Modeling a Microfluidic Device to Capture Single Muscle Fibers for Analysis

Amit Sawhney, Vratislav Kostal PhD, Maggie Donoghue PhD, and Edgar A. Arriaga PhD
Department of Chemistry

UNIVERSITY OF MINNESOTA
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Introduction

Recently, a new technique was developed in Dr. Arriaga's lab to culture single muscle fibers[1]. The cultured fibers are functional and have mitochondrial membrane potential for up to 48 hours, however the heterogeneous nature of the fibers prevent valid conclusions about ROS production and aging to be made. To be able to further analyze and provide treatment to the fibers, new technology must be developed. This study aims at creating a device based upon microfluidic theory to immobilize the fibers and thus provide a better way to analyze the fibers. In the end, we wish to fabricate a device that will test a high throughput of fibers and will allow safe treatment of drugs and quantitative measurements to be taken. To start this process, design and computer-aided simulation of the device were made.

Methods

All design and simulation of the device was conducted through Ansys software. The main suite of Ansys Workbench contains Ansys DesignModeler, Ansys CFX Mesh, and Ansys CFX/CFX-Post for the simulation and analysis of fluid flow.

The first model of the device developed was a simple two-channel unit based upon the schematic of the Whiteside[2] device. DesignModeler allowed for a drawing to be made in the x-y plane and then be extruded out 0.15 mm in the z-axis for the development of a 3D model. The dimensions of the device were simple that the inlet and outlet regions were 4mm in length, the bifurcations splitting and connecting the two channels were curved at a 1 mm radius, and the clamping region for the fibers tapered down from a 0.15 mm width to 0.075 mm (based upon data for average size for cultured fibers). This model was then meshed out using CFX Mesh with a 0.025 mm body spacing, 0.001 mm min panel length, 0.025 mm max panel length, and a 0.0125 mm 5 layer boundary around the sides of the device. This produced a mesh over 500k elements (most of which tetrahedral).

A second model trying to represent a static fiber being caught in on of the channels was made as well using the first model and inserting a geometry based upon the average length and radius of the fiber (0.430 mm and 0.074 mm respectively). After insertion of the geometry into the bottom channel, a boolean subtraction was made to cut out that area from the device, as if a fiber is blocking the region.

Simulations of a pressure driven flow were conducted on both models using CFX, which solves the full Navier-Stokes differential equations set up for a pressure driven flow through a set boundary. The fluid used was isothermal (25ºC) water and it ran through the main domain (the device) with 3 distinct boundaries: the inlet, the outlet, and walls. The walls were deemed as no-slip, the inlet had a 1.5 kPa static pressure applied and the direction of flow was that of the zero gradient, and the outlet was classified as an opening with 0 kPa static pressure (to create a pressure gradient driving the flow) and the flow was directed normal to the outlet. The turbulence model was set through the k-epsilon model to account for velocity fluctuations. This is a standard that uses a scalable wall-function approach to improve robustness and accuracy when the near-wall mesh is very fine. Post-processing and analysis was done through CFX-Post.

Results

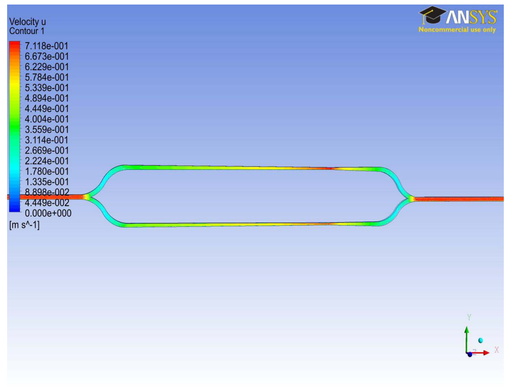

Fig. 1 Flow velocity contour plot through first 2-channel model

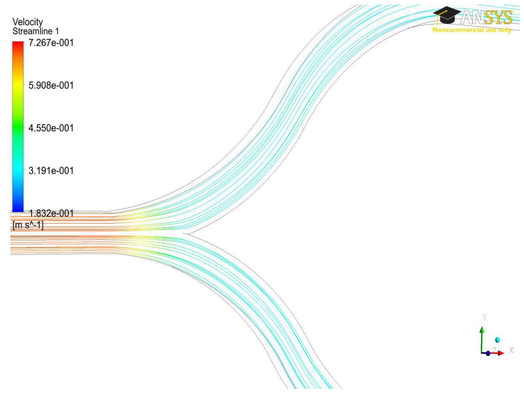

Fig. 2 Velocity streamlines showing particle movement through device splitting into the 2 channels

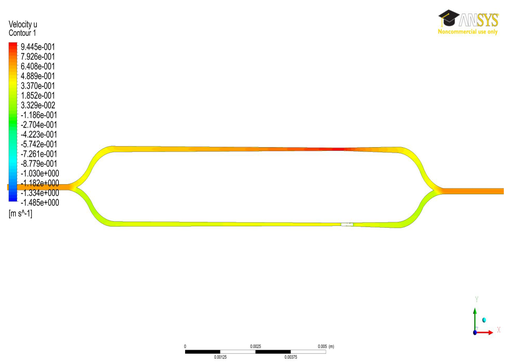

Fig. 3 Flow velocity contour plot of first model with fiber captured in bottom channel

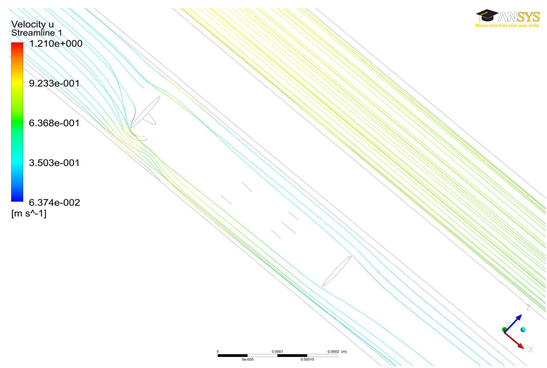

Fig. 4 Velocity streamlines showing how the flow moves around the fiber

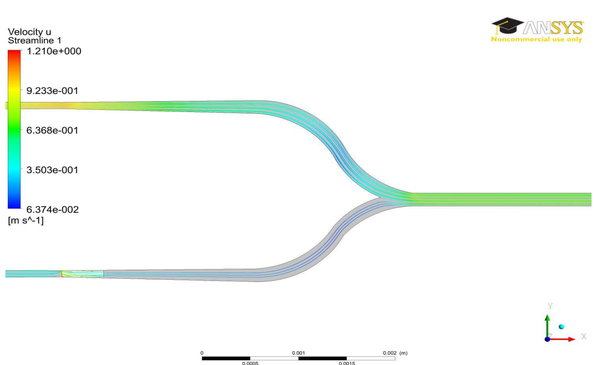

Fig. 5 Velocity streamlines indicating the difference in flow present between channels with fiber is captured

Conclusion

After countless modeling and simulation, a final design for a 2-channel model was developed. Under pressure driven flow simulations, the model showed to have a steady flow from when splitting at the bifurcation and converging at the end. This is due mostly to the radius of the curvatures allowing for a slower drift around the curves. The general flow velocity increases in the tapered area of both channels, as it should according to fluid dynamic theory. When a simulated static fiber was present in the tapered region, more flow was directed towards the other channel and the flow velocity was greatest in the opposite tapered region. The velocity streamlines generated showed that the flow was directed around the fiber successfully. Some detection of the streamlines hitting the front of the fiber are present, but the measured force was not significant.

Future

Now that a 2-channel model has been developed, more models with more channels can be developed to gain a higher throughput. These new models will be based upon the design and simulation of this 2-channel model. Then, the new models can be simulated further to make sure that allow for a steady flow. Soon CAD drawings of these 3D models will be made so that the devices can be fabricated and tested in a wet-lab setting with the actual cultured muscle fibers. After the fabrication of the devices, protocols can be developed that will measure alterations in calcium homeostasis, increase in ROS production, and loss in mitochondrial membrane potential. These measurements will take place with the use of solution delivery through the device and high-powered imaging techniques.

References

1 Arriaga, Edgar A, et al. "Analysis of Superoxide Production in Single Skeletal Muscle Fibers," Analytical Chemistry 82(11), May 2010: 4570-76.

2 Whitsides, George M. et al. "A Microfabricated Array of Clamps for Immobilization and Imaging C. elegans," Lab Chip 7, May 2007: 1515-23.