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I.   Abstract

An important field of study in microfluidics is in the realm of blood rheology in microdevices. Many types of geometries have been developed for different lab-on-chip applications for sampling and analysis. The majority of experimental and numerical studies have revolved around straight blood vessel geometries, but in recent years there have been more complex profiles analyzed, such as microbifurcations. Some devices are developed to study blood flow similar to the microvascular network, such as diverging and converging bifurcations to study arterioles, which form a closed network. Cell adhesion studies of microchannels are also common, where symmetric bifurcation and confluence has been examined. Since sharp turns as well as bifurcation and confluence are common, the hemodynamics should be examined for many different shapes and the effects of channel geometry to the adhesion phenomena should be looked at. Different devices have different goals, such as isolating circulating tumor cells from blood, separating leukocytes from blood and isolating circulating tumor cells from peripheral blood. Studies have been targeted in breast cancer, cervical cancer and smooth muscle cell applications. Some studies provide result as to the role that the hemodynamic forces have on the recruitment of the metastatic cancer cells to endothelial cells, but the effects of device geometry on adhesion isn't typically discussed formally. It has been shown that more complex geometries exhibit more non-uniform cell adhesion, adding to the confusion in the results and that an improvement in the velocity uniformity has been shown to improve the uniformity of the cell adhesion in sharp turn devices.

II.   Introduction

Different converging and diverging bifurcation studies have been shown in recent times in the biomedical microdevice field [1-5]. A representative example is used as the basis for mesh and boundary condition verification to the working fluid and flow conditions in the laboratory [1]. Examples of symmetric, asymmetric and nearly symmetric geometries have been computed similar to this case. A low cost method for fabrication was shown for biomimetic separation applications using xurography for molds to fabricate using polydimethylsiloxane (PDMS) soft lithography [5]. Blood plasma separation devices operate under the Zweifach–Fung effect, where in microcirculation, the erythrocytes, or red blood cells (RBCs) flow through a bifurcating region of a capillary blood vessel, and tend to flow into the vessel that has a higher flow rate, leaving few cells into the daughter vessel that exhibits lower flow. Other studies have been used to better understand the flow of red blood cells (RBCs) in similar geometry.

III.   Methods

Geometry was taken from past study. Commercial computational fluid dynamics (CFD) software ANSYS 15 was used for all aspects of geometry generation, mesh development, fluid analysis and optimization. Geometry was drawn in ANSYS DesignModeler and the mesh developed with approximately 200,000 elements. The simulation was computed three-dimensionally and compared well to experimental results (Figs. 1-3).
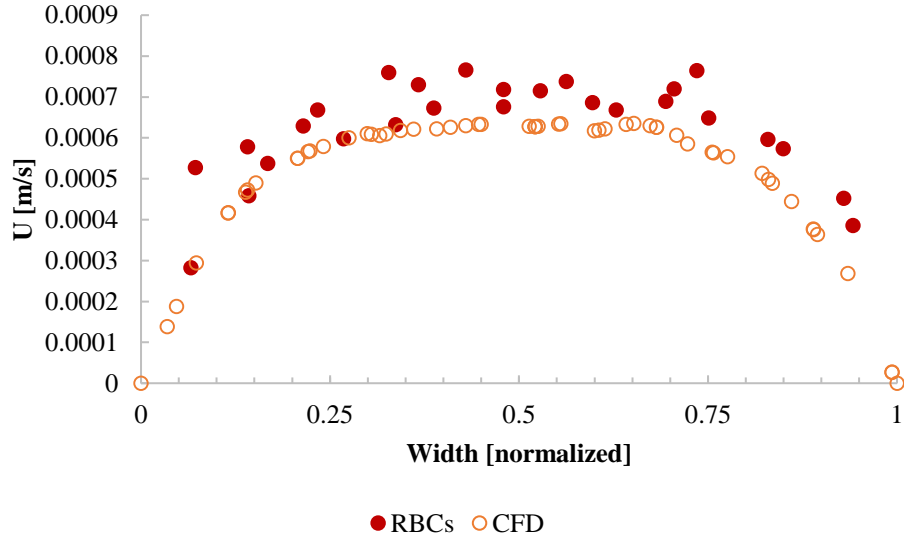
Fig. 1. Verification plot at cross section 120 μm before divergence of original geometry.
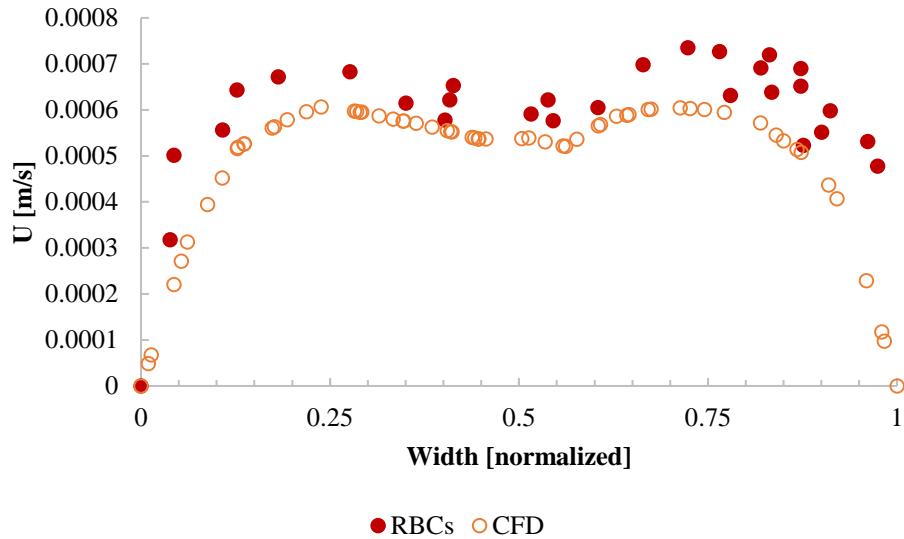
Fig. 2. Verification plot at cross section 35 μm before divergence of original geometry.
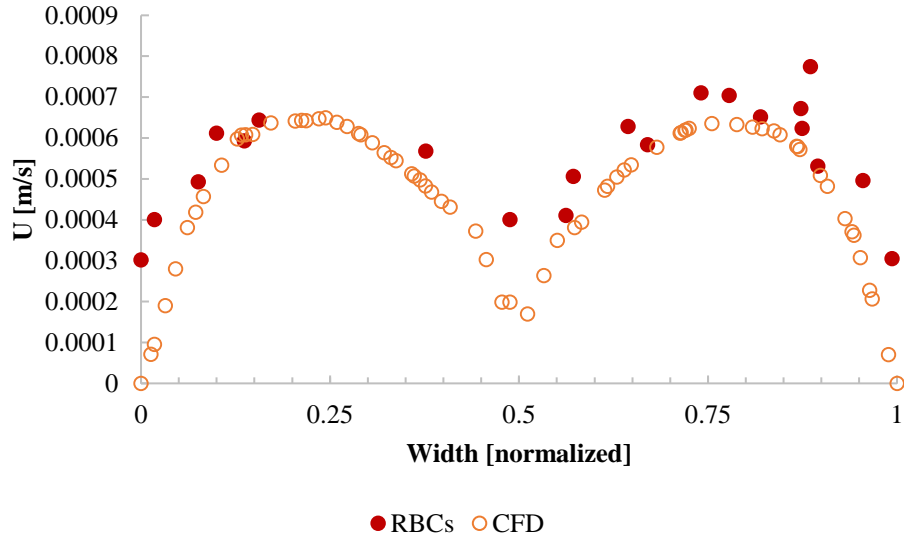
Fig. 3. Verification plot at cross section 5 μm before divergence of original geometry.

Boundary conditions were taken from previous experimental parameters, where the viscosity of blood was assumed to be 0.0045 kg/m-s with the density being 1046 kg/m^3. The mean velocity was assumed to be 0.00038 m/s [1]. The experimental work had a calculated Reynolds number of 0.0007. Blood was assumed to be Newtonian as done in previous work, continuum methods, such as the Carreau model showed little difference in this geometry and boundary condition. For future work, given greater computational expense, a much more complex and realistic multiphase approach would be more worthwhile, which considers blood as a multiphase suspension of deformable particles, and where sub-modeling occurs for the behavior of blood components. For the generation of the response surface, a Yeo-Johnson transformation was set for the output parameter of gamma uniformity index:

$$\gamma = 1 - \int_A \frac{\sqrt{(\bar{u} - u)^2}}{2 \cdot A \cdot \bar{u}} dA$$

where $\bar{u}$ is the average velocity and A is the cross sectional area. Gamma gives an indication of how uniform the flow is on a section cut and is the normalized root mean square of the difference between the local velocity and the spatial mean of the velocity integrated over the area of the clipped plane. A screening optimization with a sample size of 1000 was computed for a direct optimization to maximize the average gamma uniformity index between three clipped planes, with the left plane being stationed at 0.00300000 m from the inlet, which comes right at the divergence apex, the center plane, which is 0.00343301 m from the inlet and the right most plane, 0.00300000 m from the outlet, or 0.00386602 m from the inlet and at the convergence apex. Central composite design matrices auto-generated the design space. For the 3 variable study, which assessed inner blend, outer blend and middle blend (optimum radius turn), the auto defined setting was sufficient with 15 training runs. For the 2 variable study, which assessed outer blend and middle blend (optimum zero turn), the auto defined setting would have potentially undertrained the system with 9 runs, thus the training was stepped up to face-centered enhanced, which resulted in 17 runs. Face-centered enhanced was not selected for the 3 variable study as 29 runs would have been required, which would have increased the computational expense and may not have improved the system consistent with the increased labor.

IV.   Results and Discussion

Both the optimum zero turn and optimum radius turn studies produced improvement of the uniformity of the velocity (Tables 1 and 2), the effects of the variables and response point intersections are also shown (Fig. 4). Middle plane and center plane cross sections are shown of the velocity profiles (Figs. 5 and 6). Response surfaces between optimization methods also compared well. The screening method was compared to genetic algorithm response surfaces with 0.00% and 0.08% difference between predicted gamma uniformity index of velocity magnitude for optimum zero turn and optimum radius turn respectively. The genetic algorithm tended to show a higher amount of significant figures deeply into the noise for all variables, whereas the screening method resulted in a converged minimum and maximum of the design range for the inner and middle blends in the optimum zero turn and optimum radius turn cases respectively. However, the screening method revealed discrete results for the remaining parameters.

Table 1. Comparison between parameter values predicted from response surfaces of CFD computation.

Case	Inner Blend Radius (m)	Outer Blend Radius (m)	Middle Blend Radius (m)
Original	N/A	N/A	N/A
Optimum Zero Turn	N/A	0.00010000	0.00030198
Optimum Radius Turn	0.00004443	0.00024716	0.00050000
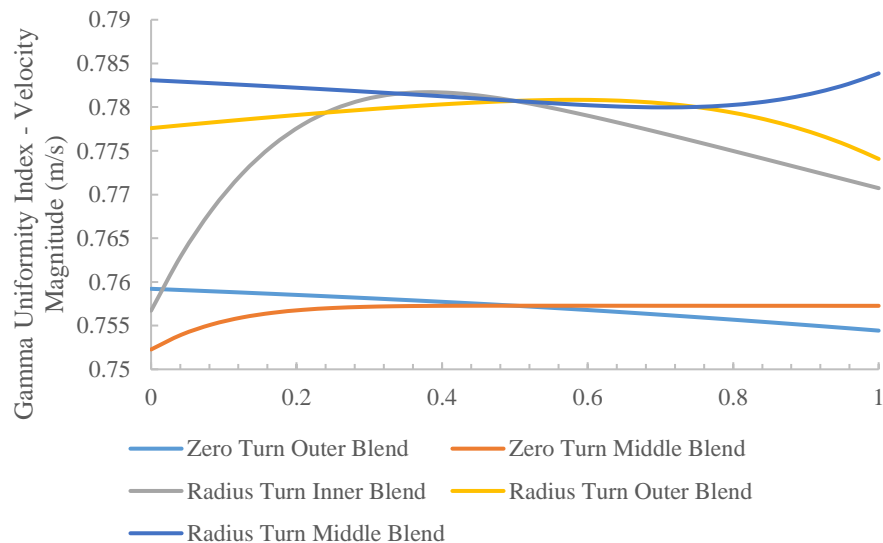
Fig. 4. Normalized plot to show decreasing and increasing parameters vs. the resulting response surface.
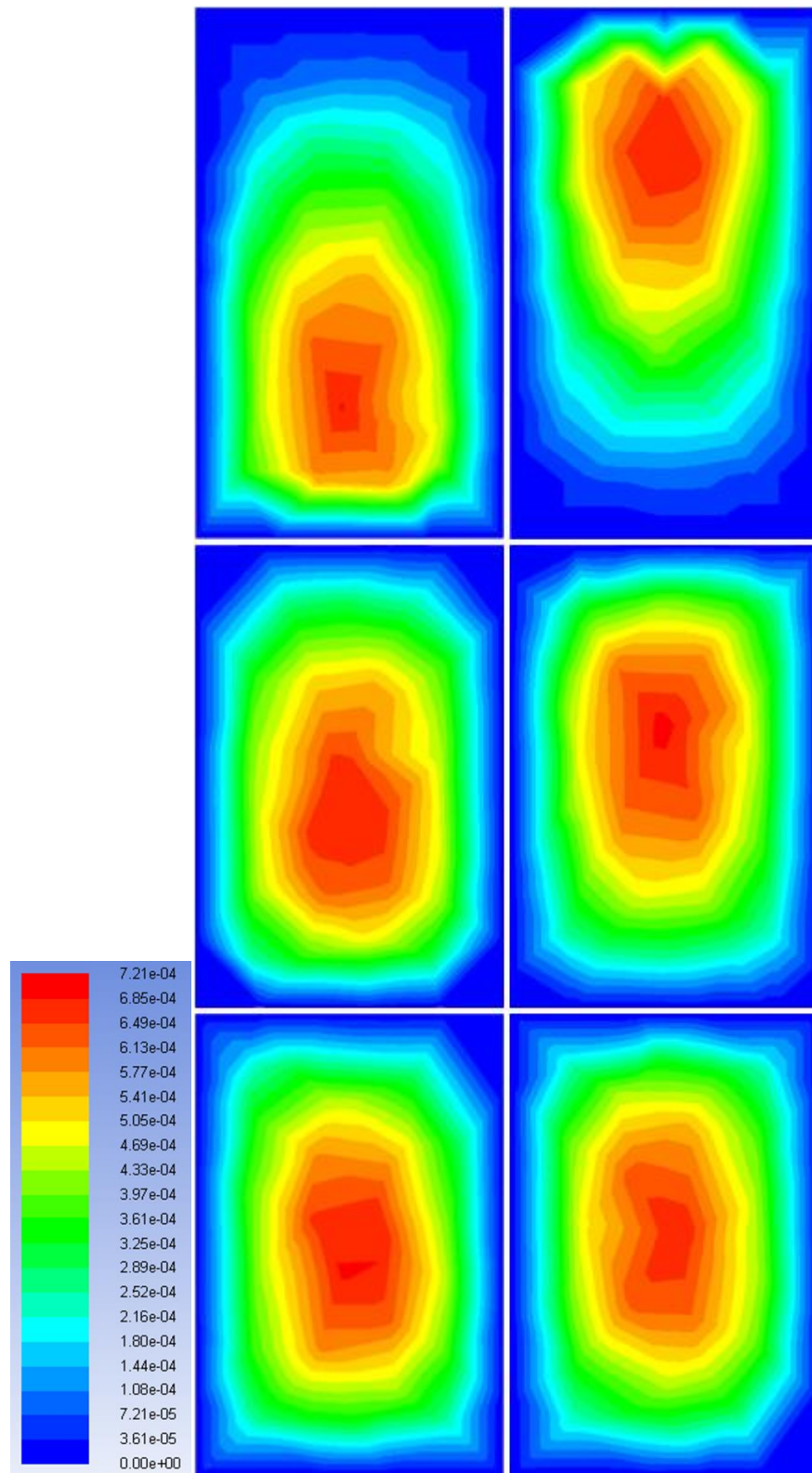
Fig. 5. Original vs. optimum zero turn vs. optimum radius turn middle plane (top to bottom), velocity magnitude cross section (m/s).
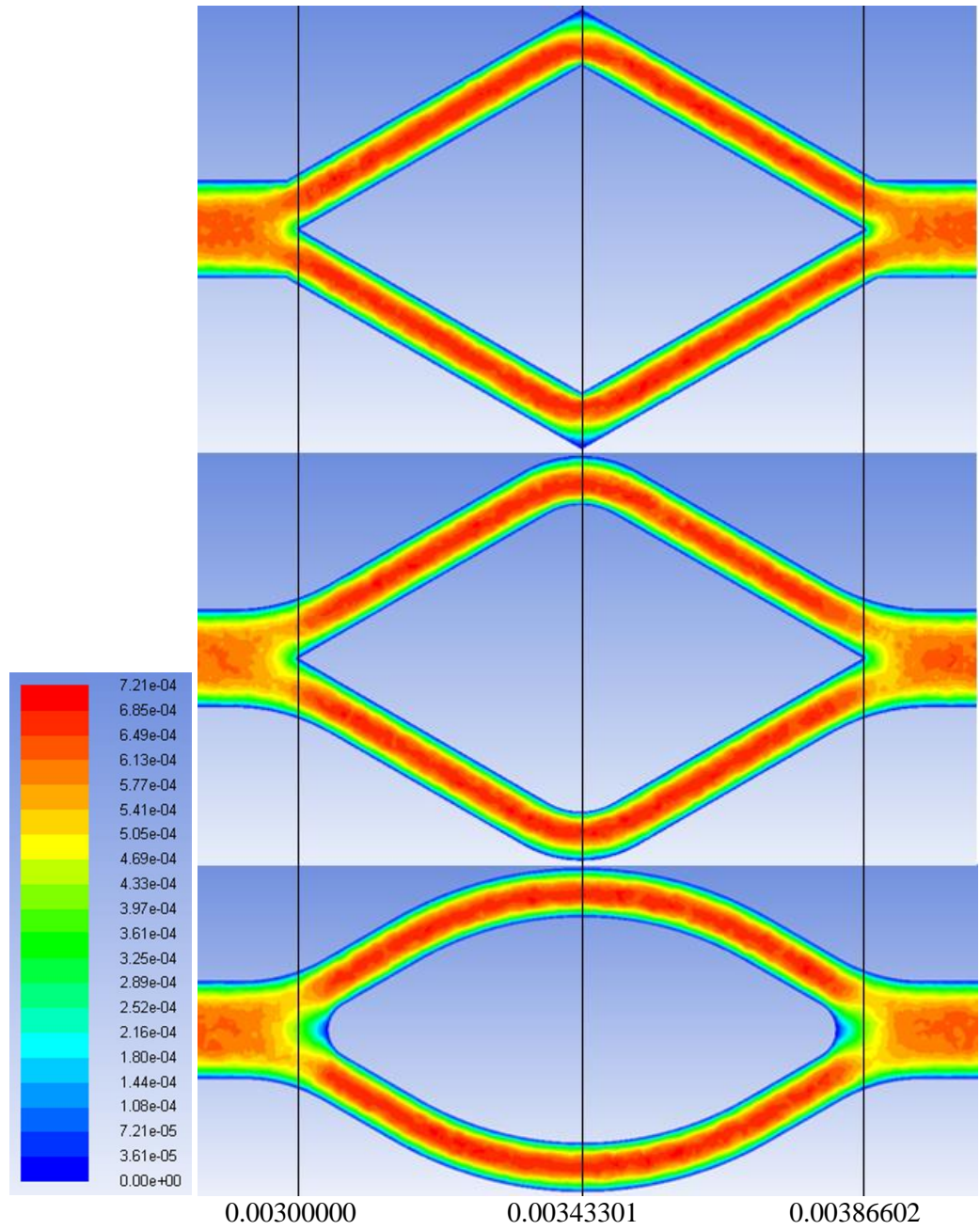
Fig. 6. Original vs. optimum zero turn vs. optimum radius turn center plane (top to bottom), velocity magnitude cross section (m/s) along *x* axis (m).

Table 2. Comparison between design of experiment prediction from response surfaces and actual result in CFD computation.

Case	Prediction (m/s)	Actual (m/s)	Percent Error	Percent Improvement Optimized Actual
Original	N/A	0.74295747	N/A	N/A
Optimum Zero Turn	0.75921000	0.75657773	0.3479%	1.83%
Optimum Radius Turn	0.78424000	0.78043222	0.4879%	5.04%

V.   Conclusion

Some bifurcating diverging and converging microchannels have a sharp diamond-like shape as the profile while others may have an ovate inner part and boundary with slightly more curvature [4]. It has been suggested that curved microchannels provide a strong platform where uniform adhesion is needed [6]. Many microchannel geometries are complex, and some are even in spiral configurations [7]. Typically, a sharp-turn in a microchannel will create near-zero velocities at a turn region, where a number of cells adhere or become collected. In a U-turn turn channel, if the edges are sharp, near-zero velocities and cell adhesion will typically occur on the outer edges, where as a full radius can have greater uniformity. Experimentation would be needed, but it may not be the case in all geometries that a round region creates less adhesion than a sharp region as indicated by the dramatic increase in lower and near-zero velocities near the divergence portion of the optimum radius turn microchannel. The zero turn microchannel produced very limited lower velocity or near-zero velocity regions, which is the typical cell adhesion region in the device. In addition, usually in a straight diverging and converging bifurcation, the confluence portion will have a cell free layer, experimentation would reveal the effects of a radius in a geometry such as that, if the cell free layer would be similar or become depleted in comparison to a sharp confluence. Near the divergence, for instance in the case of a biomedical microdevice studying cell adhesion of cancer cells, depending on the fabrication and design of the device, the resulting flow and adhesion could be affected. As expected, the addition of a radius near the apex of the middle plane greatly limited the near-zero velocity regions in comparison to the original device.

VI.   References

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