Cell rheology in microfluidic perfusion: computational and experimental approach

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Lab-on-chips for blood analysis are the ultimate trend in rapid point-of-care diagnostics and in a not-too-distant future will hopefully replace expensive and complicated laboratory tests. Very often, the development of a lab-on-chip for blood analysis concerns mainly the careful design of the microfluidic geometry. In many applications, in fact, geometry is directly related to the chip main function: for example in mixing, or in cell separation by density gradient, cell trapping... At the microscale, blood has to be regarded as a particulate fluid and computational models of blood flow in microfluidic chips should take this issue in consideration.
Our work focused on the development of computational models which simulate the rheology of erythrocytes in plasma perfused through arbitrary microfluidic geometries. Experimental validation of the computational model has been performed for simple geometries. Data on to the trajectories, velocity patterns, collisions, and membrane mechanical stress of single cells can be obtained from the simulations and used to optimize the microfluidic design. Our approach allows rapid optimization of circuits for cell manipulation, such as separation, trapping, position specific cell-cell or cell-material interaction.

The computer model consists of individual erythrocytes immersed in a lattice-Boltzmann fluid dynamics code (Fig. 1 and 2). The blood cells are modelled as elastic surface membranes, calibrated and validated using cell stretching experiments [1]. In order to improve the cell rheology properties, an experimental setup was established. In addition to the stretching experiment, also rotation, shearing, fluidic pathways and many more properties can be analyzed and compared (Fig. 3).

For the experimental validation of the computational model, microfluidic channels of variable geometries were produced in PDMS. Briefly, the high resolution film mask was purchased from Micro Lithography Services, dry-film photoresist Ordyl 355 (Elga Europe) was laminated on microscope glass slides, exposed using a self-built UV lamp, and developed by dipping method. PDMS was poured over the negative form of the channels and cured. After punching in- and outlets, the PDMS was glued on microscope glass slides. Despite our low-cost laboratory equipment, fluidic channels of 50 µm width could be obtained (Fig. 4). Fresh blood samples were diluted with RPMI cell culture medium until the desired hematocrit (Hct) was reached, typically 1 -15%. Gravity-driven perfusion was used to take videos of the blood flow under variable flow rates.

Our validated computational model can be used to rapidly predict position, velocity and membrane deformation of individual cells in arbitrary microfluidic systems. Such information could formerly only be obtained by expensive and time-consuming experimental analysis. This computational model can be particularly useful for the design of microfluidic devices where precise cell positioning and cell behavior is needed.

[1] I. Cimrák, M. Gusenbauer, T. Schrefl. Computers & Mathematics with Applications. 64(3) (2012) 278-288.

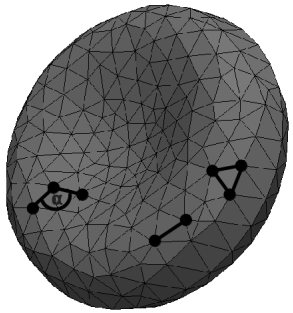

Figure 1. Computational model of erythrocyte contains around 374 surface nodes. Several types of bond connecting surface nodes are used, i.e. stretching, bending, constant area and volume to obtain correct cell elasticity and thus also rheology.

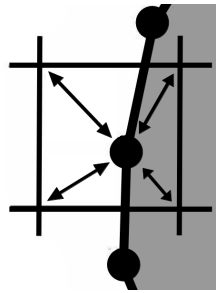

Figure 2. Correct hydrodynamic behavior of cells is obtained by the immersed boundary method. Surface nodes (red) interact with a fixed lattice Boltzmann fluidic grid. Velocity information of the fluid is transferred to the cell boundary and cell movement or change of shape is transferred back to the fluid.

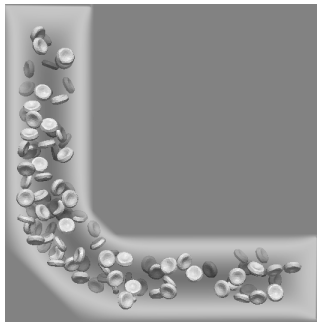

Figure 3. Simulated blood flow. Cell trajectories, cell rotation, collisions, shearing, deformations and many more cell rheology properties can be directly compared to experimental data.

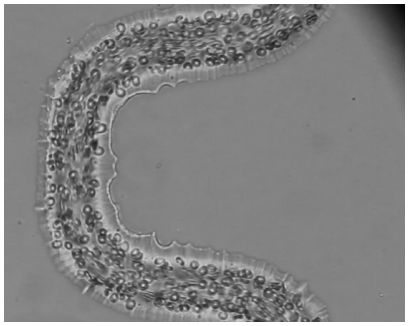

Figure 4. Diluted blood (15% Hct) perfused through a 50 µm width channel.

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