COMPUTATIONAL MECHANICS OF AN ADAPTATION MODEL FOR BLOOD VESSELS

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Summary Based on the changes of wall shear and circumferential stress experimented by the endothelial cells and smooth muscle cells respectively, a huge cascade of biological processes begin. In this work, we present a mechanical and computational model for the contraction of the smooth muscle cells and the characteristic collagen fibers turnover, which lead to stiffer vessels, due to a rise up of the blood pressure. All these processes have been modeled computationally in a finite element framework.

INTRODUCTION

The theoretical formulation of mechanical models for biological tissue is an important and enterprising challenge due to its complex and active response. The physiological adaptation of soft tissues, such as the cardiovascular system is one of the most studied fields in biomechanics. In this contribution we present a mechanical model of blood vessel to account for its microstructural evolution due to changes in its mechanical environment.

One of the most important situations of enviromental changes is hypertensive disease, characterized by an increase of the mean blood pressure and changes in wall shear stresses (WSS). Changes in the WSS are transmitted by the endothelial cells by releasing different substances into the vessel wall, which lead, e.g., to the active contraction of the smooth muscle cells (SMC) and the turnover of collagen fiber bundles. Changes in the circumferential stresses is mainly felt by the smooth muscle cells, which lead to similar releasing of substances. Some of the most important substances in these processes are: TGF $-\beta$, a growth factor involved in changes of SMC and in the turnover of collagen fibers, inhibitors of metalloproteinases TIMPs and metalloproteinase (MMPs) which are in charge of the degradation of the collagen fibers.

In this contribution, we present a mechanical model for these evolution phenomena. We present a mathematical and numerical model for the smooth muscle cell contraction and for the subsequent density growth of collagen fibers. We based these two processes on the evolution of the substances release due to the mechanosensing and mechanotransduction of the vessel wall.

We compute the non-liner equations that describe density growth in a finite element framework (see e.g. [1]). The active contraction of the smooth muscle cell is accomplished by means of a kinematic decomposition, which is also included in the finite element model. The passive mechanical characterization of the tissue is described by the classical quasi-incompressible hyperelastic formulation [2]. The main components of the vessel, elastin, SMC, and collagen are taken into account. The mechanical behavior of collagen is modeled by means of a micro-sphere based approach and where every fibril follows a worm-like chain model [3].

MODEL AND NUMERICS

The behavior of our blood vessel wall model can be separated in a passive and active part. The passive behavior is given by a quasi-incompressible model (see [2]), where the water content is characterized by the volumetric part while the isochoric part is given by the addition of elastin, collagen and smooth muscle cells. Elastin is modeled as a Neo-Hookean material, SMC are by a anisotropic 1D fibers-like model while the collagen is taken into account by a homogenizing microsphere model, where the probabilistic distribution of the fibers is considered by a Bingham statistical distribution, as

$$\Psi_{\text{col}} = \frac{1}{4\pi}\int_{\mathbb{U}^2} \hat{\rho}\psi(\bar{\lambda})\text{dA} \approx \sum_{i=1}^{id} \hat{\rho}_i w^i \psi(\overline{\lambda}_i), \tag{1}$$

where $\hat{\rho}$ is the Bingham orientation distribution function as given in [3], $\mathbb{U}^2$ is the unit sphere, $\overline{\lambda}_i$ and ψ are the isochoric stretch in the direction of the integration direction and its strain energy function respectively. Moreover, we perform a fluid dynamic simulation in order to obtain the pressure and WSS in the vessel wall and feed the model with these trigger variables. Fig 1 shows the real geometry used in our computation as well as the sketch of the information token into account in the wall. In order to provide to the model with realistic loads we perform a fluid-structure interaction simulation where pressure and WSS are computed over the internal face of the vessel wall.

The active behavior of the wall, this is the adaptation of the collagen bundles to changes in the mechanical environment, is treated by means of a a density growth model. These changes in the density of the collagen fibers are triggered by

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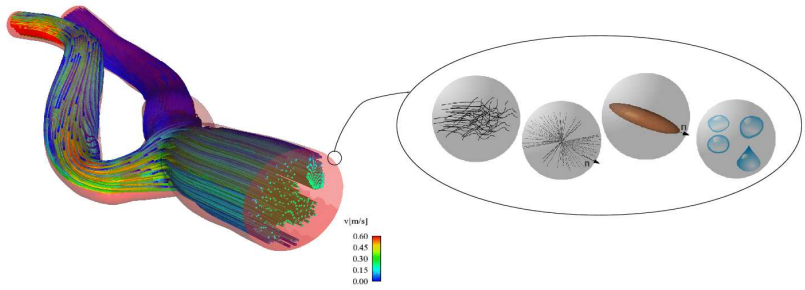


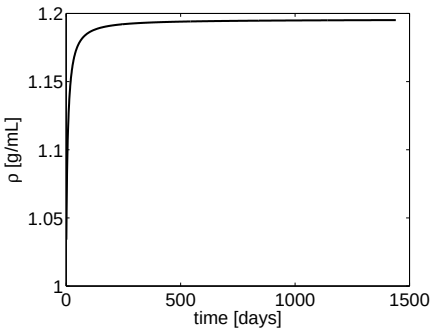
Figure 1. Patient specific geometry of a human carotid and sketch of the constituents included in the model.

different substances released by the SMC and EC cells. For the density growth, we measure the release of MMP-1, TIMP and TGF-β, which are considered the most important ones and compute its density variations as given in the following equations

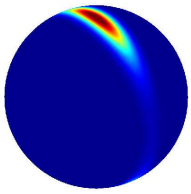
$$\dot{\rho} = \mathcal{R} \qquad \text{with} \qquad \mathcal{R} = \left[\frac{\rho}{\rho^*}\right]^{-m} \Psi(\mathbf{C}) - \Psi^*, \tag{2}$$

where $\mathcal{R}$ the source term, ρ^* is the initial density and Ψ^* a saturation value. This evolution in density can be computed implicitly by means of a Newton-Raphson scheme. The changes in these substances will set the underlying turnover of the collagen fibers.

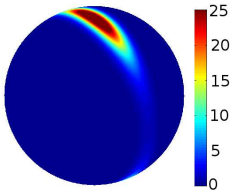
In this way, and as an example, we present Fig. 2 where the evolution of collagen due to the increase of TGF-β and the decrease of MMP is obtained. We observe an overall increase of around 20% of the initial density in a total period of time of 4 years of hypertensive disease. In Fig. 2 (b) and (c) we show the change in the statistical distribution of the collagen bundle.



(a) Evolution of the collagen density in response to both increase in TGF-β and decrease in MMP



(b) Initital Bingham distribution at t=0



(c) Final Bingham distribution at t=5000

Figure 2. Evolution of the collagen content in hypertensive patients driven by an increase in TGF-β and a decrease in MMP.

CONCLUSIONS

In the present contribution we have developed a mechanical model to study computationally the evolution of the smooth muscle cell contraction and the subsequent collagen variations of the turnover rate which lead to changes on the stiffness of the vessel wall. We develop such a model by considering the variation of the mechanical environment of the blood vessel which we study by means of a fluid structure interaction simulation for homeostatic and hypertensive values.

References

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