Variance Decomposition Techniques for Sensitivity Analysis in Stochastic / Noisy Models with Uncertain Parameters

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1. **Variance-Based Sensitivity Analysis for SODE’s**
   - Variance decomposition
   - Galerkin approximation
   - Examples

2. **Stochastic Simulations**
   - Stochastic simulators
   - Variance Decomposition
   - Examples

3. **Conclusion**
**Stochastic models**
Physical systems with

- complex small scale dynamics (MD, chemical systems, . . .)
- random forcing and source terms (finance, wind-load, . . .)
- unresolved scales (turbulence, climate modeling, . . .)

are often tackled by means of stochastic modeling where complex / unknown / unresolved phenomenons are accounted for by the introduction of noisy dynamics.

In addition to the effect of the noise, the model may involve unknown parameters: e.g. noise level, physical constants and parameters, initial conditions, . . .

Our general objective is to propagate / assess the impact of parameters uncertainty within such stochastic models while characterizing the effect of inherent noise:

global sensitivity analysis & analysis of the variance
**Stochastic ODEs**

We consider a simple system driven by random noise (Ito equation) for \( t \in [0, T] \): for

\[
dX(t) = C(X(t)) \, dt + D(X(t)) \, dW(t), \quad X(t = 0) = X_0,
\]

where

- \( X(t) \in \mathbb{R} \) is the solution,
- \( W(t) \) is the Wiener process,
- \( C(\cdot) \) is the drift function,
- and \( D(\cdot) \) is the diffusion coefficient.

The solution can be computed through MC simulation, solving (e.g.)

\[
X_{i+1} = X_i + C(X_i) \Delta t + D(X_i) \Delta W_i, \quad X_i \approx X(i \Delta t),
\]

drawing iid random variables \( \Delta W_i \sim N(0, \Delta t) \).

Sample estimate expectation, moments, quantiles, probability law, . . . , of the stochastic process \( X(t) \):

\[
\mathbb{E} \{ g(X(i \Delta t)) \} \approx \frac{1}{M} \sum_{l=1}^{M} g(X_i^l).
\]
Stochastic ODEs with parametric uncertainty

The drift function and diffusion coefficient can involve some uncertain parameters $Q$:

$$dX(t) = C(X(t); Q)dt + D(X(t); Q)dW(t), \quad X(t = 0) = X_0.$$ 

We consider that:
- $Q$ random with known probability law,
- $Q$ and $W$ are assumed independent.

The solution can be seen as a functional of $W(t)$ and $Q$: $X(t) = X(t, W, Q)$. We shall assume, $\forall t \in T$,

1. $\mathbb{E}\{X^2\} < \infty$,
2. $\mathbb{E}\left\{\mathbb{E}\{X|W\}^2\right\} \equiv \mathbb{E}\left\{X_{|W}^2\right\} < \infty$,
3. $\mathbb{E}\left\{\mathbb{E}\{X|Q\}^2\right\} \equiv \mathbb{E}\left\{X_{|Q}^2\right\} < \infty$.

We want to investigate the respective impact of $Q$, $W$ on the dynamics.
Classical sensitivity analysis
Focusing on the two first moments, global SA for the random parameters $Q$ is based on:

1. approximating the mean and variance of $X|Q$

   \[ \mathbb{E}\{X|Q\} = \mu_X(Q), \quad \mathbb{V}\{X|Q\} = \Sigma_X^2(Q), \]

2. perform a GSA of $\mu_X(Q)$ and $\Sigma_X^2(Q)$ with respect to the input parameters in $Q$.

In particular, for independent parameters $Q$, Polynomial Chaos approximations:

\[
\mu_X(Q) \approx \sum_\alpha \mu_\alpha \psi_\alpha(Q), \quad \Sigma_X^2(Q) \approx \sum_\alpha \Sigma_\alpha^2 \psi_\alpha(Q).
\]

PC expansion coefficients can be computed / estimated by means of Non-Intrusive Spectral Projection, Bayesian identification, . . .

This approach characterizes the dependence of the first moments with respect to the parameters $Q$. 
Another approach of GSA
Here, we exploit the structure of the model to take an alternative approach, inspired from the hierarchical orthogonal Sobol-Hoeffding decomposition of $X$:

$$X(W, Q) = \bar{X} + X_W(W) + X_Q(Q) + X_{W,Q}(W, Q), \quad \forall t \in T,$$

where the functionals in the SH decomposition are mutually orthogonal. In fact, the decomposition is unique and given by

- $\bar{X}(t) \doteq \mathbb{E} \{X(t)\}$,
- $X_W(t, W) \doteq \mathbb{E} \{X(t)|W\} - \mathbb{E} \{X(t)\} = X|_W(t) - \bar{X}(t)$,
- $X_Q(t, Q) \doteq \mathbb{E} \{X(t)|Q\} - \mathbb{E} \{X(t)\} = X|_Q(t) - \bar{X}(t)$.

Owing to the orthogonality of the SH decomposition, we have

$$\nabla \{X\} = \nabla \{X_W\} + \nabla \{X_Q\} + \nabla \{X_{W,Q}\},$$

from which follow the definitions of the sensitivity indices

$$S_W = \frac{\nabla \{X_W\}}{\nabla \{X\}}, \quad S_Q = \frac{\nabla \{X_Q\}}{\nabla \{X\}}, \quad S_{W,Q} = \frac{\nabla \{X_{W,Q}\}}{\nabla \{X\}}.$$
**Sensitivity indices**

The sensitivity indices

\[ S_W = \frac{\text{Var} \{ X_W \}}{\text{Var} \{ X \}}, \quad S_Q = \frac{\text{Var} \{ X_Q \}}{\text{Var} \{ X \}}, \quad S_{W,Q} = \frac{\text{Var} \{ X_{W,Q} \}}{\text{Var} \{ X \}}, \]

then measure the fraction of the variance due to

- the Wiener noise only, or intrinsic randomness \((S_W)\),
- the parameters only, or parametric randomness \((S_Q)\),
- the combined effect of intrinsic and parametric randomness \((S_{W,Q})\).

In particular, \(S_W\) measure the part of the variance that cannot be reduced through a better knowledge of the parameters.

In addition,

\[ \frac{\text{Var}_Q \{ \mu_X(Q) \}}{\text{Var} \{ X \}} = S_Q, \quad \text{but} \quad \frac{\mathbb{E}_Q \{ \Sigma^2(Q) \}}{\text{Var} \{ X \}} = S_W + S_{W,Q}. \]

From \(\Sigma^2(Q)\), one cannot distinguish the intrinsic and mixed randomness effects.
Polynomial Chaos expansion
We express the dependence of $X$ on $Q$ as a PC expansion

$$X(t, W, Q) = \sum_{\alpha} X_{\alpha}(t, W)\psi_{\alpha}(Q),$$

where

- $\{\psi_{\alpha}\}$ is a CONS of $L^2(Q, p_Q)$,
- the expansion coefficients $X_{\alpha}$ are random processes.

The random processes $X_{\alpha}(t)$ are the solutions of the coupled system of SODEs

$$dX_{\beta}(t) = \left\langle F\left(\sum_{\alpha} X_{\alpha}(t)\psi_{\alpha} ; QX\right) , \psi_{\beta}\right\rangle dt + \left\langle G\left(\sum_{\alpha} X_{\alpha}(t)\psi_{\alpha} ; Q\right) , \psi_{\beta}\right\rangle dW,$$

where $\langle \cdot , \cdot \rangle$ denotes the inner product in $L^2(Q, p_Q)$.

This system can be solved by MC simulation (upon truncation).
**PC expansion**

Assuming $\Psi_0 = 1$, it comes

$$
\mathbb{E} \{ X \} = \mathbb{E} \{ X_0 \}, \quad X_Q(Q) = \sum_{\alpha \neq 0} \mathbb{E} \{ X_\alpha \} \Psi_\alpha(Q), \quad X_W(W) = X_0(W) - \mathbb{E} \{ X_0 \},
$$

and

$$
X_{W,Q}(W, Q) = \sum_{\alpha \neq 0} (X_\alpha(W) - \mathbb{E} \{ X_\alpha \}) \Psi_\alpha(Q).
$$

Finally, the partial variances have for expression:

$$
\forall \{ X_Q \} = \sum_{\alpha \neq 0} \mathbb{E} \{ X_\alpha \}^2, \quad \forall \{ X_W \} = \forall \{ X_0 \}, \quad \forall \{ X_{W,Q} \} = \sum_{\alpha \neq 0} \forall \{ X_\alpha \}.
$$

Observe:

1. $X_Q(Q) + \mathbb{E} \{ X \} = \mu_X(Q), \quad \mu_X(Q) = \mathbb{E} \{ X \}$
2. $\sum_{\alpha} \forall \{ X_\alpha \} = \sum_{\alpha} \mathbb{E} \{ X_\alpha^2 \} - \mathbb{E} \{ X_\alpha \}^2 = \mathbb{E}_Q \{ \Sigma_X^2 \}.$
**Linear additive system**

- Consider SODE with drift and diffusion terms given by:

\[
C(X, Q) = Q_1 - X \quad D(X, Q) = (\nu X + 1)Q_2
\]

where \(Q_1\) and \(Q_2\) are independent, uniformly-distributed, random variables with mean \(\mu_{1,2}\) and standard deviation \(\sigma_{1,2}\).

- The orthonormal PC basis consists of tensorized Legendre polynomials.

- We use for initial condition \(X(t = 0) = 0\) almost surely.
Additive noise model ($\nu = 0$) with $\mu_1 = 1$, $\mu_2 = 0.1$, $\sigma_1 = \sigma_2 = 0.05$:

$$dX(Q) = (Q_1 - X(Q))dt + Q_2dW,$$

a first-order expansion suffices to exactly represent $X(Q)$.

Selected trajectories and variability ranges for $[X_k](t, W)$. The plots correspond to $k = 0, 1$ and $2$, arranged from left to right.
Multiplicative noise: $Q_1 \sim U[1, 0.05], Q_2 \sim U[0.1, 0.05], \nu = 0.2$

Sample trajectories of $[X_k], 0 \leq k \leq 2$. Top row: order 0, bottom row: order 1 with and decreasing order in $Q_1$ from left to right.
Multiplicative Noise – II

Multiplicative noise: \( Q_1 \sim \mathcal{U}[1, 0.05], Q_2 \sim \mathcal{U}[0.1, 0.05], \nu = 0.2 \)

Sample trajectories of \([X_k], 3 \leq k \leq 14\). The total order ranges from 2 (top row) to 4 (bottom row), with and decreasing order in \(Q_1\) from left to right.
Multiplicative noise: $Q_1 \sim \mathcal{U}[1, 0.05]$, $Q_2 \sim \mathcal{U}[0.1, 0.05]$, $\nu = 0.2$

Probability density functions of the modes $[X_k]$ at $t = 10$. The modes have been centered and normalized to facilitate the comparison; the standard Gaussian distribution is also reported for reference.
Mode correlations

Projections in the planes $([X_k], [X_{k'}])$ of realizations of the centered and normalized solution vector $\mathbf{X}$ at time $t = 10$, for selected indices $k' = 0, 5, 9, 14$.

<table>
<thead>
<tr>
<th>$[X_k]$ vs $[X_{k'}]$</th>
<th>$k' = 0$</th>
<th>$k' = 5$</th>
<th>$k' = 9$</th>
<th>$k' = 14$</th>
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<tbody>
<tr>
<td>$k = 0$</td>
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<td>$k = 5$</td>
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<td><img src="image7" alt="Plot" /></td>
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<td>$k = 9$</td>
<td><img src="image9" alt="Plot" /></td>
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<td>$k = 14$</td>
<td><img src="image13" alt="Plot" /></td>
<td><img src="image14" alt="Plot" /></td>
<td><img src="image15" alt="Plot" /></td>
<td><img src="image16" alt="Plot" /></td>
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Conditional trajectories

Left: trajectories for samples of $Q$ and a *fixed* realization of $W$
Right: trajectories for samples of $W$ at a *fixed* value of the parameters.
Selected trajectories of $X$ and its SH functions.
### Parametric sensitivity

<table>
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<tr>
<th>$\mu_X(Q)$</th>
<th>$\Sigma_X^2(Q)$</th>
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<tr>
<td>$\mu_X(Q) - \mathbb{E}{X}$</td>
<td>$\Sigma_X^2(Q)$</td>
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Effect of $Q_1$ and $Q_2$ of the (centered) conditional mean $\mu_X(Q) = \mathbb{E}\{X \mid Q\} - \mathbb{E}\{X\}$ and variance $\Sigma_X^2(Q) = \mathbb{V}\{X \mid Q\}$ at time $t = 10$
Evolution of the components of the total variance. Shown are variance decompositions obtained for different values of $\sigma_1$ and $\sigma_2$.

<table>
<thead>
<tr>
<th>$\sigma_1 = 0 - \sigma_2 = 0$</th>
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<tr>
<td><img src="image1" alt="Graph 1" /></td>
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<td>$\sigma_1 = 0.05 - \sigma_2 = 0$</td>
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\[ \sigma_1 = 0 - \sigma_2 = 0 \]
\[ \sigma_1 = 0 - \sigma_2 = 0.05 \]
\[ \sigma_1 = 0.05 - \sigma_2 = 0 \]
\[ \sigma_1 = 0.05 - \sigma_2 = 0.05 \]
Consider a system with additive noise and non-linear drift

\[ dX = F(X)dt + \delta dW = -\gamma(X - a)(X - b)(X - c)dt + \delta dW \]

where \( \delta > 0 \) is an additional parameter controlling the noise level, and as before \( W \) is a Wiener process. Again the IC is \( X_0 = X(t = 0) \).

Sample trajectories with \( a = 10, b = 20, c = 30, \gamma = 0.01, \) and \( \delta = 1 \). In all cases, the initial condition coincides with \( x^0 = b \).
Consider an uncertain initial condition, $Q_1 \sim \mathcal{R}[17.5, 22.5]$, and forcing amplitude, $Q_2 \sim \mathcal{R}[0.5, 1.5]$.

$$dX = F(X)dt + Q_1 dW \quad X_0 = Q_2.$$ 

- $Q_1$ and $Q_2$ independent.
- The PC representation is based on an adaptive multiwavelet basis expansion, which enables us to accommodate for bifurcation(s).
- The use of a non polynomial basis complicates the sensitivity analysis, but the framework is essentially unaltered.
Sample trajectories

Left plots: sample set of realizations of $W$, the trajectories of $X$ (time running up) for different initial conditions and two noise levels $Q_2 = 0.65$ (top plot) and $Q_2 = 1.35$ (bottom).

Right plots show for two realizations of $W$ (top and bottom), the trajectories of $X$ for a random sample set of values of $Q_1$ and $Q_2$. 

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Variance-based SA
MW expansion

Left: partitions of the parametric domain and surface plots for $X(t = 6, W)$ as a function of $Q$. 
Variance decomposition

Partial variances of $X(t)$

Variance $V_{tot}$
Variance $V_{par}$
Variance $V_{noise}$
Variance $V_{mix}$

Graph showing the variance decomposition over time ($t$) with different colored areas representing $V_{tot}$, $V_{par}$, $V_{noise}$, and $V_{mix}$. The y-axis represents the variances ranging from 0 to 120.
**Effect of Noise amplitude**

Left: comparison of the total variances $\forall \{X\}$ and total noise contributions $V_{\text{noise}} + V_{\text{mix}}$ to the variance, for two expected values of $\mathbb{E}\{\delta\} = 1$ and 2.

Right: partial variances of the stochastic process $X(t)$ for the case $\mathbb{E}\{\delta\} = 2$. 
Stochastic Simulator

Work with Omar Knio and Alvaro Moraes (KAUST)
Stochastic Systems

Stochastic systems governed by *probabilistic* evolution rules expresses by the master equation

\[
\frac{\partial P(x, t|x_0, t_0)}{\partial t} = \sum_{j=1}^{K_r} \left[ a_j(x - \nu_j)P(x - \nu_j, t|x_0, t_0) - a_j(x)P(x, t|x_0, t_0) \right],
\]

- \(P(x, t|x_0, t_0):\) probability of \(X = x\) at time \(t\), given \(X = x_0\) at time \(t_0\),
- general form \(\partial P(x, t|x_0, t_0)/\partial t = f(P(\cdot, t|x_0, t_0))\) (Markov process),
- \(x(t):\) state of the system at time \(t\),
- \(K_r\) reactions channels,
- propensity functions \(a_j\) and state-change vectors \(\nu_j \in \mathbb{Z}^{M_s}\).

Examples includes *Reactive Networks* (chemistry, biology), social networks, . . .

- Direct resolution of the master equation is usually not an option,
- Simulations of trajectories of \(X(t) \sim P(x, t|x_0, t_0)\), using a stochastic simulator.
Gillespie’s Algorithm

Given $X(t) = x$, the probability of the next reaction to occur in the $[t, t + dt]$ is

$$a_0(x) dt = dt \sum_{j=1}^{K_r} a_j(x).$$

The time to the next reaction, $\tau$, follows an exponential distribution with mean $1/a_0(x)$.

Gillespie’s Algorithm :

1. Set $t = t_0, X = x_0$.
2. Repeat until $t > T$
   - Draw $\tau \sim \exp a_0(X)$
   - Pick randomly $k \in \{1 \ldots K_r\}$ with relative probability $p_k(a_k)$
   - Update $t \leftarrow t + \tau, X \leftarrow X + \nu_k$
3. Return $X(T) \sim P(x, t|x_0, t_0)$.

From a sample set of trajectory, estimate expectation of functionals $E \{g(X)\}$. 
Sobol Analysis of the variance

For a given output $X(t)$ of a stochastic simulator, and a functional $g$, we would like:

assess the contributions of different channels (or group of channels) on the variability of $g(X)$

That is: which channel(s) is (are) responsible for most of the variance in $g(X)$?

This is not to be confused with parametric sensitivity analyses where one wants to estimate the sensitivity of $E\{g(X)\}$ with respect to some parameters $q$ in the definition of the dynamics (e.g. propensity functions).
Sobol Analysis of the variance

- \( \mathbf{N}(\omega) = (N_1, \cdots, N_D) \) a set of \( D \) independent random inputs \( N_i \),
- \( F(\mathbf{N}) \) a (second-order) random functional in \( \mathbf{N} \),

\( F(\mathbf{N}) \) has a unique orthogonal decomposition

\[
F(\mathbf{N}) = \sum_{\mathbf{u} \in \mathcal{D}} F_{\mathbf{u}}(\mathbf{N}_{\mathbf{u}}),
\]

where \( \mathcal{D} \) is the power set of \( \{1, \cdots, D\} \) and \( \mathbf{N}_{\mathbf{u}} = (N_{u_1}, \cdots, N_{u_{|\mathbf{u}|}}) \). The orthogonality condition reads

\[
\mathbb{E}\{F_{\mathbf{u}} F_{\mathbf{s}}\} = \int_{\Omega} F_{\mathbf{u}}(\mathbf{N}_{\mathbf{u}}(\omega)) F_{\mathbf{s}}(\mathbf{N}_{\mathbf{s}}(\omega)) d\mu(\omega) = 0,
\]

so

\[
\nabla\{F\} = \sum_{\mathbf{u} \in \mathcal{D} \setminus \emptyset} \nabla\{F_{\mathbf{u}}\},
\]

where \( \nabla\{F_{\mathbf{u}}\} \) are called partial variances.
Sobol Analysis of the variance (cont. . .)

From the variance decomposition,

\[ \nabla \{ F \} = \sum_{\mathbf{u} \in \mathcal{D} \setminus \emptyset} \nabla \{ F_{\mathbf{u}} \}, \]

- **First order sensitivity indices** $s_{\mathbf{u}}$: fraction of the variance caused by the random inputs $N_{\mathbf{u}}$ only

  \[ \nabla \{ F \} s_{\mathbf{u}} = \sum_{\mathbf{s} \supseteq \emptyset}^{\mathbf{s} \neq \emptyset} \nabla \{ F_{\mathbf{u}} \} \]

- **Total order sensitivity indices** $t_{\mathbf{u}}$: fraction of the variance caused by the random inputs $N_{\mathbf{u}}$ and interaction

  \[ \nabla \{ F \} t_{\mathbf{u}} = \sum_{\mathbf{s} \in \mathcal{D}}^{(\mathbf{s} \cap \mathbf{u}) \neq \emptyset} \nabla \{ F_{\mathbf{s}} \} \]

The partial variances $\nabla \{ F_{\mathbf{u}} \}$ can be expressed as **conditional variances**:

[Homma & Saltelli, 1996]

\[ \nabla \{ F_{\mathbf{u}} \} = \nabla \left\{ \mathbb{E} \{ F \mid N_{\mathbf{u}} \} \right\} - \sum_{\mathbf{s} \in \mathcal{D} \setminus \emptyset}^{\mathbf{s} \neq \emptyset} \nabla \{ F_{\mathbf{s}} \}, \]

or

\[ \nabla \{ F \} s_{\mathbf{u}} = \nabla \left\{ \mathbb{E} \{ F \mid N_{\mathbf{u}} \} \right\}, \quad \nabla \{ F \} t_{\mathbf{u}} = \nabla \{ F \} - \nabla \left\{ \mathbb{E} \{ F \mid N_{\mathbf{u}} \} \right\} = \nabla \{ F \} (1 - s_{\mathbf{u}}), \]

where $\mathbf{u} = \{1, \ldots, D\} \setminus \mathbf{u}$.

**Decomposition of the Variance = Estimation of conditional variances**
Consider two independent sample sets $\mathcal{N}^I$ and $\mathcal{N}^{II}$ of $M$ realizations of $\mathcal{N}$. The conditional variance $\nabla \{ \mathbb{E} \{ F \mid \mathcal{N}_u \} \}$ can be estimated as [Sobol, 2001]

$$\nabla \{ \mathbb{E} \{ F \mid \mathcal{N}_u \} \} + \mathbb{E} \{ F \}^2 = \lim_{M \to \infty} \frac{1}{M} \sum_{i=1}^{M} F(\mathcal{N}_u^I(i), \mathcal{N}_u^{II}(i)) F(\mathcal{N}_u^I(i), \mathcal{N}_u^{II}(i)),$$

such that

$$\hat{S}_u = \frac{1}{M} \sum_{i=1}^{M} F(\mathcal{N}_u^I(i)) F(\mathcal{N}_u^I(i), \mathcal{N}_u^{II}(i)) - \mathbb{E} \{ F \}^2 \nabla \{ F \},$$

and

$$\hat{T}_u = 1 - \frac{1}{M} \sum_{i=1}^{M} F(\mathcal{N}_u^I(i)) F(\mathcal{N}_u^{II}(i), \mathcal{N}_u^{I}(i)) - \mathbb{E} \{ F \}^2 \nabla \{ F \}$$

where $\mathbb{E} \{ F \}$ and $\nabla \{ F \}$ are the classical MC estimators for the mean and variance.

The computational complexity scales linearly with the number of indices to be computed.
Application to Stochastic Simulators

To assess the respective impacts of different reaction channels through Sobol’s decomposition of $\nabla \{g(\mathbf{X})\}$, when $\mathbf{X}$ is the output of a stochastic simulator, we need to condition $\mathbf{X}$ on the channels dynamics:

What is a particular realization of a channel dynamics?

Gillespie’s algorithm is not suited, and we have to recast the stochastic algorithm in terms of independent processes associated to each channel.

Next Reaction Formulation. [Ethier & Kurtz, 2005, Gibson & Bruck, 2000]

$$\mathbf{X}(t) = \mathbf{X}(t_0) + \sum_{j=1}^{K_r} \nu_j N_j(t_j),$$

where the $N_j(t)$ are independent standard (unit rate) Poisson processes, and the scaled times $t_j$ are given by

$$t_j = \int_{t_0}^{t} a_j(\mathbf{X}(\tau)) d\tau, \quad j = 1, \ldots, K_r.$$

Then, $g(\mathbf{X})$ can be seen as

$$g(\mathbf{X}) = F(N_1, \ldots, N_{K_r}).$$
The random functional $g(X) = F(N_1, \ldots, N_{K_r})$ can then be decomposed à la Sobol. A particular realization of a channel dynamic is identified with a realization of the underlying standard Poisson processes.

For instance, the conditional variance writes

$$
\mathbb{E} \left\{ g(X) \mid N_u = n_u \right\} = \mathbb{E} \left\{ g \left( X(t_0) + \sum_{j \in u} \nu_j n_j(t_j) + \sum_{j \in \sim} \nu_j N_j(t_j) \right) \right\},
$$

with $t_j = \int_{t_0}^t a_j(X(\tau)) d\tau$.

Note that

- in general, for fixed $n_u(t)$ the physical firing times $t_j$ remain random and depend on $N_u \sim$, even for $j \in u$
- in practice, the standard Poisson processes $N_j$ are entirely specified by their random seeds and pseudo-random number generator:

  the Poisson processes don't have to be stored but are computed on the fly
The birth-death (BD) process

Single species $S (M_s = 1)$ and $K_r = 2$ reaction channels:

\[ \emptyset \xrightarrow{b} S, \quad S \xrightarrow{d} \emptyset , \]

with propensity functions

\[ a_1(x) = b, \quad a_2(x) = d \times x . \]

We set $b = 200$, $d = 1$, and use $M = 1,000,000$ Monte Carlo samples to compute the estimates.

**Figure:** Left: Selected trajectories of $X(t)$ generated using Next Reaction Algorithm. Right: histogram of $X(t = 8)$. 
B-D process. Variance decomposition of $g(X) = X(t)$

Left: scaled first-order and total sensitivity indices (scaled by the variance) of the birth-death model and $t \in [0, 8]$. Right: long-time evolution of the first-order sensitivity indices, and of the mixed interaction term.

- Variance in $X$ is predominantly caused by the birth channel stochasticity for early time $t < 1$
- For $1 \leq t \leq 4$, the variability induced by $R_d$ only continues to grow with the population size (first order reaction), while mixed effects develops
- Eventually, effect of $R_b$ stabilize (zero-order reaction, rate independent of $X$) while effect of $R_d$ only slowly decays to benefit the mixed term (stochasticity of $N_b$ affects more and more the death process).
System with $K_r = 4$ reaction channels:

$$B_1 + 2S \xrightarrow{c_1 \to c_2} 3S, \quad B_2 \xrightarrow{c_3 \to c_4} S,$$

with $B_1$ and $B_2$ in large excess and constant population over time, $X_{B_1} = X_{B_2}/2 = 10^5$ and a single evolving species $S$ with $M_s = 1$. The propensity functions are given by

$$a_1(x) = \frac{c_1}{2} X_{B_1} x(x - 1), \quad a_2(x) = \frac{c_2}{6} x(x - 1)(x - 2), \quad a_3(x) = c_3 X_{B_2}, \quad a_4(x) = c_4 x.$$

We set $c_1 = 3 \times 10^{-7}$, $c_2 = 10^{-4}$, $c_3 = 10^{-3}$, $c_4 = 3.5$ and deterministic initial condition $X(t = 0) = 250$. Results in a bi-modal dynamic.
Schlögl model - Variance decomposition of $g(X) = X(t)$

First and total order partial variances.

Higher order partial variances.

Reaction channels $R_1$ and $R_4$ are the dominant sources of variance. Dynamic essentially additive up to $t \sim 2$
Analysis of the partial variance revealed that \( R_1 \) and \( R_4 \) are the main sources of stochasticity.

It suggests a **dominant role in selecting the bifurcation branch**, as illustrated below.

### Schlögl model - Variance decomposition of \( g(X) = X(t) \)

<table>
<thead>
<tr>
<th>(a) Conditioned on ( N_1 ) and ( N_4 )</th>
<th>(b) Conditioned on ( N_2 ) and ( N_3 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trajectories of ( X(t) ) conditioned on ( N_1(\omega) = n_1 ) and ( N_4(\omega) = n_4 ), and ( N_2(\omega) = n_2 ) and ( N_3(\omega) = n_3 ). Each sub-plot shows 10 conditionally random trajectories for fixed realizations ( n_1 ) and ( n_4 ) in (a), and ( n_2 ) and ( n_3 ) in (b).</td>
<td></td>
</tr>
</tbody>
</table>
Michaelis-Menten system

\( M_s = 4 \) species and \( K_r = 3 \) reaction channels:

\[
S_1 + S_2 \xrightarrow{c_1 \over c_2} S_3, \quad S_3 \xrightarrow{c_3} S_4 + S_2
\]

with \( a_1(x) = c_1 x_1 x_2, a_2(x) = c_2 x_3, \) and \( c_3(x) = c_3 x_3 \).

We set \( c_1 = 0.0017, c_2 = 10^{-3} \) and \( c_3 = 0.125 \), and initial conditions

\( X_1(t = 0) = 300, X_2(t = 0) = 120 \) and \( X_3(t = 0) = X_4(t = 0) = 0 \)
Michaelis-Menten system - Variance decomposition of \( g(X) = X_i(t) \)

Note: \( X_2 + X_3 = \text{const} \), the sensitivity indices for \( S_2 \) and \( S_3 \) are equal

<table>
<thead>
<tr>
<th>(a) ( S_1 )</th>
<th>(b) ( S_2 )</th>
<th>(c) ( S_4 )</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="Graph of ( S_1 )" /></td>
<td><img src="image" alt="Graph of ( S_2 )" /></td>
<td><img src="image" alt="Graph of ( S_4 )" /></td>
</tr>
</tbody>
</table>

Michaelis-Menten model: First-order and total sensitivity indices \( S_{\{j\}} \) and \( T_{\{j\}} \) for \( j = 1, \ldots, 4 \).

Plots are generated for (a) \( X_1 \), (b) \( X_2 \) and (c) \( X_4 \):

- Relative importance of \( R_1 \) and \( R_3 \) changes in time for \( S_1 \) and \( S_2 \)
- Stochastic dynamic of \( S_4 \) is essentially additive and dominated by \( R_3 \)
- Channel \( R_2 \) induces nearly no variance in \( X(t) \): here the dissociation reaction \( R_2 \) can be simply disregarded without affecting significantly the dynamics.
On the contrary, increasing $c_2$ by an order of magnitude, the effect of $R_2$ on the variances becomes apparent:

(a) $S_1$

(b) $S_2$

(c) $S_4$
Conclusion and Future Work

We have proposed

- Hybrid Galerkin / MC approach for noisy systems, can be extended to Non-Intrusive methods
- Parametric dependence assumes smoothness of the trajectories
- Development of methods and algorithms that enable variance decomposition for stochastic simulators output
- Identification of the channels dynamics with their underlying standard Poisson processes
- Assessment of the relative importance of different reaction channels on the variance

On-going and future works

- Application to more complex functional $g(X)$: exit-time, path integrals, ...(smoothness?)
- Account for parametric uncertainty in the definition of the propensity functions
- Improve stochastic simulators for computational complexity reduction, e.g. Tau-Leaping method and variance reduction methods.


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Algorithm

ALGORITHM 3. Computation of the first and total-order sensitivity indices $S_{(j)}$ and $T_{(j)}$ of $g(X(T))$.

Procedure Compute_SI($M, X_0, T, \nu_j, \{a_j\}, g$)

Require: Sample set dimension $M$, initial condition $X_0$, final time $T$, state-change vectors $\{\nu_j\}$, propensity functions $\{a_j\}$ and functional $g$

1: $\mu \leftarrow 0, \sigma^2 \leftarrow 0 \quad \triangleright\text{Init. Mean and Variance}$
2: for $j = 1$ to $K_r$ do
3: \hspace{0.5em} $S(j) \leftarrow 0, T(j) \leftarrow 0 \quad \triangleright\text{Init. first and total-order SI}$
4: end for
5: for $m = 1$ to $M$ do
6: \hspace{0.5em} Draw two independent set of seeds $s^I$ and $s^{II}$
7: \hspace{1em} $X \leftarrow \text{NRA}(X_0, T, \{\nu_j\}, \{a_j\}, \text{RG}_1(s^I_1), \ldots, \text{RG}_{K_r}(s^I_{K_r}))$
8: \hspace{1em} $\mu \leftarrow \mu + g(X), \sigma^2 \leftarrow \sigma^2 + g(X)^2 \quad \triangleright\text{Acc. mean and variance}$
9: for $j = 1$ to $K_r$ do
10: \hspace{1.5em} $X_s \leftarrow \text{NRA}(X_0, T, \{\nu_j\}, \{a_j\}, \text{RG}_1(s^{II}_1), \ldots, \text{RG}_j(s^{II}_j), \ldots, \text{RG}_{K_r}(s^{II}_{K_r}))$
11: \hspace{1em} $X_t \leftarrow \text{NRA}(X_0, T, \{\nu_j\}, \{a_j\}, \text{RG}_1(s^{II}_1), \ldots, \text{RG}_j(s^{II}_j), \ldots, \text{RG}_{K_r}(s^{II}_{K_r}))$
12: \hspace{1.5em} $S(j) \leftarrow S(j) + g(X) \times g(X_s) \quad \triangleright\text{Acc. 1-st order}$
13: \hspace{1.5em} $T(j) \leftarrow T(j) + g(X) \times g(X_t) \quad \triangleright\text{Acc. total order}$
14: end for
15: $\mu \leftarrow \mu/M, \sigma^2 \leftarrow \sigma^2/(M-1) - \mu^2$
16: for $j = 1$ to $K_r$ do
17: \hspace{1.5em} $S(j) \leftarrow S(j)/\sigma^2 - \mu^2/\sigma^2 \quad \triangleright\text{Estim. 1-st order}$
18: \hspace{1.5em} $T(j) \leftarrow 1 - (T(j)^2)/(M-1) + \mu^2/\sigma^2 \quad \triangleright\text{Estim. total order}$
19: end for
20: return $S(j)$ and $T(j), j = 1, \ldots, K_r \quad \triangleright\text{First and total-order sensitivity indices}$
21: end if
22: Return $X \quad \triangleright\text{State } X(T)$

Procedure NRA implement the Next Reaction Algorithm

Poisson processes defined by two independent sets of seeds and RNG

Obvious parallelization

ALGORITHM 2. Next Reaction Algorithm.

Procedure NRA($X_0, T, \{\nu_j\}, \{a_j\}, \text{RG}_1, \ldots, \text{RG}_{K_r}$.)

Require: Initial condition $X_0$, final time $T$, state-change vectors $\{\nu_j\}$, propensity functions $\{a_j\}$, and seeded pseudo-random number generators $\text{RG}_1, \ldots, \text{RG}_{K_r}$

1: for $j = 1, \ldots, K_r$ do
2: \hspace{0.5em} Draw $r_j$ from $\text{RG}_j$
3: \hspace{1em} $\tau_j \leftarrow 0, \tau_j^* \leftarrow -\log r_j \quad \triangleright\text{set next reaction times}$
4: end for
5: $t \leftarrow 0, X \leftarrow X_0$
6: loop
7: for $j = 1, \ldots, K_r$ do
8: \hspace{1em} Evaluate $a_j(X)$ and $dt_j = \tau_j^* - \tau_j$
9: end for
10: Set $l = \arg\min dt_j \quad \triangleright\text{pick next reaction}$
11: if $t + dt_l > T$ then
12: \hspace{0.5em} break \quad \triangleright\text{Final time reached}$
13: else
14: \hspace{1em} $t \leftarrow t + dt_l \quad \triangleright\text{update time}$
15: \hspace{1em} $X \leftarrow X + \nu_l \quad \triangleright\text{update the state vector}$
16: for $j = 1, \ldots, K_r$ do
17: \hspace{1.5em} $\tau_j \leftarrow \tau_j + a_j dt_l \quad \triangleright\text{update unscaled times}$
18: end for
19: Get $r_l$ from $\text{RG}_l$
20: $\tau_l^* \leftarrow \log r_l \quad \triangleright\text{next reaction time}$
21: end if
22: end loop
23: Return $X \quad \triangleright\text{State } X(T)$