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

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Abstract

Microgravity provides an opportunity to study systems without effects such as sedimentation, hydrostatic pressure and non-diffusive types of mass transfer. Examining biological processes under such conditions has potential applications in fields such as tissue engineering, drug testing, vaccine development, stem cell propagation and protein crystallization. Exposure to microgravity is known to cause genomic and proteomic alterations [1-4] and suppress immune cell activity that may influence cancer development [5]. The Colleges of Nanoscale Science and Engineering (CNSE), SUNY Polytechnic Institute and SpacePharma, Inc. have teamed up to develop a system, as seen in Figure 1, to study the migration of metastatic cancer cells by isolating gravity as an experimental variable and assessing its contribution to earth-based cellular function. Initial development will include lab-scale functional tests and progress to an on-ground simulator with the ultimate aim being to build a system ready for space-flight to Low Earth Orbit (LEO).

Due to limitations in simulating microgravity for experiments on earth, there is a need to model fluid flow through the culture unit of the system. This will assist with design considerations and ensure proper device function. Fluid flow simulations will be run using the CFD Module of the COMSOL Multiphysics® software for values of g ranging from 1g to microgravity and will be restricted to single phase flow (spf) under laminar conditions. Figure 2 shows a top view of simulating media flushing through the outer channels of the unit and points to the need to avoid backflow into the culture chambers. Material properties for the cell chamber base are currently chosen as those for glass but may change by accounting for confluency of adherent cells. Similar simulations for fluid flow through inner channels specifically allocated for trypsin, to lift cells, and media, to culture cells, will be used to improve design. Additionally, simulations of the transport of diluted species (tds) like a chemoattractant (EGF) will be used to test the efficiency of a chemical gradient for cell migration.

Figure 3 shows the results for simulations with preliminary designs for the culture chambers. Pinching flow at the inlet may help with circular flow and prevent the formation of dead zones. Newer designs have an elongated middle with rounded edges. Figure 4 shows the diffusion of chemoattractant (EGF) across a migration channel attached to the side of the culture chambers. This will help with testing the chemical gradient needed to initiate cell migration. Such simulations will help in choosing operational flow parameters

for the device and provide valuable information for both the lab-scale experiments as well as any future experiments in space.

Migration studies on cancer cells in true microgravity can lead to the discovery of novel therapeutic targets for their metastatic behavior. Designing a robust system to study such migration is an essential starting point. Simulations of fluid flow through the system will not only help in designing the culture chip for use in the on-ground simulator but also help ensure space-flight compatibility of the system.

Reference

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[4] TT Chang et al., Spaceflight impairs antigen-specific tolerance induction in vivo and increases inflammatory cytokines, FASEB journal : official publication of the Federation of American Societies for Experimental Biology, 10.1096(2015)

[5] DV Jhala et al., Microgravity alters cancer growth and progression, Current cancer drug targets, 14, 394-406(2014)

Figures used in the abstract

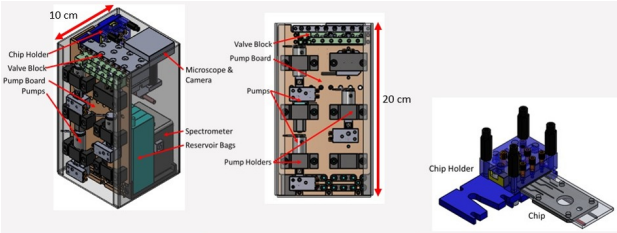

Figure 1: Illustration of the migration lab. Source: SpacePharma, Inc.

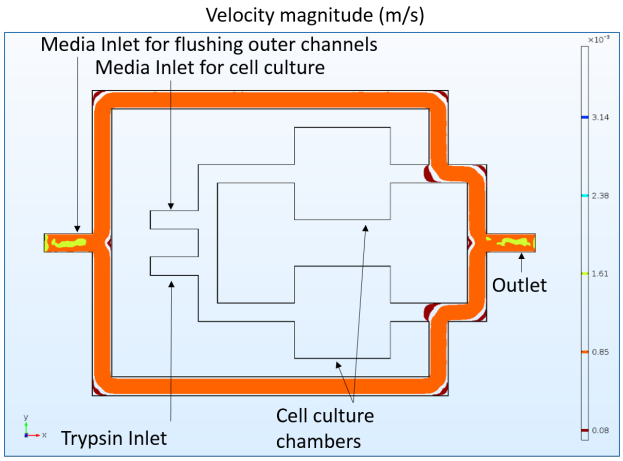

Figure 2: Top view of culture unit with a simulation of flushing media through the outer channels.

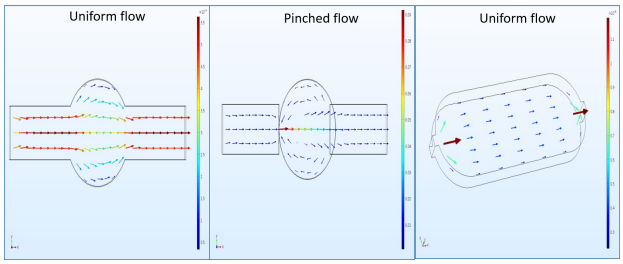

Figure 3: Simulating media flow through various iterations for the shape of the culture chamber.

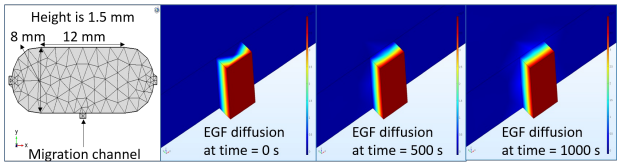

Figure 4: Simulation of diffusion of chemoattractant across migration channel.