

Solving multicomponent reaction-transport with coupled cellular trajectories and data-driven cellular activation models.

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Background: Cells release autocrine factors as well as trigger reactions on their surface that can be autocatalytic, all of which may occur in the presence of diffusive and convective transport. In these situations of quorum sensing on evolving cellular ensembles, multiscale approaches are required. Such situations include: blood clotting/bleeding under flow, biofilm formation, and angiogenesis/growth factor/tumor interactions. When blood flows over disrupted vessel surfaces, activating platelets release ADP and thromboxane, while their surface becomes catalytic for thrombin production via phosphatidylserine exposure.

Approach: Platelet calcium mobilization was measured by pairwise agonist scanning (PAS) of responses to single and pairwise delivery of low, medium, and high doses of: ADP, thromboxane mimetic (U46619), collagen mimetic (convulxin) and thrombin. A neural network model was trained with the PAS data for use in multiscale simulations. A recent multiscale model of clotting under flow (Flamm et al. Blood, 2012) was expanded for enhanced speed and accuracy. The two new modifications were: (1) the inclusion of platelet aggregate remodeling that enables growing clots to achieve more realistic shapes, and (2) the addition of particle event-driven triangular element remeshing for efficient and adaptive finite element method (FEM) solution of soluble concentrations.

Results: The remodeling scheme was implemented to allow for instantaneous local translocation and rolling of single platelets and was shown to make more physiologically consistent prediction of the clot morphology. The adaptive meshing scheme was applied to provide unstructured triangular meshes that vary along with the modulating clot contour so that better resolution and efficiency were achieved for calculation of ADP/TXA₂ release and reactive species transport. The model was able to predict platelet deposition dynamics for each patient for whole blood flowing over collagen at 200 s⁻¹ wall shear rate consistent with in-silico measurements. This approach allows efficient multiscale calculations, from the single cell to the tissue level, when the cellular ensemble has evolving structure driven by coupled species transport and prevailing hemodynamics.