MECHANICAL RESPONSE OF ENDOTHELIAL CELLS TO SHEAR FLOW AS POSSIBLE MARKER IN DEVELOPMENT OF ATHEROSCLEROSIS

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Introduction

Arterial endothelium lies right at the interface between blood flow and the aortic wall and its disruption has been hypothesized as one of the crucial players in atherosclerosis development and progression. To address the physiological conditions of arterial endothelium we conducted a study of endothelial cell behaviour under shear stress. By interconnecting tailored experiments of cells under shear flow with computational modelling, we gained further insights into the behaviour of individual cells under shear stress. The main aim of the study was to evaluate the viability and extend the capabilities of previously-developed FEM structural models of cells [1,2]. We hypothesize that excessive deformation may lead up to a disruption of the cell attachment to the underlying substrate and thus play a major role in lipid penetration through the endothelium.

Methods

Individual HUVEC cells (endothelial cells from an umbilical vein) were deformed using a microfluidic system Fluigent Flow EZ by a sequence of flow pulses, and phase images had been recorded (Fig. 1a) together with the flow measurement. The deformation has been evaluated by two image-processing methods: Centre of Mass (COM) shift [3] based on thresholding and more sophisticated Image Registration (IR) [4].
FEM calculations comprise several steps and utilize both structural and FSI analyses. Structural modelling includes determining the effective shear modulus of the complex cellular body (comprising of cytoskeleton, nucleus, membrane and cytoplasm, see Fig. 2a). FSI of the cell deformations under the previously measured flow serves as a bridge between experiments and structural modelling.

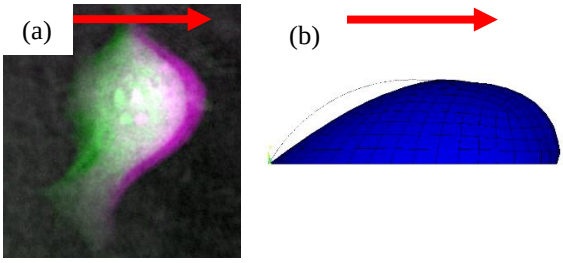

Figure 1. Cellular deformation due to shear flow in the direction indicated by a red arrow. (a) phase images of undeformed (green) and deformed (magenta) cell body and (b) non-structural Finite Element model under similar loading conditions.

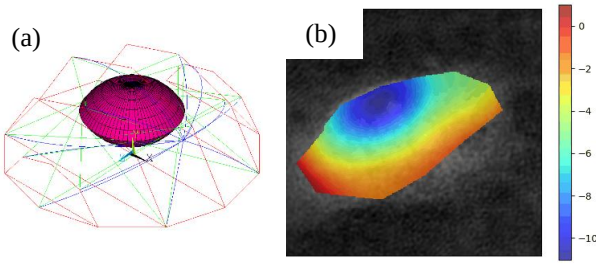

Figure 2: (a) Inner structure of the hybrid FEM model [2]. Actin bundles (red), intermediate filaments (green), microtubules (blue) and nucleus (magenta), here shown without cytoplasm and membrane. (b) Deformation field using Image Registration at the top of the first cycle.

Results

The deformation of the cell in the experimentally-computational setup has been assessed while exploring the capabilities of image processing for the shear environment (Fig. 2b). Transitioning between the mechanical behaviour of the cell under physiological loading conditions into computational modelling (Fig. 1b) helps to validate the hybrid computational model. The time dependence of cell deformation in Fig. 3 shows viscoelastic behaviour, that needs to be incorporated for reflecting reality more precisely.

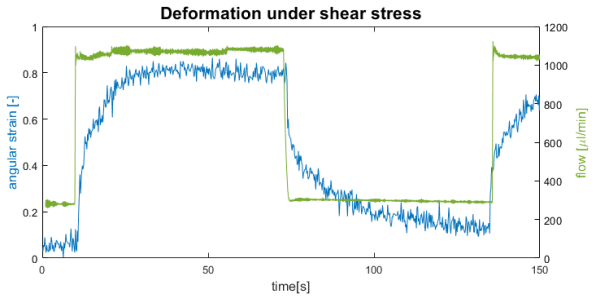

Figure 3: Cell deformation in the first cycle determined using Centre of Mass shift under shear flow.

References

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Acknowledgments

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