Predictability and Reduced Order Modeling in Stochastic Reaction Networks

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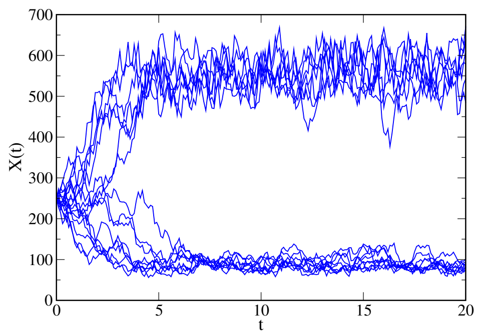
Outline

- Motivation: Stochastic Reaction Networks
- Predictability: Parametric Uncertainty Propagation using Polynomial Chaos Expansion
  - Polynomial Chaos
  - Bayesian Inference
  - Markov Chain Monte Carlo
  - Adaptive Domain Decomposition
- Dynamical Analysis: Reduced Order Modeling via Karhunen-Loève Decomposition
  - Karhunen-Loève Decomposition
  - Rosenblatt Transformation
  - Quadrature Integration
  - Adaptive Data Clustering
- Application: Schlögl Model (a benchmark bistable process)

Motivation: Stochastic Reaction Networks (SRNs)

- Reaction networks involving small number of molecules necessitate the use of *stochastic* modeling instead of the *deterministic* one. E.g.
  - Immune system signaling reactions
  - Microbial reactions
  - Surface catalytic 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
  - Numerically, Gillespie's Stochastic Simulation Algorithm (SSA, Gillespie, 1977)

Problem Definition and Methods

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

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

- Techniques employed:
  - Polynomial chaos expansion; Bayesian inference; Domain decomposition
  - Karhunen-Loève decomposition; Rosenblatt transformation; Data clusttering

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

Polynomial Chaos Expansion (PCE) - Intro

- A second order random variable $X(\boldsymbol{\theta})$ can be described by a PCE in terms of standard orthogonal polynomials Ψ_k, of associated standard random variables $\{\eta_i\}_{i=1}^{\infty}$, and spectral mode strengths c_k.

  (Wiener, 1938)(Cameron & Martin, 1947)(Ghanem & Spanos, 1991)

- Truncated PCE: finite dimension n and order p

$$X(\boldsymbol{\theta}) \simeq \sum_{k=0}^{P} c_k \Psi_k(\eta_1, \cdots, \eta_n)$$

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

- Most common standard Polynomial-Variable pairs: (continuous) Gauss-Hermite, Legendre-Uniform, (discrete) Poisson-Charlier. (Askey Scheme: Xiu & Karniadakis, 2002)

Galerkin Projection is challenged by the intrinsic noise

$$X(\boldsymbol{\theta}) \simeq \sum_{k=0}^{P} c_k \Psi_k(\boldsymbol{\eta}) = g_{\mathcal{D}}(\boldsymbol{\eta})$$

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

- Intrusive Spectral Projection (ISP)
  - ⋆ Direct projection of governing equations
  - ⋆ Leads to deterministic equations for PC coefficients
  - ∗ No explicit governing equation for SRNs
- Non-intrusive Spectral Projection (NISP)
  - ⋆ Sampling based
  - ⋆ No explicit evolution equation for X needed
  - ∗ Galerkin projection not well-defined for SRNs

Bayesian inference handles the intrinsic stochasticity well

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

$$L(\boldsymbol{c}) = P(\mathcal{D}|\boldsymbol{c}) = \prod_{i=1}^{N} \mathsf{pdf}_g(X_i)$$

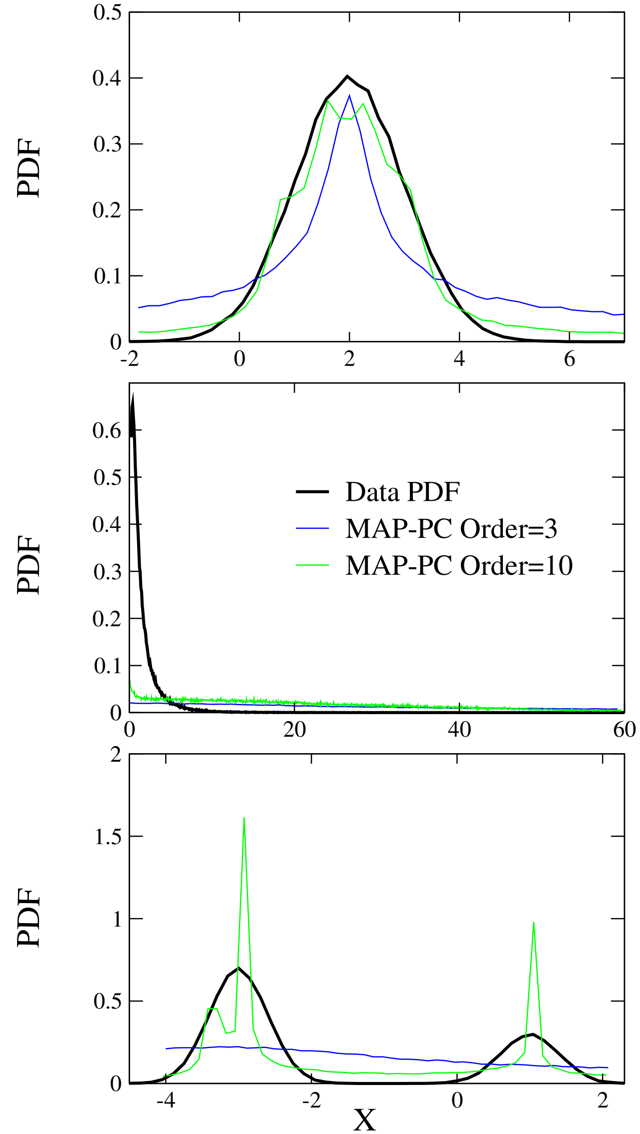
$$X \simeq \sum_{k=0}^{P} c_k \Psi_k(\eta) = g_{\mathcal{D}}(\eta)$$

- Noise model is inherent in SSA data $\mathcal{D} = \{X_i\}_{i=1}^{N}$
- Uniformly distributed priors
- Posterior exploration using Markov Chain Monte Carlo (MCMC)
- The whole posterior distribution is accessible
- Maximum a posteriori (MAP) estimate: $\boldsymbol{c}^{MAP} = \mathrm{argmax}_{\boldsymbol{c}} P(\boldsymbol{c}|\mathcal{D})$

Global PCE can fail for strongly non-linear or bimodal variables

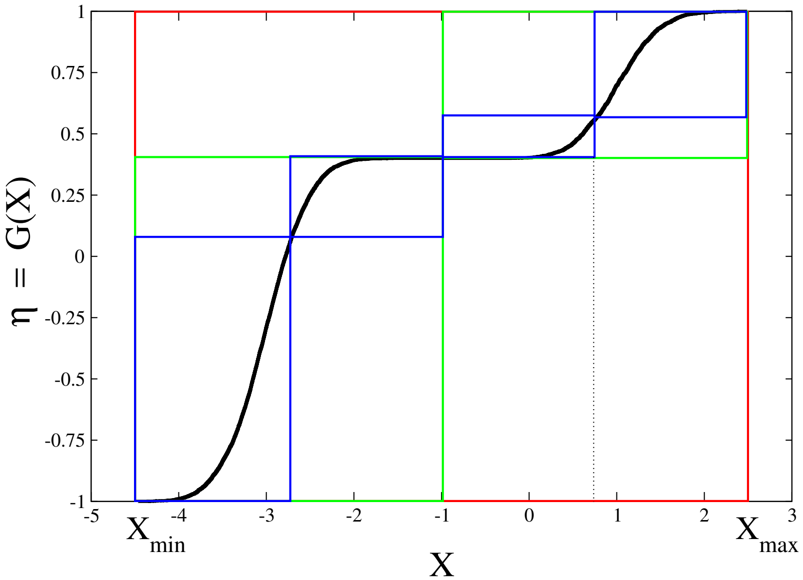
Legendre-Uniform PC

- Normal
- Lognormal
- Bimodal

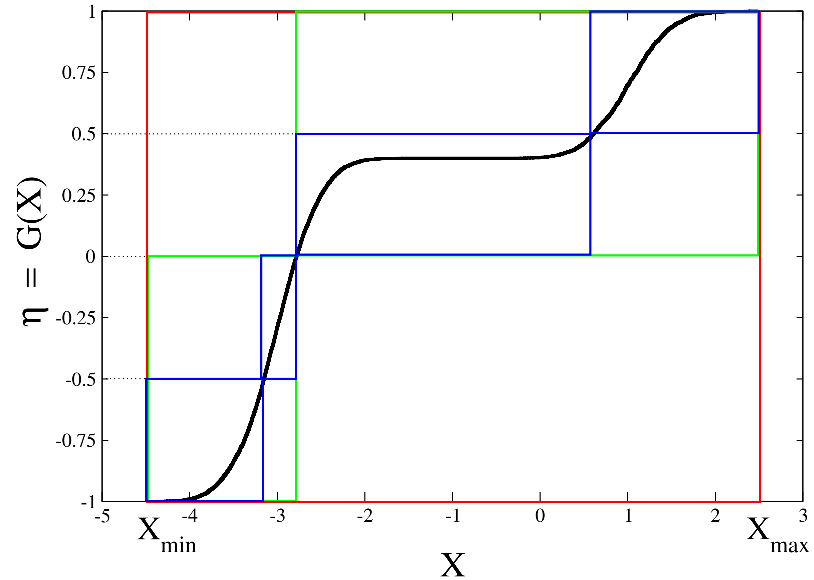


Two domain decomposition regimes available

Cumulative Distribution Function (CDF): $F(x) = P(X < x)$.
Rescaled CDF: $\eta = G(X) \equiv 2F(X) - 1$ is Uniform[-1,1].



X-domain decomposition



η-domain decomposition

Le Maître et al., 2004 - Adaptive multi-wavelet basis.

Wan & Karniadakis, 2005 - Adaptive domain decomposition.

Adaptive criterion is consistent with Kullback-Leibler 'distance'

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

Model: $X \simeq \sum_{k=0}^P c_k \Psi_k(\eta) = g_{\mathcal{D}}(\eta)$

MAP-PC samples: $\{Y_i\}_{i=1}^N$, where $Y_i = g_{\mathcal{D}}(\eta_i)$

- Log-likelihood:

$$\log L = \log P(\text{Data}|\text{Model}) = \sum_{i=1}^N \log P_Y(X_i)$$

- Target log-likelihood (the *perfect match* log-likelihood, i.e. for $\{Y_i\}_{i=1}^N = \mathcal{D}$):

$$\log L_T = \sum_{i=1}^N \log P_X(X_i)$$

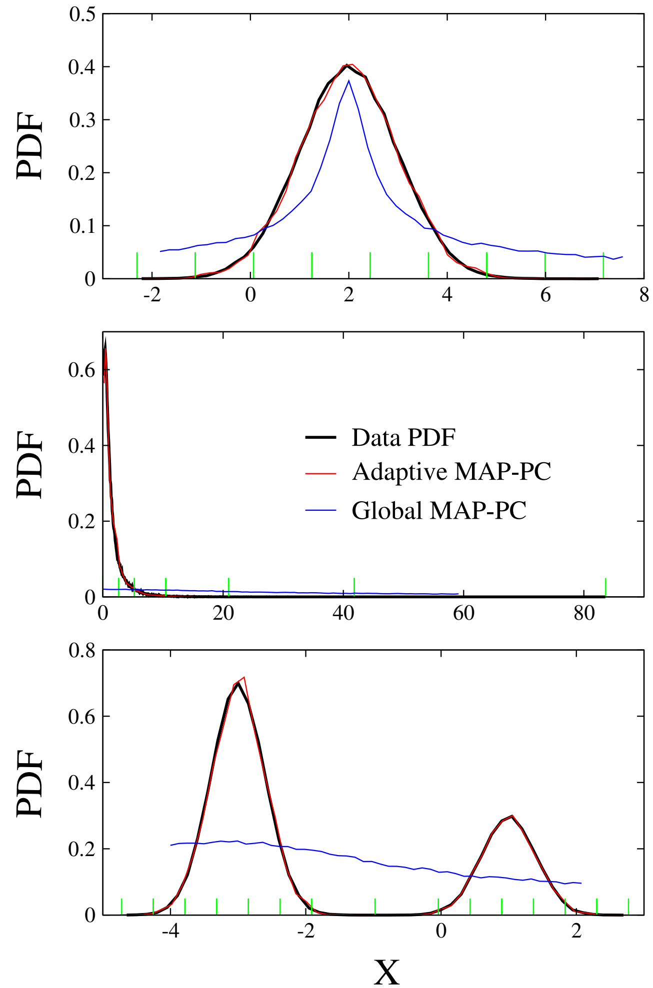
- Kullback-Leibler divergence:

$$\rho(P_X, P_Y) = \int P(z) \log \frac{P_X(z)}{P_Y(z)} dz \simeq \frac{1}{N} \sum_{i=1}^N \log \frac{P_X(X_i)}{P_Y(X_i)}$$

Multi-domain PCE captures non-linearities and bimodalities well

Legendre-Uniform multi-domain PC

- Normal
- Lognormal
- Bimodal

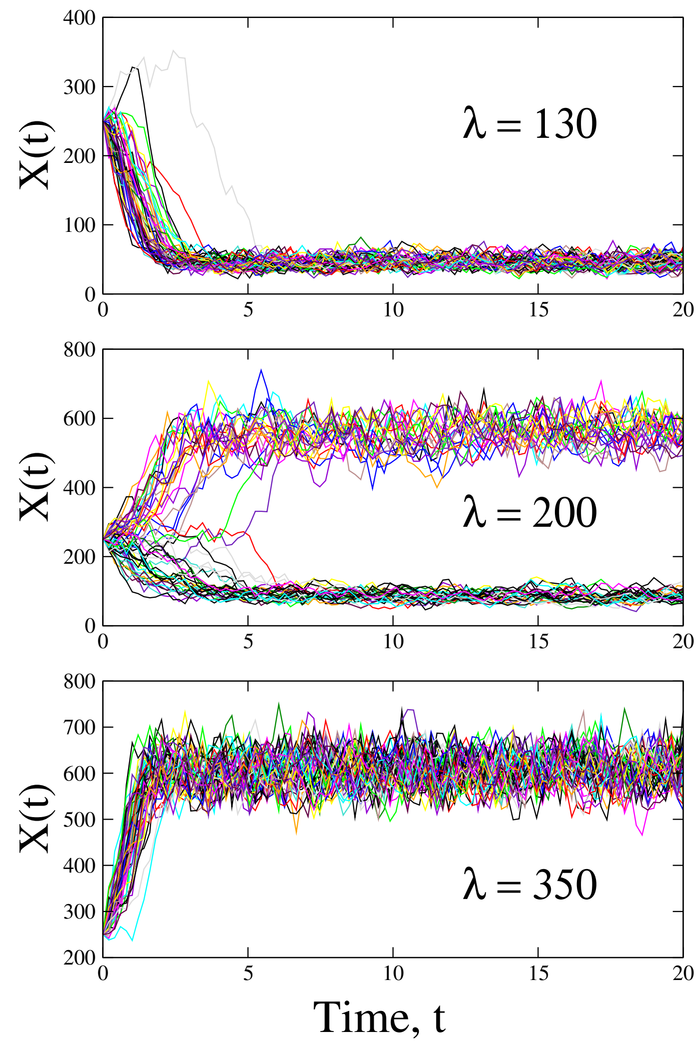


Schlögl model is a benchmark bistable process

- Reactions

$$A + 2X \underset{a_2}{\overset{a_1}{\rightleftarrows}} 3X$$

$$B \underset{a_4}{\overset{a_3}{\rightleftarrows}} X$$



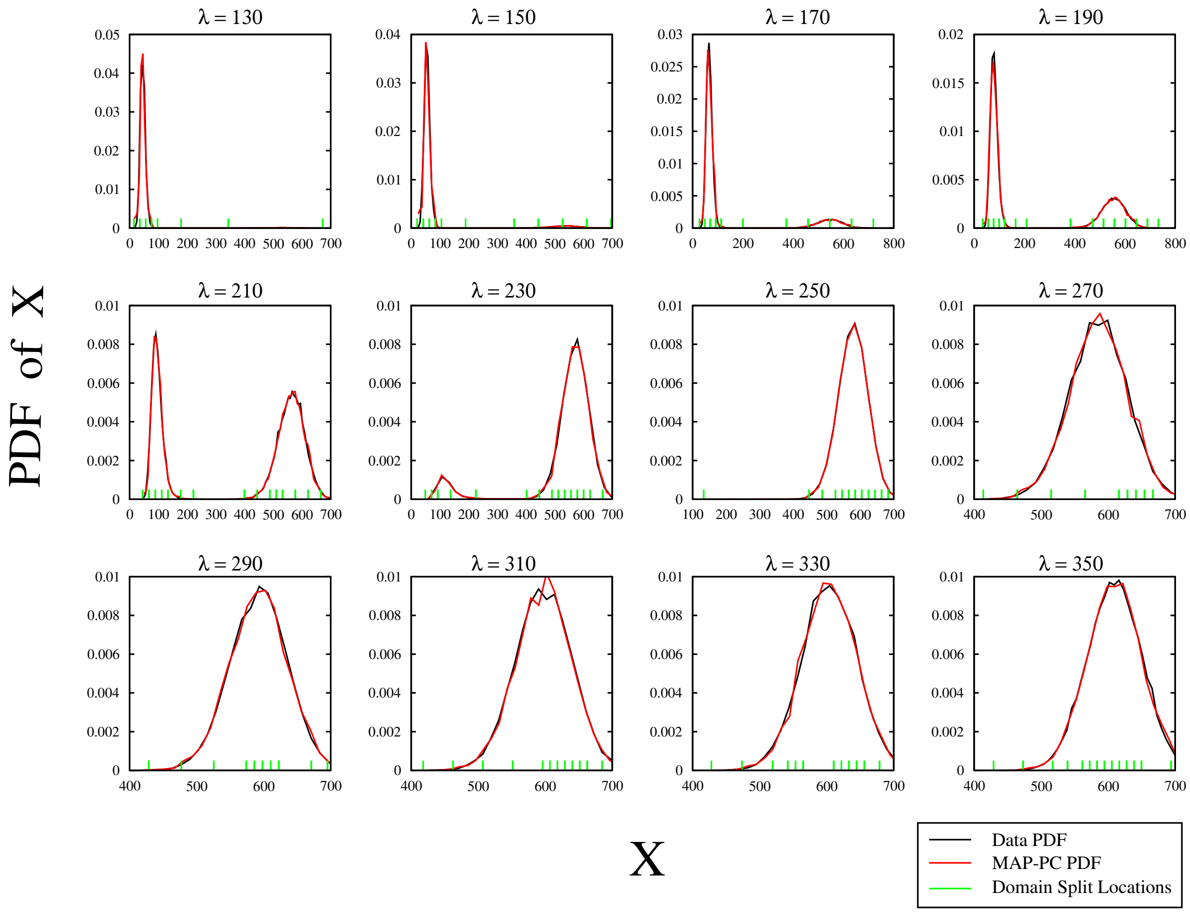
- Propensities

$$a_1 = k_1 A X(X-1)/2,$$
$$a_2 = k_2 X(X-1)(X-2)/6,$$
$$a_3 = k_3 B,$$
$$a_4 = k_4 X.$$

- Nominal parameters

$k_1 A$	0.03
k_2	0.0001
$k_3 B = \lambda$	200
k_4	3.5
A	10^5
B	$2 \cdot 10^5$
$X(0)$	250

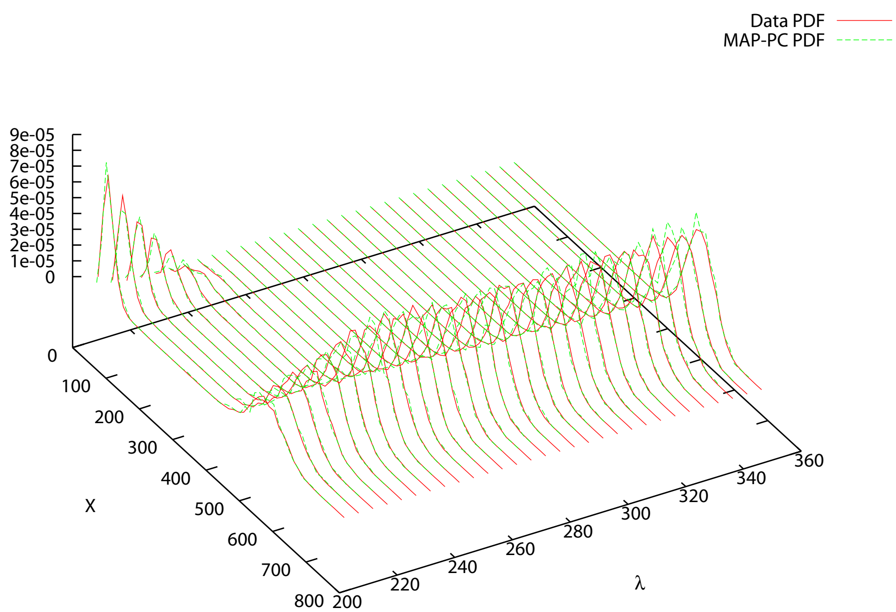
PC Inference for fixed parameter values

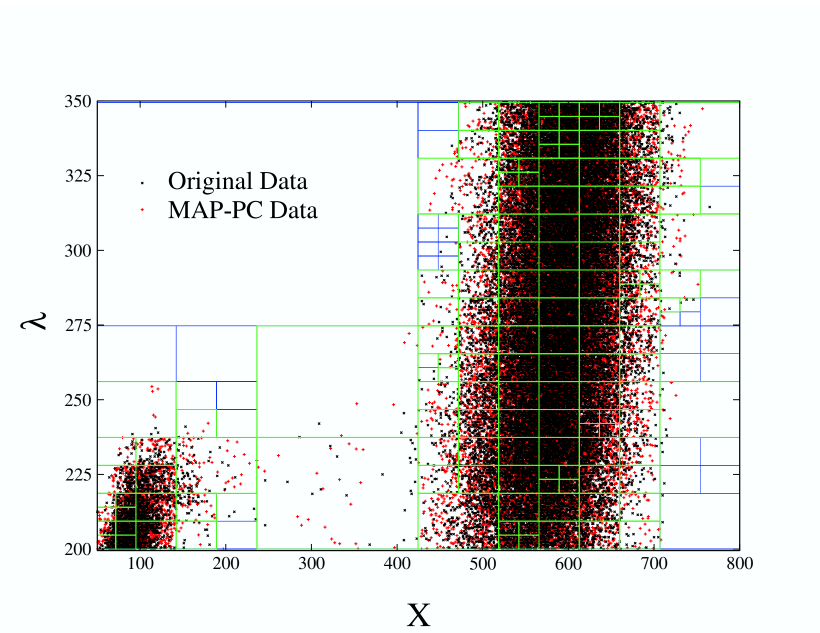


Qualitatively different behaviors across a range of λ values necessitates the parametric uncertainty introduction.

Predictability: Parametric uncertainty propagation through PCE

- Postulate parametric uncertainty $\qquad \lambda = \lambda_0 + \Delta\lambda\eta_1$
- Gather two-dimensional data $\mathcal{D} = \{(X_i, \lambda_i)\}_{i=1}^N$
- Infer the model parameters c_k's, where $X = \sum_{k=0}^P c_k \Psi_k(\eta_1, \eta_2)$
- If the representation is not satisfactory (see the criterion), split the data domain and proceed recursively





Dynamical Analysis: Big Picture

Fix the parameter $X(t,\boldsymbol{\theta},\boldsymbol{\Lambda}) \equiv X(t,\boldsymbol{\theta})$

SSA $\longleftrightarrow$ KL $\longleftrightarrow$ PCE

$$X(t,\boldsymbol{\theta}) \longleftrightarrow \xi_i(\boldsymbol{\theta})(i=\overline{1,L}) \longleftrightarrow c_{ik}(i=\overline{1,L}, k=\overline{0,P})$$

$$X(t,\boldsymbol{\theta})-\bar{X}(t) \simeq \sum_{i=1}^{L} \xi_i(\boldsymbol{\theta})\sqrt{\lambda_i} f_i(t) \simeq \sum_{i=1}^{L}\left(\sum_{k=0}^{P} c_{ik}\Psi_k(\boldsymbol{\eta})\right)\sqrt{\lambda_i} f_i(t)$$

SSA $\longleftrightarrow$ KL : Karhunen-Loève (KL) decomposition of the stochastic process

KL $\longleftrightarrow$ PCE: Polynomial Chaos expansion of each KL random variable

Karhunen-Loève Decomposition: Intro

- Separate the average:

$$X_0(t,\theta) = X(t,\theta) - \bar{X}(t)$$

- The covariance function is symmetric, bounded and positive definite. Hence, it can be expanded as a sum

$$C(t_1,t_2) = \langle X_0(t_1,\theta) X_0(t_2,\theta) \rangle = \sum_{n=1}^{\infty} \lambda_n f_n(t_1) f_n(t_2)$$

- Positive eigenvalues:

$$\int_0^T C(t_1,t_2) f_n(t_1) dt_1 = \lambda_n f_n(t_2).$$

- KL decomposition:

$$X(t,\theta) = \bar{X}(t) + \sum_{n=1}^{\infty} \xi_n(\theta) \sqrt{\lambda_n} f_n(t)$$

Karhunen-Loève decomposition leads to reduced order modeling

- KL decomposition:

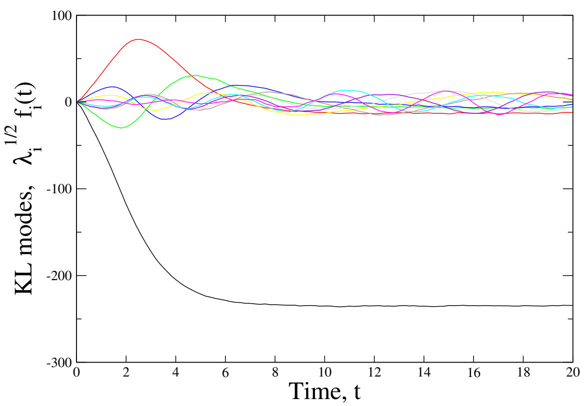
$$X(t,\theta) = \bar{X}(t) + \sum_{n=1}^{\infty} \xi_n(\theta)\sqrt{\lambda_n} f_n(t)$$

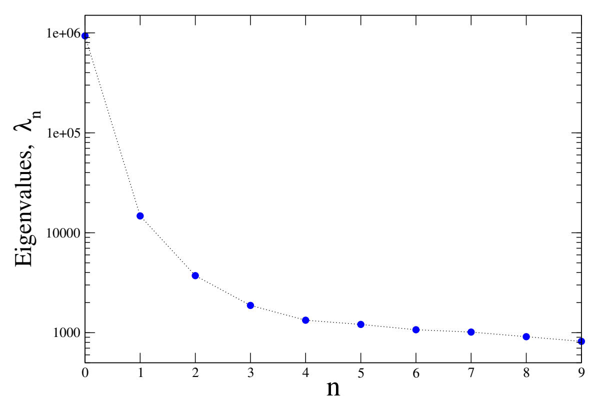
- Uncorrelated, zero-mean KL variables:

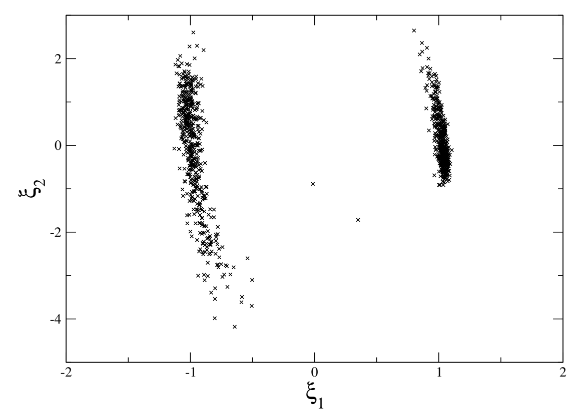
$$\langle \xi_n \rangle = 0, \qquad \langle \xi_n \xi_m \rangle = \delta_{nm}$$

- SSA(continuum) $\longleftrightarrow$ KL(discrete)

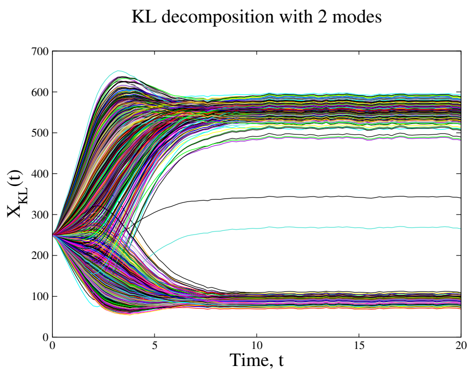
$$X(t) \longleftrightarrow \boldsymbol{\xi} = (\xi_1, \xi_2, \dots)$$

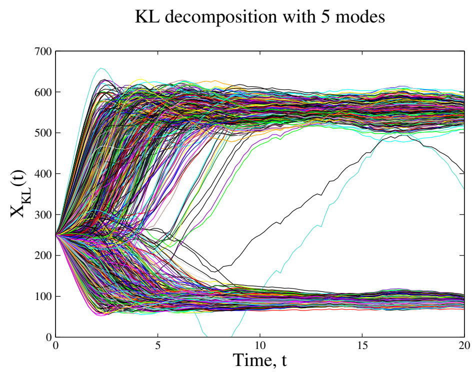


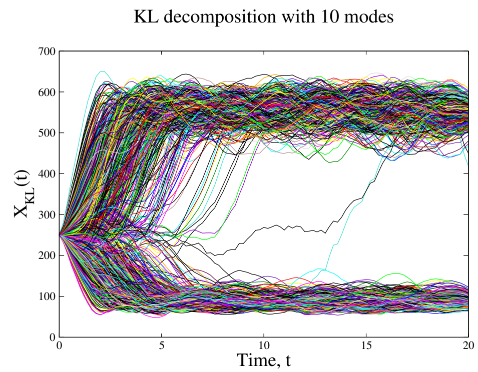


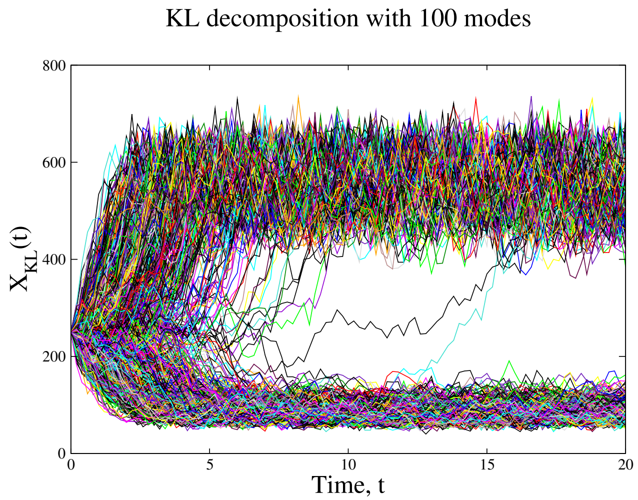


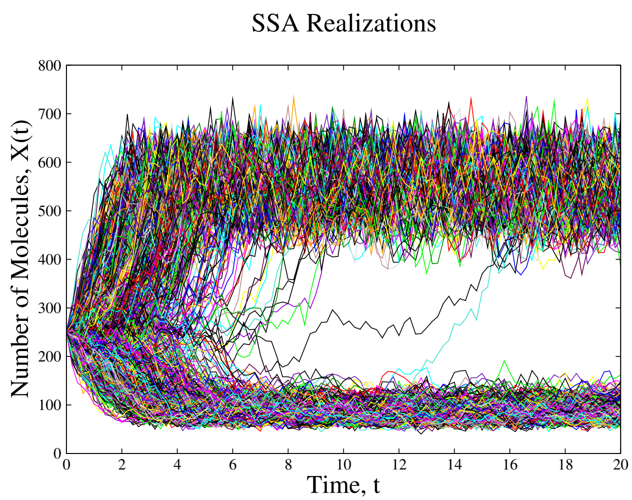
Karhunen-Loève decomposition captures each realization











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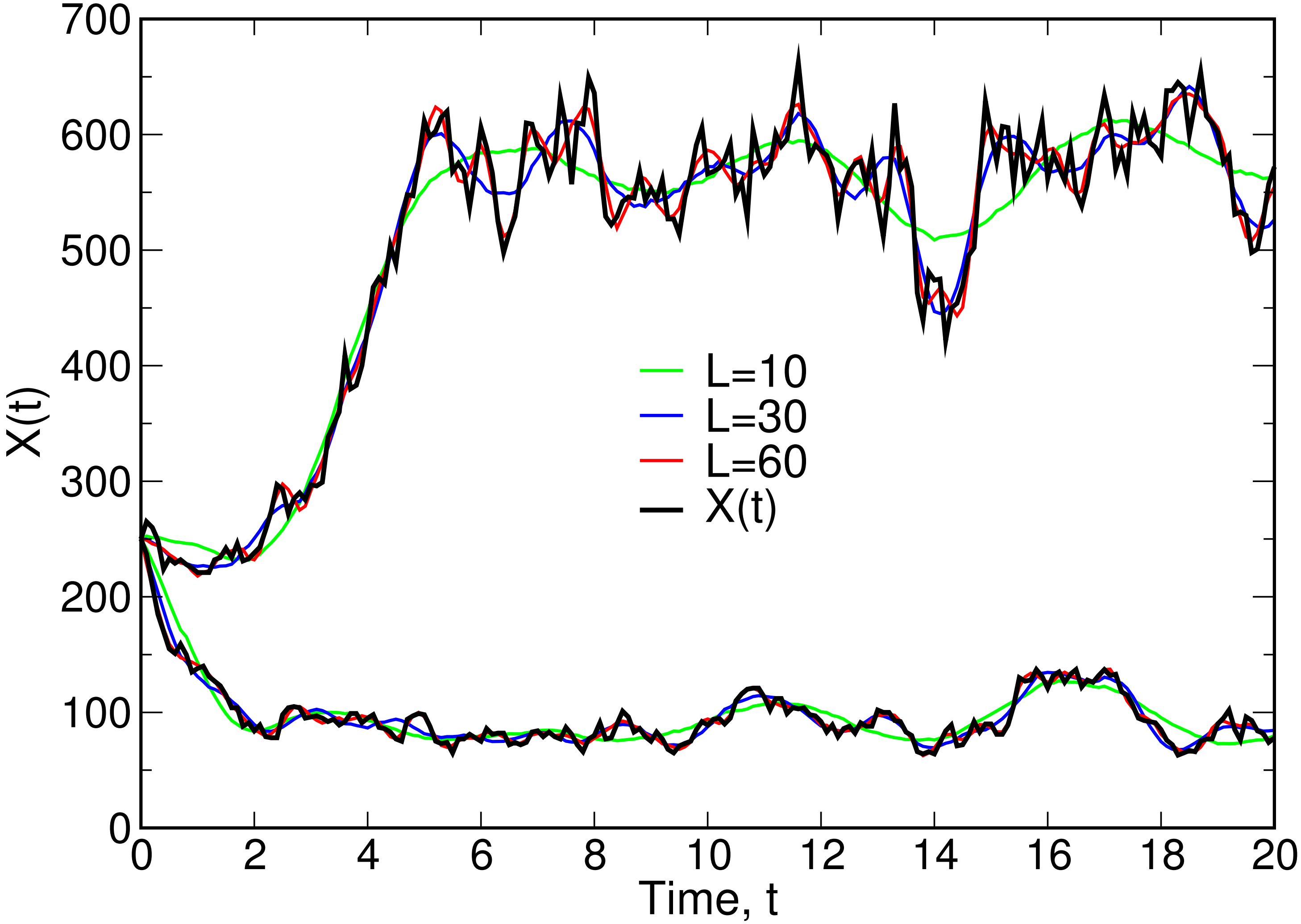

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Challenges in PC expansions of KL random variables

Need to PC-expand each of the KL random variables

$$\xi_i = \sum_{k=0}^{P} c_{ik} \Psi_k(\boldsymbol{\eta}), \text{ for } i = 1, \ldots, L$$

- Quadrature-based non-intrusive spectral projection is not well-defined

$$c_{ik} = \frac{\langle \xi_i \Psi_k(\boldsymbol{\eta}) \rangle}{\langle \Psi_k^2(\boldsymbol{\eta}) \rangle}$$

  - Employ (inverse) Rosenblatt transformation
- Multimodal variables not captured well
  - Use data clustering

Rosenblatt Transformation

- Rosenblatt transformation maps any (not necessarily independent) set of random variables $(\xi_1, \ldots, \xi_n)$ to uniform i.i.d.'s $\{\eta_i\}_{i=1}^n$ (Rosenblatt, 1952).

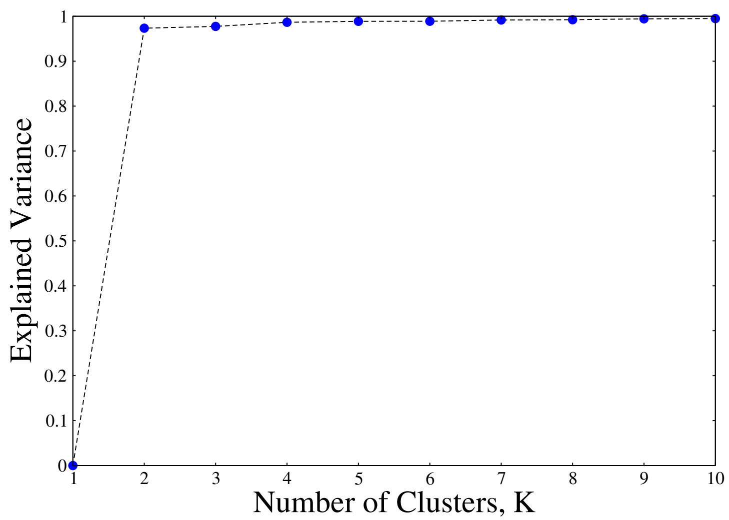
$$\begin{aligned} \eta_1 &= F_1(\xi_1) \\ \eta_2 &= F_{2|1}(\xi_2|\xi_1) \\ \eta_3 &= F_{3|2,1}(\xi_3|\xi_2, \xi_1) \\ &\vdots \\ \eta_n &= F_{n|n-1,\ldots,1}(\xi_n|\xi_{n-1}, \ldots, \xi_1) \end{aligned}$$

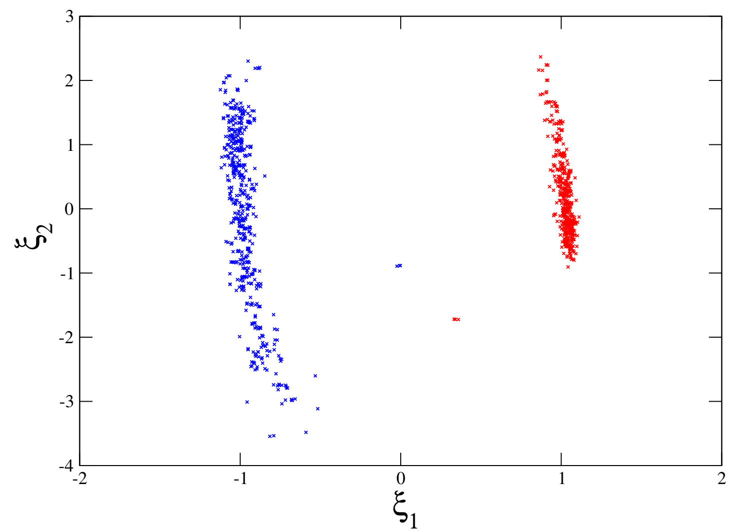
- Inverse Rosenblatt transformation $\boldsymbol{\xi} = R^{-1}(\boldsymbol{\eta})$ ensures a well-defined integration

$$\langle \xi_i \Psi_k(\boldsymbol{\eta}) \rangle = \int (R^{-1}(\boldsymbol{\eta}))_i \Psi_k(\boldsymbol{\eta}) d\boldsymbol{\eta}$$

Adaptive Data Clustering

- Finite number of KL variables: $\boldsymbol{\xi} = (\xi_1, \xi_2, \ldots, \xi_L)$
- Multidimensional data: $\{\boldsymbol{\xi}^{(i)}\}_{i=1}^{N}$
- K-Center clustering
- 'Elbow' criterion to pick initial number of clusters
- Adaptive clustering: split clusters if output is not good enough (check the Kullback-Leibler distance)





PC Mixture Model

- Divide data into K clusters with fractions p_j:

$$p_1 + p_2 + \cdots + p_K = 1$$

- Find PC expansion for ξ in each cluster:

$$\xi_{PC}^{(j)} = \sum_{k=0}^{P} \xi_k^{(j)} \Psi_k(\eta^{(j)})$$

- Superpose the results to obtain PC mixture model:

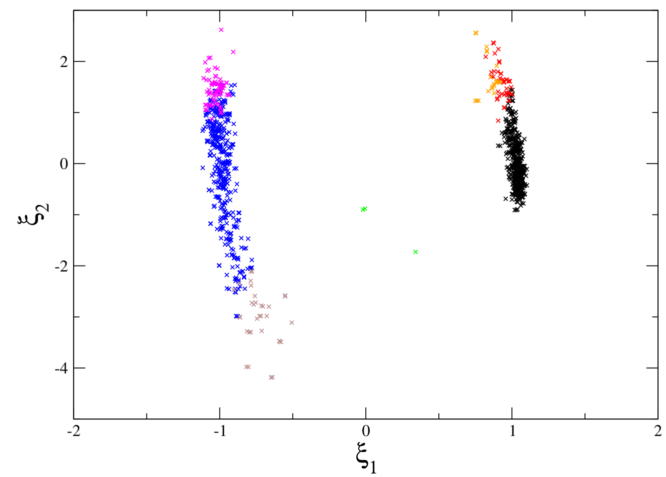
$$\xi = \xi_{PC}^{(j)} \text{ w. prob. } p_j$$

- Probability distribution function is a mixture of PC PDFs:

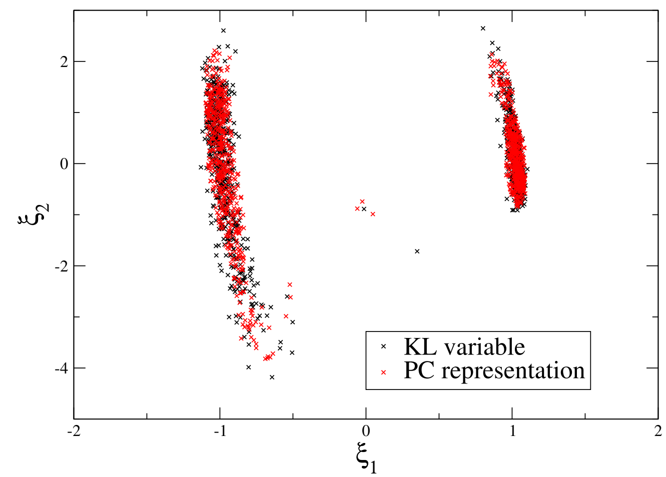
$$\mathsf{Pdf}_{\xi}(x) = p_1 \mathsf{Pdf}_{\xi_{PC}^{(1)}}(x) + \cdots + p_K \mathsf{Pdf}_{\xi_{PC}^{(K)}}(x)$$

Results for the Schlögl Model

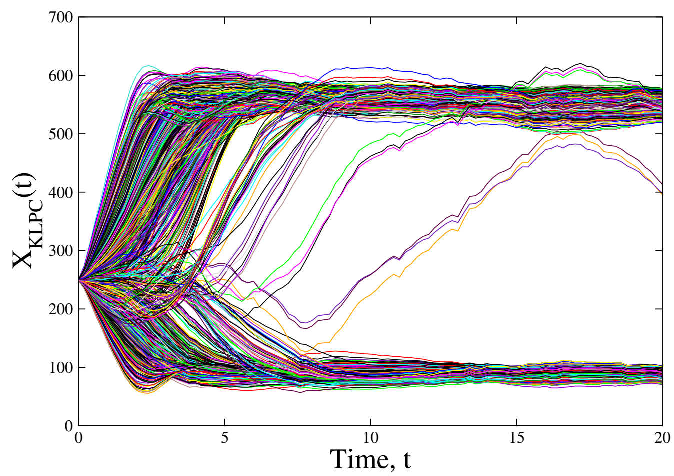
Adaptive Clustering



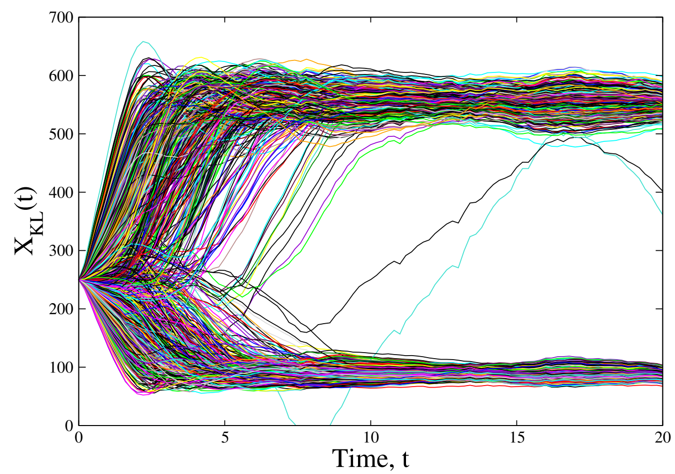
PC representation of first two KL variables



KL-PC representation, 5 KL modes, 3rd PC order



KL decomposition with 5 modes



Conclusions and Ongoing Work

- Adaptive domain decomposition with Bayesian inference allows representation of the state $X(T, \boldsymbol{\theta}, \boldsymbol{\lambda})$ across large range of parameter values
- PC mixture model with Karhunen-Loève decomposition represents the dynamics of the state $X(t, \boldsymbol{\theta}, \boldsymbol{\Lambda})$

- Dimensionality (complexity increase) studies
- Adaptive PC order
- Sparce quadrature integration or Latin Hypercube Sampling
- Combination of parameter uncertainties and time evolution

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Multi-domain PC expansion

- Partition: $-1 = a_1 < b_1 = a_2 < b_2 = \cdots = a_n < b_n = 1$

$$\mathcal{P} = \{[a_1, b_1), [a_2, b_2), \ldots, [a_n, b_n]\}$$

- Linear map: $f^I : I \equiv [a, b] \mapsto [-1, 1]$ from an interval $[a, b]$ (subscripts dropped for simplicity) to $[-1, 1]$, by

$$f^I(\xi) = \tilde{\xi} = \frac{2}{b-a}\left(\xi - \frac{a+b}{2}\right)$$

- Multi-domain PC expansion

$$X \simeq g(\xi) = \sum_{I \in \mathcal{P}} \sum_{k=0}^{P} c_k^I \Psi_k^I(\xi),$$

where

$$\Psi_k^I(\xi) \equiv 0, \text{ if } \xi \notin I$$
$$\Psi_k^I(\xi) = \Psi_k(f^I(\xi)), \text{ if } \xi \in I$$