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Quantitative analysis of spatial irregularities in RBCs flows

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ABSTRACT

The spatial irregularities of red blood cells (RBCs) in continuous pulsing flow condition in micro-channels were investigated by analyzing the time variability of optical signatures obtained by recording transmitted light variability at specific location in micro-flow channels. Different flow conditions were filmed and analyzed by the digital particle image velocimetry (DPIV) to characterize local flow velocity across the whole micro-channel and in four sub-areas selected to study the particles behaviors close to the walls and in the micro-channel bulk. Starting from a behavioral classification based on the three flow patterns identified as {*Weak Activity, Vorticity, Alignment*}, an analysis to detect the spatial irregularity in the flow distribution was carried out. The velocity gradients and four nonlinear parameters (shear rate, strain rate, vorticity, divergence) were computed from the time-varying velocity maps obtained by DPIV and used to provide a quantitative characterization of the flow features. The comparison of the results obtained in the four experiments has made possible an overall understanding of the RBC movements in different conditions and, as well, the establishment of a analysis procedure for flows spatial irregularity detection.

1. Introduction

In the last decade the two-phase microfluidics has contributed in many biological, chemical and medical researches [2,7,19]. The bi-phase flows can be obtained considering two immiscible fluids or micro-particles dispersed in a fluid, with a certain concentration [16].

Real time monitoring of blood flow components is of interest in the field of microvascular research particularly for diagnosing blood pathologies [5,6] and in the development of blood substitutes [1,9]. Blood is composed by plasma and particles and accomplishes its main functions at the micro-vascular level where red blood cells (RBCs) motion evidences the principal dynamic effects due to their preponderant numbers.

A micro-channel network can be then considered the best environment to emulate the RBCs flow in the microvascular system, so the use of microfluidic devices will play a fundamental role in the development of Lab-on-a-chip for blood flows tracking [13–15,17] and blood test [8].

In this context, the establishment of procedures to analyze the RBCs flows, as a standard two-phase microfluidics processes, becomes crucial to study their complex dynamics. In our recent works [3,4], we investigated the collective behavior of the RBCs in micro-channels and three different flow patterns were identified and characterized by the dynamical changes of the particles velocities. To enrich these results, in this paper, the spatial irregularity in RBCs flows in continuous pulsing conditions were studied in the whole micro-channel and in four sub-areas to characterize particles behavior in the bulk micro-channel and close to the walls. The investigation was carried out by using the velocity gradients and four nonlinear parameters (shear rate, strain rate, vorticity, divergence). These nonlinear parameters allowed to describe in details how the particle velocities change in the fluid stream in different experimental conditions, and quantify the spatial features of the flow patterns.

The paper is organized as follows. The Section 2 describes the experimental setup and the digital particle image velocimetry approach used in the RBCs movies analysis. The Section 3 presents the features extracted in the behavioral RBCs flow patterns by using the velocity gradients and the nonlinear parameters in the whole micro-channel and in its sub-areas.

2. Materials and methods

The investigation of the RBCs collective behaviors in a rectilinear micro-channel, in continuous pulsing conditions, was

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Fig. 1. Experimental setup scheme. The RBCs sample was pumped in the micro-channel by a peristaltic pump (Instech P625). The process was monitored optically by using a backlit white light microscope (BX51, Olympus), with a magnification of 10X and coupled with a high-speed CCD (PCA 1024, Photron).

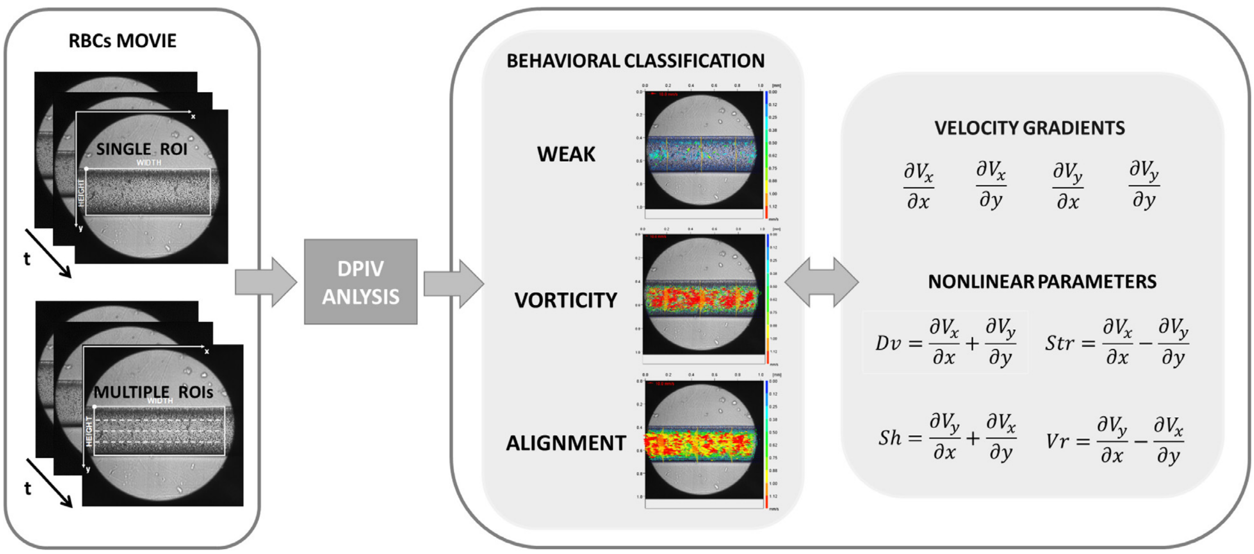

Fig. 2. The flow chart summarizes the key points in this study. The DPIV analysis from the RBCs flow movies performed on the whole micro-channel and in four sub-areas. The investigation based on the velocity gradients and nonlinear parameters to obtain a quantitative characterization of the irregularities in flow pattern behavior.

conducting by using a simplified set-up for process monitoring and the data recording. The movies collected were processed by implementing an automatic procedure based on the digital particle image velocimetry (DPIV) to compute the maps related to the changes in time of the RBCs velocity spatial distributions.

2.1. Experimental setup

RBCs sample was prepared by diluting fresh blood taken from a hamster to a concentration of 1% (hematocrit) in a phosphate buffered saline (PBS) solution. A peristaltic pump (Instech P625) controlled by an ad-hoc LABVIEW interface, was used to feed the fluid in the microfluidic rectilinear channel (SMS0104 ThinxxS), with a squared area of 320 μm^2 side and a length of 16 mm.

Four experiments are presented in which an external oscillating pressure at a frequency $f = 0.1$Hz with an amplitude varying per trial in the set $A \in \{0.1;\ 1;\ 10;\ 100\}$ mmHg was applied at the inlet of the microfluidic channel. The experiments are labelled in the discussion of the results using the values of the forcing amplitude A.

As in the scheme of Fig. 1, the process was optically monitored by a light microscope (*BX*51, Olympus) with a magnification of 10*X* coupled with a high-speed CCD (PCA 1024, Photron). Unlike most of the PIV (particle image velocimetry) analysis, in which the light used is provided by a laser, in this set-up the white light was chosen [11,12] because it is well suited in connection with CCD camera for its spectral sensitivity. Other advantages are the low cost, the simplicity and no needs of particles tracer.

Based on the microscope set-up (Olympus BX51, working distance of the objective 3.5 mm), the focal plane was placed, with a good approximation, at the center of the microchannel. The videos circumscribed an area of 1 mm^2 within the micro-channel at a distance of 8 mm from the inlet. Recording lasted 10 s with a frame rate of 125*FPS* and consist of 1200 frames with a spatial resolution of (1024×1024) px, based on the optical setup used 1 px = 1 μm.

2.2. DPIV analysis

The RBCs movies acquired were analyzed by using the digital particle image velocimetry (DPIV) [12], the output information investigated were the time-varying velocities vector maps. The analysis was carried out in the portion of the frame occupied by the micro-channel, called region of interest (ROI), whose width and height are respectively {1000, 300} px.

In the DPIV algorithm, the analysis was performed by implementing the cross-correlation between interrogation areas of two consecutive images. Specifically, the approach used was the discrete Fourier transform (DFT), that computes the correlation matrix in the frequency domain. In this work, a three-pass DFT was considered, where the three squared subsequent interrogation areas in pixel were chosen as follows: $InterrArea1 = 64$, $InterrArea2 = 32$, $InterrArea3 = 16$. The step size has been set a half of the last interrogation area, $Step = 8$. In this way, the smallest displacement investigated was of about 8 μm, close to the RBC dimension.

In [3], the analysis of the RBCs movies to compute the velocity vector maps $V(i, j, t)$ was conducted using the JPIV platform [20]. Instead in this work, the PIVlab tool for Matlab [18] was used. This gives, as output information, the matrices related to the spatial distribution of the velocity components on the horizontal and vertical directions $\{V_x(i, j, t), V_y(i, j, t)\}$.

The accuracy of the measure was taken into account using an experiment where a single-phase PBS solution was fed at the inlet

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