Microfluidic Platform for Culture and Live Cell Imaging of Cellular Microarrays

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Outline

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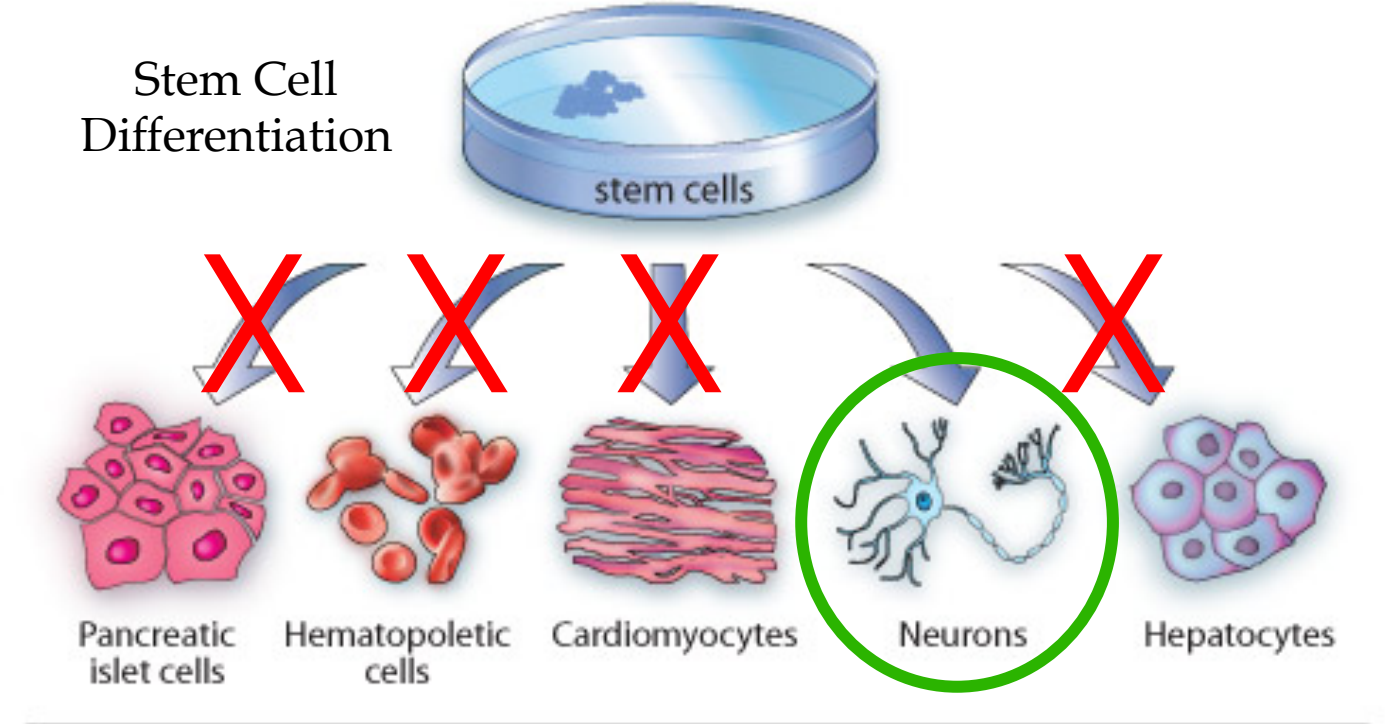
Client Description

- Dr. Randolph Ashton
  - Assistant Professor, Department of Biomedical Engineering
  - University of Wisconsin - Madison
  - Research
    - Regenerative stem cell medicine for clinical applications

http://www.engr.wisc.edu/bme/faculty/ashton_randolph.html

Motivation

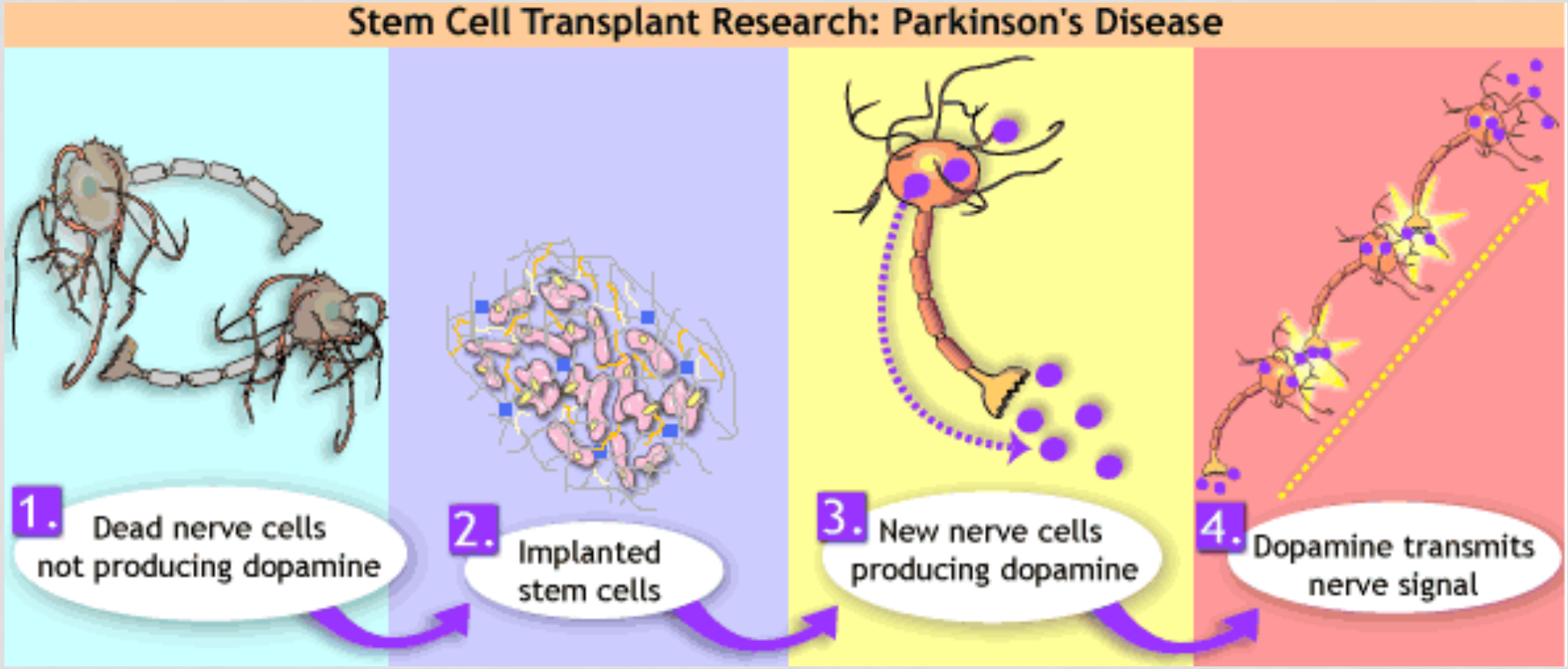
- Pluripotent stem cells differentiate into nerve cells



http://www.biologyjunction.com/stemcell_article.htm

Motivation

- Provide treatment for neurodegenerative disorders



http://www.csa.com/discoveryguides/stemcell/overview.php

Problem Statement

- Integrate cellular microarray with microfluidic platform that:
  - Is compatible with a standard microscope stage
    - Live-cell imaging and high-throughput analysis
  - Generates a concentration gradient across microarray
  - Creates a water-tight seal with microscope coverslip
  - Is reusable for multiple microarrays

- Initial focus: concentration gradient generation

Design Specifications

- Dimensions and weight
  - Platform: 158 x 105 mm
  - Microarray area: 59 x 23 mm
  - Maximum weight: 0.5 kg
- Ergonomics
- Performance requirements
  - Maximize gradient number
  - Maximize cellular pixels (r = 100 μm)
  - Long term experimentation (1 – 10 days)

Current Devices

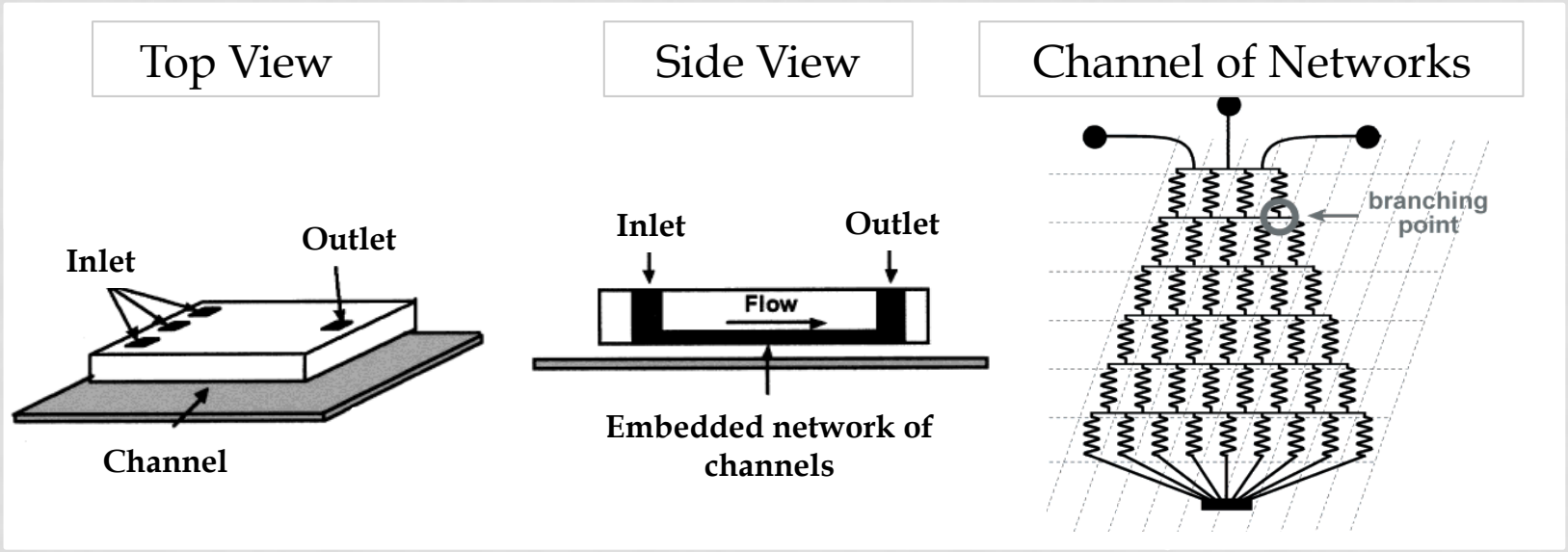
- Devices for generating concentration gradients in research
  - Christmas Tree
  - Universal
  - Source/Sink
  - Microjets

- Project novelties
  - Removable cellular microarrays
  - Long term cell culture
  - Multiple soluble factors

http://memsliu.pme.nthu.edu.tw/MSCL%20Projects/chemotaxis.htm

Design Alternatives
Christmas Tree

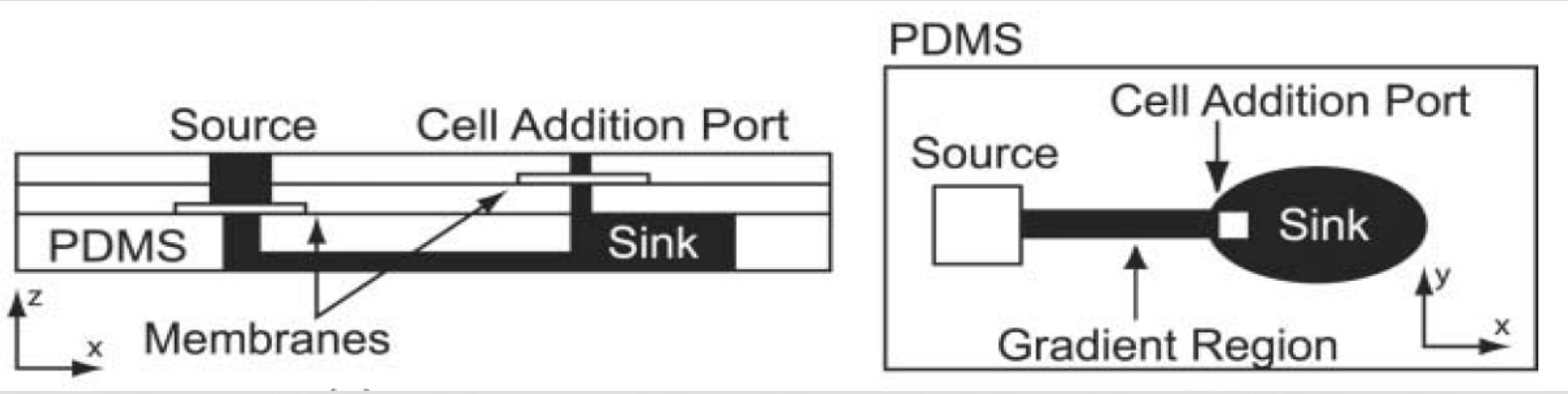
- Gradient generated in microfluidic channels
  - Inlet solutions repeatedly combined, mixed, and split
  - Each branch channel has a distinct composition
- Monotonic gradient



"Generation of solution and surface gradients using microfluidic systems" and "Generation of gradients having complex shapes using microfluidic networks"

Design Alternatives
Source/Sink Gradient Generator

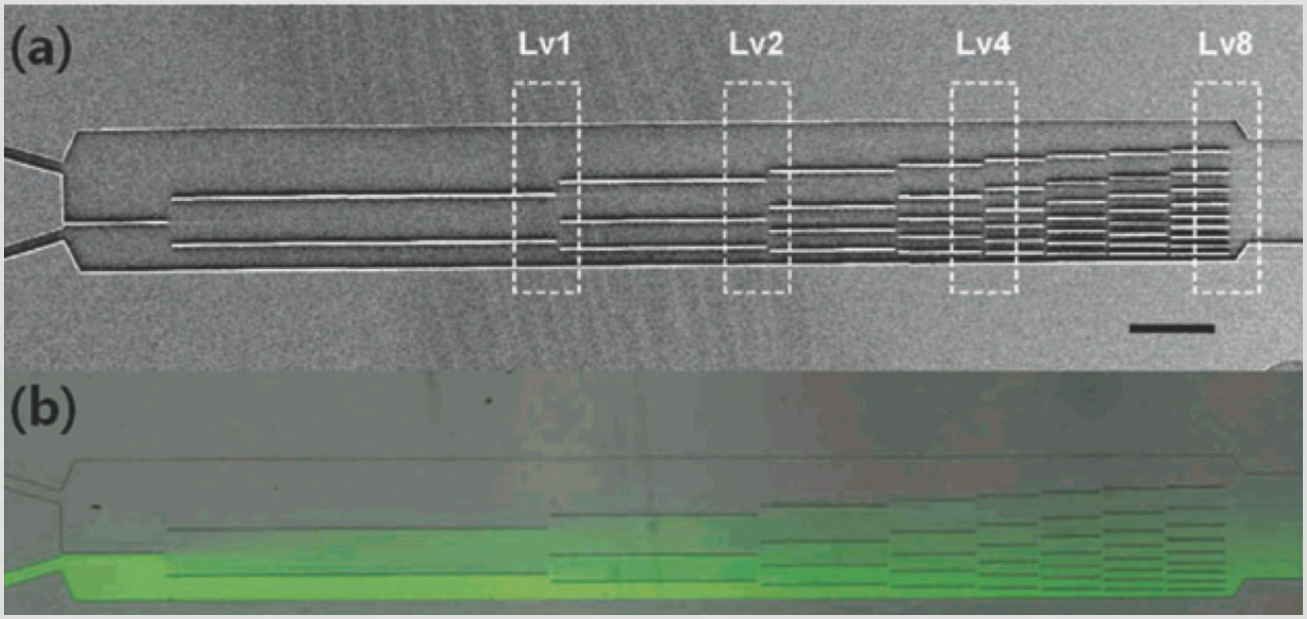
- Membrane-covered source
- Large volume sink region
- Transport from source to sink
- No fluid flow
- Transient generation period



"Characterization of a membrane-based gradient generator for use in cell-signaling studies "

Design Alternatives
Universal Gradient Generator

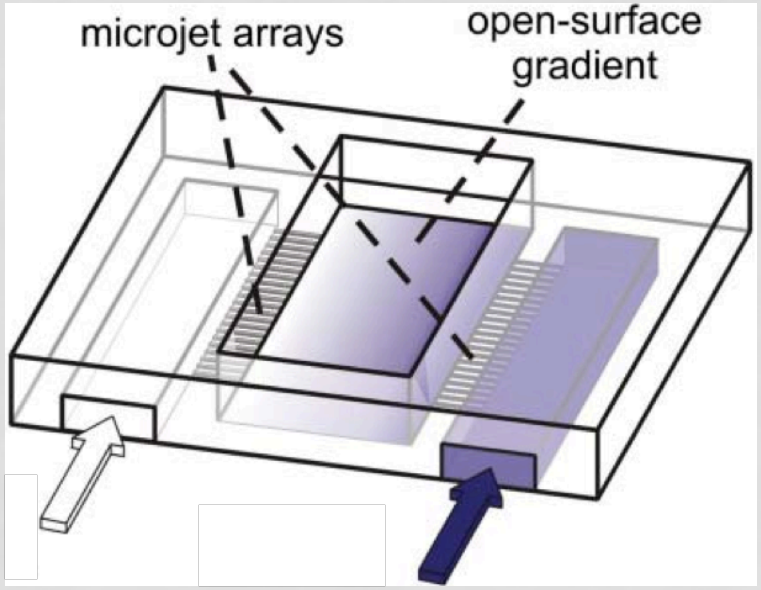
- Mimics principles of Christmas Tree
  - Flow dividers inside microfluidic channel
  - Controlled splitting and mixing of channel contents
- Monotonic gradient



"Biological applications of microfluidic gradient devices"

Design Alternatives
Microjets Device

- Pneumatically ejects fluids into microarray
- Diffusion generates gradient
- Cells not exposed to fluid flow
- Need continual supply of fresh gradient fluids



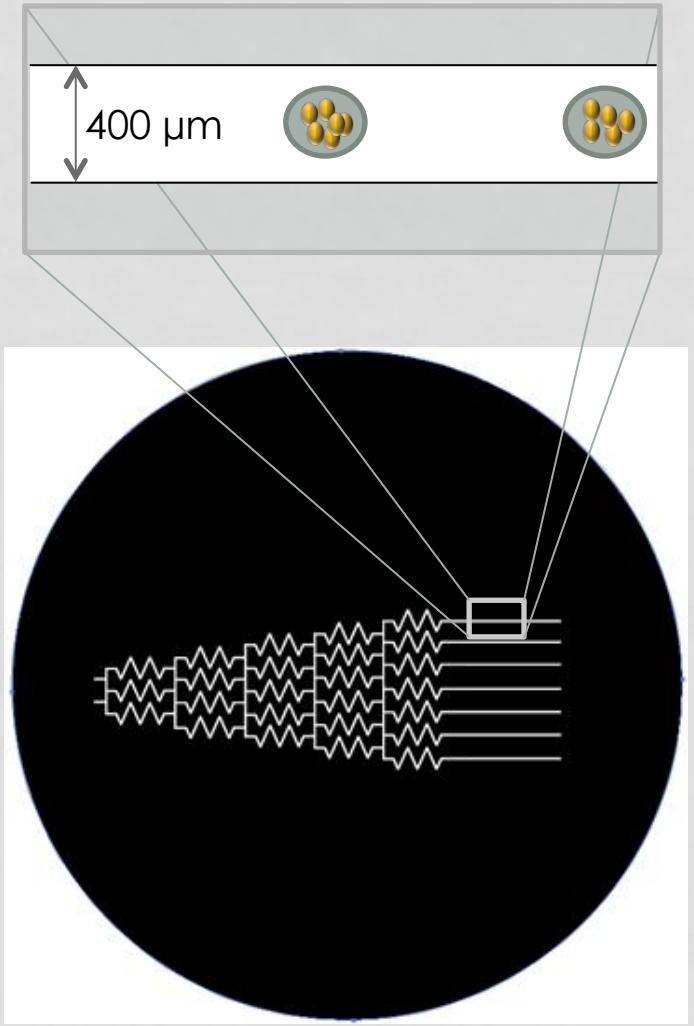
"Biomolecular gradients in cell culture systems"

Design Matrix

Category (Points)	Christmas Tree	Source/ Sink Gradient Generator	Universal Gradient Generator	Microjets Device
Ease of Fabrication (25)	22	20	20	20
Accuracy of Gradients (25)	21	17	18	18
Estimated Throughput (20)	20	20	18	20
Ergonomics (20)	20	20	13	17
Client Preference (10)	10	0	0	0
Total (100)	**93**	**77**	**69**	**75**

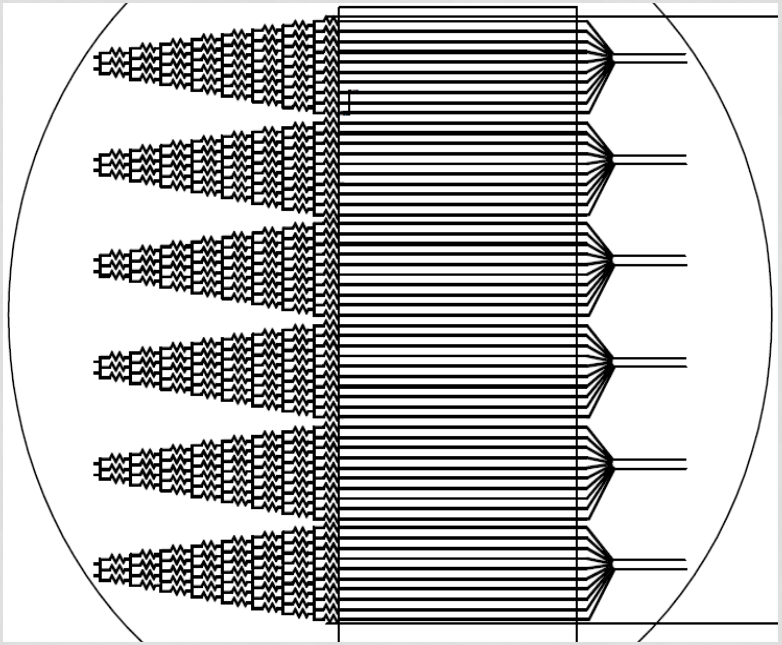
Final Design

- Christmas Tree microfluidics
  - Polydimethyl siloxane (PDMS)
  - Single channels
- Incorporation
  - Removable microarray
  - Environmental chamber



Final Design

- 6 adjacent trees
  - 12 input lines
  - Multiple soluble factors
  - Fine tuning of gradient possible



Future Work

- This Semester:
  - COMSOL analysis
  - Verify simulation
    - Fick's Law of Diffusion
  - Order photomask
  - Develop prototype
  - Integrate microarray
- Next Semester:
  - Integrate environmental chamber
  - Ensure cell viability
  - Determine cellular response

References

- V. V. Abhyankar, *et al.*, "Characterization of a membrane-based gradient generator for use in cell-signaling studies," *Lab Chip,* vol. 6, pp. 389-393, 2006.
- S. K. W. Dertinger, *et al.*, "Generation of gradients having complex shapes using microfluidic networks," *Analytical Chemistry,* vol. 73, pp. 1240-1246, 2001.
- N. L. Jeon, *et al.*, "Generation of solution and surface gradients using microfluidic systems," *Langmuir,* vol. 16, pp. 8311-8316, 2000.
- T. M. Keenan and A. Folch, "Biomolecular gradients in cell culture systems," *Lab on a Chip,* vol. 8, pp. 34-57, 2008.
- S. Kim, *et al.*, "Biological applications of microfluidic gradient devices," *Integr. Biol.,* 2010.

Questions?