Predictability in Stochastic Reaction Networks

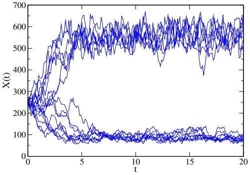
Khachik Sargsyan, Bert Debusschere, Habib Najm

Sandia National Laboratories
Livermore, CA

SIAM CSE Meeting
Reno, NV
February 28 - March 4, 2011

Stochastic Reaction Networks

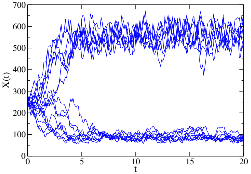
- Reaction networks involving small number of molecules necessitate the use of *stochastic* modeling instead of the *deterministic* one. E.g.
  - Microbial processes (bioenergy, bioremediation)
  - Surface catalytic reactions (fuel cells, batteries)
  - Immune system signaling reactions



- SRNs are modeled as Jump Markov Processes
  - Governed by Chemical Master Equation $\dot{P}(X(t)=n)=\sum_m A_{nm}P(X(t)=n)$
  - Reduces to deterministic Rate Equations in the large volume limit
  - Trajectories simulated by Gillespie's Stochastic Simulation Algorithm (SSA, Gillespie, 1977)

Stochastic Reaction Networks

- Reaction networks involving small number of molecules necessitate the use of *stochastic* modeling instead of the *deterministic* one. E.g.
  - Microbial processes (bioenergy, bioremediation)
  - Surface catalytic reactions (fuel cells, batteries)
  - Immune system signaling reactions



- SRNs are modeled as Jump Markov Processes
  - Governed by Chemical Master Equation $\dot{P}(X(t)=n) = \sum_m A_{nm} P(X(t)=n)$
  - Reduces to deterministic Rate Equations in the large volume limit
  - Trajectories simulated by Gillespie's Stochastic Simulation Algorithm (SSA, Gillespie, 1977)

Objective: predictability in high-d

$$X(t, \boldsymbol{\theta}, \boldsymbol{\lambda})$$

- Develop tools for *predictability*$(\boldsymbol{\lambda})$ and *dynamical analysis*(t) of SRNs accounting for
  - Inherent stochasticity $(\boldsymbol{\theta})$
  - Model/parameter uncertainty $(\boldsymbol{\lambda})$
  - Limited data

$$\mathcal{D} = \{X_i\}_{i=1}^N$$

- Predictability assessment
  - Fix t, focus on λ dependence
  - Statistical properties $Y(\lambda) = \langle f(X(\theta, \lambda)) \rangle$ have sampling noise
  - How uncertainty in λ affects uncertainty in $Y(\lambda)$ given limited data
- High dimensionality of λ

Objective: predictability in high-d

$$X(t, \boldsymbol{\theta}, \boldsymbol{\lambda})$$

- Develop tools for *predictability*($\boldsymbol{\lambda}$) and *dynamical analysis*(t) of SRNs accounting for
  - Inherent stochasticity ($\boldsymbol{\theta}$)
  - Model/parameter uncertainty ($\boldsymbol{\lambda}$)
  - Limited data

$$\mathcal{D} = \{X_i\}_{i=1}^N$$

- Predictability assessment
  - Fix t, focus on $\boldsymbol{\lambda}$ dependence
  - Statistical properties $Y(\boldsymbol{\lambda}) = \langle f(X(\boldsymbol{\theta}, \boldsymbol{\lambda}))\rangle$ have sampling noise
  - How uncertainty in $\boldsymbol{\lambda}$ affects uncertainty in $Y(\boldsymbol{\lambda})$ given limited data

- High dimensionality of λ

Objective: predictability in high-d

$$X(t, \boldsymbol{\theta}, \boldsymbol{\lambda})$$

- Develop tools for *predictability*($\boldsymbol{\lambda}$) and *dynamical analysis*(t) of SRNs accounting for
  - Inherent stochasticity ($\boldsymbol{\theta}$)
  - Model/parameter uncertainty ($\boldsymbol{\lambda}$)
  - Limited data

$$\mathcal{D} = \{X_i\}_{i=1}^N$$

- Predictability assessment
  - Fix t, focus on $\boldsymbol{\lambda}$ dependence
  - Statistical properties $Y(\boldsymbol{\lambda}) = \langle f(X(\boldsymbol{\theta}, \boldsymbol{\lambda}))\rangle$ have sampling noise
  - How uncertainty in $\boldsymbol{\lambda}$ affects uncertainty in $Y(\boldsymbol{\lambda})$ given limited data

- **High dimensionality of $\boldsymbol{\lambda}$**

High-dimensional parametric uncertainty in stochastic systems

- Statistical property $Y(\boldsymbol{\lambda}) = \langle f(X(\boldsymbol{\theta}, \boldsymbol{\lambda}))\rangle$ of interest.
  - High-dimensional parametric uncertainty ($\boldsymbol{\lambda}$)
  - Sampling noise due to limited data $\{X_i\}$
- Expectation $\langle\cdot\rangle$ filters intrinsic noise.
  - Averaging over sample realizations of X
  - Still leftover noise, width $\sim 1/\sqrt{N}$
- Polynomial Chaos expansion to represent input-output relationship
  - Sensitivity analysis
  - Surrogate model for optimization or inverse problems
  - Identify key reaction mechanisms

Polynomial Chaos expansion represents a random variable as a polynomial of a standard random variable

- Truncated PCE: finite dimension n and order p

$$Y \simeq \sum_{k=0}^{P} c_k \Psi_k(\boldsymbol{\eta})$$

with the number of terms $P+1=\frac{(n+p)!}{n!p!}$.

- $\boldsymbol{\eta}=(\eta_1,\cdots,\eta_n)$ standard i.i.d. r.v.
  Ψ_k standard orthogonal polynomials
  c_k spectral modes.

- Most common standard Polynomial-Variable pairs:
  (continuous) Gauss-Hermite, Legendre-Uniform,
  (discrete) Poisson-Charlier.

[Wiener, 1938; Ghanem & Spanos, 1991; Xiu & Karniadakis, 2002]

Polynomial Chaos expansion represents a random variable as a polynomial of a standard random variable

- Truncated PCE: finite dimension n and order p

$$Y \simeq \sum_{k=0}^{P} c_k \Psi_k(\boldsymbol{\eta})$$

with the number of terms $P+1 = \frac{(n+p)!}{n!p!}$.

- $\boldsymbol{\eta} = (\eta_1, \cdots, \eta_n)$ standard i.i.d. r.v.
  Ψ_k standard orthogonal polynomials
  c_k spectral modes.

- Most common standard Polynomial-Variable pairs:
  (continuous) Gauss-Hermite, Legendre-Uniform,
  (discrete) Poisson-Charlier.

[Wiener, 1938; Ghanem & Spanos, 1991; Xiu & Karniadakis, 2002]

Polynomial Chaos expansion represents a random variable as a polynomial of a standard random variable

- Truncated PCE: finite dimension n and order p

$$Y \simeq \sum_{k=0}^{P} c_k \Psi_k(\boldsymbol{\eta})$$

with the number of terms $P+1 = \frac{(n+p)!}{n!p!}$.

- $\boldsymbol{\eta} = (\eta_1, \cdots, \eta_n)$ standard i.i.d. r.v.
Ψ_k standard orthogonal polynomials
c_k spectral modes.
- Most common standard Polynomial-Variable pairs:
(continuous) Gauss-Hermite, Legendre-Uniform,
(discrete) Poisson-Charlier.

[Wiener, 1938; Ghanem & Spanos, 1991; Xiu & Karniadakis, 2002]

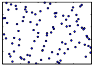
Alternative methods to obtain PC coefficients

$$Y \simeq \sum_{k=0}^{P} c_k \Psi_k(\boldsymbol{\eta}) \qquad c_k = \frac{\langle Y(\boldsymbol{\eta}) \Psi_k(\boldsymbol{\eta}) \rangle}{\langle \Psi_k^2(\boldsymbol{\eta}) \rangle}$$

The integral $\langle Y(\boldsymbol{\eta}) \Psi_k(\boldsymbol{\eta}) \rangle = \int Y(\boldsymbol{\eta}) \Psi_k(\boldsymbol{\eta}) \pi(\boldsymbol{\eta}) d\boldsymbol{\eta}$ can be estimated by

- Monte-Carlo

$$\frac{1}{K} \sum_{j=1}^{K} Y(\boldsymbol{\eta}_j) \Psi_k(\boldsymbol{\eta}_j)$$



many samples from $\pi(\boldsymbol{\eta})$

- Quadrature

$$\sum_{j=1}^{Q} Y(\boldsymbol{\eta}_j) \Psi_k(\boldsymbol{\eta}_j) w_j$$

samples at quadrature

- *Bayesian inference*

$$P(c_k | Y(\boldsymbol{\eta}_j)) \propto P(Y(\boldsymbol{\eta}_j) | c_k) P(c_k)$$

any (number of) samples

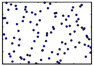
Alternative methods to obtain PC coefficients

$$Y \simeq \sum_{k=0}^{P} c_k \Psi_k(\boldsymbol{\eta}) \qquad\qquad c_k = \frac{\langle Y(\boldsymbol{\eta})\Psi_k(\boldsymbol{\eta})\rangle}{\langle \Psi_k^2(\boldsymbol{\eta})\rangle}$$

The integral $\langle Y(\boldsymbol{\eta})\Psi_k(\boldsymbol{\eta})\rangle = \int Y(\boldsymbol{\eta})\Psi_k(\boldsymbol{\eta})\pi(\boldsymbol{\eta})d\boldsymbol{\eta}$ can be estimated by

- Monte-Carlo

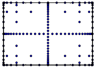
$$\frac{1}{K}\sum_{j=1}^{K} Y(\boldsymbol{\eta}_j)\Psi_k(\boldsymbol{\eta}_j)$$



many samples from $\pi(\boldsymbol{\eta})$

- Quadrature

$$\sum_{j=1}^{Q} Y(\boldsymbol{\eta}_j)\Psi_k(\boldsymbol{\eta}_j)w_j$$



samples at quadrature

- *Bayesian inference*

$$P(c_k|Y(\boldsymbol{\eta}_j)) \propto P(Y(\boldsymbol{\eta}_j)|c_k)P(c_k)$$

any (number of) samples

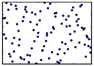
Alternative methods to obtain PC coefficients

$$Y \simeq \sum_{k=0}^{P} c_k \Psi_k(\boldsymbol{\eta}) \qquad c_k = \frac{\langle Y(\boldsymbol{\eta})\Psi_k(\boldsymbol{\eta})\rangle}{\langle \Psi_k^2(\boldsymbol{\eta})\rangle}$$

The integral $\langle Y(\boldsymbol{\eta})\Psi_k(\boldsymbol{\eta})\rangle = \int Y(\boldsymbol{\eta})\Psi_k(\boldsymbol{\eta})\pi(\boldsymbol{\eta})d\boldsymbol{\eta}$ can be estimated by

- Monte-Carlo

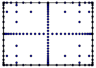
$$\frac{1}{K}\sum_{j=1}^{K} Y(\boldsymbol{\eta}_j)\Psi_k(\boldsymbol{\eta}_j)$$



many samples from $\pi(\boldsymbol{\eta})$

- Quadrature

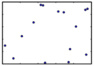
$$\sum_{j=1}^{Q} Y(\boldsymbol{\eta}_j)\Psi_k(\boldsymbol{\eta}_j)w_j$$



samples at quadrature

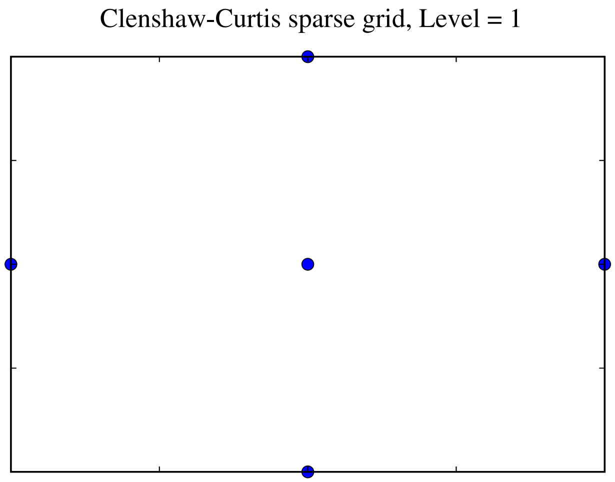
- *Bayesian inference*

$$P(c_k|Y(\boldsymbol{\eta}_j)) \propto P(Y(\boldsymbol{\eta}_j)|c_k)P(c_k)$$

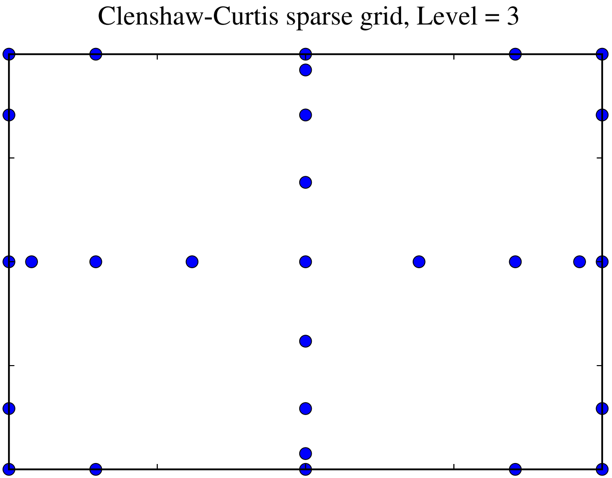


any (number of) samples

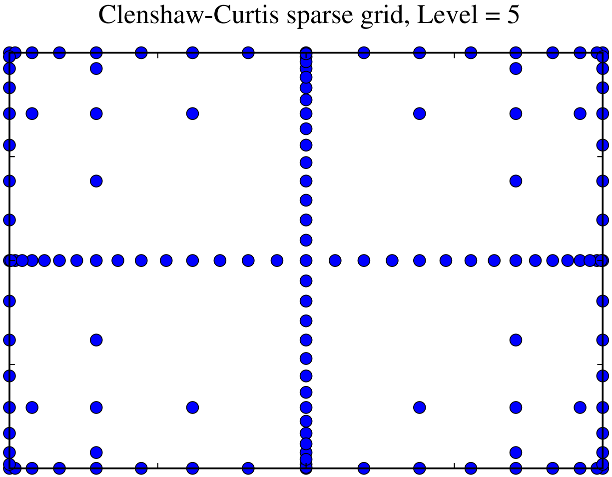
Sparse quadrature integration well-suited for high-dimensional *smooth* integrands



Sparse quadrature integration well-suited for high-dimensional *smooth* integrands



Sparse quadrature integration well-suited for high-dimensional *smooth* integrands



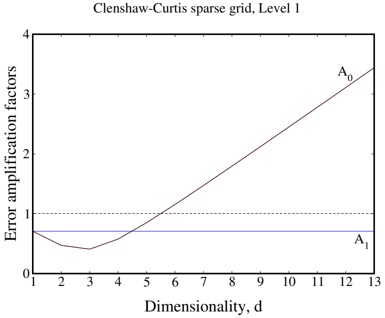
Sparse quadrature integration fails for noisy integrands

$$Y \simeq \sum_{k=0}^{P} c_k \Psi_k(\boldsymbol{\eta})$$

$$c_k = \frac{\langle Y(\boldsymbol{\eta})\Psi_k(\boldsymbol{\eta})\rangle}{\langle \Psi_k^2(\boldsymbol{\eta})\rangle}$$

$$c_k \approx \frac{1}{\langle \Psi_k^2(\boldsymbol{\eta})\rangle} \sum_{j=1}^{Q} Y(\boldsymbol{\eta}_j)\Psi_k(\boldsymbol{\eta}_j) w_j$$

Noise$_Y \sim \sigma \Longrightarrow$ Error$_{c_k} \sim A_k\sigma$



- amplification factor A_k grows with dimensionality
  - CC, level 1: $A_0 = \frac{1}{3}\sqrt{(d-3)^2 + \frac{d}{2}}, \qquad A_1 = \frac{1}{\sqrt{2}}$.
- blame the negative weights.
- for full quadrature, $\frac{1}{n^{d/2}} \le A_0 \le 1$, no amplification!

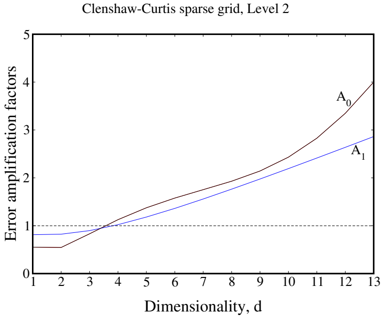
Sparse quadrature integration fails for noisy integrands

$$Y \simeq \sum_{k=0}^{P} c_k \Psi_k(\boldsymbol{\eta})$$

$$c_k = \frac{\langle Y(\boldsymbol{\eta})\Psi_k(\boldsymbol{\eta})\rangle}{\langle \Psi_k^2(\boldsymbol{\eta})\rangle}$$

$$c_k \approx \frac{1}{\langle \Psi_k^2(\boldsymbol{\eta})\rangle} \sum_{j=1}^{Q} Y(\boldsymbol{\eta}_j)\Psi_k(\boldsymbol{\eta}_j) w_j$$

Noise$_Y \sim \sigma \Longrightarrow$ Error$_{c_k} \sim A_k\sigma$



- amplification factor A_k grows with dimensionality
  - CC, level 1: $A_0 = \frac{1}{3}\sqrt{(d-3)^2 + \frac{d}{2}}$, $\qquad A_1 = \frac{1}{\sqrt{2}}$.
- blame the negative weights.
- for full quadrature, $\frac{1}{n^{d/2}} \leq A_0 \leq 1$, no amplification!

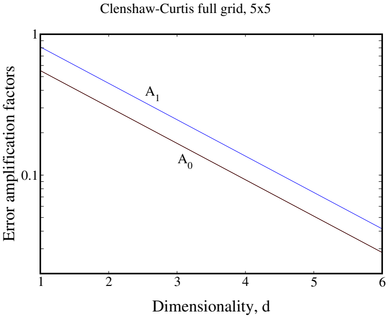
Sparse quadrature integration fails for noisy integrands

$$Y \simeq \sum_{k=0}^{P} c_k \Psi_k(\boldsymbol{\eta})$$

$$c_k = \frac{\langle Y(\boldsymbol{\eta})\Psi_k(\boldsymbol{\eta})\rangle}{\langle \Psi_k^2(\boldsymbol{\eta})\rangle}$$

$$c_k \approx \frac{1}{\langle \Psi_k^2(\boldsymbol{\eta})\rangle} \sum_{j=1}^{Q} Y(\boldsymbol{\eta}_j)\Psi_k(\boldsymbol{\eta}_j) w_j$$

$\text{Noise}_Y \sim \sigma \Longrightarrow \text{Error}_{c_k} \sim A_k\sigma$



- amplification factor A_k grows with dimensionality
  - CC, level 1: $A_0 = \frac{1}{3}\sqrt{(d-3)^2 + \frac{d}{2}}$, $\qquad A_1 = \frac{1}{\sqrt{2}}$.
- blame the negative weights.
- for full quadrature, $\frac{1}{n^{d/2}} \leq A_0 \leq 1$, no amplification!

Bayesian inference handles the intrinsic stochasticity well

$$Y = \langle X \rangle \simeq \sum_{k=0}^{P} c_k \Psi_k(\boldsymbol{\eta})$$

$$\overbrace{P(\boldsymbol{c}|\mathcal{D})}^{\text{Posterior}} \propto \overbrace{P(\mathcal{D}|\boldsymbol{c})}^{\text{Likelihood}} \overbrace{P(\boldsymbol{c})}^{\text{Prior}}$$

$$L(\boldsymbol{c}) = P(\mathcal{D}|\boldsymbol{c}) = \left(\frac{1}{\sigma\sqrt{2\pi}}\right)^N \prod_{i=1}^{N} \exp\left(-\frac{(X_i - \sum_{k=0}^{P} c_k \Psi_k(\boldsymbol{\eta}_i))^2}{2\sigma^2}\right).$$

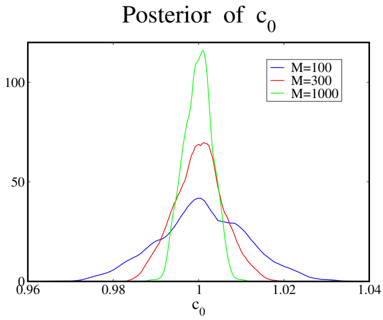
- Noise model is assumed gaussian with σ from CLT or inferred
- Uniformly distributed priors
- Posterior exploration using Markov Chain Monte Carlo (MCMC)
- The whole posterior distribution is accessible, *i.e.* uncertain response surface
- Input parameters can have arbitrary values

Posterior narrows around the true value as more samples are taken

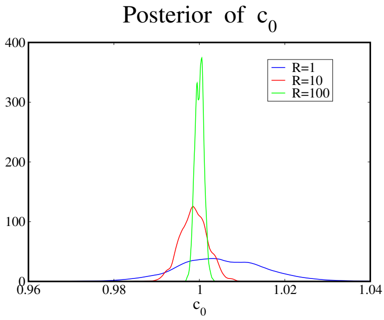
- M parameter locations
- R replicas per parameter

- Second order Legendre polynomial expansion with unit coefficients.

No noise in function evaluations, $R = 1$



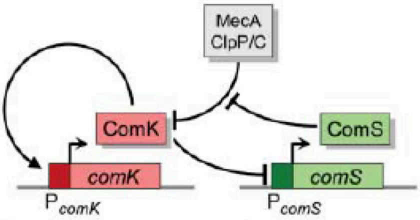
Noisy function evaluations, $M = 100$



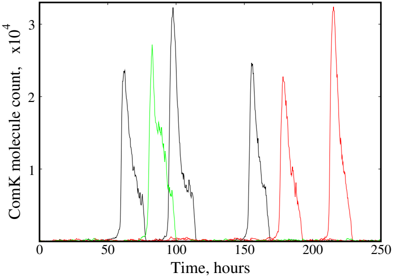
Bacillus subtilis is a soil bacterium

relevant to bioenergy and bioremediation

- 16 reactions, 11 species
- Competence in *B. Subtilis* allows uptake of external DNA
- Rapid rise in transcription factor comK molecules
- Vegetative $\rightarrow$ Competent state transition is driven by stochasticity
- Input parameters: rate constants of underlying reactions (high-d)
- Output observable: probability of competence $P_c = P(X_\infty > 5000)$



Süel et al., Science, 2007



Intrinsic stochasticity induces transition to competence

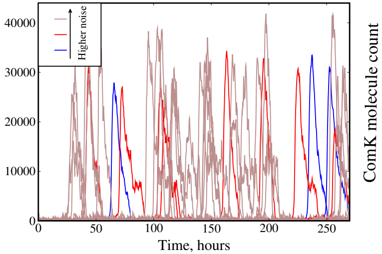
Chemical Master Equation (CME):

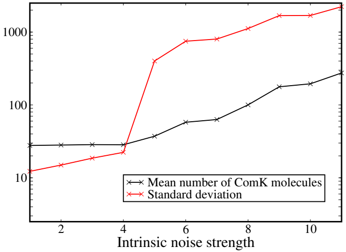
$$\frac{d}{dt}P(X(t)=n)=\sum_m A_{nm}P(X(t)=n)$$

Rate equation (ODE):

$$\frac{d}{dt}X(t)=\tilde{A}(X)$$

- No-noise or large volume limit (ODE) does not produce competence
- Many parameter combinations lead to the same ODE limit, but correspond to different effective volumes, i.e. intrinsic noise strength
- Increasing intrinsic noise leads to more frequent transitions





Intrinsic stochasticity induces transition to competence

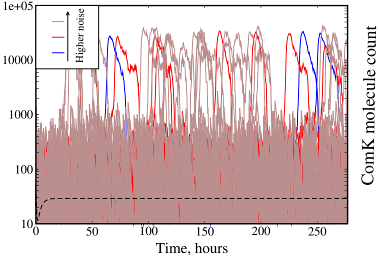
Chemical Master Equation (CME):

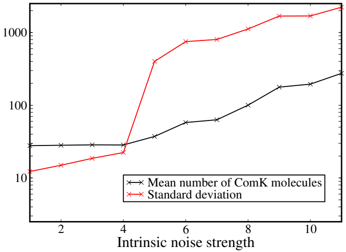
$$\frac{d}{dt}P(X(t)=n)=\sum_m A_{nm}P(X(t)=n)$$

Rate equation (ODE):

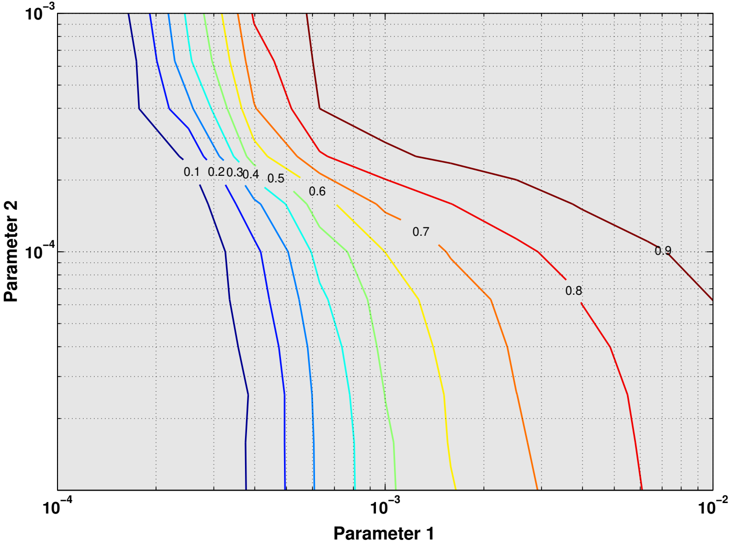
$$\frac{d}{dt}X(t)=\tilde{A}(X)$$

- No-noise or large volume limit (ODE) does not produce competence
- Many parameter combinations lead to the same ODE limit, but correspond to different effective volumes, i.e. intrinsic noise strength
- Increasing intrinsic noise leads to more frequent transitions



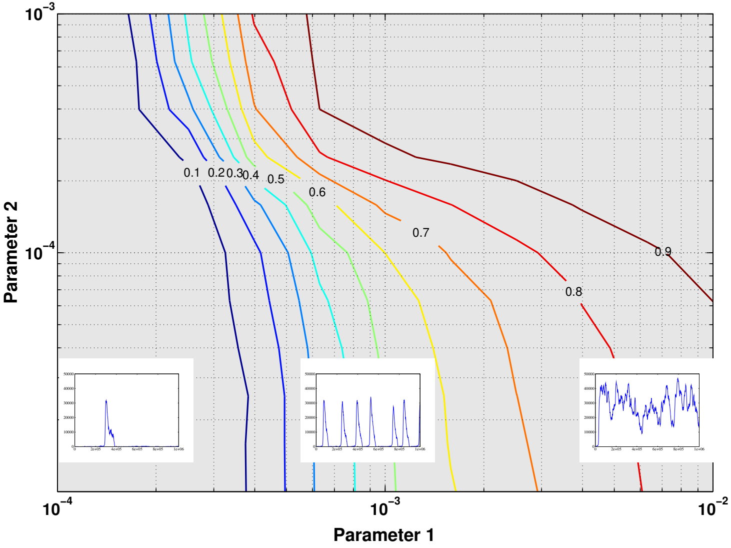


Contours of probability of competence P_c

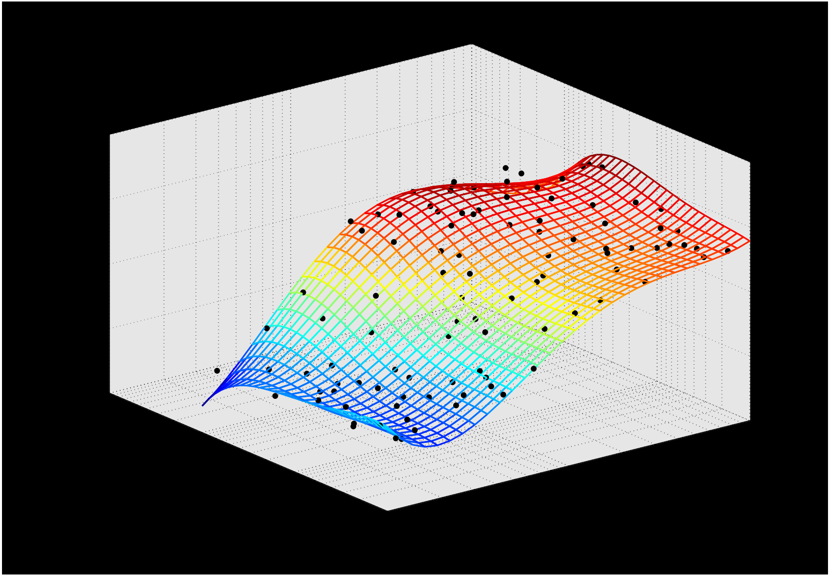


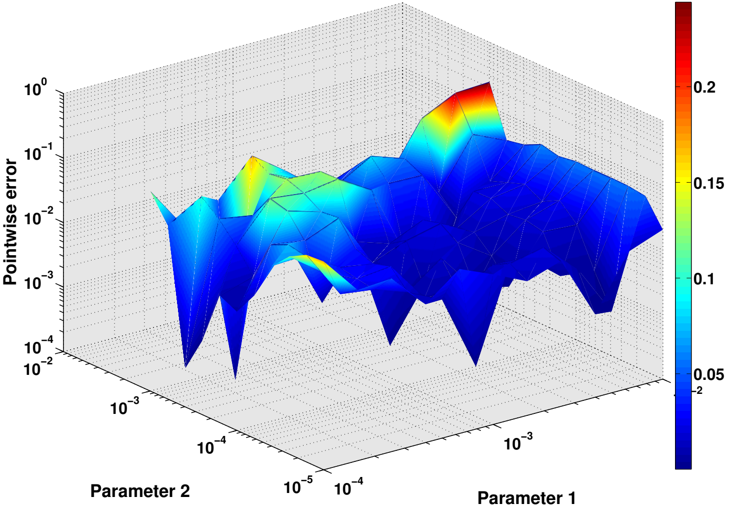
Various dynamical regimes revealed by exploring parameter space

Contours of probability of competence P_c



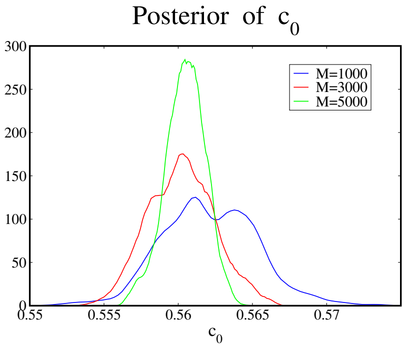
Uncertain response surface in two-parameter case, 4th order PC

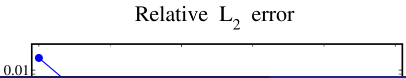



Pointwise error
10^0
10^{-1}
10^{-2}
10^{-3}
10^{-4}
10^{-2}
10^{-3}
10^{-4}
10^{-5}
Parameter 2
10^{-4}
10^{-3}
Parameter 1
0.2
0.15
0.1
0.05

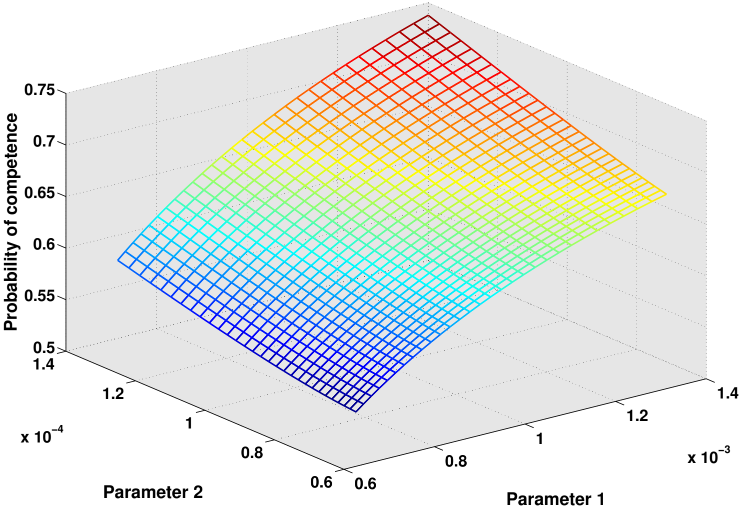
Convergence both in posterior width and order

- With more input parameter samples, posterior narrows around the true value
- Convergence in PC order is established





MAP estimate of 2-nd order response surface in 10-d case



High Dimensional Model Representation (HDMR)

breaks the function into group-wise contributions of input variables

$$f(\boldsymbol{\lambda}) = f(\lambda_1, \ldots, \lambda_d) = f_0 + \sum_i f_i(\lambda_i) + \sum_{i<j} f_{ij}(\lambda_i, \lambda_j) + \sum_{i<j<k} f_{ijk}(\lambda_i, \lambda_j, \lambda_k) + \cdots$$

Component functions are found by

$$f_0 = \int_{R^d} f(\boldsymbol{\lambda}) d\boldsymbol{\lambda}, \qquad f_i(\lambda_i) = \int_{R^{d-1}} f(\lambda_i, \boldsymbol{\lambda}_{\bar{i}}) d\boldsymbol{\lambda}_{\bar{i}} - f_0$$

$$f_{ij}(\lambda_i, \lambda_j) = \int_{R^{d-2}} f(\lambda_i, \lambda_j, \boldsymbol{\lambda}_{\bar{ij}}) d\boldsymbol{\lambda}_{\bar{ij}} - f_i(\lambda_i) - f_j(\lambda_j) - f_0$$

- Component function $f_{i_1 \ldots i_s}(\lambda_{i_1}, ..., \lambda_{i_s})$ is found by a $(d-s)$-dimensional integral. Still too high-dimensional.
- Otherwise called ANOVA decomposition (analysis of variance)
- Exact in the limit, but not unique.

High Dimensional Model Representation (HDMR)

breaks the function into group-wise contributions of input variables

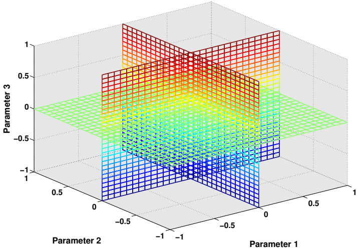
$$f(\boldsymbol{\lambda}) = f(\lambda_1, \ldots, \lambda_d) = f_0 + \sum_i f_i(\lambda_i) + \sum_{i<j} f_{ij}(\lambda_i, \lambda_j) + \sum_{i<j<k} f_{ijk}(\lambda_i, \lambda_j, \lambda_k) + \cdots$$

Component functions are found by

$$f_0 = \int_{R^d} f(\boldsymbol{\lambda}) d\boldsymbol{\lambda}, \qquad f_i(\lambda_i) = \int_{R^{d-1}} f(\lambda_i, \boldsymbol{\lambda}_{\bar{i}}) d\boldsymbol{\lambda}_{\bar{i}} - f_0$$

$$f_{ij}(\lambda_i, \lambda_j) = \int_{R^{d-2}} f(\lambda_i, \lambda_j, \boldsymbol{\lambda}_{\bar{ij}}) d\boldsymbol{\lambda}_{\bar{ij}} - f_i(\lambda_i) - f_j(\lambda_j) - f_0$$

- Two major variants:
  - Cut-HDMR
  - RS-HDMR



High Dimensional Model Representation (HDMR)

breaks the function into group-wise contributions of input variables

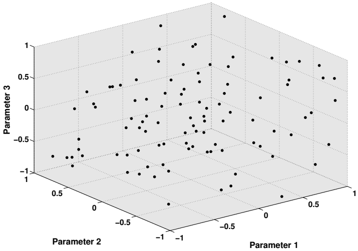
$$f(\boldsymbol{\lambda}) = f(\lambda_1, \ldots, \lambda_d) = f_0 + \sum_i f_i(\lambda_i) + \sum_{i<j} f_{ij}(\lambda_i, \lambda_j) + \sum_{i<j<k} f_{ijk}(\lambda_i, \lambda_j, \lambda_k) + \cdots$$

Component functions are found by

$$f_0 = \int_{R^d} f(\boldsymbol{\lambda}) d\boldsymbol{\lambda}, \qquad f_i(\lambda_i) = \int_{R^{d-1}} f(\lambda_i, \boldsymbol{\lambda}_{\bar{i}}) d\boldsymbol{\lambda}_{\bar{i}} - f_0$$

$$f_{ij}(\lambda_i, \lambda_j) = \int_{R^{d-2}} f(\lambda_i, \lambda_j, \boldsymbol{\lambda}_{\bar{ij}}) d\boldsymbol{\lambda}_{\bar{ij}} - f_i(\lambda_i) - f_j(\lambda_j) - f_0$$

- Two major variants:
  - Cut-HDMR
  - RS-HDMR

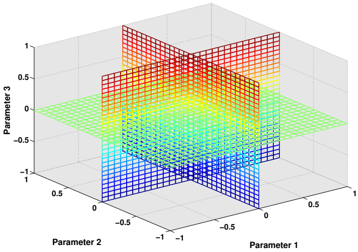


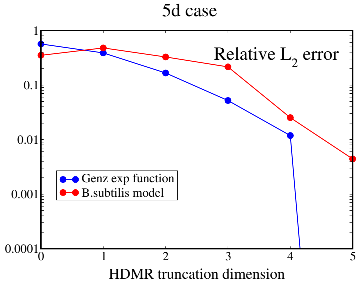
cut-HDMR disregards corners in the parameter space and does not guarantee accuracy in general

- Component functions are

$$f_0 = f(\boldsymbol{\lambda}^a), \qquad f_i(\lambda_i) = f(\lambda_i, \boldsymbol{\lambda}^a_{\bar{i}}) - f_0$$
$$f_{ij}(\lambda_i, \lambda_j) = f(\lambda_i, \lambda_j, \boldsymbol{\lambda}^a_{\bar{ij}}) - f_i(\lambda_i) - f_j(\lambda_j) - f_0$$

- Relies on values at lower-dimensional hyperplanes
- Depends on the anchor point $\boldsymbol{\lambda}^a$
- Does not account for 'corners'



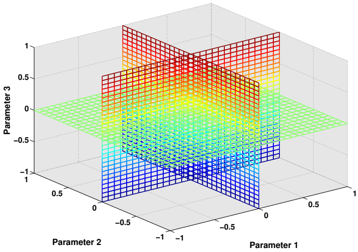


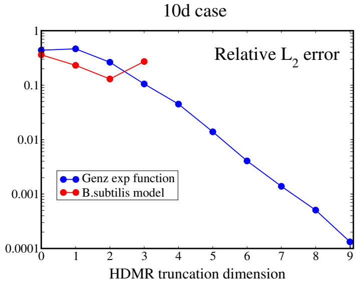
cut-HDMR disregards corners in the parameter space and does not guarantee accuracy in general

- Component functions are

$$f_0 = f(\boldsymbol{\lambda}^a), \qquad f_i(\lambda_i) = f(\lambda_i, \boldsymbol{\lambda}^a_{\bar{i}}) - f_0$$
$$f_{ij}(\lambda_i, \lambda_j) = f(\lambda_i, \lambda_j, \boldsymbol{\lambda}^a_{\bar{ij}}) - f_i(\lambda_i) - f_j(\lambda_j) - f_0$$

- Relies on values at lower-dimensional hyperplanes
- Depends on the anchor point $\boldsymbol{\lambda}^a$
- Does not account for ‘corners’





Random Sampling (RS) HDMR in principle equivalent to PC expansion with Monte-Carlo integration

$$f(\boldsymbol{\lambda}) = f(\lambda_1,\ldots,\lambda_d) = f_0 + \sum_i f_i(\lambda_i) + \sum_{i<j} f_{ij}(\lambda_i,\lambda_j) + \sum_{i<j<k} f_{ijk}(\lambda_i,\lambda_j,\lambda_k) + \cdots$$

- Component functions are found by

$$f_0 = \int_{R^d} f(\boldsymbol{\lambda})d\boldsymbol{\lambda}, \qquad f_i(\lambda_i) = \int_{R^{d-1}} f(\lambda_i,\boldsymbol{\lambda}_{\bar{i}})d\boldsymbol{\lambda}_{\bar{i}} - f_0$$

$$f_{ij}(\lambda_i,\lambda_j) = \int_{R^{d-2}} f(\lambda_i,\lambda_j,\boldsymbol{\lambda}_{\bar{ij}})d\boldsymbol{\lambda}_{\bar{ij}} - f_i(\lambda_i) - f_j(\lambda_j) - f_0$$

- MC integrals still too expensive (new random samples needed for each hyperplane)
- Represent component functions with a polynomial expansion and use same set of samples
- Equivalent to Monte-Carlo PC with reordered multiindices!
  - PC (total order): $f(\xi_1,\xi_2) = 1 + [\xi_1+\xi_2] + [(\xi_1^2-1) + \xi_1\xi_2 + (\xi_2^2-1)] + \ldots$
  - RS-HDMR: $f(\xi_1,\xi_2) = 1 + [\xi_1 + (\xi_1^2-1)] + [\xi_2 + (\xi_2^2-1)] + \xi_1\xi_2\ldots$
- In future: employ Bayesian inference on component functions.

Summary

- Polynomial Chaos expansions represent effects of uncertainties of input parameters to output statistical properties
  - Sensitivity analysis
  - Uncertainty quantification
  - Response surface construction
- Noise in function evaluations hampers quadrature methods
  - Sparse integration of noisy functions useless in high-d !
- HDMR constructions do not always guarantee accuracy with small computational effort
  - Generally still require high-d integrals
  - cut-HDMR overcomes this requirement but is not accurate enough
- Bayesian inference well-suited to handle noisy data

Acknowledgements

- Youssef Marzouk (MIT)
- Cosmin Safta (SNL)

- DOE Office of Science, Advanced Scientific Computing Research, Applied Mathematics.

Thank You!

Sandia National Laboratories is a multi-program laboratory operated by Sandia Corporation, a wholly owned subsidiary of Lockheed Martin Corporation, for the U.S. Department of Energy's National Nuclear Security Administration under contract DE-AC04-94AL85000.

Literature

- N. Wiener, “Homogeneous Chaos”, *American Journal of Mathematics*, 60(4), pp. 897-936, 1938.
- R. Ghanem and P. Spanos, “Stochastic Finite Elements: a Spectral Approach”, Springer, 1991.
- D. Xiu and G.E. Karniadakis, “The Wiener-Askey Polynomial Chaos for Stochastic Differential Equations”, *SIAM J. Sci. Comput.*, 24(2), pp. 619-644, 2002.
- O. Le Maître and O. Knio, “Spectral Methods for Uncertainty Quantification with Applications to Computational Fluid Dynamics”, Springer, 2010.

- K. Sargsyan, B. Debusschere, H. Najm and O. Le Maître,
  ”Spectral representation and reduced order modeling of the dynamics of stochastic reaction networks via adaptive data partitioning”.
  SIAM Journal on Scientific Computing, 31:6, 2010.
- K. Sargsyan, B. Debusschere, H. Najm and Y. Marzouk,
  ”Bayesian inference of spectral expansions for predictability assessment in stochastic reaction networks”.
  Journal of Computational and Theoretical Nanoscience, 6:10, 2009.