COLLEGES OF NANOSCALE
SCIENCE + ENGINEERING
SUNY POLYTECHNIC INSTITUTE

COMSOL
CONFERENCE
2016 BOSTON

SIMULATING FLUID FLOW THROUGH A CULTURE CHIP FOR CELL MIGRATION STUDIES IN MICROGRAVITY

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CASTRACANE LAB

THE PROJECT

GOAL: To study cancer cell migration in microgravity

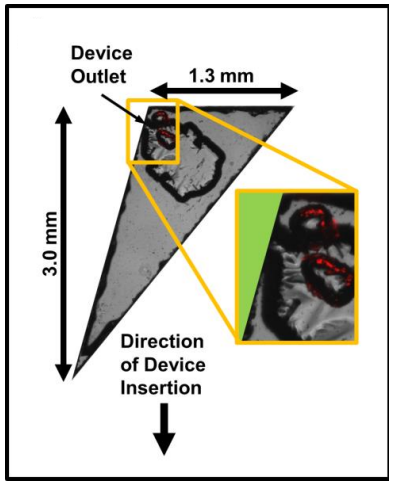
NEED: To uncover potential therapeutic targets for cancer cells

CNSE Role: Design cell migration experiments and study how migration differs in microgravity

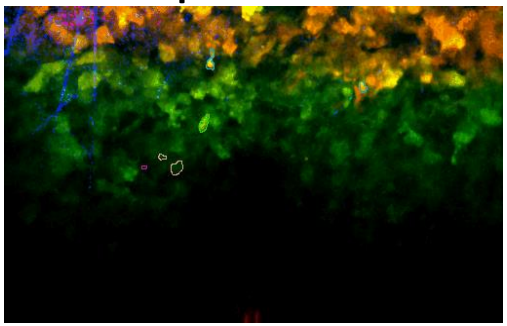
SpacePharma Role: Build an end-to-end system to facilitate such studies in Low Earth Orbit

LAB BACKGROUND - NANIVID

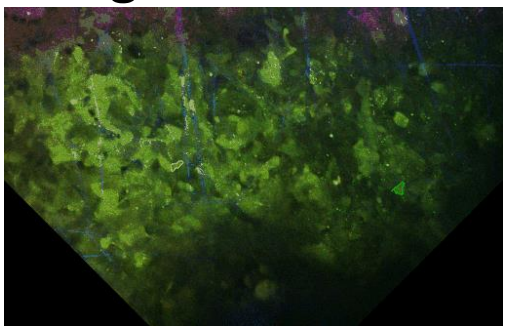
- Nano Intravital Device – an implantable device to study cancer cell migration
- Releases EGF causing migration of cancer cells



2 µM EGF



Negative Control



Scale bar: 100 µm

We are trying to rework such experiments in microgravity

Raja *et al.* (2012) | Williams *et al.* (2016)

THE MIGRATION LAB

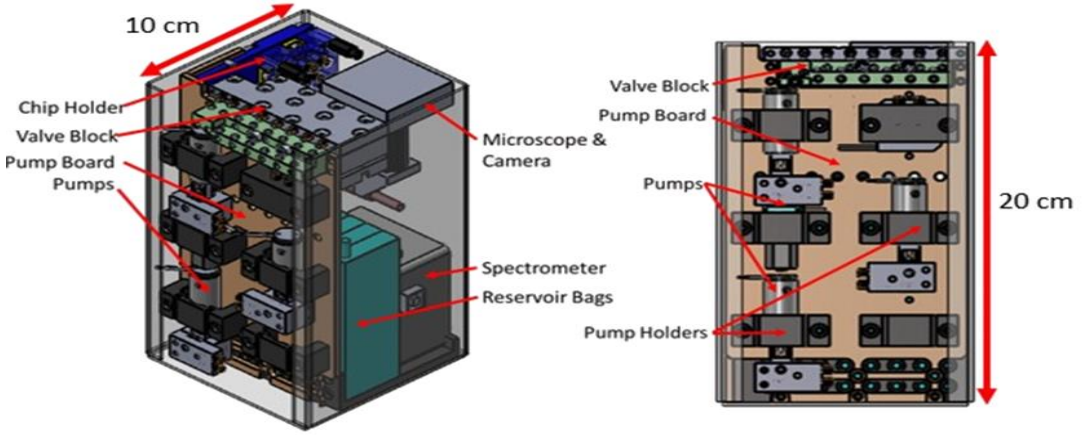
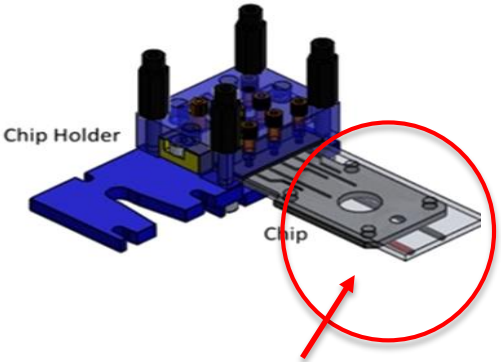


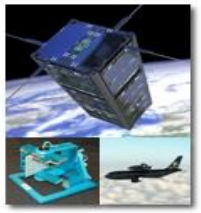
Illustration of the migration lab



We build the chips

Develop Research Strategy

Customize Lab



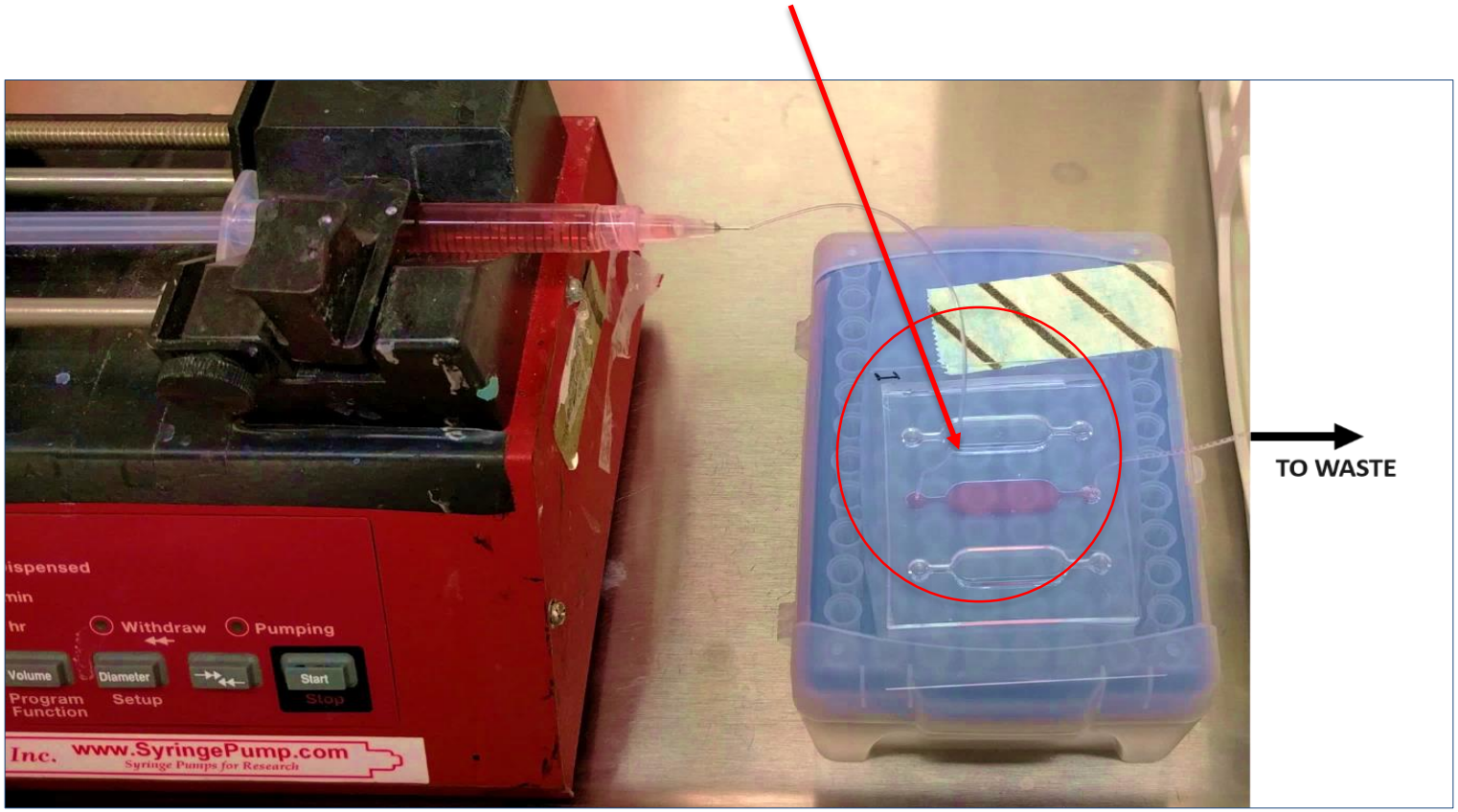
Place Lab in Microgravity

Control Experiment from Earth

Source: SpacePharma, Inc.

ROLE OF COMSOL MULTIPHYSICS

To simulate fluid flow through the chips we build



By default gravitational forces are not taken into account

Computational Fluid Dynamics Module

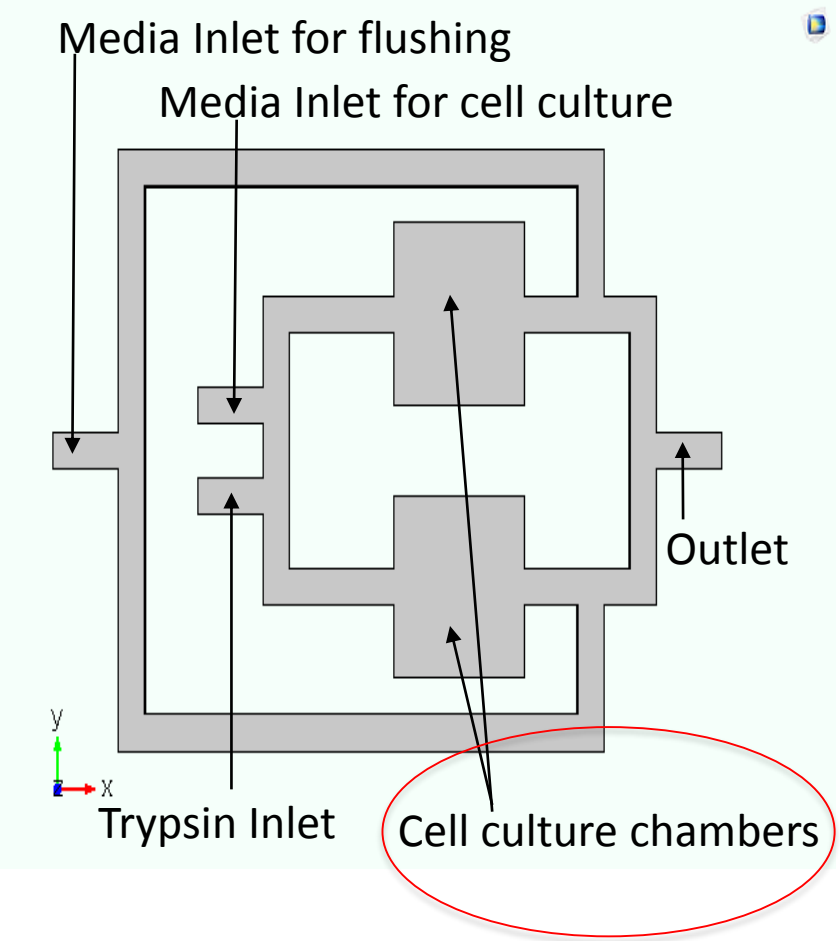
Single phase flow (spf) study on cell growth media (DMEM) under laminar conditions

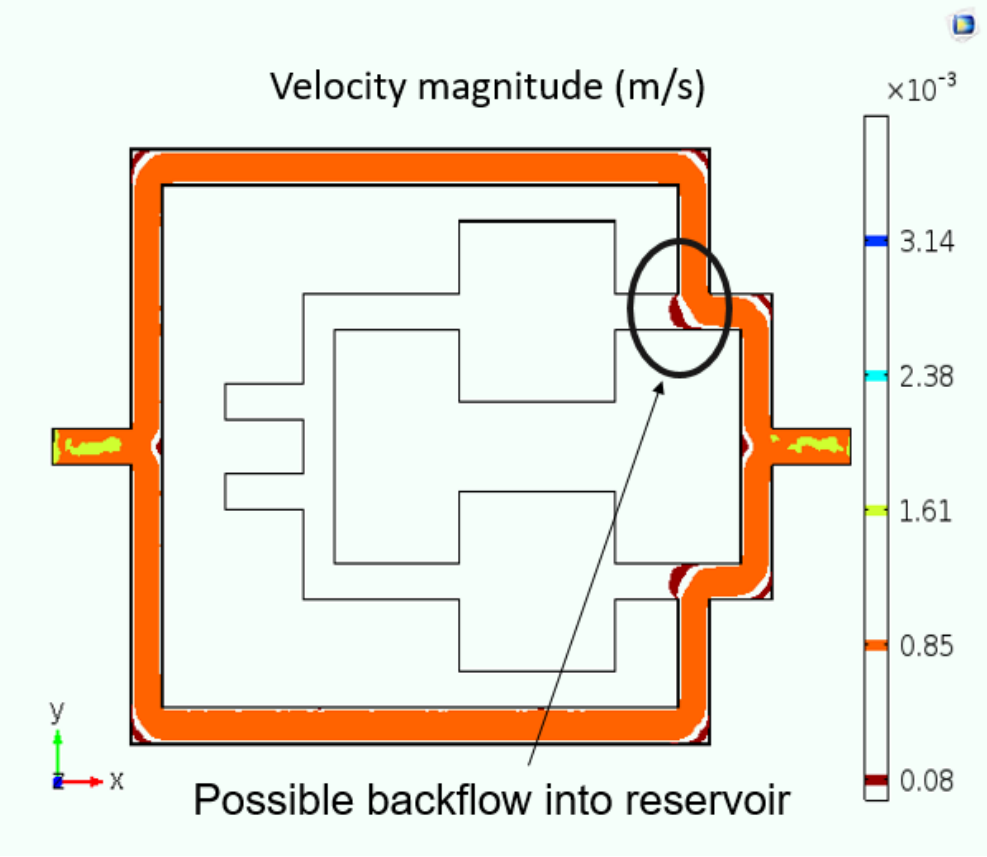
- To determine optimum shape of culture chip and operating flow rate range

Transport of diluted species (tds) study for diffusion of chemoattractant (EGF) across a migration channel

- To conduct experiments on practical timescales and estimate migration rate

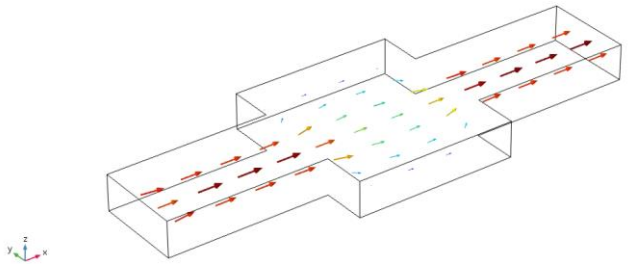
INITIAL CULTURING SYSTEM



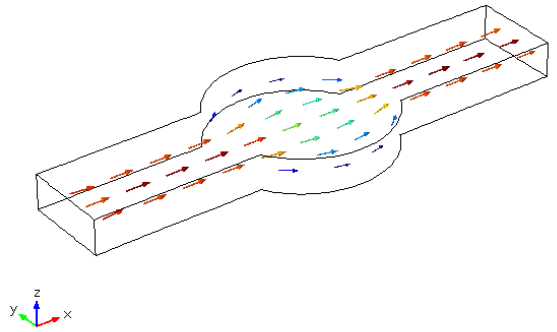


SHAPE OF CULTURE CHAMBER

Uniform flow
Rectangular chamber

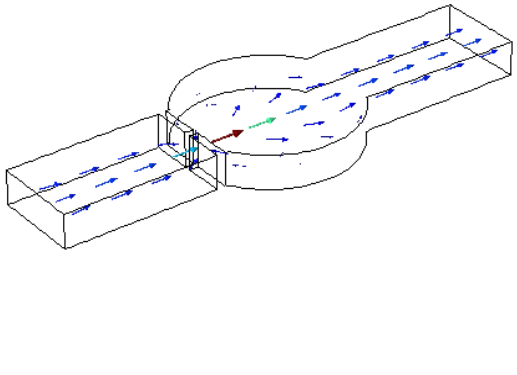


Uniform flow
Circular chamber

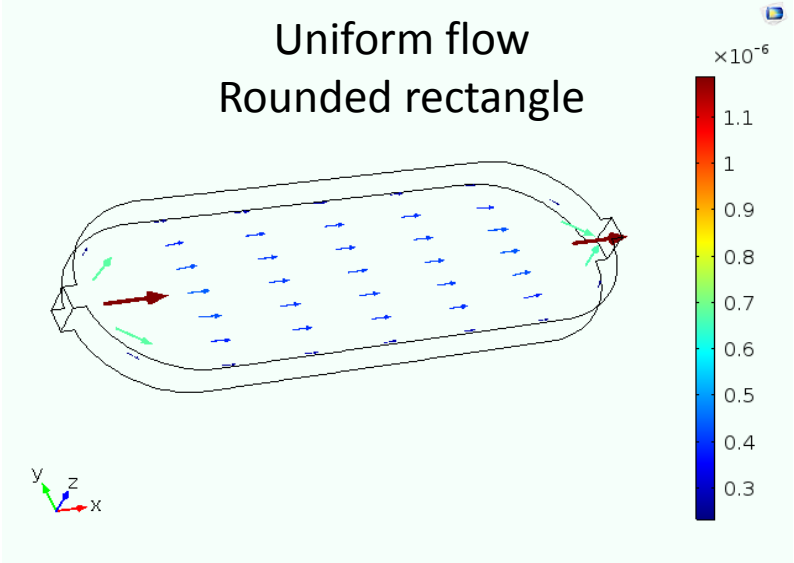


m/s

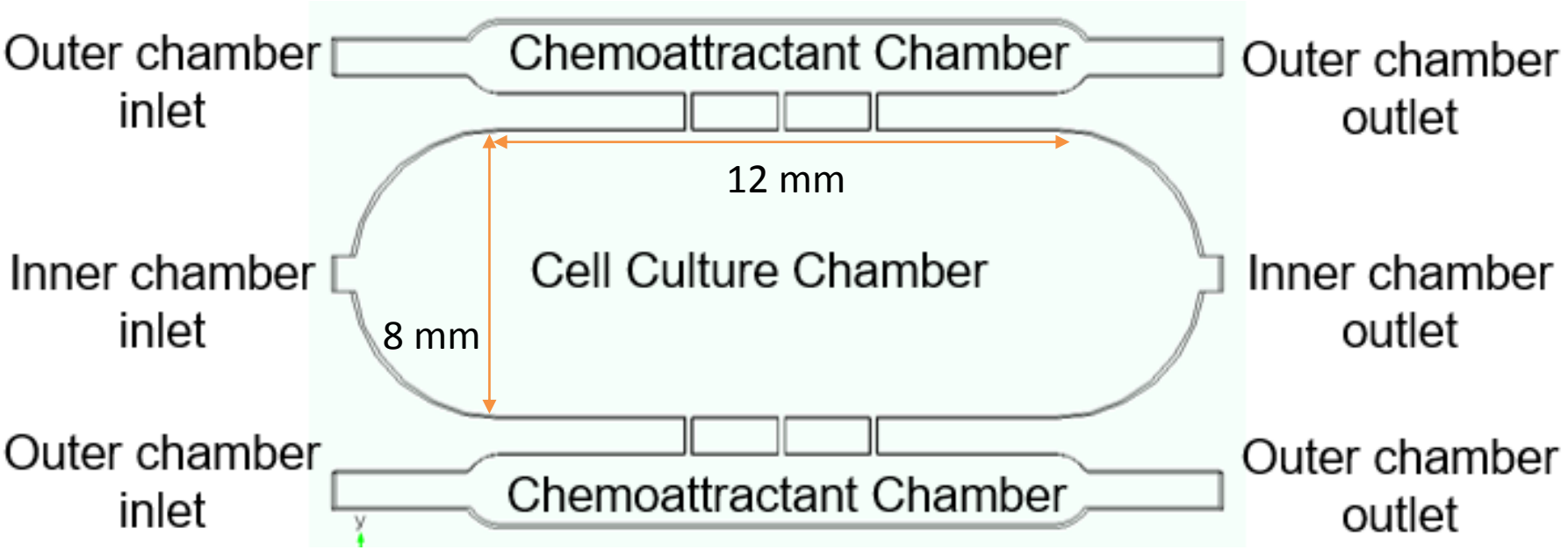
Pinched flow
Circular chamber



Uniform flow
Rounded rectangle

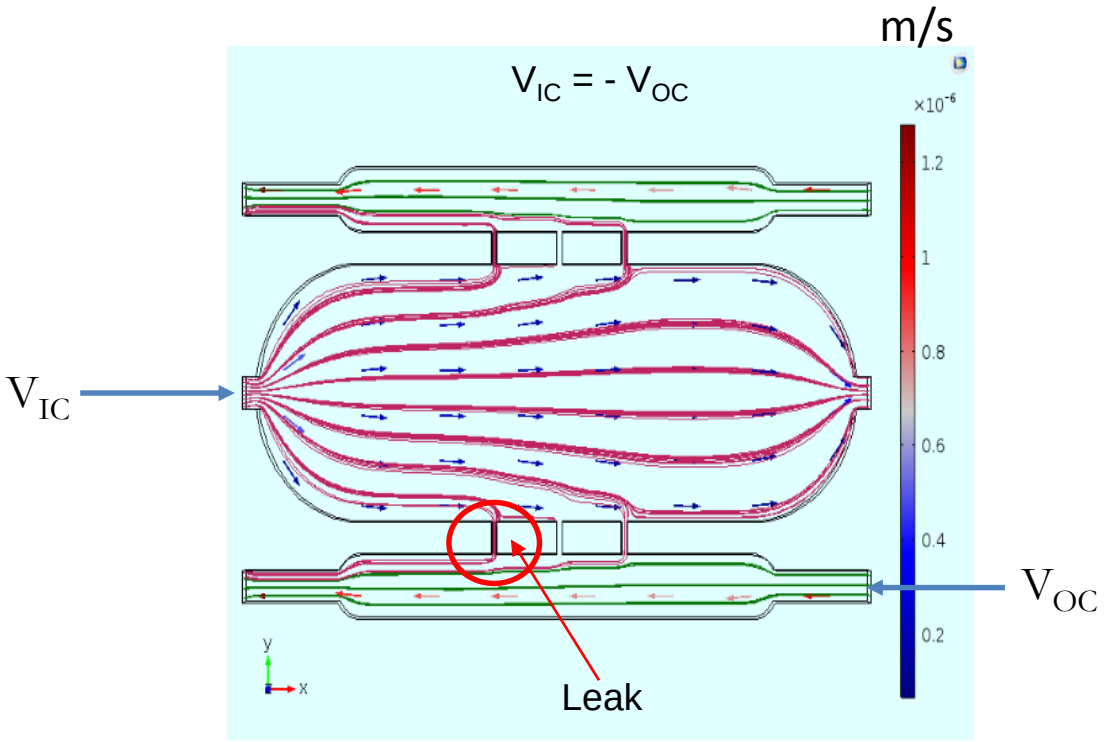


CURRENT DESIGN OF CULTURE CHIP



- Current version of the chip has 3 reservoirs
- Diameter of inlet and outlet is 1 mm
- Migration channel is 5 times narrower than inlet
- Height throughout is 1.5 mm

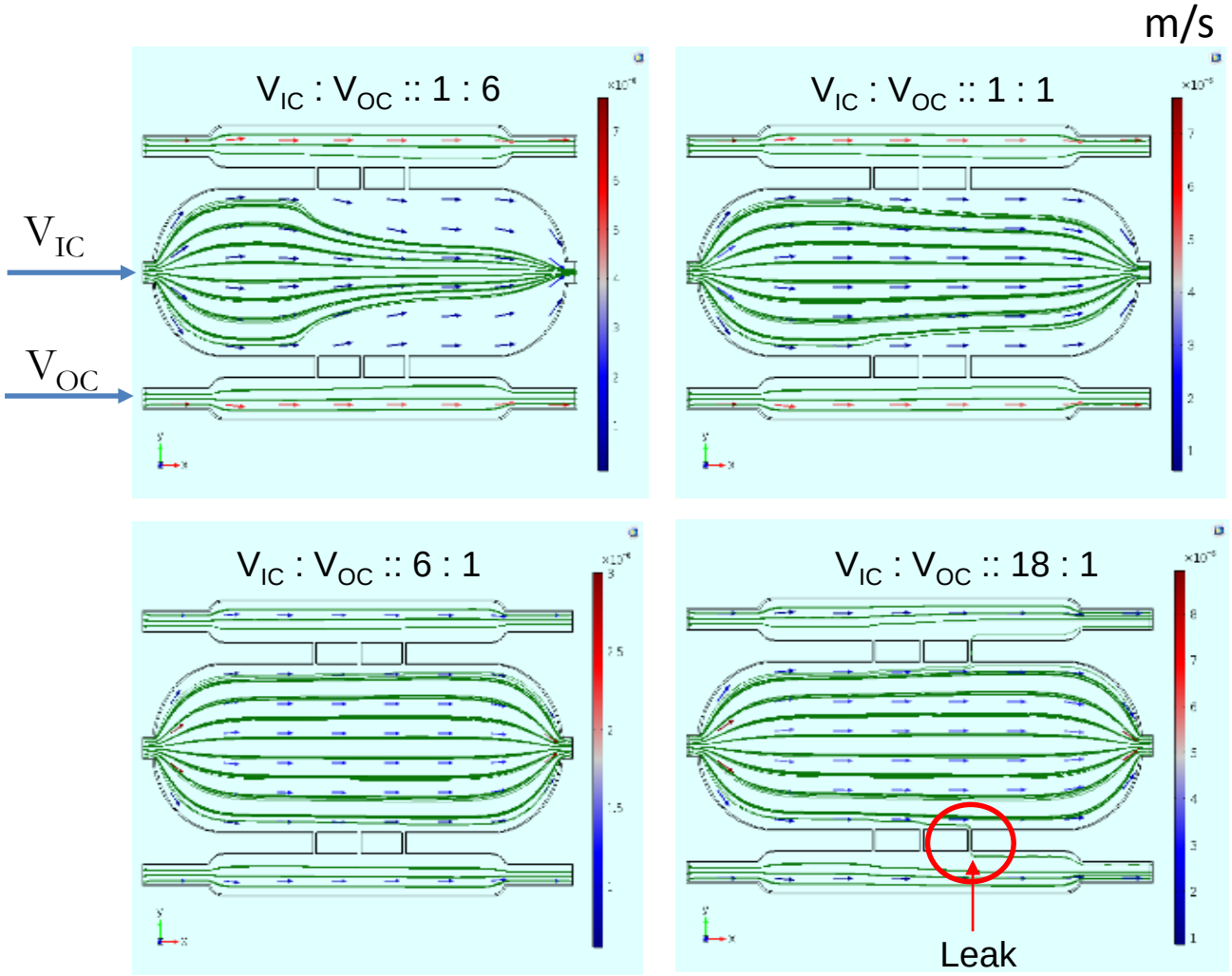
FLOW THROUGH CULTURE CHIP



Antiparallel case

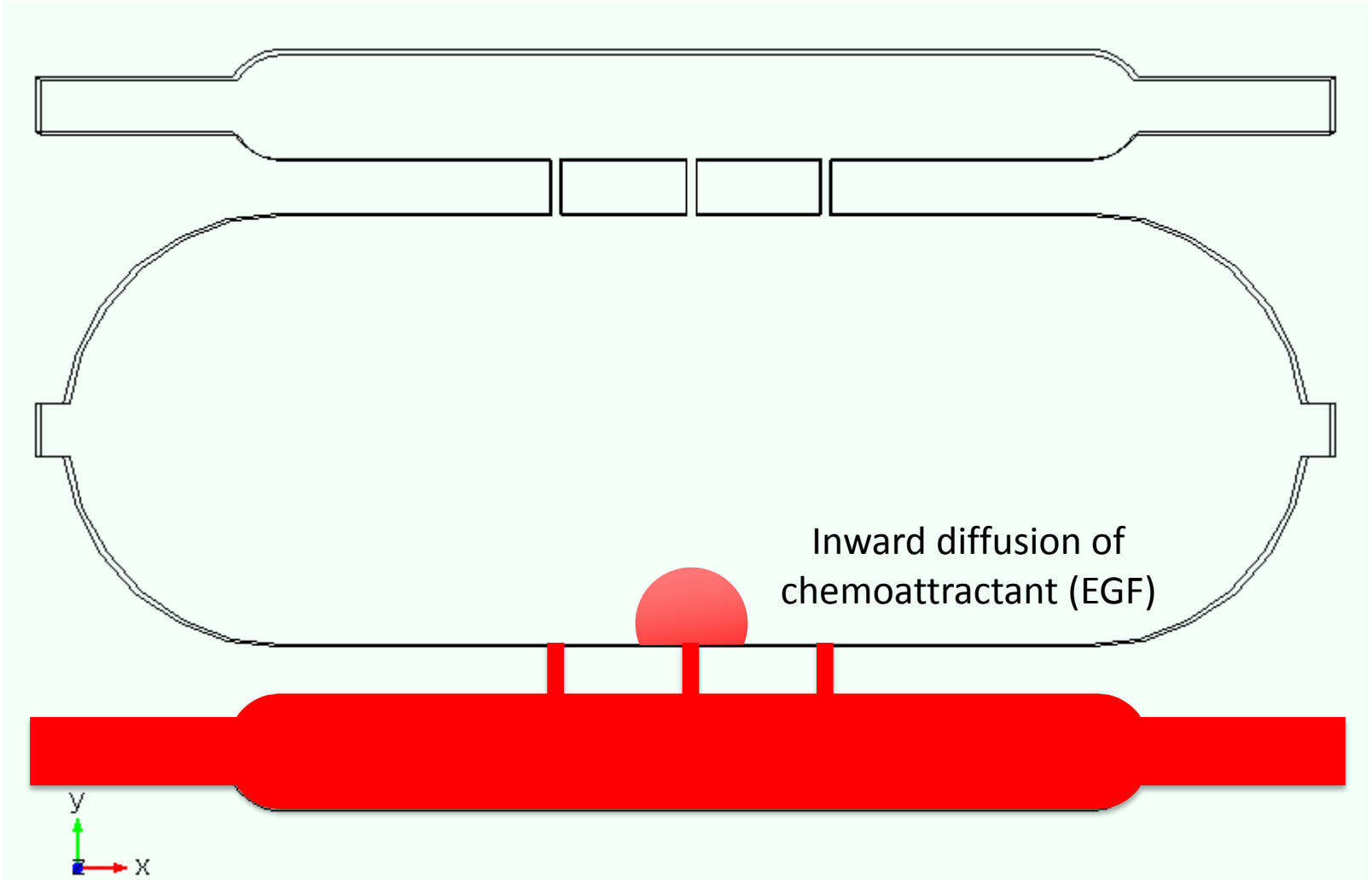
- V_{IC} = input velocity for the inner chamber
- V_{OC} = input velocity for the outer chambers
- Leakage through **all** migration channels

OPTIMAL FLOW RATE FOR CONNECTED CHIP



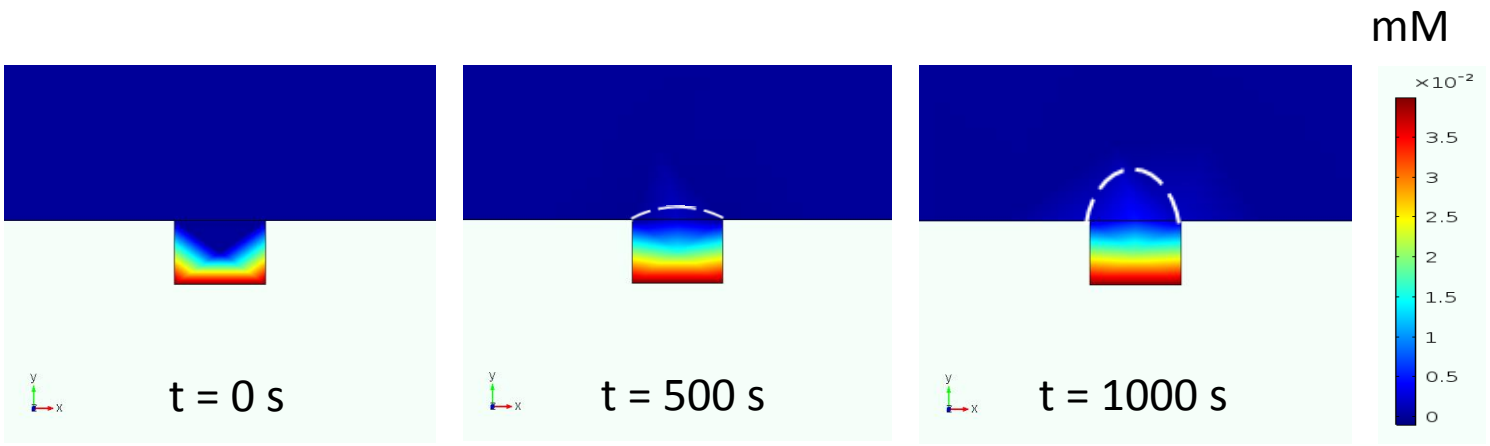
Beyond a threshold ratio, V_{IC} becomes too large in comparison to V_{OC} and media leaks through the third channel

WHAT ABOUT DIFFUSION OF EGF ?



EGF DIFFUSION

- Diffusion of 0.04 mM EGF across a 0.6 mm long channel
- Diffusion coefficient of EGF taken as 5.18 X 10^{-11} m^2/s

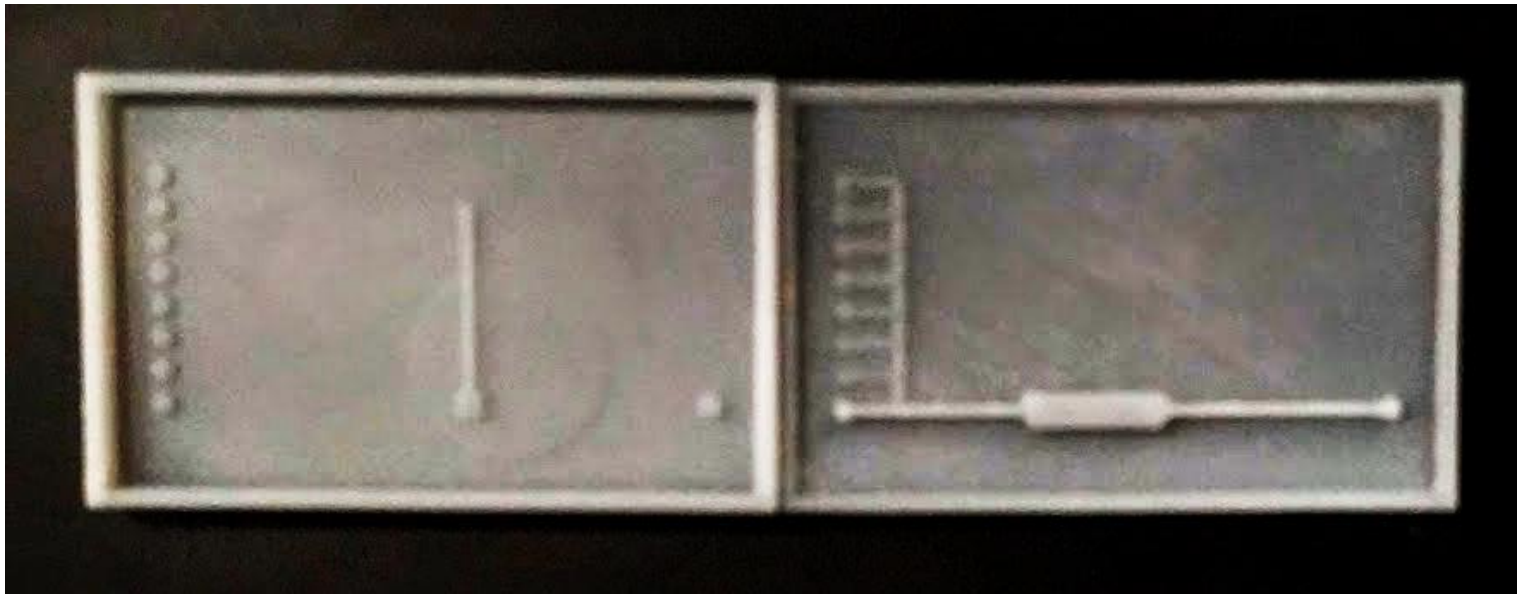


- Timescale of diffusion is practical for conducting cell migration experiments in culture chips
- Cell migration is normally a few hundred µm/hr in the presence of a chemoattractant gradient

SUMMARY

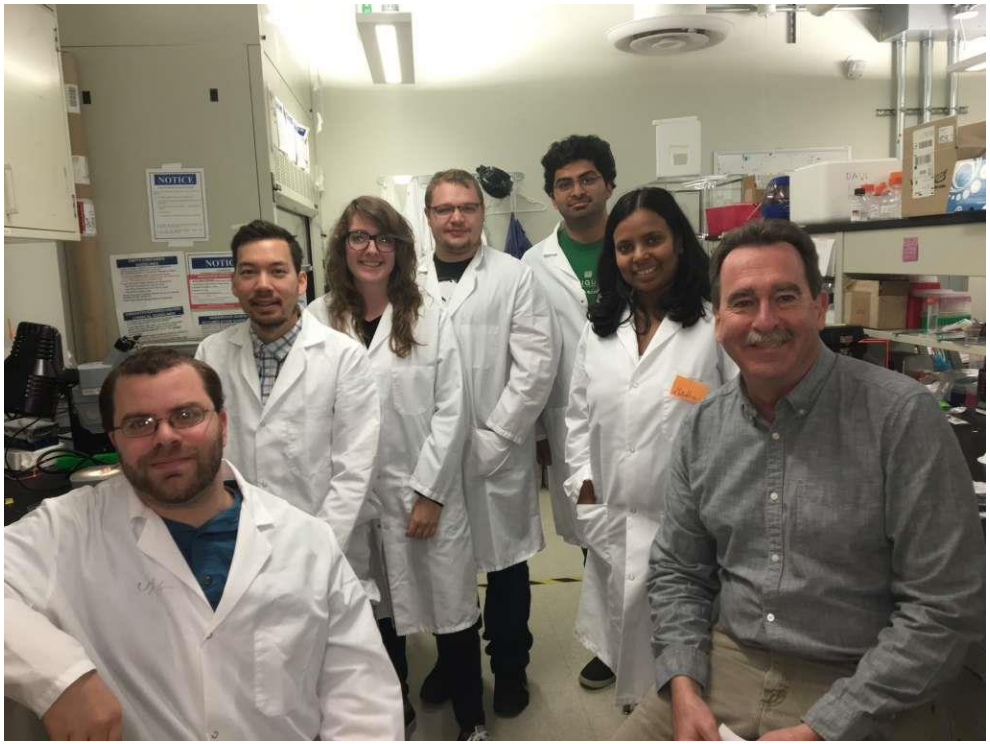
- Microgravity leads to changes in proteomic and genomic expression of cancer cells
- Migration studies in microgravity can help uncover novel therapeutic targets for metastatic behavior
- Spf studies led to improving the shape of the culture chamber and gauging an optimal operating flow rate range
- Tds studies point to the timescale over which diffusion of EGF can take place

FUTURE CHIPS



- 3D printed mold using FormLabs Form 1+
- 8 inlets, 2 outlets and a membrane

ACKNOWLEDGMENTS



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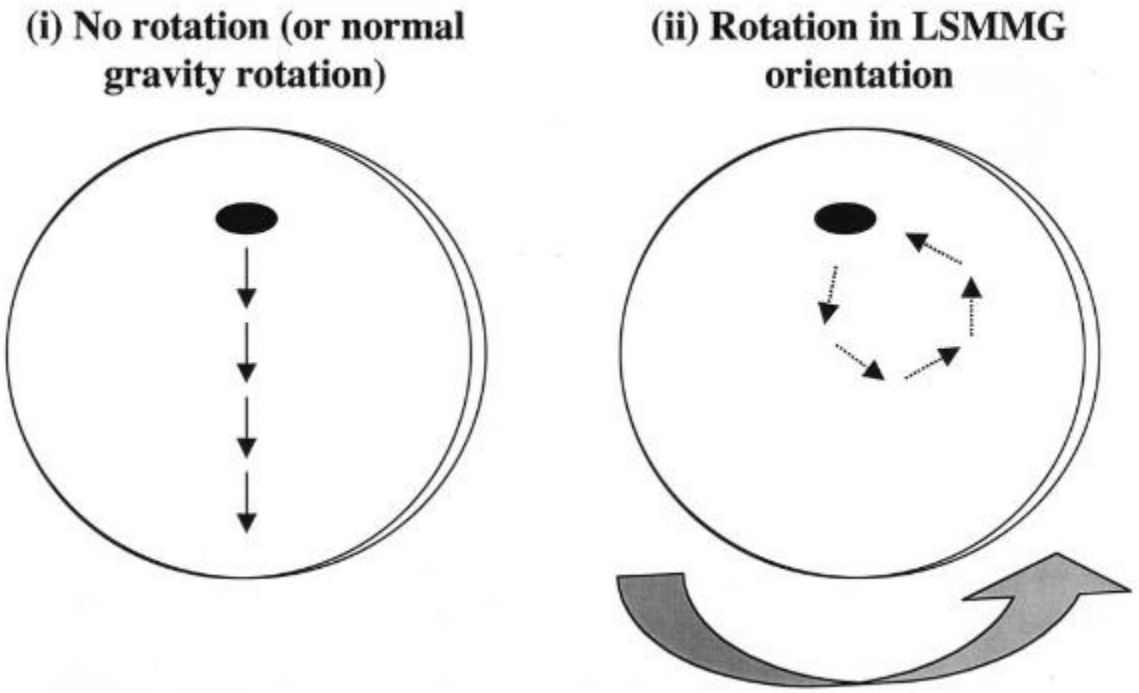
THANK YOU

SUPPLEMENTAL



Nickerson *et al.* (2004)