Applications of Uncertainty Quantification and Data Assimilation in Hemodynamics

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Motivation

- **Cardiovascular disease** (CVD): hypertension now identified as the most important single cause of mortality worldwide (stroke, aneurysm, coronary or carotid artery disease)

- Biomechanical (hemodynamic) factors play a role in pathogenesis of CVD: e.g. regions of low shear stress correlate with locations of atherosclerotic lesions, HBP, AAA

- Cardiovascular **modeling** and **simulations** are – **noninvasive** (in silico experiments) means of getting morphological and **functional information** about cardiovascular system, – complements clinical diagnosis and – improve treatment, device design/performance (e.g. heart valve prosthesis)

- Cardiovascular **modeling** is very uncertain:
  - “patient specific”, multiscale, living materials, non-standard conditions: e.g. pathology, coupling to organs and/or supports, clinical/medical imaging data acquisition and **simulations** are challenging:
    - complex geometry/meshing, nonlinear FSI, BCs, HPC...
Circulatory system

- heart $\equiv$ pump + highly branched/bifurcating network of vessels
- Contain and transport blood together with $O_2/CO_2$, nutrients, enzymes, hormones to and waste products from each of $\sim 50 \cdot 10^{12}$ cells
- Control heat/mass transfer
- Redistribute blood depending on end-organ demands (auto-regulation)
- **Closed loop system** with double circulation: – **systemic** & – pulmonary
- **Arteries**: blood vessels that carry (oxygenated) blood away from the heart: most important **aorta**
Coupled interaction btw heart and systemic circulation

- Heart: propulsion organ
  - pumping of blood (unsteady: pulsatile!) into aorta
  - maintain relatively high arterial pressure
  - almost only inertial forces (in equilibrium with pressure)

- Arterial system/flow:
  - transport of blood to tissues/organs
  - pulsating flow → more/less steady flow
  - driven by pressure gradient
  - both inertial and viscous forces
Pulse wave propagation in the arterial tree [van de Vosse 2011]

- Arteries – **distend** to accommodate sudden increase in volume caused by contraction of left ventricle (systole), then – **contract** when elastic energy is released and heart at rest (diastole)

- Regular beating (**pulse**) that follows the heartbeat and propagates in the form of pulse waves. They travel fast!

- Typical physiological scaling of vascular system: $c \sim 3 - 15 [m \cdot s^{-1}], \ T \sim 1 [s], \ \lambda \sim 3 - 15 [m]$

- Lot of **reflection** of forward waves at branching sites, peripheral impedances or sites of variation in arterial geometry/elastic properties

- Comprehension/modeling: blood circulation of blood [Harvey 1628], capacitance effect of arteries [Borelli 1680], Windkessel effect and waves [Euler 1775, Franck 1899], PWV [Moens-Korteweg 1878, Bramwell-Hill 1922]. Diagnostic potential of pulse wave modeling: e.g. flow waveform in the umbilical artery
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Hierarchy of models for arterial blood flow

Cardiovascular system is extraordinarily complex and vast! may be tackled with very diverse mathematical/computational tools

- Windkessel or lumped parameters (0D) models (ODE): overall description; relation btw pressure and flowrate at specific site; few parameters: main properties of network distal to point of interest

- [✓] Distributed (1D) models (PDE): arterial tree ≡ ∪ small segments with known geometry/mechanical properties; based on the + 1D form of Navier-Stokes equations (conservation of mass and momentum) computationally cheap

- Full (3D) models (PDE): often restrained to (patient-)specific part of arterial tree; access to detailed flow description; computationally intensive; sensitive to boundary conditions

- combinations of models or multiscale models are possible
Incorporation of uncertainty modeling
Applied to hemodynamics

Forward UQ: *global*: geom/material properties/distal BCs [Xiu 07, Chen 13] vs. *local* impact: AAA geom, carotid bifurcation geom+flow [Sankaran 11], lower limb [El Bouti 15]

**Stochastic inverse problems**: Bayesian framework with clinical data + numerical solver: femoropoplitial bypass graft [Lassila 13], PS aortic stiffness [Auricchio 15], DA EnKF [Lombardi 13]
Incorporation of **uncertainty modeling**
Applied to hemodynamics

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Effect of subject-specific activities → influence of inflow BCs and aortic stiffness on vascular response?
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Effect of subject-specific activities $\rightarrow$ influence of inflow BCs and aortic stiffness on vascular response?

$\rightarrow$ UQ of inflow BCs and of aortic stiffness

$\rightarrow$ Focus on Pulse Pressure: $PP(x)$ and Reflection Magnitude: $RM(x)$ response.
Reduced-order cardiovascular network modeling

1D model

Reduce geometrical/computational complexity. For each artery $A_i$ [Formaggia 02]:

\[
\frac{\partial A}{\partial t} + \frac{\partial AU}{\partial x} = 0
\]

\[
\frac{\partial U}{\partial t} + U \frac{\partial U}{\partial x} = -\frac{1}{\rho} \frac{\partial p}{\partial x} - \frac{f}{\rho A}
\]

\[
p = p_0 + \beta(x)(\sqrt{A} - \sqrt{A_0})
\]

\[\beta(x) = 2\rho c_0(x)^2 A_0^{-1/2} \sim \text{wall arterial stiffness at rest}\]

- incompressible and Newtonian fluid, laminar flow
- long-wave approximation (radius of curvature $\gg$ arterial radius)
- cross-sectional averages of blood velocity and pressure
- elastic (linear), homogeneous and thin arterial walls
Reduced-order cardiovascular network modeling

The characteristic system

\[ U_t + H(U)U_x = S \quad \text{with} \quad U = [A, U]^T \]
\[ W_t + \Lambda(U)W_x = LS \]

- \( H = L^{-1}\Lambda L \): Jacobian matrix of the flux
  \( W = [W_f, W_b]^T \): characteristics variables

- Strictly hyperbolic system with \( \lambda_{f,b} = U \pm c \), with wavespeed \( c \propto A^{1/4} \gg U \)

- \( \lambda_f > 0 \): information travels proximal \( \rightarrow \) distal; \( \lambda_b < 0 \): opposite
**Reduced-order cardiovascular network modeling**

Numerical solution: **Discontinuous Galerkin (DG) scheme**

DG solver [Sherwin 03] does not suffer from excessive dispersion/diffusion errors

- **Spectral/hp element solution** Legendre polynomial expansion
- **Riemann solver of Roe** same accuracy as exact RP solver
- **2nd-order Adams-Bashforth time int.** + CFL condition
- **Subject-specific in vivo validation** [Bollache 14, El Bouti 15]

✓ **Need for appropriate inflow, terminal and junction/bifurcation boundary conditions (BC)**
Convection-dominated problem with subcritical flow: one BC at both domain inlet and outlet:

- **inflow**: volume flow rate $AU(t)$ measured *in vivo* e.g. medical imaging MRI close to inlet of ascending aorta ($\sim 70$ (bpm); $70 - 100 [ml]/$stroke; CO : $6 [l/min]$)

- **terminal**: accounts for truncated peripheral vessels (small arteries, arterioles and capillaries), fluid resistance dominates over wall compliance/fluid inertia; 0D RCR model (electric circuit analog)

**Junction/bifurcation:**

- conservation of mass
- conservation of total (Bernoulli) pressure
- nonlinear system of 6 equations at each node (Newton solver)
Reduced-order cardiovascular network modeling

Uncertainty quantification challenges

UQ of pulse wave propagation in the systemic circulation is challenging:

- **complexity** of internal pulse **wave dynamics** in a **closed-loop network** (fast waves, numerous reflexions, “wave-trapping” phenomena, cause-effect relationship hard to define)

- **parametric exploration** → **curse of dimensionality** (55-artery 1D distributed model: geometry, compliance, boundary conditions, reference pressures, etc...: 227 parameters! exponential growth with bifurcation generation)

  question of the optimal choice of network topology; computational reduction:... “less is more”!
**Inflow BC model**

- For pulsatile **inflow proximal BCs** at ascending aorta: go further than the 1/2 sine wave? [Franke PhD 03], including reverse flow?

- A differentiable, periodic, function with parameters cardiac cycle $T$, mean flow rate $\bar{Q}$, peak flow rate $Q_{\text{max}}$ is defined [Stevens 03]:

$$Q_{\text{inlet}}(t) = A \times \bar{Q} \sin^{13}(\omega t) \cos(\omega t - \phi) \quad \text{with} \quad \omega = \frac{\pi}{T}$$

$\rightarrow$ the term $A$ comes from a normalizing factor,

$\rightarrow$ the phase angle $\phi \in ]0, \pi/2]$ is issued from $Q_{\text{max}}$

$$(T, \bar{Q}, Q_{\text{max}}) \sim \phi \quad \longmapsto \quad Q_{\text{inlet}}(t)$$
Stochastic inflow BCs

<table>
<thead>
<tr>
<th>dist. $\sim U$</th>
<th>$T$</th>
<th>$\bar{Q}$</th>
<th>$Q_{\text{max}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>mean $\mu$</td>
<td>$\frac{60}{70}$ (s)</td>
<td>100 (ml/s)</td>
<td>650 (ml/s)</td>
</tr>
<tr>
<td>std $\sigma_{[%\mu]}$</td>
<td>11.6%</td>
<td>5.8%</td>
<td>5.8%</td>
</tr>
</tbody>
</table>

Figure: Example of several random realizations of aortic ascending inflow rates
Aortic stiffening with age (courtesy of [Xiao 2013])

Wall stiffness (MPa)

```
1.0
1.0
0.8
0.8
0.6
0.6
0.4
0.4
0.2
0.2
```

```
Interval  Young  Middle-Aged  Elderly
1 to 2    3.01    3.36       3.57
2 to 3    3.43    5.61       6.15
3 to 4    3.52    5.32       8.11
4 to 5    4.30    6.38       8.00
5 to 6    3.56    5.06       6.24

Aortic to Iliac (1 to 6)
3.74      5.08       6.19
```

![Diagrams of arterial wall stiffness for three trunk cases. The “middle-aged” and “elderly” cases represent a 2x and 3x increase in arterial stiffness, respectively, over that of the “young” case.](image)

Top Panel: Distribution of arterial wall stiffness for three trunk cases. The “middle-aged” and “elderly” cases represent a 2x and 3x increase in arterial stiffness, respectively, over that of the “young” case.

Middle Panel: Pressure waveforms at six sites in the aorta for all three cases.

Bottom Panel: Comparison of pulse wave velocities between the three cases.
Aortic stiffness model

- The aortic stiffness $x \mapsto \beta(x)$ along the aorta is modeled as a random field discretized with a finite number of variables.
- It is assumed to be a stationary random field with a spatial correlation defined by a Gaussian kernel:

$$\text{cov}_{c_0} : (x_1, x_2) \in D \times D \mapsto \text{cov}_{c_0}(x_1, x_2) = \sigma_{c_0}(x) e^{-\frac{(x_2-x_1)^2}{2C_l^2}}.$$  

- It is expressed with the Karhunen-Loève (KL) representation:

$$c_0(x, \xi) \approx c_{00}(x) + \sum_{i=1}^{n} c_{0i}(x, \xi_i) = \mu_{c_0}(x) + \sigma_{c_0}(x) \sum_{i=1}^{n} \sqrt{\lambda_i} r_i(x) \xi_i,$$

- A correlation length $C_l \equiv l_{\text{aorta}}/3$ is chosen in accordance with experimental evidence. It is well represented with the first $n = 3$ modes.
Stochastic aortic stiffness

Figure: Example of several random realizations of the aorta stiffness random field: here, depicted as pulse wave velocities at rest $c_0$. 
Stochastic (sample-based) approximation method

- **Three UQ computations** are presented here: a reference case with 3 unknowns \((T, Q, Q_{max})\) and two augmented cases with 1 or 3 additional unknowns in the proximal (resp proximal/distal) aorta \((c_{0,1}, c_{0,2}, c_{0,3})\).

- **Non-intrusive:** pseudospectral **multivariate** (Legendre) Polynomial Chaos \((g)PC\) [Wiener 38, Ghanem 91, Xiu 02, Conrad 13] \(\Rightarrow\) flexibility of sampling-based method + fast convergence if solution regularity

**polynomial** \(L_2\) **projection** \(\rightarrow\) inner products integrals... **might be costly!**

- **Sampling:** MC \(O(K^{-\frac{1}{2}})\), Quasi MC \(O((\log K)^N K^{-1})\); quadrature/cubature + Smolyak’s algorithm \(\Rightarrow\) **sparse grids** \(O(K^{-r}(\log K)^{(N-1)(r+1)})\) based on Clenshaw-Curtis, Gauss-Patterson (less than 700 runs)... (nested) rules

\(\rightarrow\) spectral statistics: moments/correlations, pdfs, variance-based gSA (ANOVA)
Results I

Pulse pressure (PP), Area distensibility (AD) & reflection magnitude (RM) statistics

Figure: Light gray bars refer to the case of cardiovascular uncertainty modeling, while white (respectively dark gray) bars refer to the augmented case including proximal (respectively proximal-distal) aortic distensibility uncertainty modeling.
Results II
Detailed Pulse Pressure first-order Sobol’ indices: $S_T$ (a), $S_Q$ (b) and $S_{Q_{\text{max}}}$ (c)
Results III

PP correlations with heart rate and peak flow rate

Figure: Correlation coefficients $\rho_{PP,T}$ (+) and $\rho_{PP,Q_{\text{max}}}$ (○) along the arterial network versus the number of bifurcations times the metric distance from the heart.
Summary

The pulse wave propagation in arterial networks subject to uncertain inlet BCs and uncertain aortic stiffness has been investigated.

- Pulse Pressure (PP) variability mainly due to cardiac cycle period $T$ and to a lower extent to peak flow rate $Q_{\text{max}}$, not sensitive to mean flow rate $\bar{Q}$.
- Proximal PP decreases for increasing $T \rightarrow$ peripheral PP measure may overestimate central pressure subject with spontaneous tachycardia.
- High correlation ($PP_{\text{upper aorta}}, T$) and ($PP_{\text{lower aorta}}, Q_{\text{max}}$).
- The introduction of aortic stiffness uncertainty increases the variability of the system but induces a decrease of the influence of cardiac parameters.
- The effects of aortic rigidity fluctuations become important all across the system for reflection magnitude (RM) and not only downstream of the aorta, with an emphasis close to the body extremities.
- Noticeable dissymmetry between quantities predicted in left/right arms (due to different # bifurcations).
Summary

- The pulse wave propagation in arterial networks subject to uncertain inlet BCs and uncertain aortic stiffness has been investigated.
- The main results are the following:

  Pulse Pressure (PP) variability mainly due to cardiac cycle period $T$ and to a lower extent to peak flow rate $Q_{\text{max}}$, not sensitive to mean flow rate $\bar{Q}$.

  Proximal PP decreases for increasing $T \rightarrow$ peripheral PP measure may overestimate central pressure subject with spontaneous tachycardia.

  High correlation ($PP_{\text{upper aorta}}, T$) and ($PP_{\text{lower aorta}}, Q_{\text{max}}$)

  The introduction of aortic stiffness uncertainty increases the variability of the system but induces a decrease of the influence of cardiac parameters.

  The effects of aortic rigidity fluctuations become important all across the system for reflection magnitude (RM) and not only downstream of the aorta, with an emphasis close to the body extremities.

  Noticeable dissymmetry between quantities predicted in left/right arms (due to different number of bifurcations)
More details about this first part in:


Reducing uncertainties in cardiovascular simulations

Physics-based modeling is not enough! → data-driven methods

Arterial stiffness (AS): predictor of cardiovascular (CV) diseases

AS characterized by compliance & distensibility parameters, hard to measure directly in vivo Doppler Ultrasound, MRI, CT

→ inference from pulse wave velocity $c$ along arterial tree (Moens-Korteweg equation)

Data assimilation (DA): using both (indirect) observations and numerical model of the system
Patient-specific data assimilation in hemodynamics: an inverse problem (IP)

Given set of data $\mathcal{O}$ + model $\mathcal{M}$ describing state/solution $\mathbf{U}$:

$\rightarrow$ estimate parameters $\mathbf{q}$

Deterministic inversion often ill-posed (existence, uniqueness, stability)

Statistical Inference (SI) restates IP as a well-posed problem in probability space: parameters $\mathbf{q}$ are modeled as RVs

Bayesian paradigm for inference:

1. Bayesian inference

2. Bayesian filtering (unsteady IP)
Bayesian Inference

Probabilistic approach where the prior probability of parameters $q$ of a model $M$ with solution $U$ is updated using measurements of the system

$q \in \mathbb{R}^d$: unknown parameters to be inferred, $O = \{O_i\}_{i=1,...,M} \in \mathbb{R}^M$: set of measurements/observables

Bayes’ rule:

$$p_{\text{post}}(q|O) \propto L(O|q,M)p(q),$$

$p(q)$: prior density, $L(O|q,M)$: likelihood of the measurement set and $p_{\text{post}}(q|O)$ posterior density

Information to extract/use:

- estimate parameters: $(\mathbb{E}[q|O], q_{\text{MAP}}: \arg \max_{q \in \mathbb{R}^d} p_{\text{post}}(q|O))$, marginal distributions, credibility intervals
- perform UQ and sensitivity analyses based on $M$, estimate $U$
Likelihood function

→ requires introduction of model for measurement errors, e.g. for additive noise, mutually ind. from $q$:

$$O_i = U_i(q) + \epsilon_i,$$

where $U_i(q)$ is the model prediction for the $i$-th measurement

$$p(O_i|q) = p_{\epsilon_i}(O_i - U_i(q))$$

In case of normally distributed noise $p_{\epsilon_i} \sim \mathcal{N}(0, \sigma_i^2)$ & prior $p(q) \sim \mathcal{N}(\mu_q, \Sigma_q)$:

$$L(q) \equiv L(O|q, U) = \prod_{i=1}^{M} \exp \left[ -\frac{|O_i - U_i(q)|^2}{2\sigma_i^2} \right]$$

$$p_{\text{post}}(q|O) \propto \exp \left[ \sum_{i=1}^{M} -\frac{1}{2} (O - U(q))_i \Sigma_{\epsilon}^{-1} (O - U(q))_i 
- \frac{1}{2} (q - \mu_q)^T \Sigma_q^{-1} (q - \mu_q) \right]$$
Computational tasks/challenges

1. Based on all prior information, find a prior prob. density $p(q)$
   MaxEnt, Expert knowledge

2. Compute the **Likelihood** function $L(q)$: relating parameters, observations and predictions
   \[ \rightarrow \text{costly forward model appears inside the likelihood} \]

3. Develop methods to explore efficiently posterior density $p_{post}(q|\mathcal{O})$
   (Markov Chain MC methods, Metropolis-Hastings, Gibbs sampler)
   - posterior statistics may be expensive to estimate
   - MCMC has same convergence rate as MC methods
Accelerating the Bayesian Inference

Statistical-based inference challenging for complex models and High dimension → possible alleviations through complexity / dimensionality reduction

1. Build $p(q)$: SSM: Karhunen-Loève (KL) expansion [Marzouk 09, Li 06]

2. Using surrogate forward models $\hat{M}$, compute Likelihood $\hat{L}(q)$: , e.g. SSM: PC/gPC [Marzouk 07, Galbally 10, Birolleau 14], SC [Balakrishnan 03]; RBF [Bliznyuk 12]; POD [Wang 05]; Gaussian proc. [Rasmussen 03]; Optimal maps [El Moselhy 12]; local Pol. [Conrad 14]

3. Explore efficiently $\hat{p}_{\text{post}}(q|O)$ (MCMC: transition kernel; multi-stage; low-rank multi/fidelity [Cui 14]); deterministic (sparse, adaptive) quadrature/cubature for low/moderate dim. [Cools 96, Schillings13]
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Under *i.i.d.* **Gaussian** measurement errors and if $\exists \kappa, \kappa \cdot p(q) \geq 1, \exists C(O) > 0$ such that [Birolleau 14]:

$$\text{KL}(p_{post} \| \hat{p}_{post}) \leq C(O) \left( \sum_{i=1}^{M} \| U_i - \hat{U}_i \|_{L^2(p)}^2 \right)^2, \text{ with } \text{KL}(r \| s) = \int r(q) \log \left( \frac{r(q)}{s(q)} \right) dq$$
Accelerating the Bayesian Inference

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**But overwhelming difficulties for large prior-posterior distance and/or low-regularity state/parameter**
IP schematic

suitable prior-based samples $\rightarrow$ accurate surrogate over posterior region...
IP schematic

... → accurate posterior samples
IP schematic

inappropriate prior-based samples $\rightarrow$ poor surrogate over posterior region...
IP schematic

... → poor posterior samples
Model reduction for Bayesian Inference

**Idea**: construct accurate **posterior-adapted polynomial surrogate** minimizing $L_2(p_{\text{post}})$ error:

\[
\mathbb{E}_{p_{\text{post}}} \left\{ |U_i - \hat{U}_i|^2 \right\} = \int \ldots \int |U_i(q) - \hat{U}_i(q)|^2 p_{\text{post}}(q | \mathcal{O}) dq
\]

posterior measure is unknown, off-line construction of surrogate is not feasible
Model reduction for Bayesian Inference

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$L_{2(\rho_{\text{post}})}$ error:

$$
\mathbb{E}_{\rho_{\text{post}}} \left\{ |U_i - \hat{U}_i|^2 \right\} = \int \int |U_i(\mathbf{q}) - \hat{U}_i(\mathbf{q})|^2 p_{\text{post}}(\mathbf{q} | \mathcal{O})) d\mathbf{q}
$$

posterior measure is unknown, off-line construction of surrogate is not feasible

→ iterative strategy with sequence of surrogates constructed based on “posterior-adapted” samples drawn from successive $\hat{p}_{\text{post}}(\mathbf{q} | \mathcal{O})$ approximations

Surrogate candidates: **stochastic spectral approximations (PC)** [Le Maître 10]:

$$
U_i(\mathbf{q}) \approx \hat{U}_i(\mathbf{q}) \doteq \sum_{\alpha} [U_i]_{\alpha} \Psi_{\alpha}(\eta(\mathbf{q})),
$$

where $\Psi_{\alpha}$ are orth-normal multi-variate polynomials, $\mathbf{q} \mapsto \eta$ (Cholesky, SVD)
Model reduction for Bayesian Inference
Iterative surrogate model

\[
U(q) = (U_1(q) \ldots U_M(q))^T \quad \text{vector of model predictions}
\]

Goal: construct sequence of polynomial surrogates \(\hat{U}^{(k)}(q)\) for \(U(q)\) by incorporating/selecting progressively new samples to entire data set \(\mathcal{D}\)

\[
\mathcal{D} = \{(q^j, U^j, \rho^j), j = 1, \ldots, |\mathcal{D}|\} \quad \text{collected samples} \quad \text{i.e. – parameters, model predictions and confidence measures – used for the construction of the surrogates}
\]
Model reduction for Bayesian Inference

Iterative surrogate model

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Iterative approach from step \( (k) \to (k+1) \):

1. \( \mathcal{D} \) is completed by drawing new samples from \( \hat{p}_{\text{post}}^{(k)}(q|\mathcal{O}) \), based on the current surrogate \( \hat{U}^{(k)}(q) \), thanks to Markov-Chain type samplers

2. polynomial surrogate construction of \( \hat{U}^{(k+1)}(q) \) from samples in \( \mathcal{D} \), thanks to (regularized) **weighted least squared** \( (w\text{-LS}) \) residual minimization
Model reduction for Bayesian Inference

Generation of new samples

- Use of approximate posterior at step \(^{(k)}\) + MCMC methods

\[
\hat{p}_{\text{post}}^{(k)}(q|\mathcal{O}) \propto \exp \left[ \sum_{i=1}^{M} - \frac{|O_i - \hat{U}_i^{(k)}(q)|^2}{2\sigma_i^2} \right] \cdot p(q), \tag{1}
\]

- fast/cheap (polynomial) generation of new (quasi) independent samples \(q^j\)

- For each new \(q^j\) retained, \(U^j_i = U(q^j)\) computed by solving complete model

- + evaluation of a discrepancy: \((\Delta^j)^2 \triangleq \sum_{i=1}^{M} \frac{|U^j_i - \hat{U}_i^{(k)}(q^j)|^2}{2\sigma_i^2}\), that is related to a trust measure (weight): \(\rho^j \triangleq 1/ \max(\delta_t, \Delta^j)\)

Enrichment of the data set \(\mathcal{D} \leftarrow \mathcal{D} \subset \{(q^j, U^j, \rho^j)^{(k)}\}\)
Choice of samples subset $D^{(k+1)} = \{(q^j, U^j, \rho^j), j \in \mathcal{I}^{(k+1)}\} \subset D$ with $\mathcal{I}^{(k+1)} \subset \{1, \ldots, |D|\}$ from which to build the continuous model.

PCA-type parameter coordinates transformation: $q^j \xrightarrow{\text{PCA}} \eta^j$ centered/normalized for better conditioning + weight normalization over the subset $D^{(k+1)}$.

Model calculation: $U^{(k+1)}(q) = \sum_{\alpha=0}^{P} [U]^{(k+1)}_{\alpha} \Psi_{\alpha}(\eta(q))$ by regression:

$$[U]^{(k+1)}_{\alpha=0 \ldots P} \equiv u = \arg \min_{v \in \mathbb{R}^{P+1}} \sum_{j \in \mathcal{I}^{(k+1)}} \rho^j \left| U^j - \sum_{\alpha=0}^{P} \Psi_{\alpha} v_{\alpha} \right|^2 + \left( \lambda \sum_{\alpha=0}^{P} |v_{\alpha}| \right),$$

(regularized) weighted least squared residuals problem.
Simple one-dimensional test problem

Problem settings:
✓ single parameter $q$ and non-polynomial model: $U(q) = \exp[\tanh(q/2)]$
✓ standard Gaussian prior: $p(q) = \exp[-q^2/2]/\sqrt{2\pi}$
✓ single observation $O = 2.6$, likelihood maximized for $q = 3.8$

✓ for small noise level, $\sigma \ll 1$, prior and posterior are very distant
✓ a high polynomial order is required to globally approximate $U(q)$ over few standard deviations range.
One-dimensional test problem

Convergence of to the exact posteriors depending on the noise level:

<table>
<thead>
<tr>
<th>$\sigma = 0.5$</th>
<th>$\sigma = 0.1$</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="Graph" /></td>
<td><img src="image2.png" alt="Graph" /></td>
</tr>
<tr>
<td>$\sigma = 0.01$</td>
<td>$\sigma = 0.001$</td>
</tr>
<tr>
<td><img src="image3.png" alt="Graph" /></td>
<td><img src="image4.png" alt="Graph" /></td>
</tr>
</tbody>
</table>

✓ polynomial expansion with degree 5
✓ surrogates are constructed using the 10 last data points
One-dimensional test problem

Effect of polynomial degree: (noise level $\sigma = 0.05$)

<table>
<thead>
<tr>
<th>degree 2</th>
<th>degree 3</th>
</tr>
</thead>
</table>

- surrogates are constructed using the degree $\times 2$ last data points
- convergence of the surrogates and posteriors
Higher-dimensional test problem

Problem setting:
✓ same number $d > 1$ of parameters in $\mathbf{q}$ and observations: $\mathbf{U}(\mathbf{q}) \in \mathbb{R}^d$
✓ $U_i(\mathbf{q}) = \exp[\tanh(q_i/2) + i \times \|\mathbf{q}\|/10]$, for $i = 1, \ldots, d$
✓ $\mathbf{q}$ with independent standard Gaussian prior
✓ PC construction of the surrogates of $U_i$ with polynomial degree
✓ observations $O_i$ set to $U_i(2, \ldots, 2)$
✓ assume same noise level $\sigma_i = \sigma$ for all observations

For validation purposes:
✓ generation of 10,000 independent sample points from the exact posterior
✓ point-wise comparison of $p_{\text{post}}^k(\mathbf{q}|O)$ and $p_{\text{post}}(\mathbf{q}|O)$
✓ **Empirical Monte Carlo estimation of the surrogate error**

$$\mathbb{E}_{p_{\text{post}}} \left\{ \| \mathbf{U} - \hat{\mathbf{U}}^{(k)} \|^2 \right\} = \int \cdots \int \| \mathbf{U}(\mathbf{q}) - \hat{\mathbf{U}}^{(k)}(\mathbf{q}) \|^2 p_{\text{post}}(\mathbf{q}|O)) d\mathbf{q}$$
Higher-dimensional test problem

Convergence of surrogates error with polynomial degree \((d = 3)\):

✓ surrogates constructed from the \(2 \times \) basis dimension last data
✓ noise level 0.01

Monitoring of the weights: carries information on convergence!
Arterial stiffness (AS): predictor of cardiovascular (CV) diseases

Structural/func. changes in arteries are age-related or $\propto$ CV risk factors

AS characterized by compliance & distensibility parameters, hard to measure in vivo Doppler Ultrasound, MRI, CT

→ inference from pulse wave velocity $c$ along arterial tree (Moens-Korteweg equation)
In vivo arterial stiffness estimation in cardiovascular networks

Arterial stiffness (AS): predictor of cardiovascular (CV) diseases

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Doppler Ultrasound, MRI, CT

$\rightarrow$ inference from pulse wave velocity $c$ along arterial tree (Moens-Korteweg equation)

Physiological scaling of vascular system

$c \sim 3 - 15 [m \cdot s^{-1}], \quad T \sim 1 [s], \quad \lambda \sim 3 - 15 [m]$

Hemodynamics: nonlinear FSI problem

with closed distribution network + incompressible fluid
Patient-specific arterial stiffness calibration on 7-artery left lower limb model

Parameters: \( c_0 \equiv \exp(q) \in \mathbb{R}^{d=7} \) network AS with \( p(q) \sim \mathcal{N}(\mu_q, \Sigma_q) \), hyperbolicity condition [Xiu 07]

\( \mu_q \) from [Sherwin 2001]; \( \Sigma_q \) based on \( c_{vq} \sim 15 - 20\% \)

Measurements: non-invasive patient-specific (ultrasound echo-tracking):
\( O \equiv \left| \left( \mathbf{U}^{\text{sys}} - \mathbf{U}^{\text{dia}} \right) / \mathbf{U}^{\text{dia}} \right| \in \mathbb{R}^{M=3} \) in arteries \( A_{2,4,6} \) with noise \( \epsilon \sim \mathcal{N}(0, \Sigma_O) \) \( (U_i \) maybe \( A \) or \( U) \)

Iterative surrogate model: parallelized 1D FSI hemodynamic code \((h \sim 0.25\text{cell/cm}; p = 4)\); sampling \( |\mathcal{I}^{(k)}| = 3 N_{PC} (N_0) \); basis: Hermite polynomial of TD with \( N_0^{(0)} = 1 \); w–LS solver

Posterior sampling: parallel MCMC chains
(Metropolis-Hastings scheme)
Sample trust-indices/bandwidth, selected polynomial order

(a) 10^0 10^2 10^4
(b) 1 2 3 4
(c) 0 50

Dec. 13th 2016 – Didier Lucor (LIMSI-CNRS) 42 / 49
Adaptive vs. iterative surrogates (averaged) trust-indices

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Posterior $\hat{p}_{\text{post}}(c_0|\mathcal{O})$ mean statistics convergence
Posterior $\hat{p}_{\text{post}}(c_0|\mathcal{O})$ std statistics convergence
1- and 2-dimensional posterior $\hat{p}_{\text{post}}(c_0|O)$ marginals

← Global surrogate model (Gauss-Hermite sparse grid $\nu = 3$: 785 runs)
1- and 2-dimensional posterior $\hat{p}_{\text{post}}(c_0|\mathcal{O})$ marginals

← Global surrogate model (Gauss-Hermite sparse grid $\nu = 4$: 3921 runs)
1- and 2-dimensional posterior $\hat{p}_{\text{post}}(c_0|\mathcal{O})$ marginals

← Global surrogate model (Gauss-Hermite sparse grid $\nu = 5$: 16703 runs)
1- and 2-dimensional posterior \( \hat{p}_{\text{post}}(c_0|O) \) marginals

← Iterative local surrogate model (MC grid \( N_{\text{max}} \approx 1000 \) runs)
Summary

Statistical-based inference challenging in HD spaces for systems with computationally expensive forward models

Possible alleviations through dimensionality reduction → surrogate model constructed with fewer samples than required to characterize the posterior

Using prior information only is inefficient as the surrogate must be accurate over the posterior distribution support

Surrogate model is incrementally optimized to minimize $L^2_{p_{post}}$ error

Non-intrusive stochastic spectral methods of low orthogonal polynomial order are great candidates if local regularity in forward model w.r.t. parameters (weighted / regularized) least-square methods, with updated sample set is a flexible & robust framework for this approach

Significant reductions in number of model evaluations used for posterior sampling
Perspectives / future work

**Control residual sampling error**: obtain convergence rate estimates to guide sampling bandwidth and weight function selection

**Include prior hyperparameters** and reduced-order **model inadequacy** to the calibration

**Improve MCMC sampling/convergence** through fine local tuning of proposal distribution thanks to the surrogate model, use local approximation derivatives

UQ & inference on AS + effect of **lumped parameter outflow models for boundary conditions**: correlations btw different vessel generation levels, pressure waves reflection magnitude, wave entrapment phenomena, etc...

**Use information gain theory** to guide practitioners: best data acquisition sites and function utility
Final thoughts on the place of UQ in numerical hemodynamics today

Deterministic simulation

3D (local patient-specific) model - 0D/1D BCs or ROM/BC & data+

0D/1D models & data

Full body scale DNS & data++
Final thoughts on the place of UQ in numerical hemodynamics today

Source of uncertainties: computational geometry, mathematical models, physical/material parameters, boundary conditions, external sources/forces/supports, clinical/physiological data, flow split,…
Final thoughts on the place of UQ in numerical hemodynamics today

UQ of low-order models → ✓ robustness of hemodynamic response “trends”
✓ guidance for most/least sensitive parameters for “intermediate-order” models
✓ conceptual shift from patient–specific (PS) to patient-probable approach