A dynamic-IB Method for Computing the Vascular Journey of micrometric Carriers in Narrow Capillaries

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Abstract

In vascular targeted therapies, blood-borne carriers should realize sustained drug release from the luminal side towards the diseased tissue. In this context, such carriers are required to firmly adhere vascular walls for a sufficient period of time while resisting hydrodynamics perturbations induced by the blood flow. Here, a hybrid computational model, combining a Lattice Boltzmann (LBM) and Immersed Boundary Methods (IBM), is proposed for predicting the dynamics of rigid and deformable adhesive micro-carriers navigating a capillary with physiological hematocrit. Red cells and particles are modeled as a collection of mass-spring elements responding to a bending resistance, an elastic potential and total enclosed volume conservation constraint. Furthermore, particle surfaces are uniformly decorated with adhesive molecules (ligands) interacting with receptors disposed on the walls. Particle adhesion is modeled as a short-range ligand-receptor interaction and in term of formation and destruction probability functions that discriminate whether a chemical bond can be formed or destroyed. If a bond is established an attractive elastic force is activated. The interaction between blood cells and particles is characterized in two different situations. Firstly, particle transport and adhesion are characterized in terms of their ability to reach the capillary peripheries (margination rate) and firmly adhere the vasculature. This analysis is carried out systematically by varying particles' and cells' releasing positions and stiffness in a 10 μm capillary with physiological hematocrit. Then, the strength of adhesion of already adhering particles in narrow capillaries traversed by blood cells is measured as a function of cell and particle shape and stiffness. These data demonstrate that stiffness weakly influence the margination rate while significantly affect the ability of such constructs to efficiently interact with the endothelium by forming stable chemical bonds.

References

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