Multiscale Modeling of Hematologic Disorders

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Modeling of hematologic disorders, in genetic diseases (sickle cell anemia) or in infectious diseases (e.g. malaria), is now feasible using mesoscale modeling that can be at the spectrin level but also it can include thousands of red blood cells (RBCs), hence allowing accurate studies of blood rheology. We have developed several multiscale models of RBCs that can be used in simulations of blood flows in small arteries and capillaries, based on a single component or a two-component, i.e. treating separately the lipid bilayer and cytoskeleton. Both models allow us to investigate the salient features of hematologic disorders involving increased viscosity of the blood and adhession of RBCs to the endothelium. In this talk we will focus in particular on the adhesion dynamics of malaria and especially sickle cell anemia, which explains clinical symptoms associated with vasoocclusion crises.

In particular, vasoocclusion crisis is a key hallmark of sickle cell anemia. Although early studies suggest that this crisis is caused by blockage of a single elongated cell, recent experiments have revealed that vasoocclusion is a complex process triggered by adhesive interactions among different cell groups in multiple stages. However, the quantification of the biophysical characteristics of sickle cell anemia remains an open issue. Based on dissipative particle dynamics, we develop a multiscale model for the sickle red blood cells (SS-RBCs), accounting for diversity in both shapes and cell rigidities, to investigate the precise mechanism of vasoocclusion. First, we investigate the adhesive dynamics of a single SS-RBC in shear flow and static conditions, and find that the different cell groups (SS2: young-deformable SS-RBCs, ISCs: rigid-irreversible SS-RBCs) exhibit heterogeneous adhesive behavior due to the diverse cell morphologies and membrane rigidities. We quantify the observed adhesion behavior (in static conditions) in terms of a balance of free energies due to cell adhesion and deformation, and propose a power law that relates the free-energy increase as a function of the contact area. We further simulate postcapillary flow of SS-RBC suspensions with different cell fractions. The more adhesive SS2 cells interact with the vascular endothelium and trap ISC cells, resulting in vasoocclusion in vessels less than 15 microns depending on the hematocrit. Under inflammation, adherent leukocytes may also trap ISC cells, resulting in vasoocclusion in even larger vessels.