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Effect of geometric singularities on plasma separation performance in cascade Zweifach-Fung bifurcations

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Abstract

Series of different geometric singularities (extractions) were integrated and characterized regarding their enhancement of blood plasma separation performance of cascade Zweifach-Fung bifurcations. Flow fields and particle trajectories evolving in geometric perturbations were studied by Computational Fluid Dynamics (CFD) simulation and the model was verified experimentally also. The development of cell-depleted layer near the channel walls due to lift and shear forces were analyzed considering the applied flow rates and the geometric variation of singularities. An optimal flow rate was defined to avoid cell recirculation in the extractions to be deteriorating purity of the proposed plasma. The branch-to-branch development of the cell-depleted layer thickness was studied to prove the improvement of the separation technique due to the integrated inertial subsystems. The separation efficiencies of different geometries were defined and calculated and the optimal singularity shape was selected for further development the proposed Zweifach-Fung effect driven plasma separation system.

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Keywords: microfluidics; Lab-On-a-Chip; plasma separation

1. Introduction

Several medical diagnostic tests are based on human blood as sample solution due to its complex and representative marker molecule composition considering pathological issues. Most of these tests require separation of plasma or serum from the whole blood. Recent development of microfabricated Lab-on-a-Chip systems provides outstanding

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solutions for analytical problems although integration of high performance continuous separation function is challenging. Passive microfluidic inertial plasma separation structures could be promising candidates due to their relatively simple structure and fabrication technology. [1] Zweifach-Fung bifurcation type microscale separation systems utilize viscous lift and shear forces evolving in the low Reynolds regime and developing a cell-depleted layer near the channel walls. This structure could provide excellent plasma purity in single branch [2] however in case of cascade separation systems purity is deteriorated subsequently from branch to branch due to the thinning of the cell-depleted layer. In our work the possible recovery of the cell-free layer after each bifurcation was studied considering inertial forces evolving in special geometrical singularities to improve the separated plasma purity.

2. Materials and methods

2.1. Geometry and microfabrication

Six different geometric perturbations were designed to aid the development and recovery of cell free layer before each cascade side branches (see Fig. 3). These perturbations were 250-1000 μm long and 335-600 μm wide. The main channels were 100 μm and the side branches were 10 μm wide each.

The microfluidic channels were realized in Polydimethylsiloxane (PDMS) using soft lithography technique. SU-8 negative photoresist was patterned to form the moulding replica. [3] At the final step of the fabrication process, PDMS was sealed to glass plate by low temperature bonding after oxygen plasma treatment.

2.2. Numerical modeling and validation

COMSOL Multiphysics was used to calculate a laminar and stationary velocity field by solving the Navier-Stokes equation. The pre-calculated velocity field then was used for the calculation of particle trajectories. The particle tracing based model calculates, follows and depicts the individual particle trajectories according to the hydrodynamic drag force described by Stokes' law. The lift force was not considered due to the low Reynolds number and the small difference between the particle and water density. Laminar inflow boundary condition was applied on the inlet with different average velocities and zero pressure was set at the outlet. On the channel walls, no slip boundary conditions were defined for the laminar flow model and bounce boundary was used for the trajectory model as summarized in Table 1. Spherical particles were used as an approximation of the cell geometry and this approach was in accordance with the experimental methods, as well.

To validate the results of the calculations we have used yeast cells to model the red blood cells in a possible blood analyte as their size characteristic and distribution is similar to the red blood cells [4]. Dark field microscopy was used to follow particle trajectories facilitating the recording of the light scattered from the cells crossing the light beam. Local cell concentration from the lateral distribution of the scattered light intensities, i.e. from the local brightness levels of the image were estimated.

Table 1. Summary of boundary conditions for the numerical model

Boundary	Model	Boundary condition	Values
Inlet	CFD	Laminar inflow with average flow velocity	0.01 - 0.05 - 0.1 - 0.5 1 - 5 μL/s
Inlet	Trajectory	Particle inlet	100 particles with uniform density
Channel wall	CFD	No slip	-
Channel wall	Trajectory	Bounce	-
Outlet	CFD	Pressure	0 Pa
Outlet	Trajectory	Freeze	-

3. Results

3.1. Flow velocity field and particle trajectory model

The velocity fields were calculated and visualized experimentally also as demonstrated in Fig. 1 in case of a representative geometry. At low flow rate regime the velocity field is stable however an order of magnitude increase in the flow rate results in recirculations and vortices in the channel (see Fig. 1.B) which was reproduced experimentally also. These recirculations need to be avoided as they can compromise the purity of the separated plasma. The cell free layer was also deteriorated at higher flow rates as presented in Fig. 1.C.

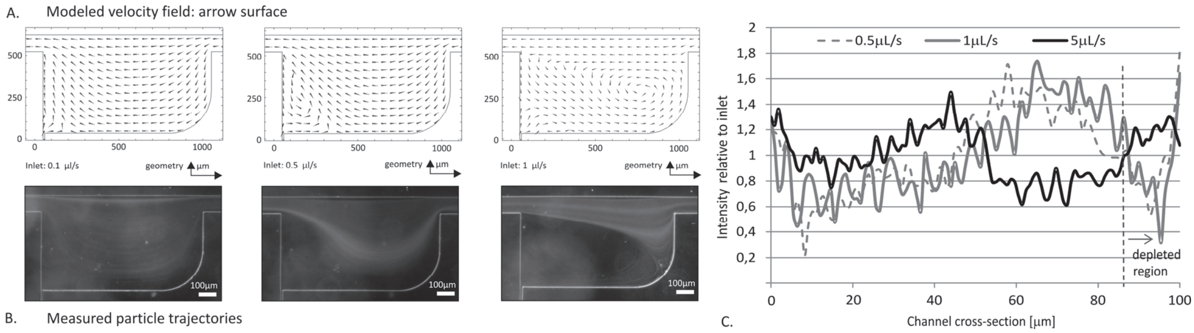

Fig. 1. Modeled flow velocity fields (A.) in a representative singularity in case of different injected flow rates compared to the experimentally recorded particle trajectories (B.). Moffatt recirculation evolves at higher flow rates and deteriorates the cell-depleted layer at the outlet of the singularities (C.).

Particle trajectories modeled in COMSOL Multiphysics were in a good agreement with the experiments demonstrating the development of cell free layer near the channel wall applying adequate (in this case 0.5µL/s) flow rate as shown in Fig. 2.

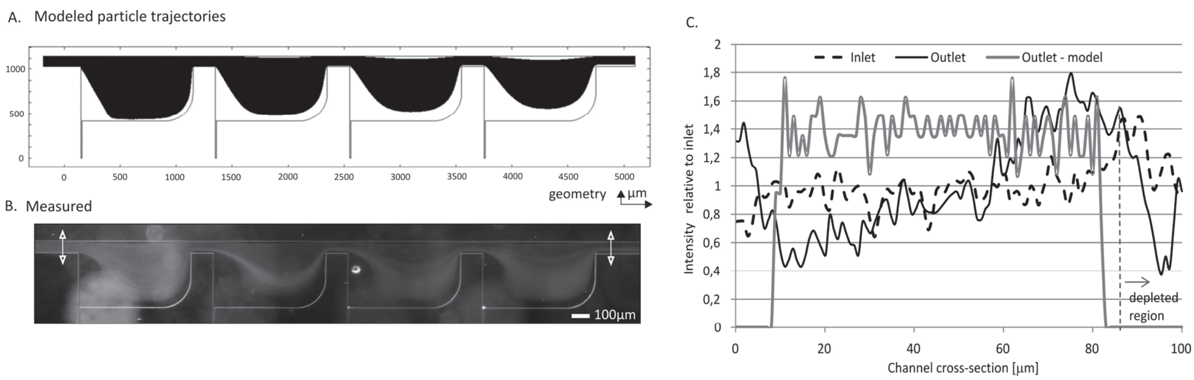

Fig. 2 Modeled (A.) and experimentally recorded (B.) particle trajectories representing the development of depleted layer after the geometric singularity: periodic widening of the channel. The particle distribution and the measured scattered light intensities (C.) in the outlet plane demonstrate the effect of lateral migration at an adequate flow rate.

3.2. Efficiency of plasma separation

The separation efficiency of the developed microfluidic structures were defined as the ratio of the sum of the plasma flow rate at the outlets of the daughter channels and the inlet flow rate. The calculated values are summarized in Table

2. Although the efficiencies seem to be in similar range in the case of geometries 2-5 the smaller singularities tend to have better outlet efficiencies.

Table 2. Modeled plasma separation efficiency at the six different geometric singularities. We proposed the 6th geometry as the most promising one for further studies and integration into the enhanced plasma separation system.

	1th geometry	2nd geometry	3rd geometry	4rd geometry	5th geometry	6th geometry
Geometries						
Plasma separation efficiency	0.43%	0.98%	1.08%	1.1%	1.37%	2.29%

4. Conclusion

Series of geometric singularities (six types of different expansions) were integrated with bifurcations branching from main stream channel in order to reveal their inertial effects on particle movement in the Zweifach-Fung type plasma separation systems. Flow behavior and particle distribution affected by geometric perturbations were characterized by Computational Fluid Dynamics (CFD) module of COMSOL Multiphysics (solving pressure and velocity field) and Particle Tracing Module (calculating particle trajectories). Test structures were fabricated in Polydimethylsiloxane (PDMS) and the performance of the different geometries was characterized experimentally recording particle trajectories by dark field microscopy applying different flow rates.

We proved that applying adequate flow rate regime (0.5 – 1µL/s) the inertial forces in geometrical singularities led to the recovery of the cell-free layer after the bifurcations although higher flow rates generate Moffat recirculation deteriorating the plasma purity. The effects of lateral migration processes were shown both in measurements and model results. The plasma separation efficiencies of the different geometries were estimated to define the most promising geometry to be integrated into the enhanced cascade type Zweifach-Fung plasma separation systems.

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