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In vitro Blood Flow in Circular PDMS Microchannels: Effect of the Flow Rate and HematocritValdemar GARCIA¹; Ricardo DIAS^{1,3}; Teresa CORREIA^{2,4}; Rui LIMA^{1,3}; Elisa PINHEIRO¹; Diana PINHO¹; Pedro RODRIGUES¹

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Recently, Lima et al. [1] has performed confocal micro-PIV measurements on the blood flow through straight PDMS microchannel. In that study they have observed that the formation of the cell free layer is enhanced as the cross section ratio increases. However, the cross section ratio is not the only parameter that contributes for the creation of the cell-free layer. Hence, several other physical and hemorheological factors (such as flow rate, hematocrit, viscosity and cell deformability) need to be investigated in order to make use on the physics of microfluidics to either develop new lab-on-chip devices or to optimize the design of the existent microfluidic chips. The main aim of the present study is to show the effect of both flow rate and hematocrit on the blood flow and cell behaviour. The circular polydimethylsiloxane (PDMS) microchannels were fabricated by using wire casting technique and the experiments were carried out by using dextran 40 containing different fractions of red blood cells (RBCs). The in vitro blood flow was measured by means of video microscopy and image analysis. Additionally, the pressure drop was also measured.

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Measuring the Cell-Free Layer in Circular MicrochannelsCatia FIDALGO¹; Antonio SA¹; Rui LIMA^{1,2}; Monica OLIVEIRA^{2,3}; Takuji ISHIKAWA⁴; Yohsuke IMAI⁴; Takami YAMAGUCHI⁵

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One of the most interesting hemodynamic phenomenon observed both in vivo and in vitro studies is known as Fahraeus-Lindqvist effect, in which the apparent blood viscosity decreases as the tube diameter is reduced, for narrow tubes (< 300 µm). The physical reason behind this phenomenon is the creation of a marginal cell-free layer at regions adjacent to the tube wall. Although intensively studied, the complex formation of the cell-free layer has not yet been convincingly described mainly due to multi-physical and hemorheological factors that affect this phenomenon. The main purpose of this experimental work is to study the effect of the hematocrit (Hct) and temperature on the thickness of the cell-free layer in both glass capillaries and circular polydimethylsiloxane (PDMS) microchannels using an optical technique. The internal diameter of the glass and PDMS microchannels are 100 µm and 73±2 µm, respectively. The microchannels were placed on the stage of the inverted microscope and the temperature of the stage was adjusted by means of a thermo plate controller. The flow rate of the working fluids was controlled using a syringe pump. The images were recorded using a confocal microscopy system and transferred to the computer to be evaluated in Image J (NIH) using different plug-ins (MTrackJ and FeatureJ). The recorded images show a clear formation of a cell-free layer of variable thickness depending on experimental conditions.

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Deformation Behavior of Multiple Red Blood Cell in a Capillary Vessel with BifurcationsXiaobo GONG¹; Shu TAKAGI²

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The detailed deformation of multiple red blood cells in capillary flows is investigated computationally and hydrodynamics in the capillary flow accompanied with the deformation of red blood cells are analyzed. The membrane of red blood cell is modeled as a hyperelastic thin-shell and the immersed boundary method is used for the fluid-structure coupling in the present simulations. Numerical results show that the apparent viscosity in the capillary flow increases with the increase of the shear coefficient in the membrane of red blood cell, while this change for the viscosity is not obvious when the stiffness of the membrane changes. The distribution of multiple red blood cells in a capillary with branches is also simulated which shows that the apparent viscosity in the flow and the distribution of the cells affect each other interactively.

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Drift and Fluctuating Motion of Artificial Platelet during Adhesion Process Near the WallHiroaki TOBIMATSU¹; Antoine PARAGON¹; Yosuke OKAMURA²; Shinji TAKEOKA²; Ryo SUDO¹; Kazuo TANISHITA¹

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INTRODUCTION: Development of platelet substitute is necessary to overcome platelet transfusion problems, the limitation of short-term storage and the risk of viral and bacterial infections. To overcome these problems, the development of platelet substitutes is necessary to achieve long-term storage and avoidance of viral infections. An important mechanical aspect of platelet adhesion to vessel wall is a microscopic motion. Especially, a lateral motion of platelet plays a key role of transportation and adhesion to injured vessel wall in hemostasis process. Previous studies reported that the presence of Near Wall Excess (NWE: concentration of platelet near wall region in blood flow) largely contributes to the adhesion of platelet. However, because of short trajectory of the particle, the previous studies based on fixed-point measurement could not reveal the mechanism of lateral transport. To obtain long trajectories including lateral motion, we built a travelling stage of microscope for tracking particles moving through flow channel and estimated the lateral motion which contributes to NWE and adhesion.

MATERIALS AND METHODS: We employed recombinant Glycoprotein Ib alpha conjugated latex beads (rGPIba-LB) as platelet substitute. These particles were observed at wall shear rate (WSR) of 200, 500, and 1000 /s with hematocrit of 0 and 40% of washed red blood cells in rectangular flow channel which had vWf surface. To observe long trajectories of the particles, the field of view of the microscope was moved from the entrance to the exit by travelling stage. We tracked the particle as Lagrangian method and separated the trajectory of particle with drift and fluctuating motion, and investigated quantitatively the motion which contributes to NWE and adhesion to the wall surface.

RESULTS AND DISCUSSION: Trajectories of rGPIba-LB were tracked from obtained movies. Then lateral gradient which reflects a drift motion of the particle toward the wall and dispersion coefficient which reflects a fluctuating motion of the particle were calculated. The rGPIba-LB moved only along axial direction with 0% hematocrit. As hematocrit increases, rGPIba-LB moved toward near the wall (about 0.9R) and the position was similar to that of NWE in previous studies. The dispersion coefficient increased near the wall and as WSR and hematocrit increased. Although the lateral gradient showed that rGPIba-LB moved toward the center of the flow channel on the wall, high dispersion coefficient near the wall induced rGPIba-LB to interact with the wall surface. These results showed that fluctuating motion is enhanced with the presence of RBC and high shear, and the particle motion near the wall includes low drift motion and high fluctuating motion.

CONCLUSION: We concluded the particle which has drift motion with high fluctuating motion induced by the presence of RBC and high shear contributes to interact to the wall surface and adhesion from NWE region.

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Mechanics of Human Red Blood Cell and the Smallest Limiting Geometries it can Flow ThroughMing DAO^{1,2}; Igor V. PIVKIN^{1,2}; Guillaume DEPLAINE³; Pierre A. BUFFET³; Subra SURESH^{1,2}

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The exquisite deformability of the human red blood cell (RBC) is essential to its physiological function which requires continuous circulation through narrow capillaries and even narrower splenic slits during about 120 days. Numerous diseases are associated with marked shape and deformability alterations of the RBC. Induced either by mutations of RBC cytoskeleton proteins in inherited disorders such as hereditary spherocytosis, or by the malaria parasite *P. falciparum* (amongst others), these alterations impair the RBC ability to overcome size-limiting deformability constraints in the human microcirculation. Analytical, continuum-based and molecular-level modeling have been applied to study the relation between RBC shape/deformability versus the critical conditions of capillaries and splenic slits (limiting dimensions, geometry, and pressure differentials). These findings have been cross-validated by biological experiments using filters, and ex-vivo perfusion of human spleens. This integrative bio-physical approach will be now applied to more precisely explore key determinants of RBC microcirculation in physiology and disease.



The aim of this study is to investigate relationship between mesh patterns and mechanical properties in the closed-cell stent structure. Multiple types of mesh patterns were designed and the differences of characteristic due to the patterns were studied by deformation analysis using computational analyses based on FEM. We validated numerical model with bending and compressive experiments by fabricated stent sample. The results of this study show that the bending stiffness of a closed cell model can be changed with its structure for all stent models. This behavior is explained considering the different stent cell geometries which set by geometrical parameters. Bending moment of 0.16 Nmm at a curvature index of 0.06 radmm⁻¹, which is efficient for cerebrovascular stent.

Therefore, bending stiffness for closed-cell stent depend on the geometry configure of the stent cell. It decreased by the geometry of the stent cell stretched to the circumferential direction of the stent. Mechanical flexibility equal to open cell structure was obtained in the closed-cell structure by varying geometrical configure of stent cell.

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Micro-flow Visualization of in vitro Blood through a Microchannel with a Bifurcation and Confluence

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Micro-visualization techniques have been used to investigate the in vitro blood flow through straight glass capillaries. Although the glass microchannels present certain similarities to in vivo microcirculation, it is also clear that these kind of in vitro experiments differ from microvessels in several respects, such as: elasticity of microvessels, effect of the endothelial surface layer and microvascular networks composed with short irregular vessel segments which are linked by numerous bifurcations and convergences. Thus it was not surprising that several studies on blood flow in glass microtubes and in microvessels have yielded conflicting results with respect to blood viscosity and flow resistance. The main purpose of this work is to improve our understanding about the effect of a bifurcation and convergence on the rheological properties of in vitro blood. The microchannel containing a bifurcation and confluence will be fabricated in PDMS by using a soft lithography technique. The flow behaviour of both pure water (PW) and dextran 40 (Dx40) containing about 14% (14Hct) of human red blood cells (RBCs) will be investigated by means of a confocal micro-PTV system. Additionally, the experimental measurements obtained with PW will be also compared numerically by using the commercial finite element software package POLYFLOW®.

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Blood-on-chips: Flow through Complex Geometries

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Blood is a complex body fluid, composed of cells and plasma, which holds a massive amount of information about several physiological and pathologic events happening throughout the body. Hence, blood sampling and analysis are used extensively in traditional clinical laboratories for the diagnosis of several diseases. Since the inception of microfluidics, there has been a growing interest, by both microfluidic and biomedical communities, to develop blood-on-chip devices as an alternative tool for the diagnosis of major diseases, such as cancer and cardiovascular diseases. Therefore, it is essential to understand the blood flow behaviour involved in this kind of microfluidic channels in order to design reliable blood-on-a-chip devices able to efficiently treat and diagnose a variety of diseases. The present experimental study shows the effect of micro-scale contractions and expansions, such as those found in an artificial stenosis, on the blood flow and cell behaviour. The micro-channels were fabricated in PDMS using softlithography and the experiments were carried out by using dextran 40 containing different fractions of human erythrocytes. The in vitro blood flow was measured by means of a high-speed video microscopy system composed with an inverted microscope, a high-speed camera and a thermo plate to control the surrounding temperature.

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Inertial Based Spiral Microfluidics for Fractionating Stem Cells into Different Stages of Cell Cycle

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We introduce a microfluidics based approach to cell cycle synchronization using inertial forces in spiral microchannels. Cell cycle synchronization is an important technique for the exact study of cell properties, biological processes and regulatory mechanisms within the cell. Animal cells can be synchronized by inhibiting DNA replication in the S phase using chemicals such as hydroxyurea, methotrexate or aphidicolin (1). Synchronized cultures can also be obtained via non-chemical means which include serum starvation (2) and contact inhibition (3). These techniques have the ability to obtain large numbers of partially synchronized dividing cells but the metabolism of the synchronized cells is often modified, leading to unbalanced growth of cells and disrupted progression through the cell cycle. Counterflow centrifugal elutriation is another commonly used synchronization technique which separates living cells based on cell sizes that correspond to the various stages of cell cycle (4). Unlike chemical and growth limiting methods, centrifugal elutriation does not affect the metabolism of cells. However, the need for large operating equipment set-up has limited the wide application of this technique within the biological community. Recently, size based particle separation in microfluidic systems have been developed based on the principles of inertial migration (5). In spiral shaped microchannel, under Poiseuille flow condition, particles of different sizes equilibrate at distinct positions along the microchannel cross-section under the influence of inertial lift and Dean drag forces. Using this principle, we have size fractionated human mesenchymal stem cells (hMSCs) so that relatively pure populations of G1, S and G2/M phase cells can be obtained. The flow throughput of this technique is high (typically 1-2ml/min), allowing one to fractionate large (~1-2 x 10⁶) number of cells. If optimized, this device could find diverse applications in the biological studies of many different cell types.

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Study of Temperature-Dependent Deformability of Red Blood Cells Using Microfluidic Bottleneck Array

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Red Blood Cells (RBCs) undergo repeated deformation as they traverse blood capillaries and organs; the deformability of RBCs is therefore crucial for normal blood circulation. The loss of RBC elasticity is central to the pathophysiology of several potentially severe diseases, such as sickle-cell anemia and malaria. In the context of malaria, Plasmodium falciparum exports proteins which alter the structure of the spectrin network, and as a consequence, host RBCs stiffen upon infection. Studies show that the deformability of parasitized RBCs is most significantly impaired at febrile temperature (Marina Marinkovic, Monica Diez-Silva, Ivan Pantic, Jeffrey J. Fredberg, Subra Suresh, and James P. Butler, *Am J Physiol Cell Physiol* 296: C69-C64, 2009). This observation suggests that temperature may