S32: Computational Models of Thrombosis

S32-1 The contact activation system in device-related thrombosis

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Biomaterial surfaces used in blood-coated medical devices initiate blood coagulation that may lead to device malfunction or thromboembolism. To reduce thrombosis risk in this type of devices computational fluid dynamics (CFD) is often used to predict the formation of thrombus. The current work consists in the coupling of a CFD solver with a biochemical scheme that generates thrombin considering the contact activation system (CAS). A strategy is proposed to initiate the coagulation reactions by contact activation of factor XII with the device wall. In this view, a boundary condition is introduced which relates the species diffusive wall flux to the surface reaction rate of factor XII activation. This new predictive method contrasts with conventional in-vivo models in which the reactions are initialized at user-defined and arbitrary injury sites. The model of Chatterjee et al. 2010 was applied to a backward facing step geometry (BFS) inspired from the experimental setup of Taylor et al. 2014. The results show a significant amount of thrombin generated in the recirculation region formed behind the BFS. Interestingly, this result was obtained without a priori knowledge of the regions prone to thrombosis. Qualitatively results align well with the experimental data which showed that the thrombus forms behind the BFS, in the recirculation zone area. Our results thus show that accounting for the CAS provides a novel strategy to initiate thrombus formation. The current strategy coupled to existing models that consider platelet activity and thrombus growth may lead to a predictive pipeline for device-related thrombosis.

References

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S32-2 Development of a Device-Induced Computational Thrombosis Model

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Thrombosis remains an obstacle in current blood-contacting devices, primarily due to regions of disturbed flow. Specifically, regions of high shear stress activate platelets and regions of low wall shear rate allow for platelet adhesion and thrombus growth. Both of these phenomena occur in regions of flow separation. A computational model capable of predicting device-induced thrombosis on a macroscopic scale and relatively quickly, compared to existing models, would be useful in the device development process. A single-scale thrombosis model was modified to predict device-induced thrombosis. Bulk concentrations of platelets (non-activated and activated) and a chemical activator are considered. A power law model is used to predict platelet activation based on the local shear stress, and a non-linear weighting function is used to quantify thrombus deposition based on the local wall shear rate. A modified Brinkman term is added to the Navier-Stokes equations to account for a

growing thrombus by modeling it as a porous material. In summary, a model that predicts macroscopic thrombus is presented to achieve the goal of expediting the cardiovascular device design process.

S32-3 Reduced-order computational modeling of thrombogenic potential in large arteries

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Computational modeling of large artery thrombosis is challenging for several reasons. First, it involves a wide range of spatial and temporal scales. Blood flow dynamics span up to centimeters, while platelet interaction and near-wall chemical concentration boundary layers are on the order of microns. Second, the underlying processes are highly complex and in some cases not fully understood. Simulation of the coagulation cascade alone, for example, requires the knowledge of dozens of reaction rates and initial conditions, many of which are not well known. The goal of this work is the development of reduced-order techniques for the modeling of thrombogenic potential in large arteries. We will first discuss a method for bridging the gap between length scales in the mass transport problems associated with thrombotic processes. Due to the high Peclet and Schmidt numbers associated with these types of problems, coagulation enzymes are expected to be concentrated in micron-scale boundary layers near the vessel wall. Based on these physics, we develop a model that converts the three-dimensional micron-scale transport problem to one that can be solved as a two-dimensional problem on the vessel wall surface, greatly reducing computational cost. Second, we will discuss a framework for developing reduced-order models of the coagulation cascade. This framework utilizes nested genetic algorithm optimizations to both reduce the number of model species and optimize the rate constants of the resulting reactive network. These reduced-order models have lower model complexity and computational cost, while potentially reproducing essential dynamics of the full reactive system.