## Introduction to Bayesian Inference and Uncertainty Propagation

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*Essentially, all models are wrong, but some are useful,* George E.P. Box, Industrial Statistician.

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### "We":

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Michael Hays, Billy Oates (Florida State University)

Brian Williams (LANL), Russell Hooper, Brian Adams, Vince Mousseau (Sandia)

Emre Tatli and Yixing Sung (Westinghouse)

# Modeling Strategy

General Strategy: Conservation of stuff

$$\begin{array}{c|c} \mathsf{Stuff} \longrightarrow \\ x & x + \Delta x \end{array}$$

 $\frac{dStuff}{dt} = \text{Stuff in - Stuff out + Stuff created - Stuff destroyed}$ 

Continuity Equation:

 
$$\frac{\partial(\rho\Delta x)}{\partial t} = \phi(t, x) - \phi(t, x + \Delta x)$$

$$\Rightarrow \lim_{\Delta x \to 0} \frac{\partial \rho}{\partial t} = \lim_{\Delta x \to 0} \frac{\phi(t, x) - \phi(t, x + \Delta x)}{\Delta x}$$



**Density:**  $\rho(t, x)$  - Stuff per unit length or volume

**Rate of Flow:**  $\phi(t, x)$  - Stuff per second

More Generally:

$$\Rightarrow \frac{\partial \rho}{\partial t} + \frac{\partial \Phi}{\partial x} =$$
Sources - Sinks

# **Example 1: Weather Models**

Observable Quantity

## **Challenges:**

- Coupling between temperature, pressure gradients, precipitation, aerosol, etc.;
- Models and inputs contain uncertainties;
- Numerical grids necessarily larger than many phenomena; e.g., clouds
- Sensors positions may be uncertain; e.g., weather balloons, ocean buoys.



- Assimilate data to quantify uncertain initial conditions and parameters;
- Make predictions with quantified uncertainties.



## **Equations of Atmospheric Physics**



Constitutive Closure Relations: e.g.,

$$S_{m_2} = S_1 + S_2 + S_3 - S_4$$

where

1

## **Ensemble Predictions**

#### **Ensemble Predictions:**



#### **Cone of Uncertainty:**



## **Ensemble Predictions**

#### **Ensemble Predictions:**



#### **Cone of Uncertainty:**



### **General Questions:**

- What is expected rainfall in Research Triangle on February 25?
- What are average high and low temperatures?
- What is predicted average snow fall?
- Note: Quantities are statistical in nature.

# Example 2: Pressurized Water Reactors (PWR)



### Models:

- Involve neutron transport, thermal-hydraulics, chemistry.
- Inherently multi-scale, multi-physics.

CRUD Measurements: Consist of low resolution images at limited number of locations.

# Example: Pressurized Water Reactors (PWR)

#### **Challenges:**

• Models linear in the state but function of 7 independent variables:

 $r = x, y, z; E; \Omega = \theta, \phi; t$ 

- Very large number of inputs or parameters; e.g., 100,000. Parameter selection critical.
- Codes can take hours to days to run.

**Example:** Shearon Harris outside Raleigh





#### **UQ Questions:**

- What is peak operating temperature?
- What is expected level of CRUD buildup?
- What is associated risk?
- What is expected profit for new design?

Example 3: HIV Model for Characterization and Control Regimes

#### **HIV Model: Notes:** 21 parameters $\dot{T}_1 = \lambda_1 - d_1 T_1 - (1 - \varepsilon) k_1 V T_1$ [Adams, Banks et al., 2005, $\dot{T}_2 = \lambda_2 - d_2 T_2 - (1 - f\varepsilon) k_2 V T_2$ 2007] $\dot{T}_{1}^{*} = (1 - \varepsilon)k_{1}VT_{1} - \delta T_{1}^{*} - m_{1}ET_{1}^{*}$ $\dot{T}_{2}^{*} = (1 - f\varepsilon)k_{2}VT_{2} - \delta T_{2}^{*} - m_{2}ET_{2}^{*}$ $\dot{V} = N_T \delta(T_1^* + T_2^*) - cV - [(1 - \varepsilon)\rho_1 k_1 T_1 + (1 - f\varepsilon)\rho_2 k_2 T_2]V$ Notation: $E \equiv \frac{dE}{dE}$ $\dot{E} = \lambda_E + \frac{b_E(T_1^* + T_2^*)}{T_1^* + T_2^* + K_b} E - \frac{d_E(T_1^* + T_2^*)}{T_1^* + T_2^* + K_d} E - \delta_E E$ **Compartments:** d<sub>1</sub> $\begin{array}{c} \lambda_1 \\ \hline T_1 \\ \hline \rho_1 \end{array}$ m<sub>1</sub> λE $V_{I}$ ) (1- $\varepsilon_{2}$ ) $N_{T}\delta$ ε2Ντδ VNI E δ<sub>E</sub> ρ2 т2\* $T_2$ $(1-f\epsilon_1)k_2$ $m_2$ do δ

Uninfected Infectious Infected Non-infectious Immune Effectors Target Cells Virus Target Cells Virus (CTLs)

# Example: HIV Model for Characterization and Treatment Regimes

**HIV Model:** Several sources of uncertainty including viral measurement techniques **Example:** Upper and lower limits to assay sensitivity



## UQ Questions:

- What are the uncertainties in parameters that cannot be directly measured?
- What is optimal treatment regime that is "safe" for patient?
- What is expected viral load? Issue: very often requires high-dimensional integration!

• e.g., 
$$\mathbb{E}[V(t)] = \int_{\mathbb{R}^{21}} V(t,q) \rho(q) dq$$

*Experimental results are believed by everyone, except for the person who ran the experiment*, source anonymous, quoted by Max Gunzburger, Florida State University.

## Example 4: SIR Cholera Model

#### Model:





Model Parameter	Symbol	Units	Values
Rate of drinking $B_L$ cholera	β <sub>L</sub>	$\frac{1}{\text{week}}$	1.5
Rate of drinking $B_H$ cholera	β <sub>H</sub>	week	7.5 (*)
$B_L$ cholera carrying capacity	κ <sub>L</sub>	$\frac{\# \text{ bacteria}}{m\ell}$	10 <sup>6</sup>
$B_H$ cholera carrying capacity	К <sub>Н</sub>	$\frac{\# \text{ bacteria}}{m\ell}$	<u>κ</u> 700
Human birth and death rate	b	$\frac{1}{\text{week}}$	1560
Rate of decay from $B_H$ to $B_L$	x	week	<u>168</u> 5
Rate at which infectious individuals spread $B_H$ bacteria to water	ξ	# bacteria # individuals.mℓ.week	70
Death rate of $B_L$ cholera	δ	$\frac{1}{\text{week}}$	$\frac{7}{30}$
Rate of recovery from cholera	γ	$\frac{1}{week}$	$\frac{7}{5}$

# Example: SIR Cholera Model

Strategy: Time-dependent global sensitivity indices; later talk by Pierre Gremaud



parameter

#### Model:





Model Parameter	Symbol	Units	Values
Rate of drinking $B_L$ cholera	βL	$\frac{1}{\text{week}}$	1.5
Rate of drinking $B_H$ cholera	β <sub>H</sub>	week	7.5 (*)
$B_L$ cholera carrying capacity	κ <sub>L</sub>	$\frac{\# \text{ bacteria}}{m\ell}$	10 <sup>6</sup>
$B_H$ cholera carrying capacity	К <sub>Н</sub>	$\frac{\# \text{ bacteria}}{m\ell}$	$\frac{\kappa_L}{700}$
Human birth and death rate	b	$\frac{1}{\text{week}}$	1560
Rate of decay from $B_H$ to $B_L$	X	week	<u>168</u> 5
Rate at which infectious individuals spread $B_H$ bacteria to water	ξ	$\frac{\# \text{ bacteria}}{\# \text{ individuals} \cdot m\ell \cdot \text{week}}$	70
Death rate of $B_L$ cholera	δ	$\frac{1}{\text{week}}$	$\frac{7}{30}$
Rate of recovery from cholera	γ	week	$\frac{7}{5}$

# Steps in Uncertainty Quantification

**Note:** Uncertainty quantification requires synergy between statistics, mathematics and application area.



# Model Calibration and Uncertainty Propagation

### Sources of Uncertainty:

- Model
- Parameters
- Sensor measurements
- Initial conditions

Parameters: Reduced set

$$q = [b_E, \delta, d_1, k_2, \lambda_1, K_b]$$

### Strategy:

- Quantify uncertainty in parameters
- Propagate uncertainty through model

Example: HIV model  

$$\dot{T}_{1} = \lambda_{1} - d_{1}T_{1} - (1 - \varepsilon)k_{1}VT_{1}$$

$$\dot{T}_{2} = \lambda_{2} - d_{2}T_{2} - (1 - f\varepsilon)k_{2}VT_{2}$$

$$\dot{T}_{1}^{*} = (1 - \varepsilon)k_{1}VT_{1} - \delta T_{1}^{*} - m_{1}ET_{1}^{*}$$

$$\dot{T}_{2}^{*} = (1 - f\varepsilon)k_{2}VT_{2} - \delta T_{2}^{*} - m_{2}ET_{2}^{*}$$

$$\dot{V} = N_{T}\delta(T_{1}^{*} + T_{2}^{*}) - cV - [(1 - \varepsilon)\rho_{1}k_{1}T_{1} + (1 - f\varepsilon)\rho_{2}k_{2}T_{2}]V$$

$$\dot{E} = \lambda_{E} + \frac{b_{E}(T_{1}^{*} + T_{2}^{*})}{T_{1}^{*} + T_{2}^{*} + K_{b}}E - \frac{d_{E}(T_{1}^{*} + T_{2}^{*})}{T_{1}^{*} + T_{2}^{*} + K_{b}}E - \delta_{E}E$$
squares
$$q)]^{2}$$

Point Estimates: Ordinary least squares

$$q^{0} = \arg\min_{q} \frac{1}{2} \sum_{j=1}^{N} [\upsilon_{j} - f(t_{j}, q)]^{2}$$

Note: Scaling critical since parameter values vary by 8 orders of magnitude.

**Optimization Results:** 

b <sub>E</sub>	δ	<i>d</i> <sub>1</sub>	k <sub>2</sub>	$\lambda_1$	K <sub>b</sub>
0.30	0.68	$9.1  imes 10^{-3}$	$1.22  imes 10^{-4}$	$9.95  imes 10^{3}$	88.5

#### **Data and Prediction of Immune Effector Response E:**



**Note:** Point estimates but no quantification of uncertainty in:

- Model
- Parameters
- Data

#### **Goals:**

- Replace point estimates with distributions.
- Construct credible and prediction intervals.
- Natural in a Bayesian framework

## Statistical Inference

**Goal:** The goal in statistical inference is to make conclusions about a phenomenon based on observed data.

**Frequentist:** Observations made in the past are analyzed with a specified model. Result is regarded as confidence about state of real world.

• Probabilities defined as frequencies with which an event occurs if experiment is repeated several times.

• Parameter Estimation:

o Relies on estimators derived from different data sets and a specific sampling distribution.

o Parameters may be unknown but are fixed and deterministic.

**Bayesian:** Interpretation of probability is subjective and can be updated with new data.

• Parameter Estimation: Parameters are considered to be random variables having associated densities.

# **Bayesian Inference: More General Model**



$$m{s}_i = m{E}m{e}_i + m{arepsilon}_i$$
 ,  $i = 1, ..., N$   
 $\hat{igsilon}_{m{arepsilon}_i} \sim N(0, \sigma^2)$ 

Parameter: Stiffness E

Strategy: Use model fit to data to update prior information



Non-normalized Bayes' Relation:

$$\pi(E|s) = e^{-\sum_{i=1}^{N} [s_i - Ee_i]^2/2\sigma^2} \pi_0(E)$$



# **Bayesian Inference**



- Prior Distribution: Quantifies prior knowledge of parameter values
- Likelihood: Probability of observing a data given set of parameter values.
- Posterior Distribution: Conditional distribution of parameters given observed data.

### **Problem:** Can require high-dimensional integration

- e.g., HIV Model: p = 6 23!
- Solution: Sampling-based Markov Chain Monte Carlo (MCMC) algorithms.

• Metropolis algorithms first used by nuclear physicists during Manhattan Project in 1940's to understand particle movement underlying first atomic bomb.

## Markov Chain Monte Carlo Methods

### Strategy:

- Sample values from proposal distribution  $J(q^*|q^{k-1})$  that reflects geometry of posterior distribution
- Compute  $r(q^*|q^{k-1}) = \frac{\pi(\upsilon|q^*)\pi_0(q^*)}{\pi(\upsilon|q^{k-1})\pi_0(q^{k-1})}$ 
  - \* If  $r \ge 1$ , accept with probability  $\alpha = 1$
  - \* If r < 1, accept with probability  $\alpha = r$

**Intuition:** Consider flat prior  $\pi_0(q) = 1$  and Gaussian observation model



Algorithm: [Haario et al., 2006] – MATLAB, Python



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Algorithm: [Haario et al., 2006] – MATLAB, Python





Algorithm: [Haario et al., 2006] – MATLAB, Python





Algorithm: [Haario et al., 2006] – MATLAB, Python





## **Bayesian Model Calibration – HIV Example**

Model: 
$$\dot{T}_1 = \lambda_1 - d_1 T_1 - (1 - \varepsilon)k_1 V T_1$$
  
 $\dot{T}_2 = \lambda_2 - d_2 T_2 - (1 - f\varepsilon)k_2 V T_2$   
 $\dot{T}_1^* = (1 - \varepsilon)k_1 V T_1 - \delta T_1^* - m_1 E T_1^*$   
 $\dot{T}_2^* = (1 - f\varepsilon)k_2 V T_2 - \delta T_2^* - m_2 E T_2^*$   
 $\dot{V} = N_T \delta(T_1^* + T_2^*) - cV - [(1 - \varepsilon)\rho_1 k_1 T_1 + (1 - f\varepsilon)\rho_2 k_2 T_2] V$   
 $\dot{E} = \lambda_E + \frac{b_E(T_1^* + T_2^*)}{T_1^* + T_2^* + K_b} E - \frac{d_E(T_1^* + T_2^*)}{T_1^* + T_2^* + K_b} E - \delta_E E$ 

#### **Verification:** Why do we trust results??

• Compare results from different algorithms; e.g., DRAM and Gibbs

**Parameter Chains and Densities:**  $q = [b_E, \delta, d_1, k_2, \lambda_1, K_b]$ 



# Chain Convergence (Burn-In)

#### **Techniques:**

- •Visually check chains
- Statistical tests
- •Often abused in the literature





# Propagation of Uncertainty in Models – HIV Example

### **Parameter Densities:**



#### Techniques:

- Sample from parameter densities to construct prediction intervals for Qol.
- Slow convergence rate  $O(1/\sqrt{M})$
- 100-fold more evaluations required to gain additional place of accuracy.
- Significant numerical analysis used to efficiently propagate densities.



# Use of Prediction Intervals: Nuclear Power Plant Design

**Subchannel Code (**COBRA-TF): numerous closure relations, ~70 parameters

Nu: Nusselt number  $Nu = 0.023 Re^{0.8} Pr^{0.4}$  Re: Reynolds number Pr: Prandtl number

**Rod** cluster control assembly

Bottom

nozzle

op nozzle

-Plug

Pellet

Fuel rod

Fuel tube

Grid

Fuel rod

Control rod

quide thimble

**Industry Standard:** Employ conservative, uniform, bounds

i.e., [0, 0.046], [0, 1.6], [0,0.8]

e.g., Dittus—Boelter Relation

### **Bayesian Analysis:** Employ conservative bounds as priors



**Note:** Substantial reduction in parameter uncertainty

# Use of Prediction Intervals: Nuclear Power Plant Design

Strategy: Propagate parameter uncertainties through COBRA-TF to

determine uncertainty in maximum fuel temperature



### Notes:

• Temperature uncertainty reduced from 40 degrees to 5 degrees

• Can run plant 20 degrees hotter, which significantly improves efficiency

Ramification: Savings of 10 billion dollars per year for US power plants Issues:

- We considered only one of many physical relations
- Nuclear regulatory commission takes years to change requirements and codes

Good News: We are now working with Westinghouse to reduce uncertainties.

# Steps in Uncertainty Quantification



Parameter Selection: Required for models with unidentifiable or noninfluential inputs

• e.g., HIV and SIR model

## **Parameter Selection Techniques**

**Issue:** Parameters often not *identifiable* in the sense that they are uniquely determined by the data.

### SIR Model:

$$\frac{dS}{dt} = \delta N - \delta S - \underline{\gamma k} I S \quad , \ S(0) = S_0 \qquad \text{Susceptible}$$
$$\frac{dI}{dt} = \underline{\gamma k} I S - (r + \delta) I \quad , \ I(0) = I_0 \qquad \text{Infectious}$$
$$\frac{dR}{dt} = rI - \delta R \qquad , \ R(0) = R_0 \qquad \text{Recovered}$$

#### **Response:**

$$y = \int_0^5 R(t, q) dt$$

**Note:** Parameter set  $q = [\gamma, k, r, \delta]$  is not identifiable

Later Talk: Pierre Gremaud -- A Biased Introduction to Global Sensitivity Analysis

## SIR Disease Example

### SIR Model:

$$\frac{dS}{dt} = \delta N - \delta S - \gamma k I S \quad , \ S(0) = S_0 \qquad \text{Susceptible}$$
$$\frac{dI}{dt} = \gamma k I S - (r + \delta) I \quad , \ I(0) = I_0 \qquad \text{Infectious}$$
$$\frac{dR}{dt} = rI - \delta R \qquad , \ R(0) = R_0 \qquad \text{Recovered}$$



# Local Sensitivity Analysis

#### Local Sensitivities: Consider



**Conclusion:** Response most sensitive to *r* and  $\delta$ 

#### Limitations:

- Does not accommodate potential uncertainty in parameters.
- Sensitive to units and magnitudes of parameters.

# **Global Sensitivity Analysis**

**Global Sensitivities:** Sample parameters from uniform distributions; e.g.,

$$\gamma \sim \mathcal{U}(\gamma_{\ell}, \gamma_{r})$$
  
 $\gamma_{\ell} = \gamma_{nom} - 0.2\gamma_{nom}$   
 $\gamma_{r} = \gamma_{nom} + 0.2\gamma_{nom}$ 

**Recall:** MATLAB command to sample M samples from U(a,b)

$$>> q = a + (b - a) * rand(M, 1)$$



**Conclusion:** Response most sensitive to *r* and  $\delta$ 

### Advantage:

• Quantifies how uncertainties in response apportioned to uncertainties in parameters -- Basis for Analysis of Variance (ANOVA).

## Variance-Based Methods

**Sobol Representation:** For now, take  $Q_i \sim \mathcal{U}(0, 1)$  and  $\Gamma = [0, 1]^p$ 

Take

$$f(q) = f_0 + \sum_{i=1}^{p} f_i(q_i) + \sum_{1 \le i < j \le p} f_{ij}(q_i, q_j)$$

With appropriate assumptions,

$$f_{0} = \int_{\Gamma} f(q) dq$$
$$f_{i}(q_{i}) = \int_{\Gamma^{p-1}} f(q) dq_{\sim i} - f_{0}$$

#### Variances:

$$D_i = \int_0^1 f_i^2(q_i) dq_i$$
$$D = \operatorname{var}(Y)$$

**Sobol Indices:**  $S_i = \frac{D_i}{D}$ 

Analogy: Taylor or Fourier series



**Statistical Interpretation:** 

$$D_i = \operatorname{var}[\mathbb{E}(Y|q_i)] \Rightarrow S_i = rac{\operatorname{var}[\mathbb{E}(Y|q_i)]}{\operatorname{var}(Y)}$$

## Morris Screening: Random Sampling of Approximated Derivatives

**Example:** Consider uniformly distributed parameters on  $\Gamma = [0, 1]^{p}$ 



**Elementary Effect:** 

$$d_i^j = rac{f(q^j + \Delta e_i) - F(q^j)}{\Delta}$$
 , *i<sup>th</sup>* parameter , *j<sup>th</sup>* sample

Global Sensitivity Measures: r samples

$$\mu_{i}^{*} = \frac{1}{r} \sum_{j=1}^{r} |d_{i}^{j}(q)|$$
  
$$\sigma_{i}^{2} = \frac{1}{r-1} \sum_{j=1}^{r} \left( d_{i}^{j}(q) - \mu_{i} \right)^{2} , \quad \mu_{i} = \frac{1}{r} \sum_{j=1}^{r} d_{i}^{j}(q)$$

## SIR Disease Example

#### SIR Model:

$$\frac{dS}{dt} = \delta N - \delta S - \gamma k I S \quad , \ S(0) = S_0 \qquad \text{Susceptible}$$
$$\frac{dI}{dt} = \gamma k I S - (r + \delta) I \quad , \ I(0) = I_0 \qquad \text{Infectious}$$
$$\frac{dR}{dt} = rI - \delta R \qquad , \ R(0) = R_0 \qquad \text{Recovered}$$

**Note:** Parameter set  $q = [\gamma, k, r, \delta]$  is not identifiable

#### **Assumed Parameter Distribution:**

$$\begin{split} & \gamma \sim \mathcal{U}(0,1) \ , \ k \sim \textit{Beta}(\alpha,\beta) \ , \ r \sim \mathcal{U}(0,1) \ , \ \delta \sim \mathcal{U}(0,1) \\ & \text{Infection} & \text{Interaction} & \text{Recovery} & \text{Birth/death} \\ & \text{Coefficient} & \text{Rate} & \text{Rate} \end{split}$$

#### **Response:**

$$y = \int_0^5 R(t,q) dt$$

## SIR Disease Example

#### **Global Sensitivity Measures:**



**Result:** Densities for  $R(t_f)$  at  $t_f = 5$ 



Influential Parameters

**Note:** Can fix non-influential parameters  $\gamma$ , *k* 

#### Note: More during the project!

# **Concluding Remarks**

### Notes:

- UQ requires a synergy between engineering, statistics, and applied mathematics.
- Model calibration, model selection, uncertainty propagation and experimental design are natural in a Bayesian framework.
- Goal is to predict model responses with quantified and reduced uncertainties.
- Parameter selection is critical to isolate identifiable and influential parameters.
- Surrogate models critical for computationally intensive simulation codes.
- Codes and packages: Sandia Dakota, R, MATLAB, Python, nanoHUB.
- *Prediction is very difficult, especially if it's about the future*, Niels Bohr.



