

Multiscale modeling of nanocarrier (NC) hydrodynamics in blood flow

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Nanocarrier (NC) transport in blood vessels involves hydrodynamic and thermodynamic interactions, which collectively dictate efficacy in targeted drug delivery applications. We investigate two important transport effects of (1) the effect of blood particulates in defining the hydrodynamic fields in simple and complex vascular geometries, and (2) hydrodynamic interactions for NCs of complex shapes.

We focus on the *ab-initio* modeling of the non-Newtonian rheology of the blood flow and compute the effective viscosity and diffusion (mobility) tensor under various hydrodynamic conditions. The flow is resolved by performing direct numerical simulations of the Navier-Stokes equations via a finite element method implementation of the arbitrary Lagrangian-Eulerian (ALE) approach [1]. In a simple geometry of single cylindrical vessel tube, the effect of red blood cells (RBCs) is considered by introducing them as hard spheres; flow profiles in the longitudinal section with two different volume fractions of RBCs are analyzed. We find that the flow profiles are similar to developed velocity profile of a Casson fluid under pressure-driven flow [2] in a cylindrical channel, which allows us to determine the effective viscosity based on the Casson model [2]. The Batchelor and Green model [3] of effective viscosity for hard sphere suspensions is also used for comparison, and the result is consistent with the prediction of Casson model. Therefore, our numerical simulation shows that the consideration of hard sphere interactions for RBCs captures the expected non-Newtonian nature of the blood and successfully describes the essential physics of blood rheology due to the presence of particulates. Extension of these simulations to branched geometries is currently being pursued. The circulatory system is comprised of blood vessels with irregular geometries with branched vessel structures, where a vessel with a large diameter bifurcates into a series of tubes with smaller diameter. Such structures gain importance in the context of targeted drug delivery since the partitioning of nanocarriers into the branched structures is affected by a variety of features like the vessel diameter, the angle and location of the branch. We have demonstrated previously in [1] that the ALE framework is highly sensitive to the resolution of the computational mesh and as a result adaptive meshing techniques are an integral part of this framework. We have improved the implementation of the adaptive framework to make it viable for the simulations of branched structures.

Similar to vessel geometries, the shape of NCs also plays a crucial role in targeted drug delivery [4]. Hence in order to quantify the flow and association properties of oblate NCs we have developed a framework with capabilities to simulate nanoparticles with arbitrary shapes. We introduce the quaternion framework for rotational motion [5], and two collision models [6], namely, (a) an impulse-based model for wall-particle collision, and (b) the short-range repulsive Gay-Berne potential [7] for particle-particle collisions. Using this extended model, we study the more realistic structures of red blood cells and NCs (such as ellipsoid, discoid, spherocylinder) with hydrodynamic and thermodynamic interactions and also extend our work to deformable elastic particles [8]. By comparing the results with hard sphere models, we can improve the current theoretical models and quantify the binding dynamics and interactions of arbitrary shaped NCs.

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