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ScienceDirect
Comput. Methods Appl. Mech. Engrg. 297 (2015) 167–190
Computer methods in applied mechanics and engineering
www.elsevier.com/locate/cma

# Impact of geometric uncertainty on hemodynamic simulations using machine learning

Sethuraman Sankaran[a,*], Leo Grady[b], Charles A. Taylor[c,d]

[a] HeartFlow Inc., 1400, Seaport Blvd, Building B, Redwood City, CA 94063, USA
[b] R& D, HeartFlow Inc., 1400, Seaport Blvd, Building B, Redwood City, CA 94063, USA
[c] CTO, HeartFlow Inc., 1400, Seaport Blvd, Building B, Redwood City, CA 94063, USA
[d] Stanford University, 443 Via Ortega, Stanford, CA 94305, USA

Received 3 February 2015; received in revised form 27 August 2015; accepted 30 August 2015
Available online 15 September 2015

**Abstract**

In the cardiovascular system, blood flow rates, blood velocities and blood pressures can be modeled using the Navier–Stokes equations. Inputs to the system are typically uncertain, such as (a) the geometry of the arterial tree, (b) clinically measured blood pressure and viscosity, (c) boundary resistances, among others. Due to a large number of such parameters, efficient quantification of uncertainty in solution fields in this multi-parameter space is challenging. We use an adaptive stochastic collocation method to quantify the impact of uncertainty in geometry in patient-specific models. We develop a novel subdivision method to define the stochastic space of geometries. To accelerate convergence and make the problem tractable, we use a machine learning approach to approximate the simulation-based solution. Towards this, a reduced order model of the Navier–Stokes equations is developed using a segmental resistance analog boundary conditions (ratio of pressure to flow). Using an offline database of pre-computed solutions, we compute a map (rule) from the features to solution fields. We achieve significant speed-up (of a few orders of magnitude) by approximating the simulation-based solution using a machine learning predictor. A bootstrap aggregated decision tree was found to be the best predictor among many candidate regressors (correlation coefficient of training set was 0.94). We demonstrate stochastic space convergence using the adaptive stochastic collocation method, and also show robustness to the choice of geometry parameterization. The sensitivities to geometry obtained using machine learning had a correlation coefficient of 0.92 with the values obtained using finite element simulations. Segments with significant disease in the larger arteries had the highest sensitivities. Terminal segments are more sensitive to dilation and proximal healthy segments are more sensitive to erosion. Sensitivity to geometry is highest when geometric resistance is comparable to net downstream resistance.



*Keywords:* Sensitivity analysis; Hemodynamics; Machine learning; Stochastic collocation; Geometric uncertainty

* Corresponding author. Tel.: +1 607 2274154; fax: +1 650 368 2564.
*E-mail addresses:* ssankaran@heartflow.com (S. Sankaran), lgrady@heartflow.com (L. Grady), ctaylor@heartflow.com, taylorca@stanford.edu (C.A. Taylor).

http://dx.doi.org/10.1016/j.cma.2015.08.014
0045-7825/

## 1. Introduction

Computer simulations are becoming increasingly powerful for understanding mechanisms of disease, diagnosing disease and devising treatment strategies in the human circulatory system [1–3]. Such simulations can be chiefly classified as hemodynamic simulations to compute spatio-temporal evolution of blood flow rate and pressure, fluid–structure interaction to capture wall motion and wall stresses [4], and growth and remodeling simulations [5–7] to predict long term evolution of arterial properties in health and disease. There has been a significant increase in the clinical applicability of computational tools, owing to sophistication in image acquisition, better understanding of boundary conditions, interaction between wall motion and fluid flow, and arterial remodeling mechanisms [8]. Such tools have shown significant promise in assessing the functional significance of coronary artery disease [9–12], prediction of atherosclerosis [13], aneurysm growth [6,7], failure mechanism in bypass grafts [14], outcome of stenting, outcome of pediatric surgeries [15–17], etc. In this paper, we restrict attention to hemodynamic simulations.

Uncertainties that arise in hemodynamic simulations include (a) flow rate and pressure at inlets/outlets to the model, (b) lumped parameter boundary conditions such as resistances and capacitances, (c) clinical variables such as blood viscosity and density, and (d) uncertainty in reconstructed lumen geometry. Imaging data using techniques such as magnetic resonance imaging (MRI) or computed tomography (CT) are used to reconstruct the arterial lumen geometry [18], but can be noisy due to motion and registration artifacts, blooming artifacts, motion of the arteries during the cardiac cycle, etc [19,20]. Assumptions such as constant blood viscosity [21], approximation of micro-vessels using lumped parameter boundary conditions, and population averaged empirical laws give rise to more sources of uncertainties. Here, we restrict discussion to the impact of geometry in quantifying uncertainties in hemodynamic simulations of the coronary artery. Impact of clinical parameters such as flow rate and boundary conditions have been explored earlier [22]. We will focus attention on blood flow simulations in human coronary arteries and derived quantity of significant utility in diagnosing the severity of coronary artery disease, the fractional flow reserve (FFR). FFR is defined as the ratio of blood flow rate under conditions of maximal hyperemia (reduced myocardial bed resistance) at a given location to the hypothetical value if no disease were present in the coronary artery. Under modest assumptions, the FFR can be shown to be equal to the ratio of local coronary artery blood pressure to aortic blood pressure under maximal hyperemic conditions.

Clinically, FFR is measured in the cardiac catheterization laboratory using a pressure wire during the intravenous administration of adenosine to elicit maximal hyperemic response [23]. Measurement of FFR has emerged as the gold-standard for determining which lesions in the coronary arteries are flow-limiting and should be stented and which patients should be treated medically [24–26]. Recent developments in patient-specific CFD modeling have enabled the computation of FFR noninvasively from CT data [9], referred to as $\text{FFR}_{\text{CT}}$. Data from three multicenter clinical trials indicates that this technology significantly improves the noninvasive assessment of coronary artery disease [10–12]. Thus, the assessment of the sensitivity of patient-specific coronary artery blood flow simulations is of significant interest as these tools are currently being used for clinical decision-making. However, there is still scope for improvement of $\text{FFR}_{\text{CT}}$ and understanding of sources of error compared to invasive measurements. For example, geometric sensitivity information can aid in identifying regions of the patient-specific model that require extra attention during review, which is the motivation for the present work.

In the past decade, various methods have been developed to quantify uncertainty in partial differential equations (PDEs). Some of these have been used in hemodynamic simulations [14,22] to quantify the impact of uncertainties in inlet blood flow rate, lumped parameter resistances and capacitances, and simple geometric parameters such as angle of anastomosis in bypass grafts and representative stenotic radius. Recently, Steinman and co-workers performed computational simulations to evaluate sensitivities in quantities such as wall shear stress and oscillatory shear index to variations in blood rheology, secondary flows, etc. in human subjects [19,20]. These were some of the first studies showing the relationship between fluctuations in input parameters and output quantities for patient-specific cardiovascular simulations. However, a comprehensive assessment of diverse sources of uncertainties including clinical and geometrical variables on patient-specific models has not been performed to-date owing to the following challenges — (a) depending on the size of the arterial tree, it is computationally intractable to quantify the impact of a large number of uncertain variables, and (b) parameterizing and defining shape-space for patient-specific geometries has not yet been performed. Quantifying uncertainties can help us compute the coefficient of variation, sensitivity as well as the probability distribution of quantities of interest. These, in turn, can impact diagnostic capability as well as prediction of disease progression. For instance, a cutoff of 0.8 in $\text{FFR}_{\text{CT}}$ is used to determine the treatment protocol.