Effects of Flow and Diffusion on Blood Coagulation in Platelet Poor Plasma: A Two-way Coupling Between Hemodynamics and Biochemistry

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Abstract

Introduction
Blood coagulation is an intricate network of enzymatic reactions and it is part of the hemostatic process which aims to stop bleeding in a damaged vessel. In addition to this coagulation cascade of reactions, several factors interact to ultimately form a clot at the site of injury (e.g. vasoconstriction, platelet activation and aggregation). Describing the coupling between each involved sub-process is a challenging task of medical importance and relevance, since the balance between clotting and bleeding is a delicate equilibrium, whose regulation is vital to avoid pathologies like stroke, venous thrombosis, pulmonary embolism, hemophilia or infarction [1,2]. The power and versatility of numerical simulation can give a detailed insight on the factors influencing these diseases, helping in their prediction and prevention.

The subject of this study is the coagulation network in platelet poor plasma. This network is initiated with the exposure of a particular triggering factor (i.e. tissue factor exposed on the wound), followed by a number of sequential activation reactions and thwarted by inhibition proteins. In addition, it is enriched by positive and negative feedback loops which make it a well-regulated and robust process. The last step of the coagulation network is the production of fibrin which polymerizes and thereby forming a gel-like mesh.

The phenomena involved in blood coagulation (schematically represented in Figure 1) range from the biochemical to the hemodynamic field in a two-way coupling and on different time and spatial scale. In the vessel, plasma species are affected by both advection and diffusion and they react in the plasma with each other, but also on the wall with membrane-bounded species. A system of 47 non-linear partial differential equations is implemented for this advection-diffusion-reaction problem to simulate the dynamics of the plasma species, while the membrane proteins are represented by 11 ordinary differential equations set on the wall. Blood flows inside the vessel and its velocity field is affected by the clot formation, as the clot develops and obstructs blood flow. A modified version of the Navier-Stokes equations is used for blood, where the viscosity depends on fibrin concentration. As soon as fibrin reaches a certain threshold, the viscosity changes from the viscosity of blood to the higher viscosity of clot, resulting in an obstruction of the flow field [3,4,5].

Use of COMSOL Multiphysics®
To investigate the effect of flow and biochemistry alterations, a 2D vessel is introduced with a distribution of tissue factor on the bottom wall. A study on wound size, initial concentration of tissue factor, shear rate and diffusion is performed with the Chemical Reaction Engineering and CFD Modules of COMSOL Multiphysics®. The threshold values of these parameters are analyzed to determine whether the coagulation network is either activated or impaired. Variations of these factors are performed to investigate their influence on fibrin production together with the clot formation. In particular, analyses on the following features are performed: the time required for the complete activation of the cascade, the strength in fibrin production, the thrombus dimension, the location where it is formed at first and its growth velocity.

Reference

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Figures used in the abstract
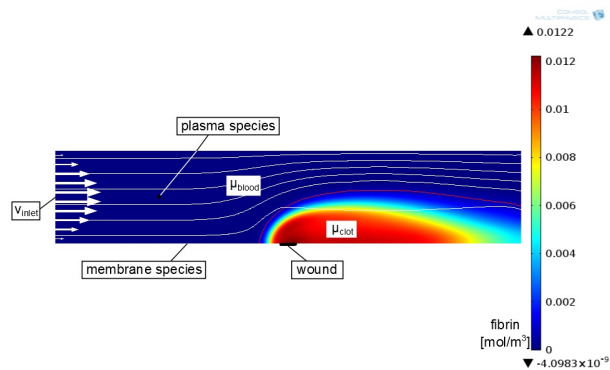
Figure 1: Surface concentration of fibrin together with the contour line (red line) equal to 600 nM which identifies the clot extension. Streamlines of the velocity field (white lines). Site of injury (black bold line at the bottom boundary). Velocity field at the inlet (white arrows).