A lumped parameter delay differential equation model of large arteries that captures reflection phenomena and integrates with modular models of the cardiovascular system.

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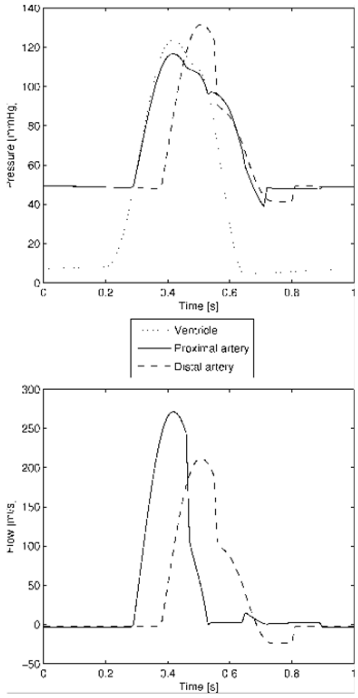
Introduction. Mathematical models of physiology in general, and the cardiovascular system in particular, in combination with modern inference methodology, may enable a quantitative interpretation of monitoring data acquired in acute care settings[1]. In this context, lumped parameter models play an important role since they preserve direct physiological interpretability while at the same time minimizing the number of unknown parameters and states. Thus, they help to improve the conditioning of the inverse problem of state and parameter estimation that possibly presents the largest obstacle to practical bedside implementation of such approaches. Any model-based data interpretation approach is naturally restricted to accessing the information content in observed phenomena that the underlying mechanistic model can capture. An area where mechanistic models suitable for integration into a modular lumped parameter representation of the cardiovascular system are scarce is that of reflection phenomena within the arterial circulation, although these are important in generating the observed morphology of arterial pressure and flow curves. This is particularly important for peripheral measurement locations such as the radial artery, which are common in clinical practice. One class of previously described models uses partial differential equation formulations, which allow great flexibility and physical realism, at the expense of increased computational expense and parameter and state space dimensionality, with corresponding adverse effects on inverse problem conditioning. Others make, for the purposes of ab initio simulation, overly simplifying assumptions such as impedance matching at artery termination points and thus require realistic pressure or flow waveforms as input rather than being able to generate them (e.g., [2]). Finally, frequency domain formulations (e.g., [3]), while computationally advantageous, do not lend themselves to convenient interfacing with modular time domain models. Here, we present a time-domain mathematical model of the large arteries which is capable of ab initio simulation of arterial pressure and flow waveforms with realistic morphology using a minimal number of state variables and parameters. We then interface it to a simple model of the cardiovascular system to demonstrate its suitability for the applications described above. **Methods.** Initially following[2], we start from the d'Alembert form of the general solution of the Telegrapher's Equation. This decomposes the general solution of this one-dimensional partial differential equation describing a lossless transmission line used to represent a large artery as an elastic tube additively into forward and backwards propagating waves. We then impose boundary conditions representing influx and outflux against Ohmic resistances under general time varying input and output pressures. The resulting equations can equivalently be expressed in a form that further decomposes the current forward and backward propagating waves



additively into a function of known current and past state variables and parameters of the overall model and past values of the forward and backward propagating waves themselves. For comparable input resistance, output resistance, and characteristic impedance of the artery, it can be seen that the contribution of the latter term is small. Using this formulation, recursive substitution into this set of equations is therefore capable of generating time domain formulations of this model that come arbitrarily close to the true solution of the full partial differential equation and can be expressed as a system of delay differential equations. As proof of concept, we integrate an implementation of this model resulting from one iterative substitution with a simple monoventricular time-varying elastance model of the heart attached to an "aortic" (arterial side) valve and a "tricuspid" venous side valve implemented as pressure difference dependent resistances and linearly compliant representations of the distal arterial and venous components of the circulation. The model was implemented in MATLAB™ using the *dde23* delay differential equation solver. Numerical stability at non-smooth points where the pressure difference across the valves changes sign (i.e., the opening and closing times) is achieved using the *dde23* event detection mechanism, which is used to identify these points and restart integration appropriately. **Results.** Model behaviour proved to be numerically robust. The model quickly settles into quasi-steady state behaviour from reasonable but non-steady- state initial conditions and is capable of producing waveforms with many key morphological properties of real arterial pressure and flow waveforms. In spite of the low dimensional parametrization (essentially two parameters for the arterial tube + approx. a dozen to completely parametrize the entire cardiovascular system model for arbitrary heart rates, valvular resistances etc.), dependence of waveform morphology on the simulated location of measurement within the artery was captured in a physiologically plausible way (figure shows one cardiac cycle after initial equilibration). **Discussion.** The presented model is capable of capturing key morphological properties of the arterial pressure and flow waveforms utilizing a small number of parameters and states that retain direct physiological interpretability. Through its generic formulation which, at the interfaces, allows for arbitrary time varying pressures, it can seamlessly be integrated into modular lumped parameter models of the cardiovascular system, as illustrated by the simple example above. In addition to direct utilization in the application areas outlined above, future extensions will include systematic exploration of the possible benefits of utilizing higher order iterative substitutions and adaptation to more realistic physical representations of the arterial system, including branched vessel arrangements.

References

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