

MULTISCALE MODELING OF VASCULAR ADAPTATION PROCESSES: ACHIEVEMENTS AND FUTURE PERSPECTIVES

Claudio Chiastra

PoliTo^{BIO}Med Lab, Department of Mechanical and Aerospace Engineering, Politecnico di Torino, Turin, Italy

Background

Vascular adaptation is the ability of blood vessels to adapt throughout life depending on genetic programming and biochemical processes in response to multiple stimuli, including mechanical and hemodynamic forces [1]. Major cardiovascular diseases, such as atherosclerosis, are characterized by vascular adaptation processes. These processes are governed by multifactorial and multiscale networks of events involving feedback mechanisms, cause-effect relationships and mutual interactions of components across different spatial (i.e., from molecules to cells and tissues/organs) and time (i.e., from seconds to days and years) scales [2]. In the last decades, researchers have applied a wide variety of approaches to investigate adaptation events, conducting extensive *in vitro*, *in vivo* and *in silico* research. In this context, multiscale computational models inspired by systems biology principles are emerging as powerful tools to bridge *in vitro* models of single-scale phenomena to *in vivo* models of the whole system of interest.

Recent Advances

Both continuum and discrete modelling strategies are options for the investigation of vascular adaptation [2]. Recently, our research group has developed a multiscale agent-based modelling framework, integrating both continuum and discrete approaches, which is able to include components across different spatio-temporal scales and capture the dynamic interplay of the events characterizing vascular adaptation (Fig. 1). The framework is composed by three different modules simulating (i) hemodynamics and/or solid mechanics with a continuum approach, (ii) arterial wall remodeling in response to hemodynamic, mechanical, inflammatory stimuli through an agent-based model (ABM) of cellular dynamics and (iii) monocyte gene expression, providing an inflammatory stimulus to the ABM. The framework has been applied to study atherosclerosis [3], restenosis after balloon angioplasty [4] and in-stent restenosis [5]. While in [3,4] idealized models were built, in [5] a patient-specific model of stented superficial femoral artery, which integrates the effects of hemodynamics and monocyte gene expression on cellular dynamics, was developed. After proper calibration, the latter model was able to describe the 1-month arterial wall remodeling following stent deployment.

Future directions

Despite the multiscale agent-based modelling frameworks presented herein are promising tools for the study of vascular adaptation, major challenges regards

Claudio Chiastra is Associate Professor of Industrial Bioengineering at Politecnico di Torino (Italy). In 2014, he obtained his PhD in Bioengineering at Politecnico di Milano (Italy). In 2014-2016, he was Post-Doc researcher at Erasmus MC (Netherlands) and Politecnico di Milano in a joint collaboration between the two institutions. Following a period as Assistant Professor at Politecnico di Milano, in 2019-2021 he served as tenure-track Assistant Professor at Politecnico di Torino. His present research mainly focuses on cardiovascular biomechanics. He is author of 73 publications in peer-reviewed journals, 5 book chapters and 160 contributions to International and National Conferences. He serves as Associate Editor for Scientific Reports and Frontiers in Cardiovascular Medicine.

(i) the reduction of the computational costs, (ii) the process of model verification, calibration and validation against large patient-specific data sets, (iii) the inclusion of multi-omics data, defining patients' molecular signature at the local level. Future research efforts are expected to address these challenges, thus advancing the multiscale computational solutions for a better understanding of the vascular diseases, and management of diagnosis, prognosis and treatment.

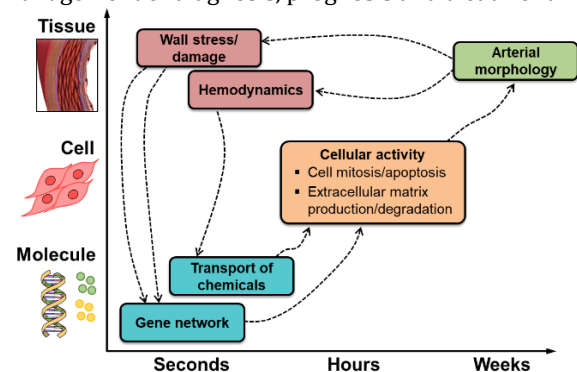


Figure 1: General representation of our multiscale framework of vascular adaptation.

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