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A SEQUENTIAL FILTERING-BASED FRAMEWORK FOR PATIENT-SPECIFIC PARAMETER ESTIMATION AND SUBSEQUENT MULTISCALE CFD SIMULATIONS

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Significant advances in computational modelling of biological flows over the past decades have resulted in sophisticated numerical models to represent human circulation and predict its behaviour. Such models typically include multiscale modelling where the region of interest is represented by complex 3D model/geometry, developed with the aid of medical images, while the rest of the circulation is represented by appropriate lower-order boundary conditions such as lumped parameter models. Assuming one has an accurate representation of the patient geometry around the area of interest, one must also specify personalised boundary conditions to analyse and predict patient-state. It is natural that such boundary conditions be estimated by using some set of clinical measurements, typically pressure and flow at several locations, in the patient. There are three questions associated with the process of such an estimation procedure: first, can one *a priori* determine the set of measurements which are sufficient to estimate the parameters; second, how can one efficiently estimate the parameters and the associated confidences from the measured data; and third, what can one do if some of the measurements needed to identify the parameters are not available or cannot be physically measured. Here, some computational tools and ideas towards answering these three questions are presented.

The three questions posed above are discussed in the context of multiscale CFD simulations in the human cardiovascular system. The flow in the 3D domain is modelled by incompressible Navier-Stokes equations and the boundary conditions are represented by a three-element Windkessel model at each outlet. The use of a reduced order model, which abstracts the 3D domain into a lumped parameter model, is advocated to explore the three aforementioned questions owing to its computational simplicity. In order to identify the set of measurements that are sufficient for parameter estimation, i.e. to identify what to measure and where to measure, the use of generalised sensitivity functions [1] is proposed. These functions are also used to study the effect of measurements on the estimates of parameters, to study the correlation between the parameters, and to identify regions in time where the measurements make most contribution towards each parameter estimate. The results of the last analysis can help identify where, in time, more measurements should be taken to improve parameter estimates. For the second question of efficiently estimating the parameters from the noisy measurements, the use of a sequential filtering-based method, namely the unscented Kalman filter (UKF) [2, 3], is presented. Such an approach is computationally efficient, and takes into account both the uncertainty in initial conditions of the dynamical system and uncertainties in the measurements. Since parameter estimation is performed on a reduced order model, the parameter estimates are only as good as the reduced order model. To alleviate this difficulty an iterative algorithm that utilises the results of a few full 3D simulations and iteratively improves the reduced order model, and hence the parameter estimates, is presented. The efficacy of such a method is shown when applied to a real case of a patient-specific coarctation. The results of this case-study are presented to show less than 3% and 10% discrepancy between the 3D simulations and clinically measured quantities in two physiological states of rest and exercise, respectively. The predictive capabilities of such an approach are also demonstrated.

The last question of addressing the question of 'missing data', the case where only a part of the measurements required for parameter estimation are available, is difficult to address. To this cause two approaches are discussed: first, to complement the measurement set with modelling assumptions, such as flow-splits taken from literature or clinically expected measurements of mean/min/max pressures; and second, to adopt a Bayesian framework where the underlying philosophy is to construct a prior based on the general knowledge of the cardiovascular system and use the posterior (prior conditioned on the set of data that was measured) in lieu of missing measurements. While the former approach is easy to implement, it requires clinical expertise and might be restrictive on the solution. The latter approach, although more general, requires careful construction of extensive priors which requires availability of data-sets for a statistically significant population of patients.

To summarise, a computational framework for parameter estimation and subsequent CFD simulations in the human cardiovascular system is presented and discussed. Computational tools that can be used under such a framework are also presented.

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