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Mechanotransduction at the endothelial interface

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ABSTRACT

Nowadays, numerical simulations deal with fluid-structure interaction because of the strong coupling between the blood dynamics and the compliant wall mechanics. The wall displacements determine the local time-dependent size of the blood vessel lumen. Although the blood flow simulations in any explored segment of the vasculature are carried out in a deformable fluid domain, the numerical results remain questionable because: (1) the material constants are most often not known in vivo, and (2) the vessel wall is assumed to be a more or less passive material. Time-dependent hemodynamic stresses indeed govern the functioning of vascular cells, mainly endothelial and smooth muscle cells. The size of the computational domain depends on the controled motions of the blood vessel wall. Several substances released by endothelial cells acts either as vasodilators or vasoconstrictors. Various signaling pathways are involved in stress-mediated changes in production of the regulators of the vasomotor tone.

Stimulus-specific interconnected signaling pathways, which includes timing, amplitude, and duration (transient or sustained) of signaling responses for coordinated behavior in time and space, as well as intracellular translocations for optimized reaction compartmentation and protein recruitments for specific cluster formation, relate extracellular signals to the expression of nuclear transcription factors of specific genes. In addition to the flow governing equations coupled to the equations of the wall mechanics, the set of equations to be solved incorporate the equations that describe the biochemical reaction cascades triggered by stresses imposed by the flowing blood on the flexible wall. The temporal dynamics of signaling networks are commonly described by chemical kinetics equations, one for each time-dependent molecule involved in the chemical transformation. Model of cell signaling pathways of short-term vascular regulation is based on deterministic form of differential equations following a reductionist strategy. Biochemical simulations use BIOCHAM software (Calzone et al., 2006).

REFERENCES

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