Introduction to uncertainty quantification
An example of application in medicine

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Introduction

- The systematic quantification of the uncertainties affecting the dynamics of a system and the characterization of the uncertainty of its outcomes is critical for engineering design and analysis, where risks must be reduced as much as possible.
- Uncertainties stem naturally from our limitations in measurements, predictions and manufacturing, and we can say that any dynamical system used in engineering is subject to some of these uncertainties.
- This lecture presents an overview of the mathematical framework used in Uncertainty Quantification (UQ) analysis and introduces the use of Polynomial Chaos approximation in UQ.
- First, a very simple toy problem in UQ will be studied in order to introduce the mathematical tools. Then, an application of UQ in medicine wil be presented.

Uncertainty quantification : a toy problem

- Before studying a real problem, let study a very simple situation : consider the model made of a scalar linear ODE :

$$y' = -ay$$

with a given initial condition

$$y(0) = 1$$

- In this model, a is a parameter known with a finite accuracy (for instance a is uniformly distributed in $[1, 3]$) and the output of the model is the value

$$S = y(1)$$

.

- The question is : can we define (or approximate) the uncertainty at the exit of the model given the uncertainty at the input ?

Uncertainty quantification : a toy problem

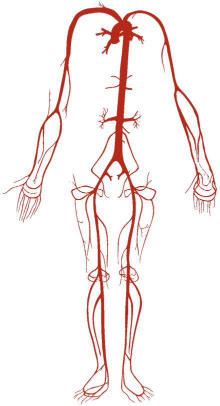
To study this problem, the following mathematical notions are now presented :

- Basic notions in probability and statistics
- The naive Monte Carlo approach
- The best polynomial approximation (in the appropriate L^2 norm)
- The orthogonal basis of polynomials (case of Legendre polynomials)
- The Gauss-Legendre quadrature method

A Scilab implementation of these tools will be proposed to solve the toy problem.

The medical application

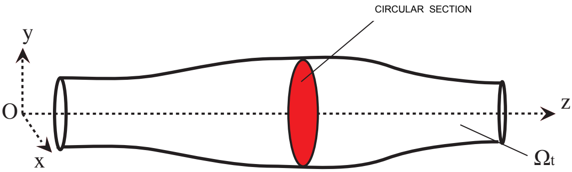
- The numerical simulation of blood flow in the human arterial tree is a very complex problem, as it involves, in the more general approach, 3D fluid/structure simulations.



The medical application

- In order to reduce the computational cost, a simplified fluid/structure model for the blood flow in the arterial tree is used (direct problem).
- The parameters are patient-specific and are obtained with the help of a non invasive, non costly experimental device.
- An uncertainty quantification for the patient-specific parameters is presented.

The 1D model



- For a given artery, the domain Ω_t is assumed to be cylindrical along the *Oz* axis and of constant length *L*.
- A simplified fluid/structure interaction model is derived on this geometry.
- References : *Formaggia, Nobile, Quarteroni* (2001),*Sherwin et al.* (2003), *Gerbeau et al.* (2005), *Stergiopoulos et al.* (2009).

The 1D model : the equations

- For a given artery, the two unknowns $A(t,z)$ (cross section) and $Q(t,z)$ (mean flux) satisfy the following set of equations :

$$\frac{\partial A}{\partial t} + \frac{\partial Q}{\partial z} = 0$$
$$\frac{\partial Q}{\partial t} + \frac{\partial}{\partial z}\left(\frac{Q^2}{A}\right) + \frac{A}{\rho}\frac{\partial P}{\partial z} + K_r\frac{Q}{A} = 0$$

- An elastic linear law closes the system :

$$P - P_{ext} = \beta(z)\left(\sqrt{A(z,t)} - \sqrt{A_0(z)}\right)$$

The 1D model : the discretization scheme

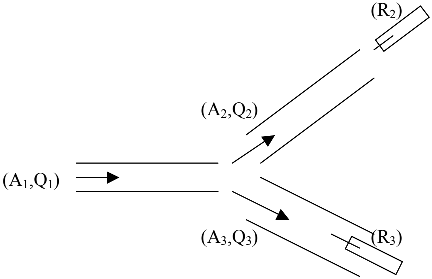
- The equations are discretized in time in their conservative form by using a second order Taylor Galerkin scheme :

$$U^{n+1} = U^n - \Delta t \frac{\partial}{\partial z}(F^n + \frac{\Delta t}{2}\frac{\partial F}{\partial U}^n B^n) - \frac{\Delta t^2}{2}(\frac{\partial B}{\partial U}^n \frac{\partial F^n}{\partial z} - \frac{\partial}{\partial z}(\frac{\partial F}{\partial U}^n \frac{\partial F^n}{\partial z})) + \Delta t(B^n + \frac{\Delta t}{2}\frac{\partial B}{\partial U}^n B^n)$$

- The spatial discretization is then done by using linear finite elements on a subdivision of $[0, L]$.
- As $\lambda_1 > 0$ and $\lambda_2 < 0$, the system is completed by two appropriate boundary conditions, one at each end for the characteristic variables W_1 and W_2.
- After some algebraic manipulations, it can be seen that a pressure profile can be imposed at the entrance.

The 1D model : network and boundary conditions

- At a bifurcation in a network of arteries, three additional conditions are imposed (conservation of mass and two pressure conditions).



- Resistance conditions are put at the exit to simulate the effect of the downtream resistance network.

Uncertainty quantification

- Once the patient-specific parameters of the model have been found, the robustness of these parameters must be studied.
- A non intrusive method called uncertainty quantification by polynomial chaos can been chosen.
- It consists in choosing an uncertainty probability distribution function for n parameters and to study the uncertainty of a a well chosen quantity at the exit.
- The chosen quantity at the exit, here the pulse pressure at position x, $PP(x)$, can be decomposed in an orthonormal polynomial basis of the form :

$$PP(x,\omega) = \sum_{j=0}^{M-1} a_j(x)\psi_j(\xi_1(\omega), \xi_2(\omega), ..., \xi_n(\omega))$$

Uncertainty quantification

- The deterministic coefficients are obtained by a non intrusive method in the following way :

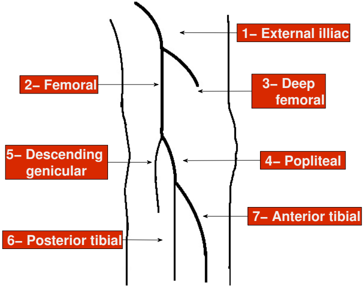
$$a_j(x) = \frac{< PP(x,.), \psi_j(\xi(.)) >}{< \psi_j^2(\xi(.)) >}$$

for $1 \leq j \leq M = \frac{(n+p)!}{n!p!}$.

- A Gauss quadrature can be used for the computation of the multi-dimensional integral.
- In case of a large n, a sparse grid interpolation technique is required to reduce the computational cost.

Numerical reconstruction of an arterial network from echotraking (patient P1)

- The arterial network studied here, is made of 7 arteries of the lower limb.



- The echotracking measurements consist in 4 velocity profiles (arteries 1,2 4 and 6) and 3 cross section profiles (arteries 1, 2 and 4).
- The cross section measurement at artery 1 is taken as the entrance condition.

The 'patient P1' optimal parameters

	Patient P1			Patient P2		
Artery	$\overline{A_0}$ (cm^2)	$\overline{c_0}$ (m/s)	$\overline{R}$	$\overline{A_0}$ (cm^2)	$\overline{c_0}$ (m/s)	$\overline{R}$
1 : El	**0.53**	4.99	-	**0.53**	6.57	-
2 : Fem	**0.47**	11.96	-	**0.38**	11.80	-
3 : DF	0.27	7.39	0.48	0.32	7.58	0.7
4 : Po	**0.40**	10.51	-	**0.34**	8.85	-
5 : Ge	0.32	9.93	0.42	0.22	13.47	0.33
6 : PT	0.23	11.61	0.95	0.24	11.67	0.68
7 : AT	0.22	9.91	0.73	0.13	14.12	0.97

TABLE: The mean optimal parameters for Patients P1 and P2 after 10 CMA-ES runs.

Robustness study of the 'patient P1 model'

- Three uncertainty analysis for patient P1 have been carried out :
  - 2 studies on local parametric uncertainty, namely the section $A_{0,k}$ and pulse wave velocity at rest $c_{0,k}$ for artery 3 and 6 respectively.
  - 1 study on the effect of external parametric uncertainty, namely peripheral resistances $(R_m)_{m\in\{3,5,6,7\}}$ at the exit.
- The random parameters for this three cases are thus respectively $(A_{0,3}, c_{0,3})$, $(A_{0,6}, c_{0,6})$ and (R_3, R_5, R_6, R_7).
- The type of uncertainty that has been chosen is of uniform type with a $\pm 25\%$ variation around the deterministic value.
- A polynomial chaos approximation of order 3 is chosen. A Gauss (respectively sparse grid) quadrature have been used for case 1 and 2 (respectively 3).

Robustness study of the 'patient P1 model'

Artery denomination	$A_{0,3}$, $c_{0,3}$ (N=2)	$A_{0,6}$, $c_{0,6}$ (N=2)	$R_{\{3,5,6,7\}}$ (N=4)
1 : external iliac	1.37	0.17	1.91
2 : femoral	2.90	5.56	10.44
3 : deep femoral	2.86	1.58	4.71
4 : popliteal	2.58	5.74	14.38
5 : genicular	1.95	6.02	14.46
6 : posterior tibial	**4.37**	**7.76**	**16.26**
7 : anterior tibial	3.96	3.64	15.73

TABLE: The pulse pressure (PP) coefficient of variation (in percentage) for each artery and for the three UQ studies.

Robustness study of the 'patient P1 model'

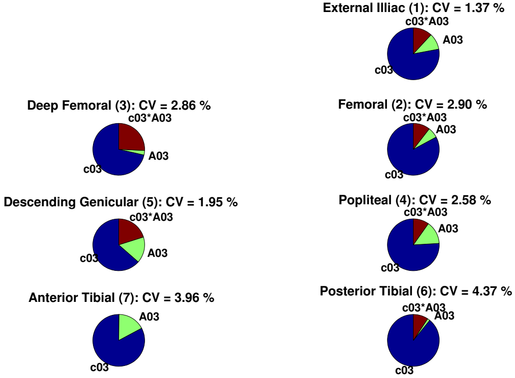


FIGURE: Patient P1 : First and second order Sobol coefficients contribution to PP uncertainty for the first UQ computation.

Robustness study of the 'patient P1 model'

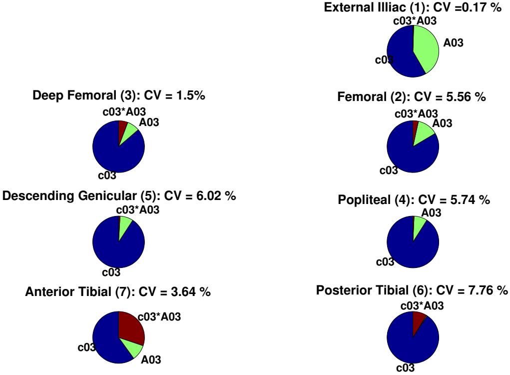


FIGURE: Patient P1 : First- and second-order Sobol coefficients contribution to PP uncertainty for the second UQ computation.

Robustness study of the 'patient P1 model'

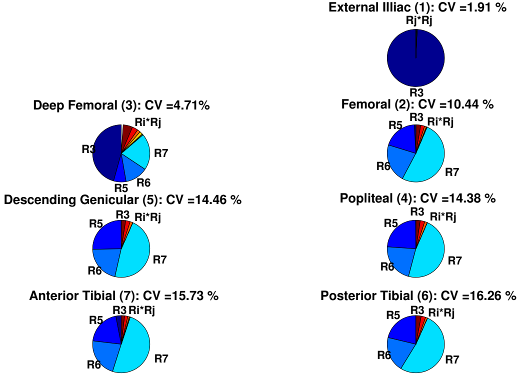


FIGURE: Patient P1 : First- and second-order Sobol coefficients contribution to PP uncertainty for the third UQ computation.

References

- "Cardiovascular Mathematics Modeling and simulation of the circulatory system", *Editors : Formaggia, Luca, Quarteroni, Alfio, Veneziani, Alessandro, Springer*, 2009.
- " Optimisation robuste et application à la reconstruction du réseau artériel humain", PhD (in french), Tamara El Bouti, 2015.
- "A robust and patient-specific hemodynamic model of the lower limb based on non invasive arterial measurements" (with T. El Bouti, D. Lucor), *Journal of Biomechanical and Engineering*, 139(1), 2016.