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Effects of arterial wall models and measurement uncertainties on cardiovascular model predictions

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ABSTRACT

We developed a methodology to assess and compare the prediction quality of cardiovascular models for patient-specific simulations calibrated with uncertainty-hampered measurements. The methodology was applied in a one-dimensional blood flow model to estimate the impact of measurement uncertainty in wall model parameters on the predictions of pressure and flow in an arterial network. We assessed the prediction quality of three wall models that have been widely used in one-dimensional blood flow simulations. A 37-artery network, previously used in one experimental and several simulation studies, was adapted to patient-specific conditions with a set of three clinically measurable inputs: carotid–femoral wave speed, mean arterial pressure and area in the brachial artery. We quantified the uncertainty of the predicted pressure and flow waves in eight locations in the network and assessed the sensitivity of the model prediction with respect to the measurements of wave speed, pressure and cross-sectional area. Furthermore, we developed novel time-averaged sensitivity indices to assess the contribution of model parameters to the uncertainty of time-varying quantities (e.g., pressure and flow). The results from our patient-specific network model demonstrated that our novel indices allowed for a more accurate sensitivity analysis of time-varying quantities compared to conventional Sobol sensitivity indices.

1. Introduction

The greatest challenges for the daily clinical application of cardiovascular models are the process of model personalization and choice of model complexity (Donders et al., 2015; Huberts et al., 2013; Eck et al., 2015a). The amount of clinical measurements of model input parameters necessary to generate a patient-specific model should be low to reduce the burden on the patient and the costs to the clinic. As a model becomes more complex, more input parameters are needed, but the model prediction becomes more certain as the physiology is better approximated. For more input parameters, the uncertainty in the model prediction may be increased due to measurement uncertainty (Eck et al., 2015a). Uncertainty quantification (UQ) can be applied to find the optimal balance between uncertainty of the model prediction and input parameters. Sensitivity analysis (SA) can be applied to assess the influence of input parameters on model predictions, e.g., with Sobol indices (Saltelli et al., 2008). Non-influential parameters can be fixed to population average values (parameter fixing) and the most influential parameters selected for the clinical measurement protocol (input prioritization) (Donders et al., 2015; Eck et al., 2015a). Conventional Sobol indices are generally applied for scalar model outputs. We present a novel method for assessing the influence of input parameters on time-varying quantities, such as pressure and flow waves in arterial networks.

In the field of cardiovascular modeling, some researchers have applied UQ and SA (Xiu and Sherwin, 2007; Leguy et al., 2011; Chen et al., 2013; Huberts et al., 2013; Donders et al., 2015; Eck et al., 2015b; Biehler et al., 2015). All of these publications were focused on model personalization, but none investigated the application of models with different complexities. The aim of this paper is to demonstrate how UQ and SA can help to identify the optimal balance between framework uncertainty and model input uncertainty. We focus on the choice of wall models, describing the non-linear elastic behavior of arterial walls, in one-dimensional blood flow models (1D-BFM).

The simulated arterial network is a synthetic network with 37 arteries (Matthys et al., 2007); thus, experimental data for model validation are available. This network has been extensively used for assessing the accuracy of numerical simulations (Matthys et al., 2007; Alastruey et al., 2011; Xiu and Sherwin, 2007; Boileau et al., 2015). The simulations were performed with a 1D-BFM, which was verified in a recent benchmark study (Boileau et al., 2015) and applied in another study involving UQ and SA (Eck et al., 2015b).

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We consider three wall models with different complexities that are commonly integrated in 1D-BFM. The first model, henceforth denoted as the *quadratic* model, is by far the most used model in publications with 1D-BFMs (Boileau et al., 2015). This model is based on Laplace's law under the assumption that arteries behave like thin-walled tubes (Sherwin et al., 2003). The second model, henceforth the *logarithmic* model, was derived from experimental data by Hayashi et al. (1980) and has been applied in a 1D-BFM in Eck et al. (2015b). The third model, henceforth denoted as the *arctan* model, is based on the experimentally derived compliance pressure relationship by Langewouters et al. (1985) and was introduced by Stergiopulos et al. (1995), who modified the model to be more adaptive to clinical measurements, i.e., pulse wave velocity, pressure and area. This model has been applied in 1D-BFMs (Reymond et al., 2009, 2011; Vardoulis et al., 2013).

Several methods have been proposed in the literature to adapt wall models in 1D-BFM to a (patient) specific condition, and such methods can be grouped as follows: (i) a fitting procedure (i.e., estimation of model parameter) to a set of available measurements (Leguy et al., 2010; Willemet et al., 2013) and (ii) the calibration of wall models to patient-specific measurements at single locations in the network (Eck et al., 2015b; Reymond et al., 2009, 2011; Matthys et al., 2007; Sherwin et al., 2003). Because measurements in clinical settings are costly, time intensive, and burdensome to the patient, we focused on the calibration of the wall models from a limited amount of non-invasively measurable data.

2. Methodology

2.1. One-dimensional wave propagation model

We applied the model framework presented by Eck et al. (2015b) for UQ and SA in a 1D-BFM, which has been validated against other BFMs (1D and 3D) and experiments (Boileau et al., 2015).

2.2. Wall models

The elastic wall models applied in 1D-BFM are simplified algebraic relationships $A(P)$ (Eck et al., 2015b; Boileau et al., 2015), relating arterial lumen area A and the transmural pressure P. The derivative of $A(P)$ with respect to P provides an equation for the arterial compliance $C(P)$:

$$C(P) = \frac{dA}{dP}. \tag{1}$$

According the fluid dynamics equations for one-dimensional arteries, the wave speed in an arterial segment is:

$$c(P) = \sqrt{\frac{A(P)}{\rho C(P)}}, \tag{2}$$

with blood density $\rho = 1050\ \mathrm{kg\ m^{-3}}$.

2.2.1. Quadratic model

The *quadratic* area–pressure relationship (Sherwin et al., 2003) is defined as:

$$A(P) = \left((P - P_s)\frac{A_s}{\lambda} + \sqrt{A_s}\right)^2, \tag{3}$$

where λ is referred to as the stiffness coefficient and A_s is the area at the reference pressure P_s. The compliance function derived from Eqs. (1) and (3) is:

$$C(P) = \frac{2A_s}{\lambda}\left((P - Ps)\frac{A_s}{\lambda} + \sqrt{A_s}\right). \tag{4}$$

2.2.2. Logarithmic model

The *logarithmic* area–pressure relationship (Hayashi et al., 1980) is defined as:

$$A(P) = A_s\left(1 + \frac{1}{\beta}\ln\left(\frac{P}{P_s}\right)\right)^2, \tag{5}$$

where β is called the stiffness coefficient and A_s is the area at the reference pressure P_s. The compliance function derived from Eqs. (1) and (3) is:

$$C(P) = \frac{2A_s}{\beta P}\left(1 + \frac{1}{\beta}\ln\left(\frac{P}{P_s}\right)\right). \tag{6}$$

2.2.3. Arctan model

The *arctan* model was first applied in a 1D-BFM by Reymond et al. (2009) as a compliance equation:

$$C(P) = C_s\left(a + \frac{b}{1 + \left(\frac{P - P_m}{P_w}\right)}\right), \tag{7}$$

where C_s is the reference compliance at the reference pressure P_s. Furthermore, P_m and P_w are shape parameters of the original model by Langewouters et al. (1985), and a and b are scaling coefficients introduced by Stergiopulos et al. (1995). Integration of Eq. (7) leads to the following area–pressure relationship:

$$A(P) = A_1 + aPC_s + bP_wC_s\arctan\left(\frac{P - P_m}{P_w}\right), \tag{8}$$

with $A_1 = A_s - aP_sC_s + bP_wC_s\arctan\left(\frac{P_s - P_m}{P_w}\right)$ and A_s is the area at P_s.

2.3. Calibration to measurements

Calibration of wall models and the network from a limited set of data is essential when simulating patient-specific hemodynamics. Thus, we focused on the calibration of these models from three measurements in an individual: $\{A^M, P^M, c^M\}$, where c^M is the carotid–femoral wave speed, A^M is the time-averaged area, and P^M is the mean pressure at the brachial artery.

To calibrate a wall model to a given $\{A^M, P^M, c^M\}$, we first simply set $A_s = A^M$ and $P_s = P^M$. Then, the wall model coefficients (λ, β, C_s) can be estimated from c^M by inserting the area and compliance equations of each model into Eq. (2). Equations can be found in Sherwin et al. (2003) for λ (*quadratic* model), in Eck et al. (2015b) for β (*logarithmic* model) and in Reymond et al. (2009) for C_s (*arctan* model).

Calibration of a generic network to a given $\{A^M, P^M, c^M\}$ combines both the calibration of wall models and the suggestions of Vardoulis et al. (2013) and Reymond et al. (2011). The first step in the procedure is to set the reference area and pressure at the measurement site, letting $A^S_m = A^M$ and $P^S_m = P^M$. Next, the A_s and P_s of the remaining arteries i are adjusted to maintain their initial ratios to the measurement point as in the generic network (marked with ^{G}), i.e.,

$$A^S_i = \frac{A^S_m}{A^G_m}A^G_i, \quad P^S_{si} = \frac{P^S_m}{P^G_m}P^G_i.$$

Finally, the carotid–femoral wave speed of the now specific network is calibrated to c^M by scaling the wall model coefficients (λ, β, C_s) with a common factor.

2.4. Stochastic modeling

To quantify model uncertainty and analyze its sensitivity to particular input parameters, we followed the guidelines proposed by Eck et al. (2015a). The non-intrusive polynomial chaos method