Computational Modeling of Platelet Aggregation and Blood Coagulation
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Abstract
Coupled, intricate systems exist to maintain the fluidity of the blood in the vascular system while allowing for the rapid formation of a solid clot to prevent excessive blood loss subsequent to vessel injury. These systems can be invoked as part of the body’s normal defense mechanism against blood loss, but these same systems are also invoked during unwanted, pathological and perhaps life threatening clot formation. Indeed, these systems can be seen as a delicate balancing act continually occurring to control clot formation and lyse in order to prevent hemorrhage without causing thrombosis. Despite more than a century of research in blood biochemistry, platelet and vascular wall biology, and fluid dynamics, the complexity of blood clotting under flow has precluded quantitative and predictive modeling. Yet, quantitative modeling of blood function under flow could have numerous diagnostic and therapeutic uses.

Challenges
So, I stub my toe and start bleeding profusely but then my blood clots and saves my life, right? What’s so hard about that?
If you want a detailed understanding of what is going on, plenty. There are three requirements that make things difficult:
• The blood needs to continue flowing throughout the body.
• Chemical reactions involved must occur fast enough to have the clot start forming at the site of injury instead of downstream.
• Clotting should be localized to the injury site, despite activated chemicals washing downstream.
These requirements have been handled biologically by a system that involves
• Complex flows
• Interactions between flow and objects
  – Objects are active, moving, and deformable
  – Examples include red blood cells or platelets
• Long cascades of chemical reactions
  – Occur within the fluid and on cell surfaces
  – Have multiple feedback and control loops, enabling several orders of magnitude signal amplification
  – Exhibit threshold behavior
• Chemical and cell transport
• Chemically induced phase transitions (polymORIZATION)
These numerous challenges translate into complex models involving:
• Coupled nonlinear PDEs
• Dynamic fluid-structure interactions
• Complicated networks of kinetic equations
• Multiple spatial and temporal scales

Key Mechanisms of Coagulation

Governing Equations
Navier-Stokes Equations
\[ \frac{\partial \mathbf{u}}{\partial t} + \mathbf{u} \cdot \nabla \mathbf{u} = -\nabla p + \nu \nabla^2 \mathbf{u} + \mathbf{f} \]
Fluid-Structure Interaction Equations
\[ \frac{\partial \mathbf{X}}{\partial t} + \mathbf{u} \cdot \nabla \mathbf{X} = D_t \Delta \mathbf{X} + R_i(t) \]

Chemical equations
\[ \frac{\partial c_i}{\partial t} + \mathbf{u} \cdot \nabla c_i = D_i \Delta c_i + R_i(t) \]
Reactive boundary conditions
\[ R_i = k_{bp} \mathbf{b}_i - k_{db} \mathbf{c}_i + k_{bc} \mathbf{b}_i \mathbf{c}_i + R_i(t) \]

References