MULTI-SCALE DPD MODELS FOR RED BLOOD CELLS IN HEALTH AND DISEASE

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We have constructed a Dissipative Particle Dynamics (DPD), multi-scale model (MS-RBC) of normal and diseased (malaria, sickle-cell) red blood cells(RBC). Depending on the application, the cell membrane is represented with hundreds or even thousands of DPD-particles connected by viscoelastic springs into a triangular network in combination with out-of-plane elastic bending resistance. Model parameters are derived from a variety of single-cell, static and dynamic tests. RBC aggregates (rouleaux) are modeled with the addition of inter-cellular adhesive forces (Morse potential). Without adjustment of parameters the model RBCs are then suspended in a neutrally buoyant Newtonian solvent of DPD particles. Calculated in uniform shear flow, the viscosities of the simulated suspensions are in excellent agreement with measured values for healthy and malaria infected blood with respect to variation of strain rate and hematocrit (H). We have also developed a low-dimensional model (LD-RBC) constructed as a closed ring of only 10 large hard DPD-particles (colloids). These are connected by worm-like chain springs combined with bending resistance. The LD-RBC model can represent the force-extension data of real RBCs over the entire range of measured cell deformations for healthy and for malaria infected RBCs. LD-RBC suspensions capture the experimental data for the viscosity of blood and its cell-free layer in tube flow, and do so with computational savings of about 1/50 relative to their MS-RBC counterparts. Sickle erythrocytes exhibit abnormal morphology and membrane mechanics in the deoxygenated state due to the polymerization of the interior hemoglobin. The representation of the irregular and varied shapes of sickle cells is being addressed by: i. mapping the biconcave shape of healthy RBCs into irregular configurations, ii. coarse-grained modeling of the polymerization of the interior hemoglobin into rigid structures which deform the enclosing membrane. The latter is a more faithful model of the sickleing process, but is computationally expensive for multi-cell applications. When the model RBC suspensions are driven through small tubes,(**diameters 20-150 microns)**, the cross-stream stress gradient induces radial migration of the suspended RBCs. At 30% tube hematocrit the main effects are a cell-free layer (CFL) at the wall and a peak in H near the centerline. Analytical theories have attempted two-phase modeling of blood flow in tubes with a Newtonian plasma CFL, and a non-Newtonian bulk fluid with uniform H in the rest of the cross-section. However, simulations show H to be non-uniform, and that in the larger tubes the velocity profiles beyond the CFL are essentially parabolic with some flattening near the centerline. At the flow rates of these simulations aggregation has only minor effects for adhesive forces at healthy levels. The simulation results are compared where possible with experimental data for blood flow in glass tubes. To bring the small-tube flow simulations closer to the 'in vivo' micro-circulation we have devised a coarse-grained model of the glycocalyx layer which separates the blood components from the epithelial cells of the vessel walls.