MODELLING VASCULAR TONE REGULATION: AN INTEGRATIVE APPROACH FROM MOLECULAR TO SYSTEMIC LEVEL

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Introduction

The physiological behaviour of the cardiovascular system is highly affected by the mechanical response of arterial segments, that is in turn dependent from both tissue histological architecture and the contractile tone of smooth muscle cells. The former depends mainly on the different amount and arrangement of constituents (mainly, elastin and collagen fibers), while the latter on chemical drivers of vasoactivity, such as nitric oxide (NO) and reactive oxygen species (e.g., ROS and PN). Moreover, arterial segments undergo a continuous remodelling, that is changes in their structure (e.g., thickening, stiffening, or narrowing). Remodelling is driven by biochemical pathways (involving growth factors – GFs – and enzymes such as matrix metalloproteinases – MMPs) that are activated when the mechanical state (i.e., stresses and/or strains) is non-homeostatic, [1,2]. When remodelling is dysfunctional, pathologies, like chronic hypertension, develop.

It is also noteworthy that the problem is highly multiscale since global hemodynamic conditions (e.g., heart rates, resistance of downstream vasculature) highly affect local flow conditions, and hence the local pressure field and the internal stresses affecting biochemical pathways and remodelling. Detailed high dimensional models (2D or 3D) can generally be used to simulate local hemodynamics of specific arterial sites, while the whole arterial tree is generally described through low dimensional descriptions (i.e., lumped 1D approaches).

Methods

This work presents a comprehensive multi-scale and multi-field computational framework that accounts for: i) a lumped 1D description of the macroscale arterial tree; ii) a continuum 3D model at the microscale of the local chemo-mechano-biological response of arterial tissues (accounting for passive and active tissue behavior); iii) biochemical-dependent vasoconstriction and vasodilation (the NO-ROS-PN biochemical chain), and biochemical-dependent tissue remodeling (the GFs-MMPs biochemical chain). Simulations from 3D chemo-mechano-biological models drive how parameters of the lumped description vary as function of segment dilation, as well as tissue histology and vasoconstriction. An illustrative representation of the proposed methodology is reported in Fig. 1a.

Results

The applicative case study investigates the relationship between arterial vasodilation and vasoconstriction with physical exercise. Figure 1b shows the short-term response of the arterial system during and after 1 hour exercise. The model predicts a release of vasodilatators (NO), a decrease of vasoconstrictors (ROS), and a hemodynamic response leading to the maintenance of quasi-homeostatic shear stresses on endothelial cells in the intima.

The obtained numerical results are consistent with available experimental data for normal and spontaneously hypertensive phenomena.
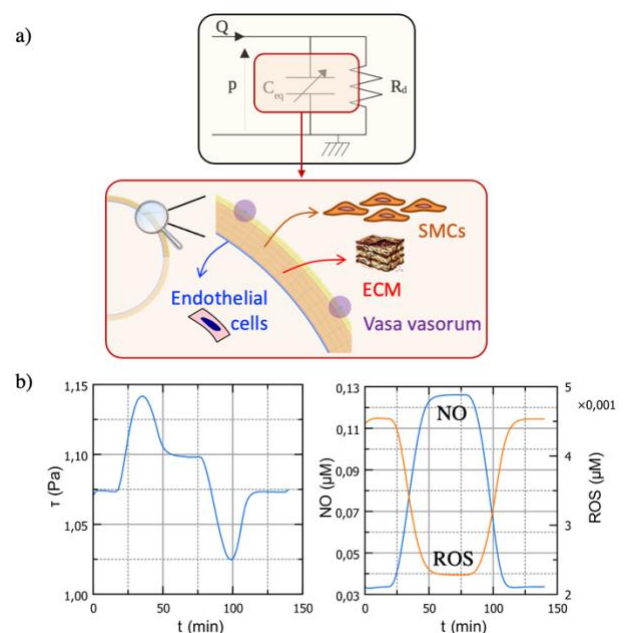

Figure 1: (a) Multi-scale and chemo-mechano-biology rationale. (b) Arterial short-term active response predicted by the model: vasodilation during 1h exercise.

Conclusions and Future studies

On-going studies are addressing the coupling of the framework with growth and remodeling mechanisms [3], and the reproduction of animal studies [4].

References

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