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Original Research Article

Lumped models of the cardiovascular system of various complexity

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ABSTRACT

Purpose: The main objective is to accelerate the mathematical modeling of complex systems and offer the researchers an accessible and standardized platform for model sharing and reusing.

Methods: We describe a methodology for creating mathematical lumped models, decomposing a system into basic components represented by elementary physical laws and relationships expressed as equations. Our approach is based on Modelica, an object-oriented, equation-based, visual, non-proprietary modeling language, together with Physiolibrary, an open-source library for the domain of physiology.

Results: We demonstrate this methodology on an open implementation of a range of simple to complex cardiovascular models, with great complexity variance (simulation time from several seconds to hours). The parts of different complexity could be combined together.

Conclusions: Thanks to the equation-based nature of Modelica, a hierarchy of subsystems can be built with an appropriate connecting component. Such a structural model follows the concept of the system rather than the computational order. Such a model representation retains structural knowledge, which is important for e.g., model maintainability and reusability of the components and multidisciplinary cooperation with domain experts not familiar with modeling methods.

1. Introduction

Our motivation for lumped-parameter mathematical modeling in physiology includes teaching, studying and explaining clinical situations, developing educational simulators, demonstrating significant physiological regulations and pathological phenomena, as well as analysis of control loops, design of control strategies and model identification. To fulfill these needs, we require a robust simulation tool.

The first prerequisite to compare and integrate models is to have one tool or environment in which all the models may run

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together. Secondly, the tool and the methodology must allow flexible extensions of the models and a possibility to effectively refactor them. Often the description of models in literature contains mistakes (as reported in [1]) and even when the source code is provided, a reimplementation is usually required to integrate the model, due to language or methodological incompatibilities. In addition, the resulting model should be understoodable also for domain experts, who are not familiar with the exact modeling methodology, which is becoming hard to achieve, as the models grow in complexity [2].

The nestor of integrative physiological modeling, A.C. Guyton, introduced large schematics of overall regulation of blood pressure in his prominent article [3], an iconic demonstration of the complex nature of bodily regulations. The model itself was implemented originally in procedural Fortran language, later, with the advent of advanced block-oriented languages, re-implemented in Simulink [4] to reflect the same visuals. Similar to Simulink, a number of other block-oriented approaches exists, namely AmeSim, Scicos, LabView, or VisSim. However, the complexity of the model increased during the transition from Guyton's original model to more complex HumMod's [5], implemented in custom XML format. The model becomes too complex to re-implement and maintain it using block-oriented tools.

The family of XML based modeling mark-up languages, such as SBML [6] or CellML [7] have a lot of attention in biomedical modeling community, but we find them too demanding to maintain large models with. Some other equation-based tools were employed in the field of biomedical engineering, namely JSim [8] or Berkeley-Madonna [9], but as they are not object-oriented, the reuse, maintenance and integration of other models is complicated.

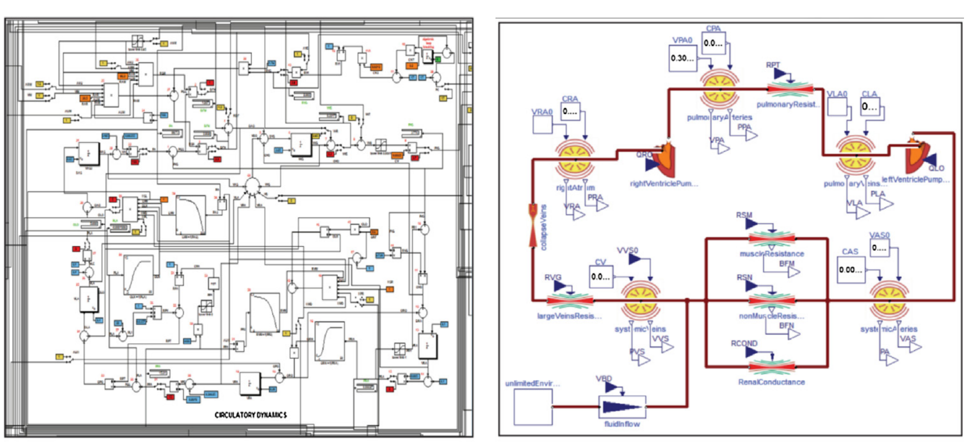
The object-oriented approach of Modelica for complex models has been suggested already by Cellier and Nebot [2]. Brunberg introduced the HumanLib, first Modelica library for cardiovascular modeling [10]. de Canete [11] reported, that the Modelica approach significantly reduced the modeling effort and facilitated the model reuse. Other benefits of equation-based, object-oriented implementation of the pulsatile cardiovascular system over a block-oriented approach are described in detail in [12]. Therefore, an alternative implementation of the HumMod model was introduced in the object-oriented acausal Modelica language as Physiomodel [13]. Fig. 1 illustrates, that the model structure in block-based modeling language (here Simulink) corresponds rather with a computational algorithm, while the model structure in Modelica is more similar to the modeled reality itself.

Although the usage of object oriented modeling, which could offer great universality, has already been embraced in the field, a comprehensive open-source modeling workbench is still missing. The goal of this paper is to offer a standardization in the field of physiological modeling by offering a modern methodology together with a free workbench for cardiovascular modeling. The methodology should be easy to use and understandable also for domain experts not familiar with the particular modeling tool. It should offer simple composability of modules and provide robust extensibility. It should be possible to combine the submodels as required by the planned usage (as envisioned in [14]). Moreover, the platform should be open to non-commercial tools.

2. Materials and methods

Based on our experience in developing and integrating compound models, we think that the following features are the most important for building comprehensible complex models of human physiology with an integrative approach:

1. Equation-based modeling – the relations among variables of a physical system are expressed declaratively in a model using general algebraic or differential-algebraic equations. The causality (i.e. the solution) of the model of a physical system is left to a modeling tool, which figures out the dependent and independent variables during model compilation. In an equation-based model, a minor structural



A) B)

Fig. 1 – The implementation of the core part of Guyton's model: (A) Circulatory dynamics – the detailed structure of the central part of the Guyton's model implemented in Simulink, preserving the original Guyton's schematics, (B) The same part of the model implemented in Modelica using concepts of physical equation-based modeling. This implementation contains connected instances of two pumps (of the right and left heart ventricles), elastic vascular compartments and resistances.