Summary

Giulia Cardillo

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Understanding and modeling fluid dynamics and transport processes in the human body is a crucial aspect in biomedical research, which has received a growing attention in the last decades.

In the present thesis, three mathematical models are described. Three different biomedical issues, where fluid dynamical aspects are of paramount importance, are modeled: i) Fluid-structure interactions between cerebro-spinal fluid pulsatility and the spinal cord (analytical modeling); ii) Enhanced dispersion of a drug in the subarachnoid space (numerical modeling); and iii) Thrombus formation and evolution in the cardiovascular system (numerical modeling).

The cerebrospinal fluid (CSF) is a liquid that surrounds and protects the brain and the spinal cord. Insights into the functioning of cerebrospinal fluid are expected to reveal the pathogenesis of severe neurological diseases, such as syringomyelia that involves the formation of fluid-filled cavities (syrinxes) in the spinal cord. Furthermore, in some cases, analgesic drugs – as well drugs for treatments of serious diseases such as cancers and cerebrospinal fluid infections – need to be delivered directly into the cerebrospinal fluid. This underscores the importance of knowing and describing cerebrospinal fluid flow, its interactions with the surrounding tissues and the transport phenomena related to it. In this framework, we have proposed: a model that describes the interactions of the cerebrospinal fluid with the spinal cord that is considered, for the first time, as a porous medium permeated by different fluids (capillary and venous blood and cerebrospinal fluid); and a model that evaluates drug transport within the cerebrospinal fluid-filled space around the spinal cord –namely the subarachnoid space–.

The third model deals with the cardiovascular system. Cardiovascular diseases are the leading cause of death worldwide, among these diseases, thrombosis is a condition that involves the formation of a blood clot inside a blood vessel. A computational model that studies thrombus formation and evolution is developed, considering the chemical, bio-mechanical and fluid dynamical aspects of the problem in the same computational framework. In this model, the primary novelty is the introduction of the role of shear micro-gradients into the process of thrombogenesis.

The developed models have provided several outcomes. First, the study of the fluid-structure interactions between cerebro-spinal fluid and the spinal cord has shed light on scenarios that may induce the occurrence of Syringomyelia. It

was seen how the deviation from the physiological values of the Young modulus of the spinal cord, the capillary pressures at the SC-SAS interface and the permeability of blood networks can lead to syrinx formation. The computational model of the drug dispersion has allowed to quantitatively estimate the drug effective diffusivity, a feature that can aid the tuning of intrathecal delivery protocols.

The comprehensive thrombus formation model has provided a quantification tool of the thrombotic deposition evolution in a blood vessel. In particular, the results have given insight into the importance of considering both mechanical and chemical activation and aggregation of platelets.