Towards personalised dynamic models of the cardiovascular system

Karolina Tlałka[1,2], Ian Halliday[2], Andrew Narracott[2], Maciej Malawski[1,3]

[1]Sano Centre for Computational Medicine, Czarnowiejska 36, 30-054 Kraków, Poland
[2]Division of Clinical Medicine, The University of Sheffield, Western Bank, S10 2TN, Sheffield, United Kingdom
[3]Faculty of Computer Science, AGH University of Kraków, Al. Mickiewicza 30, 30-059, Kraków Poland
{k.tlalka,m.malawski}@sanoscience.org, {ketlalka1, i.halliday, a.j.narracott}@sheffield.ac.uk

1. Introduction

Personalisable physics-driven modelling is a powerful tool to support clinical decisions and medical research [1]. There are some basic requirements, which must be met by models to promote clinical utility: (i) ability to represent physiological processes, (ii) simplicity, which decreases computational costs of model quantification and personalization, (iii) explainability, which is crucial to foster clinical trust in the model. In this work, we present our approach to personalization of reduced-order cardiovascular (CV) models with neuro-regulation.

2. The problem

Currently, most CV models are assumed to have constant input parameter values. However, homeostasis is constantly challenged by external factors, such as orthostatic stress [2]. In a healthy subject, regulation mechanisms, such as baroreflex (neural control of the CV system), constantly modify the physiological state in response to those changes [3]. In patients with baroreflex impairment, symptoms such as dizziness and fainting can occur during their exposure to the orthostatic stress [4]. Incorporating "active" baroreflex control into a "passive" CV system model allows one to analyse conditions connected with baroreflex failure [2]. This leads to a more accurate model, but also increases the computation time, and introduces new parameters which are notoriously difficult to measure, what makes personalization harder [2].

3. Background

The zero-dimensional approach is widely used for modelling the entire CV system [5-7]. Baroreflex models are inspired by physiological mechanism of modifying the properties of CV system by neural control [3,5,7]. They are described within control theory, providing regulation of arterial pressure by negative a feedback mechanism. The control problem is usually analysed at a local scale [3], which is a computationally efficient solution, but it may not be accurate, because of the nonlinearity of the model, introduced by e.g. cardiac function [1,2]. Computational expense arising from the need for a global analysis and the number of parameters forces one to focus on model reduction i.e. parsimony of CV models, parameter subset selections and model quantification [2] as an essential prelude to any attempt at personalization.

4. Solution to the problem

In this research we are focused on the whole process of model development. We gradually increase the structural complexity of the CV model, to find the solution which is physiologically

adequate *and* easy to personalize. We quantify the global sensitivity (see [1]) and orthogonality of candidates, to improve understanding of physiological processes connected with orthostatic response and analyze interactions between parameters and identify the most influential [2]. We use this knowledge to inform personalization process and achieve patient-specific models of human response to orthostatic challenge [2]. We have developed two CV models of graded complexity and performed local and global sensitivity analysis, to determine which input parameters influence pressures in the system and cardiac output [1] in the absence of any disturbance. We observed significant differences between global and local sensitivity patterns, for a model with a systemic and pulmonary circulation [1], which suggests the importance of higher order interactions between parameters and a need for global methods in characterizing the problem. Currently we are working on the personalization of CV models with a four-chamber heart, in the response to induced central hypovolemia [2]. We utilize global sensitivity analysis and optimization to fit our model response to the experimental data [2] such as [8]. Throughout, we use the Julia programming language, leveraging its extensive libraries, which allow one efficiently to solve our differential equation problem formulation and the associated global optimization problems. We utilize High Performance Computing, to perform parallelized global sensitivity analyses, screening of the search space, and optimization [2].

5. Conclusions and future work

Personalisation of dynamic CV models is a very challenging task, because of high uncertainty in input parameters, nonlinearity and computational expense. In this research, we address the balance between simplicity and physiological relevance. We will seek for a principled, versatile and portable (ideally universal) method for calibration of CV models to different orthostatic challenges. This will allow us quickly to conduct *in silico* studies of various experimental settings and move our models one step closer to the clinic.

References

1. Tlałka K et al. (2024), Sensitivity analysis of closed-loop one-chamber and four-chamber models with baroreflex. PLOS Computational Biology 20(12): e1012377.
2. Tlałka K et al. (2025), Personalisation of a fully closed-loop lumped-parameter cardiovascular model with baroreflex in response to orthostatic stress. Article in preparation.
3. Olufsen MS et al. (2006), Modeling baroreflex regulation of heart rate during orthostatic stress. American Journal of Physiology – Regulatory, Integrative and Comparative Physiology 291:5, R1355-R1368.
4. James MA, Potter JF (1999), Orthostatic blood pressure changes and arterial baroreflex sensitivity in elderly subjects. Age and Ageing, Vol. 28, Issue 6, 522-530.
5. Ursino M (1998), Interaction between carotid baroregulation and the pulsating heart: a mathematical model. American Journal of Physiology – Heart and Circulatory Physiology 275:5, H1733-H1747.
6. Shi Y et al. (2011), Review of zero-D and 1-D models of blood flow in the cardiovascular system. Biomedical engineering online, 10, 33.
7. Heldt T (2004), Computational models of cardiovascular response to orthostatic stress, Doctoral Thesis, Harvard University – MIT Division of Health Sciences and Technology.
8. Hoiseth et al. (2015), Tissue oxygen saturation and finger perfusion index in central hypovolemia: influence of pain. Critical care medicine, 43(4), 747-756.