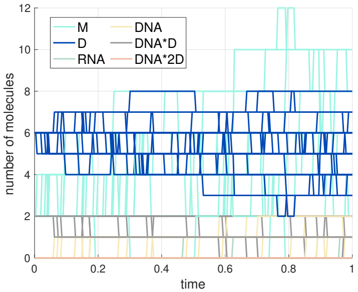
$$
\begin{aligned}
\mathrm{RNA} &\xrightarrow{\theta_1} RNA + M, & \mathrm{M} &\xrightarrow{\theta_2} \varnothing,\\
\mathrm{DNA} \cdot \mathrm{D} &\xrightarrow{\theta_3} RNA + DNA \cdot D, & \mathrm{RNA} &\xrightarrow{\theta_4} \varnothing,\\
\mathrm{DNA} + \mathrm{D} &\xrightarrow{\theta_5} DNA \cdot D, & \mathrm{DNA} \cdot \mathrm{D} &\xrightarrow{\theta_6} DNA + D,\\
\mathrm{DNA} \cdot \mathrm{D} + \mathrm{D} &\xrightarrow{\theta_7} DNA \cdot 2D, & \mathrm{DNA} \cdot \mathrm{2D} &\xrightarrow{\theta_8} DNA \cdot D + D,\\
2 \cdot \mathrm{M} &\xrightarrow{\theta_9} D, & \mathrm{D} &\xrightarrow{\theta_{10}} 2 \cdot M,
\end{aligned}
$$

$$
\bar{a}_{10}(t, \bar{\mathbf{z}}') = \mathbb{E}\left[\theta_{10} \boldsymbol{Z}_2(t) \mid \boldsymbol{Z}_2(t) = \bar{\mathbf{z}}'; \boldsymbol{Z}(0) = \boldsymbol{z}_0\right] = \theta_{10} \bar{\mathbf{z}}'
$$

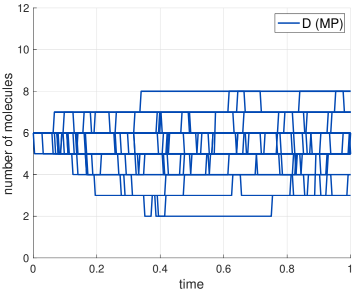
Reaction $j = 10$ is given in closed form and reactions $j = 1, 2, 3, 4$ do not occur in the projected process since $\boldsymbol{\nu}'_j = 0$.

# Markovian Projection: Numerical Experiments

Full-dimensional SRN (TL)




MP-SRN (TL)




30 sample paths generated with TL[3] with step size $\Delta t = 2^{-8}$.

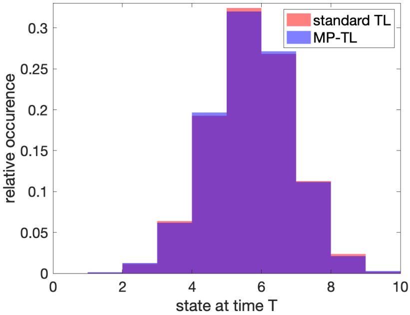
[3] Tau-Leap (TL) is the forward Euler approximation of Kurtz's random time-change representation

# Markovian Projection: Numerical Illustration

Goutsias's model of regulated transcription

(d=6, J=10, $\bar{d} = 1$)

$P(\boldsymbol{x}) = x_2$




Relative occurrences of states at final time $T$ with $10^4$ sample paths comparing the TL estimate of $P(\boldsymbol{X}(t)) \mid_{\{\boldsymbol{X}_0=\boldsymbol{x}_0\}}$ and the MP estimate of $\bar{\boldsymbol{S}}(T) \mid_{\{\boldsymbol{X}_0=\boldsymbol{x}_0\}}$.

# Standard Markovian Projection for Filtering

**Step 1**: Construct projected SRN $\bar{\boldsymbol{Z}}'$ and estimate its propensities $\bar{a}_j$ using MC or $L^2$ regression.

$$\boldsymbol{Z} = \begin{pmatrix} \boldsymbol{X}' \\ \boldsymbol{X}'' \\ \boldsymbol{Y} \end{pmatrix} \xrightarrow{\text{MP}} \bar{\boldsymbol{Z}}' = \begin{pmatrix} \bar{\boldsymbol{X}}' \\ \bar{\boldsymbol{Y}} \end{pmatrix}$$

**Step 2**: Apply FFSP to solve the filtering problem for $\bar{\boldsymbol{Z}}'$ with dimension $d' \ll d$:

$$\bar{\pi}'^{\boldsymbol{y}}(\boldsymbol{x}', t) := \mathbb{P}\left(\bar{\boldsymbol{X}}'(t) = \boldsymbol{x}' \mid \bar{\boldsymbol{Y}}(s) = \boldsymbol{y}(s), 0 \leq s \leq t\right).$$

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**Note**

The MP theorem only states $\boldsymbol{Z}'(t) \overset{d}{=} \bar{\boldsymbol{Z}}'(t)$ for each $t$, which implies

$$\mathbb{P}\left(\boldsymbol{X}'(t) = \boldsymbol{x}' \mid \boldsymbol{Y}(t) = \boldsymbol{y}(t)\right) = \mathbb{P}\left(\bar{\boldsymbol{X}}'(t) = \boldsymbol{x}' \mid \bar{\boldsymbol{Y}}(t) = \boldsymbol{y}(t)\right).$$

But there is no guarantee that $\bar{\pi}'^{\boldsymbol{y}}$ will be equal to $\pi'^{\boldsymbol{y}}$.

⚠ Recall: $\pi'^{\boldsymbol{y}}(\boldsymbol{x}', t) := \mathbb{P}\left(\boldsymbol{X}'(t) = \boldsymbol{x}' \mid \boldsymbol{Y}(s) = \boldsymbol{y}(s), \boxed{0 \leq s \leq t}\right).$

# Filtered Markovian Projection (FMP)

**Recall**: for the MP SRN $\bar{\boldsymbol{Z}}'$ we have $\bar{\pi}'^{\boldsymbol{y}} \neq \pi'^{\boldsymbol{y}}$

**Idea**: construct another SRN that preserves the conditional distribution

**Theorem (Ben Hammouda et al. 2025)**

*Let $\boldsymbol{Z} = \left(\boldsymbol{X}', \boldsymbol{X}'', \boldsymbol{Y}\right)^\top$ be a non-explosive $d$-dimensional SRN (Assumption A.1) and let $\boldsymbol{Z}'(t) := \left(\boldsymbol{X}'(t), \boldsymbol{Y}(t)\right) \in \mathbb{Z}_{\geq 0}^{d'}$. Define a $d'$-dimensional stochastic process $\tilde{\boldsymbol{Z}}'(t) = \left(\tilde{\boldsymbol{X}}'(t), \tilde{\boldsymbol{Y}}(t)\right)$ via independent Poisson processes $\tilde{R}_1, \ldots, \tilde{R}_J$ as*

$$\tilde{\boldsymbol{Z}}'(t) = \tilde{\boldsymbol{Z}}'(0) + \sum_{j=1}^{J} \tilde{R}_j \left( \int_0^t \tilde{a}_j \left( \tilde{\boldsymbol{Z}}'(s), s \right) ds \right) \boldsymbol{\nu}_j', \quad t \in [0, T]$$

*where $\boldsymbol{\nu}_j'$ are stochiometric vectors of $\boldsymbol{Z}'$, $\tilde{\boldsymbol{Z}}'(0) \stackrel{d}{=} \boldsymbol{Z}'(0)$ and*

$$\tilde{a}_j(\tilde{\boldsymbol{z}}', t) := \mathbb{E}[a_j(\boldsymbol{Z}(t)) | \boldsymbol{Z}'(t) = \tilde{\boldsymbol{z}}', \boldsymbol{Y}(s) = \boldsymbol{y}(s), s \leq t].$$

*Then $\tilde{\boldsymbol{Z}}'(t)$ has the same conditional on $\left\{ \tilde{\boldsymbol{Y}}(s) = \boldsymbol{y}(s), s \leq t \right\}$ distribution as $\boldsymbol{Z}'(t)$ conditional on $\{\boldsymbol{Y}(s) = \boldsymbol{y}(s), s \leq t\}$ for any $t \in [0, T]$.*

# FMP for Filtering

**Step 1**: Construct projected SRN $\tilde{\boldsymbol{Z}}'$

$$\boldsymbol{Z} = \begin{pmatrix} \boldsymbol{X}' \\ \boldsymbol{X}'' \\ \boldsymbol{Y} \end{pmatrix} \xrightarrow{\text{FMP}} \tilde{\boldsymbol{Z}}' = \begin{pmatrix} \tilde{\boldsymbol{X}}' \\ \tilde{\boldsymbol{Y}} \end{pmatrix}$$

and estimate its propensities with Particle Filter

$$\tilde{a}_j(\tilde{\boldsymbol{z}}', t) = \mathbb{E}\left[a_j(\boldsymbol{Z}(t)) \mid \boldsymbol{Z}'(t) = \tilde{\boldsymbol{z}}', \boldsymbol{Y}(s) = \boldsymbol{y}(s), 0 \leq s \leq t\right]$$

**Step 2**: Apply FFSP to solve the filtering problem for $\tilde{\boldsymbol{Z}}'$ with dimension $d' \ll d$:

$$\tilde{\pi}'^{\boldsymbol{y}}(\boldsymbol{x}', t) := \mathbb{P}\left[\tilde{\boldsymbol{X}}'(t) = \boldsymbol{x}' \mid \tilde{\boldsymbol{Y}}(s) = \boldsymbol{y}(s), 0 \leq s \leq t\right].$$

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**Note**

The FMP theorem guarantees $\pi'^{\boldsymbol{y}} = \tilde{\pi}'^{\boldsymbol{y}}$:

$$\mathbb{P}\left[\boldsymbol{X}'(t) = \boldsymbol{x}' \mid \boldsymbol{Y}(s) = \boldsymbol{y}(s), s \leq t\right] = \mathbb{P}\left[\tilde{\boldsymbol{X}}'(t) = \boldsymbol{x}' \mid \tilde{\boldsymbol{Y}}(s) = \boldsymbol{y}(s), s \leq t\right].$$

# Error analysis

- We have an approximation $\tilde{\pi}^{M,\Delta t}_{FFSP} \approx \pi$ with the following error sources
  - **Projection error** due to the approximation of $\tilde{a}_j$ with $M$ particles.
  - **Truncation error** due to the state space truncation in FFSP method.
  - **ODE solver error** due to the discretization of FFSP system with time step $\Delta t$.
  - The **model reduction error** is zero (Theorem 2).
- The total error is decomposed as follows:

$$\left|\pi(\boldsymbol{x}', t) - \tilde{\pi}^{M,\Delta t}_{FFSP}(\boldsymbol{x}', t)\right| \leq \underbrace{\left|\pi(\boldsymbol{x}', t) - \tilde{\pi}(\boldsymbol{x}', t)\right|}_{\text{Model reduction error}} + \underbrace{\left|\tilde{\pi}(\boldsymbol{x}', t) - \tilde{\pi}^{M}(\boldsymbol{x}', t)\right|}_{\text{Projection error}}$$

$$+ \underbrace{\left|\tilde{\pi}^{M}(\boldsymbol{x}', t) - \tilde{\pi}^{M}_{FFSP}(\boldsymbol{x}', t)\right|}_{\text{Truncation error}} + \underbrace{\left|\tilde{\pi}^{M}_{FFSP}(\boldsymbol{x}', t) - \tilde{\pi}^{M,\Delta t}_{FFSP}(\boldsymbol{x}', t)\right|}_{\text{ODE solver error}}$$

# Error analysis

In practice, we have an approximation $\tilde{\pi}^{M,\Delta t}_{FFSP} \approx \pi$ with the following error sources

- **Projection error** due to the approximation of $\tilde{a}_j$ with $M$ particles.
- **Truncation error** due to the state space truncation in FFSP method.
- **ODE solver error** due to the discretization of FFSP system with time step $\Delta t$.

**Theorem (Ben Hammouda et al. 2025)**

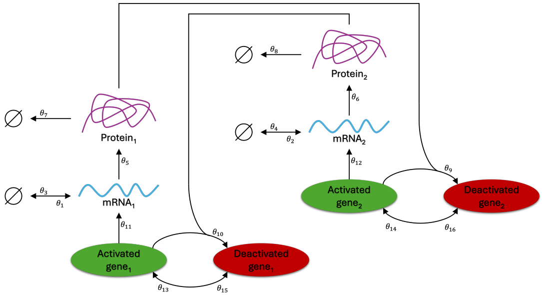
*Under some assumptions (see (Ben Hammouda et al. 2025) for more details), we show*

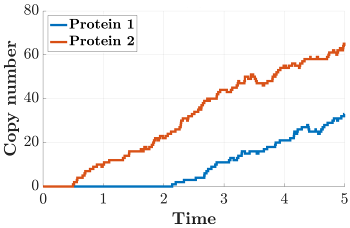
$$\mathbb{E}\left[\left|\left|\pi(\mathbf{x}', t) - \tilde{\pi}^{M,\Delta t}_{FFSP}(\mathbf{x}', t)\right|\right|_1\right] \leq \frac{C_1}{\sqrt{M}} + \mathcal{E}_{FFSP} + C_2 \Delta t^p$$

✓ We can control $\mathcal{E}_{FFSP}$ and $C_2 \Delta t^p$ with little cost since the state space of projected SRN is relatively small (potentially one-dimensional).

# Example 1: Bistable Gene Switch Network

Consider the following SRN (Gupta et al. 2021) with: 2 observed and 6 hidden species, and 16 reactions.



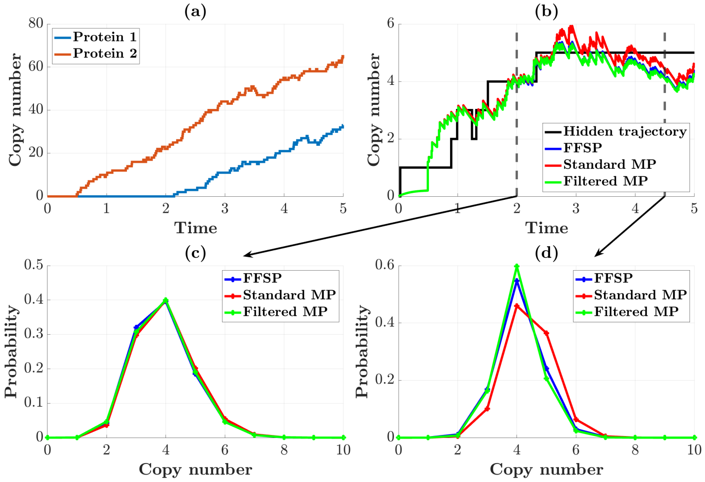




Observed trajectory of Protein$_1$ and Protein$_2$.

**Task:** Estimate the distribution of the mRNA$_2$ copy number, i.e.,

$$\pi'(x', t) := \mathbb{P}\left\{ mRNA_2(t) \,\middle|\, \begin{bmatrix} protein_1(s) = y_1(s) \\ protein_2(s) = y_2(s) \end{bmatrix}, 0 \leq s \leq t \right\}$$

# Bistable Gene Switch Network: Numerical Results



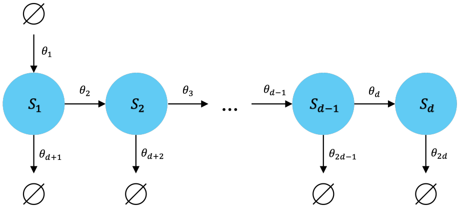

(a) Observed trajectories, (b) Estimated conditional mean, (c)-(d) Estimated conditional distribution at times $t = 2$ and $t = 4.5$.

# Bistable Gene Switch Network: Numerical Results

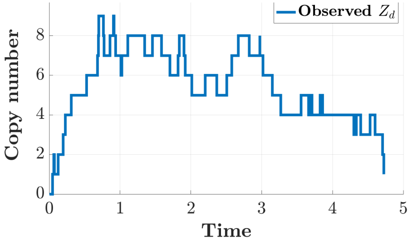
| | Dimension of hidden space | # of hidden states | CPU time in seconds |
|---|---|---|---|
| FFSP (full model) | 6 | 15 376 | 846.4 s |
| MP-FFSP (projected model) | 1 | 31 | 5.1 s |
| FMP-FFSP (projected model) | 1 | 31 | 5.7 s |

The Computational complexity of solving the filtering equations with FFSP for full and projected models.

# Example 2: Linear Cascade Model (Gupta et al. 2021)




Reactions in linear cascade SRN



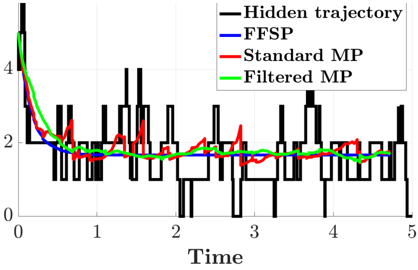

Observed trajectory of $S_d$.

**Task:** Estimate the the distribution of $S_1$ given that $S_d$ is observed, i.e.,

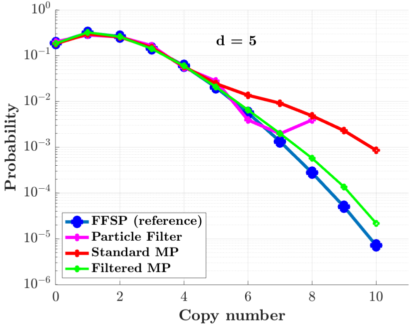
$$\pi'(x', t) = \mathbb{P}\left\{Z_1(t) \,|\, Z_d(s) = y(s), 0 \leq s \leq t\right\}$$

# Linear Cascade Model: Numerical Results

$$d = 5$$

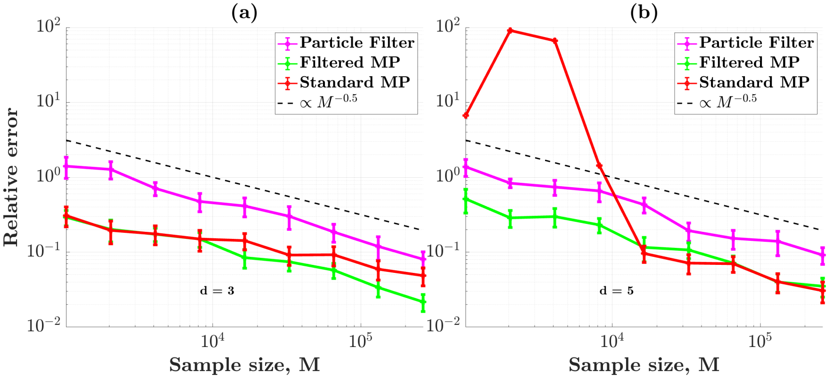



Estimated conditional mean
$\mathbb{E}\left[Z_1(t) \,|\, Z_d(s) = y(s), s \leq t\right]$



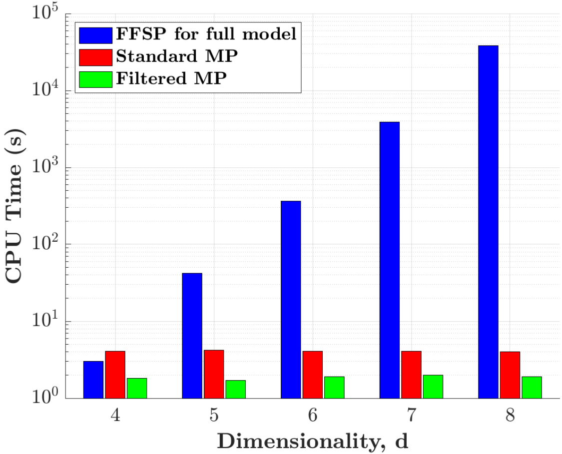

Estimated conditional distribution
$\mathbb{P}\left\{Z_1(T) \,|\, Z_d(s) = y(s), s \leq T\right\}$
in log scale

# Linear Cascade Model: Numerical Results




Relative error for estimating $\mathbb{P}[Z_1(T) \geq 8 \mid Z_d(s) = y(s), 0 \leq s \leq T] \approx 10^{-4}$. (a) the 3-dimensional model. (b) the 5-dimensional model.

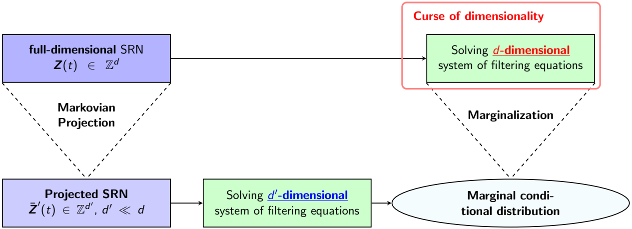
# Linear Cascade Model: Numerical Results




Computational cost versus dimension for solving the filtering problem

# Conclusion

- Existing filtering methods for SRNs are not efficient in the **high dimensional** setting.
- Filtered Markovian Projection (FMP) guarantees convergence, improves accuracy and efficiency compared to particle filters, and mitigates the curse of dimensionality faced by FFSP when applied to the full model:
  1. Employs a reduced-variance particle filter to estimate the jump intensities of the projected process (obtained via Markovian projection),
  2. Solves the filtering equations in a low-dimensional space.



# Work in Progress and Future Directions

- Adapt FMP from (Ben Hammouda et al. 2025) to settings with noisy and discrete observations.
- Extend FMP to include parameter estimation (via particle filters or other Bayesian inference methods)$\Rightarrow$ higher gains expected, but more challenging.
- Combine MP with particle filters to reduce sample degeneracy and improve tail accuracy (Djurić et al. 2013; Snyder et al. 2008), in particular, using filtered MP as Control Variate for particle filters.
- Explore Koopman-based decompositions to separate time scales (Li et al. 2023) $\Rightarrow$ reduce dimensionality w.r.t. number of reactions.

# Related References

## Thank you for your attention!


1. **C. Ben Hammouda, M. Chupin, S Münker, and R Tempone. "Filtered Markovian Projection: Dimensionality Reduction in Filtering for Stochastic Reaction Networks". In: arXiv preprint arXiv:2502.07918 (2025)**

   Accompanying code can be found here:
   Git repository: Markovian-Projection-in-filtering-for-SRNs

2. C. Ben Hammouda, N. Ben Rached, R. Tempone, and S. Wiechert. "Automated importance sampling via optimal control for stochastic reaction networks: A Markovian projection–based approach". In: *Journal of Computational and Applied Mathematics* 446 (2024), p. 115853

3. C. Ben Hammouda, N. Ben Rached, R. Tempone, and S. Wiechert. "Learning-based importance sampling via stochastic optimal control for stochastic reaction networks". In: *Statistics and Computing* 33.3 (2023), p. 58

# References I


[1] David F Anderson and Thomas G Kurtz. *Stochastic analysis of biochemical systems*. Springer, 2015.

[2] Alan Bain and Dan Crisan. *Fundamentals of stochastic filtering*. Vol. 3. Springer, 2009.

[3] James L Beck and Konstantin M Zuev. "Rare event simulation". In: *arXiv preprint arXiv:1508.05047* (2015).

[4] C. Ben Hammouda, N. Ben Rached, and R. Tempone. "Importance sampling for a robust and efficient multilevel Monte Carlo estimator for stochastic reaction networks". In: *Statistics and Computing* 30.6 (2020), pp. 1665–1689.

[5] C. Ben Hammouda, N. Ben Rached, R. Tempone, and S. Wiechert. "Automated importance sampling via optimal control for stochastic reaction networks: A Markovian projection–based approach". In: *Journal of Computational and Applied Mathematics* 446 (2024), p. 115853.

# References II


[6] C. Ben Hammouda, N. Ben Rached, R. Tempone, and S. Wiechert. "Learning-based importance sampling via stochastic optimal control for stochastic reaction networks". In: *Statistics and Computing* 33.3 (2023), p. 58.

[7] C. Ben Hammouda, M. Chupin, S Münker, and R Tempone. "Filtered Markovian Projection: Dimensionality Reduction in Filtering for Stochastic Reaction Networks". In: *arXiv preprint arXiv:2502.07918* (2025).

[8] C. Ben Hammouda, A. Moraes, and R. Tempone. "Multilevel hybrid split-step implicit tau-leap". In: *Numerical Algorithms* 74.2 (2017), pp. 527–560.

[9] Fred Brauer, Carlos Castillo-Chavez, and Carlos Castillo-Chavez. *Mathematical models in population biology and epidemiology*. Vol. 2. Springer, 2012.

# References III


[10] Corentin Briat, Ankit Gupta, and Mustafa Khammash. "A Control Theory for Stochastic Biomolecular Regulation". In: *SIAM Conference on Control Theory and its Applications*. SIAM. 2015.

[11] Nai-Yuan Chiang, Yiqing Lin, and Quan Long. "Efficient propagation of uncertainties in manufacturing supply chains: Time buckets, L-leap, and multilevel Monte Carlo methods". In: *Operations Research Perspectives* 7 (2020), p. 100144.

[12] Petar M Djurić and Mónica F Bugallo. "Particle filtering for high-dimensional systems". In: *2013 5th IEEE International Workshop on Computational Advances in Multi-Sensor Adaptive Processing (CAMSAP)*. IEEE. 2013, pp. 352–355.

[13] Lorenzo Duso and Christoph Zechner. "Selected-node stochastic simulation algorithm". In: *The Journal of chemical physics* 148.16 (2018).

[14] Elena D'Ambrosio, Zhou Fang, Ankit Gupta, and Mustafa Khammash. "Filtered finite state projection method for the analysis and estimation of stochastic biochemical reaction networks". In: *bioRxiv* (2022), pp. 2022–10.

[15] Michael B Elowitz, Arnold J Levine, Eric D Siggia, and Peter S Swain. "Stochastic gene expression in a single cell". In: *Science* 297.5584 (2002), pp. 1183–1186.

[16] Radek Erban and S Jonathan Chapman. *Stochastic modelling of reaction–diffusion processes*. Vol. 60. Cambridge University Press, 2020.

[17] Stewart N Ethier and Thomas G Kurtz. *Markov processes: characterization and convergence*. Vol. 282. John Wiley & Sons, 2009.

[18] Zhou Fang, Ankit Gupta, and Mustafa Khammash. "Stochastic filtering for multiscale stochastic reaction networks based on hybrid approximations". In: *Journal of Computational Physics* 467 (2022), p. 111441.

[19] D. T. Gillespie. "Approximate accelerated stochastic simulation of chemically reacting systems". In: *Journal of Chemical Physics* 115 (July 2001), pp. 1716–1733. DOI: 10.1063/1.1378322.

[20] John Goutsias. "Quasiequilibrium approximation of fast reaction kinetics in stochastic biochemical systems". In: *The Journal of chemical physics* 122.18 (2005), p. 184102.

[21] John Goutsias and Garrett Jenkinson. "Markovian dynamics on complex reaction networks". In: *Physics reports* 529.2 (2013), pp. 199–264.

[22] Ankit Gupta, Christoph Schwab, and Mustafa Khammash. "DeepCME: A deep learning framework for computing solution statistics of the chemical master equation". In: *PLOS Computational Biology* 17.12 (Dec. 2021), pp. 1–23. DOI: 10.1371/journal.pcbi.1009623.

[23] SebastianC. Hensel, JamesB. Rawlings, and John Yin. "Stochastic Kinetic Modeling of Vesicular Stomatitis Virus Intracellular Growth". English. In: *Bulletin of Mathematical Biology* 71.7 (2009), pp. 1671–1692. ISSN: 0092-8240.

[24] H. Solari J. Aparicio. "Population dynamics: Poisson approximation and its relation to the langevin process". In: *Physical Review Letters* (2001), p. 4183.

[25] Diederik P Kingma and Jimmy Ba. "Adam: A method for stochastic optimization". In: *arXiv preprint arXiv:1412.6980* (2014).

# References VII

[26] Ruikun Li, Huandong Wang, and Yong Li. "Learning slow and fast system dynamics via automatic separation of time scales". In: *Proceedings of the 29th ACM SIGKDD Conference on Knowledge Discovery and Data Mining*. 2023, pp. 4380–4390.

[27] Brian Munsky and Mustafa Khammash. "The finite state projection algorithm for the solution of the chemical master equation". In: *The Journal of chemical physics* 124.4 (2006).

[28] Natalija Novak, Leticia Tordesillas, and Beatriz Cabanillas. "Adverse rare events to vaccines for COVID-19: From hypersensitivity reactions to thrombosis and thrombocytopenia". In: *International reviews of immunology* 41.4 (2022), pp. 438–447.

[29] Jean Peccoud and Bernard Ycart. "Markovian modeling of gene-product synthesis". In: *Theoretical population biology* 48.2 (1995), pp. 222–234.

[30] NR Srinivasa Raghavan and N Viswanadham. “Stochastic models for analysis of supply chain networks”. In: *Proceedings of the 2002 American Control Conference (IEEE Cat. No. CH37301)*. Vol. 6. IEEE. 2002, pp. 4714–4719.

[31] Arjun Raj, Charles S Peskin, Daniel Tranchina, Diana Y Vargas, and Sanjay Tyagi. “Stochastic mRNA synthesis in mammalian cells”. In: *PLoS biology* 4.10 (2006), e309.

[32] Christopher V Rao and Adam P Arkin. “Stochastic chemical kinetics and the quasi-steady-state assumption: Application to the Gillespie algorithm”. In: *The Journal of chemical physics* 118.11 (2003), pp. 4999–5010.

[33] Muruhan Rathinam and Mingkai Yu. “State and parameter estimation from exact partial state observation in stochastic reaction networks”. In: *The Journal of Chemical Physics* 154.3 (2021).

# References IX


[34] Elijah Roberts, Andrew Magis, Julio O Ortiz, Wolfgang Baumeister, and Zaida Luthey-Schulten. "Noise contributions in an inducible genetic switch: a whole-cell simulation study". In: *PLoS computational biology* 7.3 (2011), e1002010.

[35] Chris Snyder, Thomas Bengtsson, Peter Bickel, and Jeff Anderson. "Obstacles to high-dimensional particle filtering". In: *Monthly Weather Review* 136.12 (2008), pp. 4629–4640.

[36] Yong Wang, Jill Waters, Marco L Leung, Anna Unruh, Whijae Roh, Xiuqing Shi, Ken Chen, Paul Scheet, Selina Vattathil, Han Liang, et al. "Clonal evolution in breast cancer revealed by single nucleus genome sequencing". In: *Nature* 512.7513 (2014), pp. 155–160.

[37] Christoph Zechner and Heinz Koeppl. "Uncoupled analysis of stochastic reaction networks in fluctuating environments". In: *PLoS computational biology* 10.12 (2014), e1003942.