Simulating Fluid Flow through a Culture Chip for Cell Migration Studies in Microgravity

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INTRODUCTION

Exposure to microgravity is known to alter genomic and proteomic expression [1-4] and suppress immune cell activity [5]. Both of these changes may influence cancer development. By studying cancer cells in this environment, we may uncover novel therapeutic targets. SUNY Polytechnic Institute and SpacePharma, Inc. have teamed up to study the effect of microgravity on cancer cell migration. This will be achieved using a device to conduct cell-based experiments both in on-ground simulators and in Low Earth Orbit (LEO). To optimize operational flow parameters and design, simulations of fluid flow through the devices were run using the Computational Fluid Dynamics module of COMSOL Multiphysics 5.2.

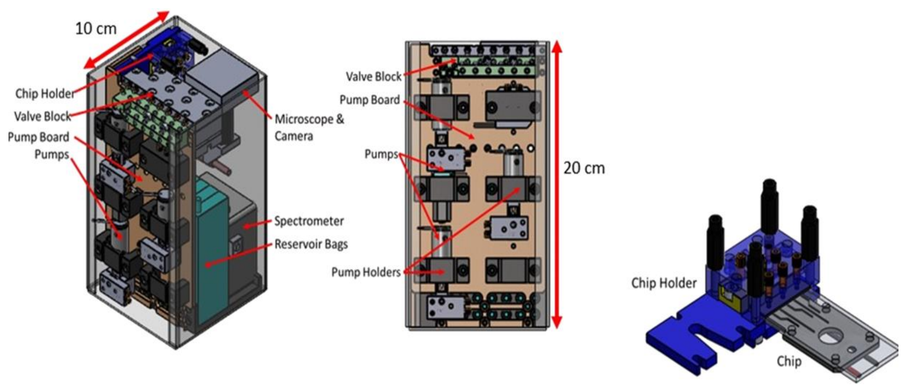

Figure 1: Illustration of the migration lab. Source: SpacePharma, Inc.

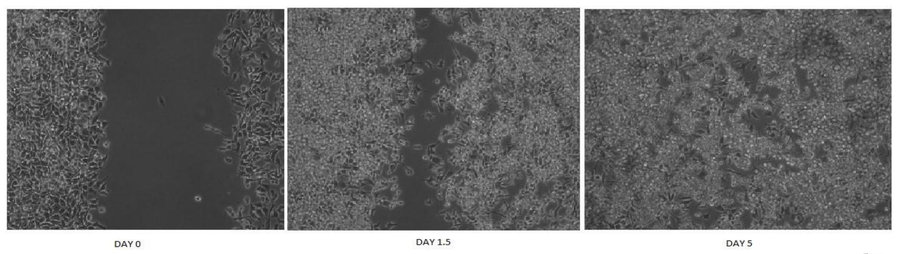

Figure 2: Wound healing assay using Mena^{INV} MDA-MB-231 cells to demonstrate cell migration. Scale bar: 100 µm.

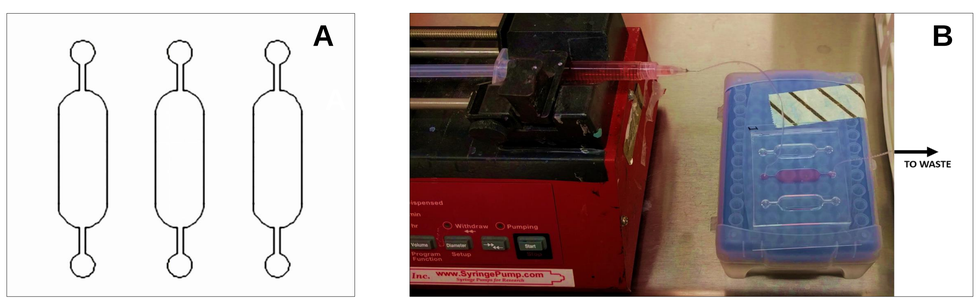

Figure 3: A) CAD representation of cell culture chips. B) Setup for conducting cell culture experiments within a chip.

COMPUTATIONAL METHODS

The Computational Fluid Dynamics (CFD) module of COMSOL Multiphysics 5.2 was used for all fluid flow simulations. Two separate studies were conducted. A Single Phase Flow (spf) study was used for flow of media through the outer channels and the culture chambers. A migration channel with dimensions of 0.6 X 1 X 1.5 mm was attached to the side of a culture chamber and a Transport of Diluted Species (tds) study was used for diffusion of the chemoattractant (EGF with a diffusion coefficient of D = 5 X 10^{-11} m^2/s) across the migration channel. The equations used in the laminar flow and diffusion studies were as follows.

LAMINAR FLOW

$$\rho(u \cdot \nabla)u = \nabla \cdot [-pI + \mu(\nabla u + (\nabla u)^T] + F$$

$$\rho \nabla \cdot (u) = 0$$

with $u = -U_0 n$ (INLET) and

$$[-pI + \mu(\nabla u + (\nabla u)^T]n = -p_0 n \text{ (OUTLET)}$$

DIFFUSION

$$\frac{\partial c_i}{\partial t} + \nabla \cdot (-D_i \nabla c_i) = R_i$$

$$N_i = -D_i \nabla c_i$$

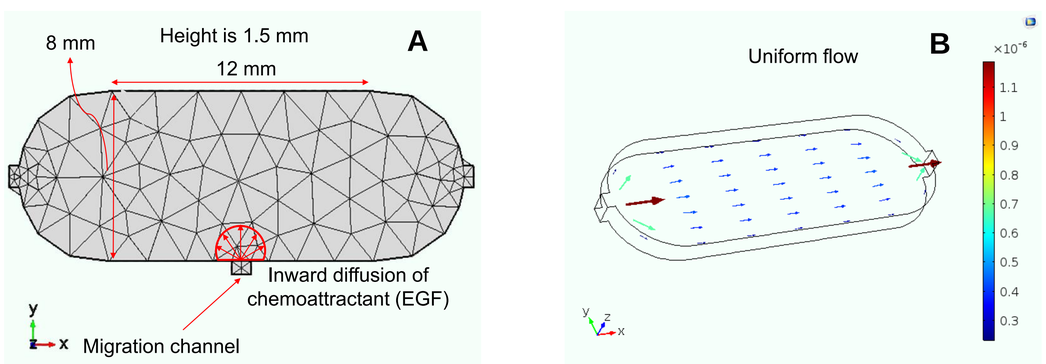

Figure 4: A) COMSOL drawing of the chip with free triangular meshing. Future designs will feature multiple chips connected by migration channels. B) Simulation of uniform flow through the latest version of the chip at a flow rate of 180 µL/min. Note the elongated middle and rounded edges.

RESULTS

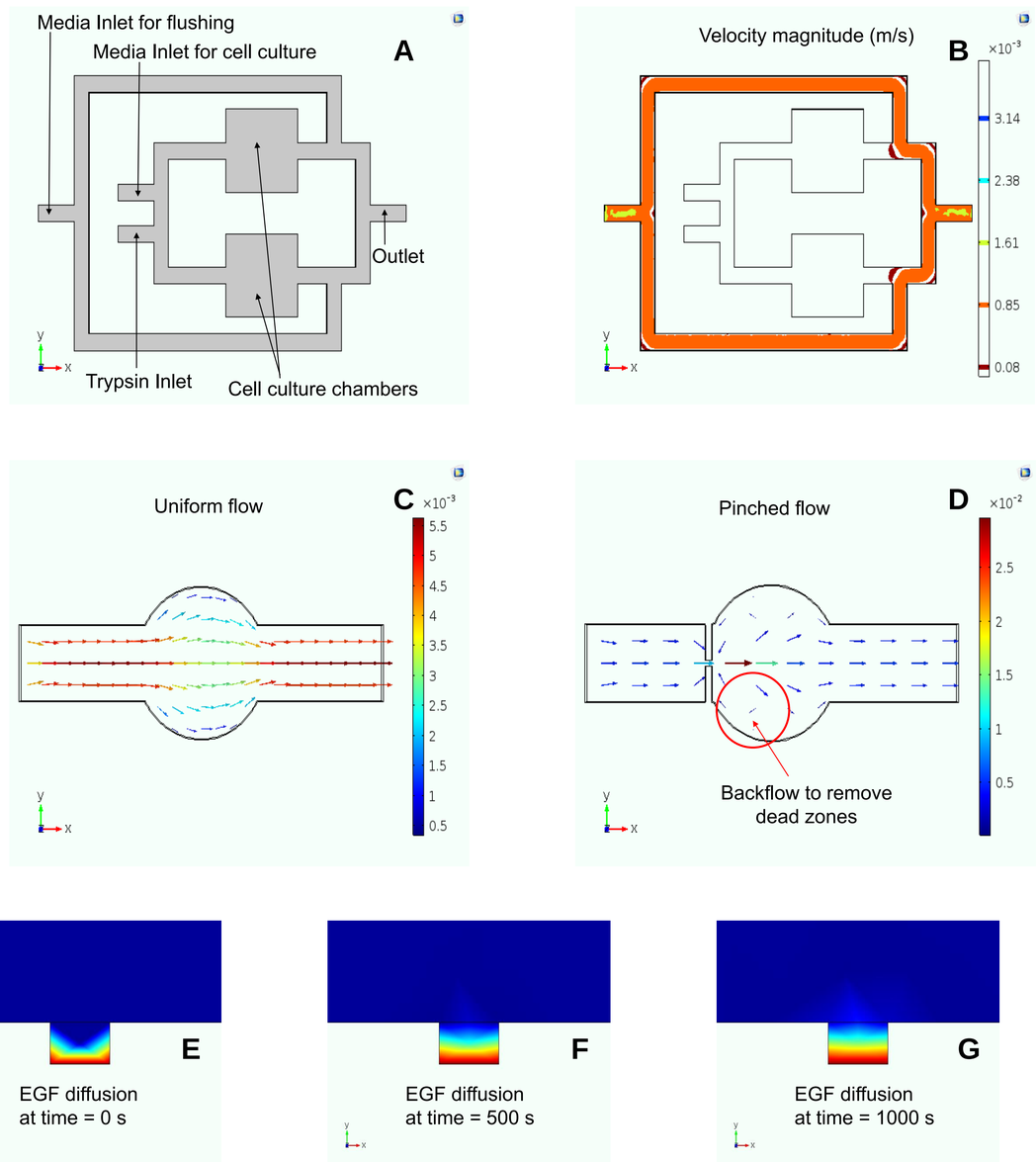

Figure 5: A) COMSOL drawing of the entire culture unit with channels for media and trypsin (to lift cells while passaging). B) Simulation of flushing media through the outer channels of the culture unit. An iso-surface velocity plot is used to show the path taken by the media. Note that there is a chance of backflow into the cell culture chambers. C) Simulation of fluid flow through a circular culture chamber to promote uniform flow and prevent 'dead zones' within the chamber. D) The same simulation with pinched flow at the inlet to aid with circular flow and removing 'dead zones' if present. E), F) & G) Simulation of diffusion of 40 µM EGF through a migration channel (as shown in Figure 4A) attached to the side of the chip at 0, 500 and 1000 s respectively.

CONCLUSIONS AND FUTURE WORK

Preliminary simulations point to the need for using chips with rounded edges and an elongated middle to ensure maximum growth and minimum 'dead zones'. The timescale for EGF diffusion through migration channels is suitable for cell migration studies akin to traditional wound healing assays. Future work – Experiments to study cell migration using chips with integrated migration channels.

ACKNOWLEDGMENTS

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