S28:Rheology and microstructure of cellular blood flow

S28-1 Effect of internal viscosity on suspension rheology of red blood cells

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We present a numerical analysis of the rheology of a suspension of red blood cells (RBCs) in a wall-bounded shear flow in the Stokes flow regime for a wide range of viscosity ratio (from 0.1 to 10) between the cytoplasm and plasma. An RBC is modeled as a biconcave capsule, or a Newtonian fluid enclosed by a thin elastic membrane, which follows the Skalak constitutive law. The problem is solved by GPU computing, coupling the lattice-Boltzmann method for the fluid dynamics with the finite element method for the membrane dynamics. The volume-of-fluid method and front-tracking method are employed to update the viscosity on the fluid mesh. Since our numerical model successfully demonstrates the behavior of single RBC and also multi-cellular interaction, we apply it for the problem of hemorheology. Our numerical results show that the deformation mode of RBCs continuously changes from rolling to swinging motion as increasing volume fraction of RBCs. The deformation of RBCs is evaluated by the Taylor parameter, and the contribution of individual deformed RBCs to the bulk suspension rheology is quantified by using the stresslet tensor. We also investigate the effects of shear rate and volume fraction of RBCs on those values, and reveal the relationship between the deformation mode of individual RBCs and bulk suspension of rheology.

S28-2 Hemolytic behavior of human red blood cells caused by osmotic pressure difference -Visualization of hemoglobin behavior by use of light absorption characteristics

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The hypotonic swelling and hemolysis of red blood cells (RBCs) has been studied in terms of the changes in shape and volume of RBCs as well as the time required for hemolysis. For a detailed investigation of the process leading from swelling to hemolysis of single RBC, we applied a visualization method of the hemoglobin by use of the light absorption characteristics to the experiment of the hypotonic hemolysis.

Human RBCs from healthy volunteers were washed with PBS and diluted by mannitol-adenine-phosphate solution. After a hypotonic solution (0.1wt% NaCl aq.) was added to the RBC solution, the swelling behavior was observed and recorded by a microscope with EMCCD camera. A bandpass filter was installed at the lamination in order to irradiate the light of the wavelength close to the hemoglobin maximum absorption. Based on the Lambert-Beer law, the light absorbance is proportional to the medium concentration and thickness. The hemoglobin molarity contained in single RBC was calculated from the absorbance measured by use of the brightness values in the experimental results.

Before adding the hypotonic solution, the light absorption of a RBC is weaker at the center than that around the edge. The local difference in thickness of biconcave shape was visualized. The hemoglobin

mass results in 128pg, which is slightly larger than the MCH (30～35pg) but roughly on the same order. After adding the hypotonic solution, the concave disappears and strong absorption arises at the center, indicating the change of RBC shape into spherical due to the swelling. As the hemolysis occurs, the gradual decrease of hemoglobin in the RBC is obtained. From the time variation of the hemoglobin mass, the shape, and the volume of RBC, the onset of the hemolysis is suggested.

S28-3 Effects of red blood cells on blood flow in micro vessel network: in vitro experiment and computer simulation

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A blood flow behavior with multiple red blood cells was examined by using in vitro experimental measurements for Polydimethylsiloxane (PDMS) channel constructed for micro vessel network. Blood flow velocity was determined by tracing individual red blood cells as markers in the blood, while flow velocity of the purified water was determined by using fluorescent particles as the markers. In the measurement, flow rate distribution was different between blood and purified water. Red blood cells tended to increase blood flow resistance, affecting the flow rate distribution in the vessel network. Experimental results could be mechanically explained by computer simulations based on a phenomenological hematocrit-apparent viscosity relationship, as well as by those based on coupled analysis of blood plasma flow and motions of deformable red blood cells.

S28-4 Capillary flow imaging with genetically-engineered red blood cells in the living animal brains

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Cellular function in our body relies on continuous supply of blood. Understanding interplays between information processing in the cells and flow states consisting of blood plasma and blood cells is therefore crucial to prevent and treat any diseases related to blood flow disturbances. Here, we developed a fluorescence-based novel imaging technique for capillary blood flow using genetically-engineered rat models in which red blood cells (RBCs) express fluorescent proteins. The fluorescent RBCs and blood plasma labeled with sulforhodamine 101 were simultaneously captured with two-photon laser scanning microscopy in the animal brains under anesthesia conditions. Automatic segmentation by means of machine learning software were applied to assign the pixels into RBC or plasma for the vessels imaged. Then, a width of the plasma and RBC flow was calculated at the cross-section of the vessels. Apparent dwell time of the fluorescent RBCs were also quantified in each pixel along a centerline of the vessels to map spatiotemporal features of the capillary RBC flow. As expected, a larger width of the plasma flow than RBC's were successfully visualized in the parenchyma arteioles and venules. According to pulsation, a thickness of the plasma layer largely fluctuates in the arterioles, but less in the venules. For capillaries (< 8 μm in diameter), intermittent distribution of the plasma and RBCs along the vessels was characterized. The results demonstrated that distribution of capillary flow varies among the multiple networks as well as within the singe

vessels over time, independent of changes in diameters of the capillaries. In conclusion, the present imaging techniques will allow for fluorescently capturing RBC flow and cellular activity simultaneously in the capillary beds.

S28-5 Fluid dynamical study of preferential distributions of blood cell components in microchannel flows

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It has long been known that red blood cells (RBCs) in blood flow through microvessels are depleted near the vessel wall, whereas platelets have enhanced concentrations in this RBC-depleted marginal layer. In order to elucidate the mechanism of these preferential distributions, we performed two types of in vitro experiments, investigating effects of RBC deformability on the axial migration of RBCs and the margination of platelets, respectively. In the first type experiment, we measured the cross-sectional distributions of normal or hardened RBCs flowing through capillary tubes with high spatial resolution by a newly devised observation system. In the second type experiment, we adopted platelet-sized fluorescent particles for platelet substitutes to measure the particle distribution in the cross section of circular or rectangular tubes in the presence of RBCs, using a confocal laser scanning microscope system. The first type experiments demonstrated that normal RBCs showed significant axial accumulation, but hardened RBCs were dispersed widely over the tube cross section dependent on the degree of hardness. The second type experiments indicated that, in rectangular tubes, platelet-sized particles mixed in normal RBC suspensions were concentrated near four corners in the cross section, although in circular tubes they were concentrated near the entire circumference of the tube wall. For particles mixed in highly hardened RBC suspensions, their margination was scarcely observed in both tube flows. These results suggest that preferential distributions of RBCs and platelets can be attributed to high deformability of RBCs, which induces axial accumulation of RBCs and platelets are expelled into the marginal layer where RBCs are depleted, due to the interaction with RBCs.