



# **Graphene Microfluidics for Dynamic, Electron Microscopic Bio-Imaging**

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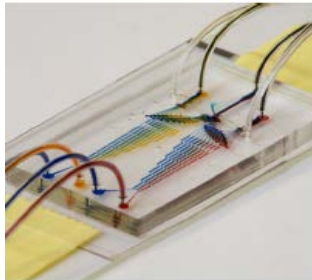
# Outline

- **Background & Motivation**
- **Research Strategy**
- **Proposed Studies**
  - **Specific objectives**
  - **Preliminary results**

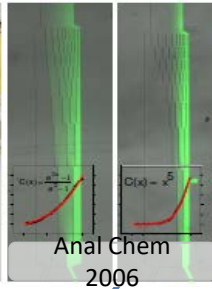
# Microfluidics for Biophysics

## Cell dynamic studies

**Gradient Switching**



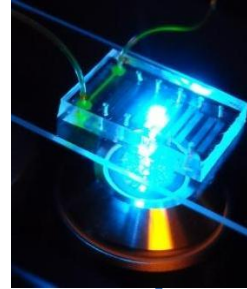
**Universal Gradient**



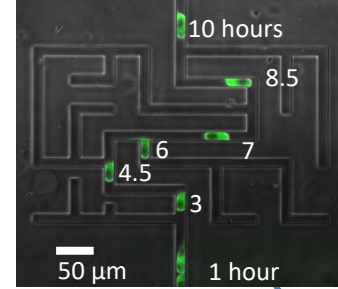
**Whole Blood**



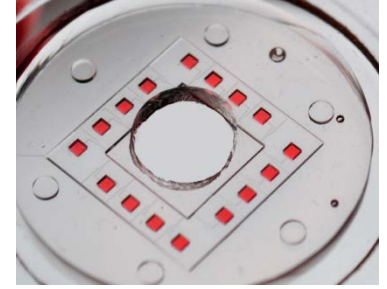
**Clinical Samples**



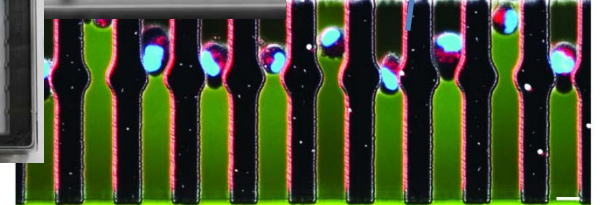
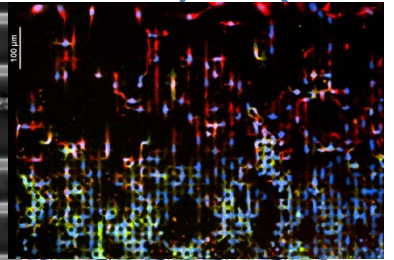
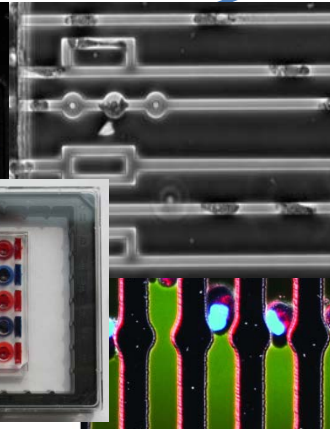
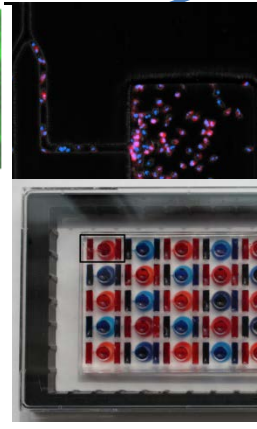
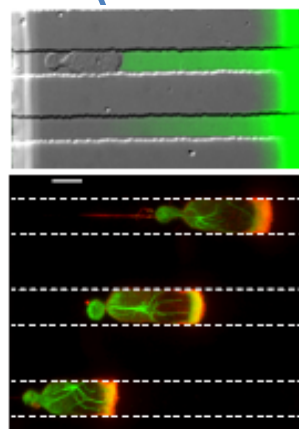
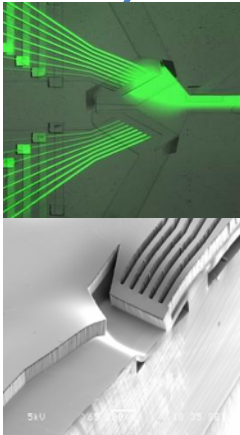
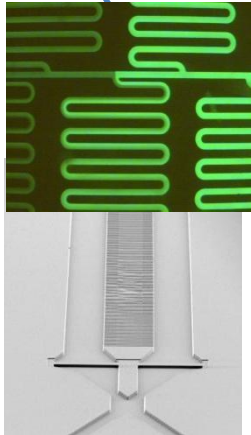
**Self Guidance of Cancer Cells**



**Cell-cell Interactions during Chemotaxis**



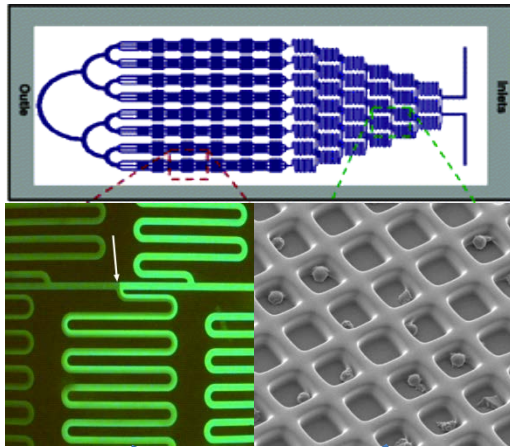
2004 2005 2006 2007 2008 2009 2010 2011 2012 2013



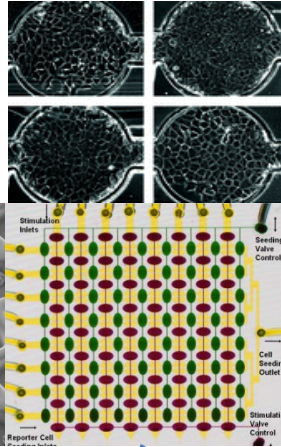
# Microfluidics for Biophysics

## Single- through multi-cell analysis

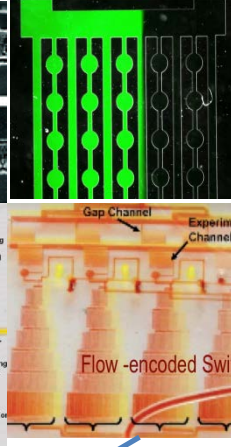
Single cell arrays



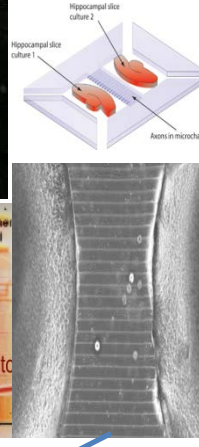
Complex cell line arrays



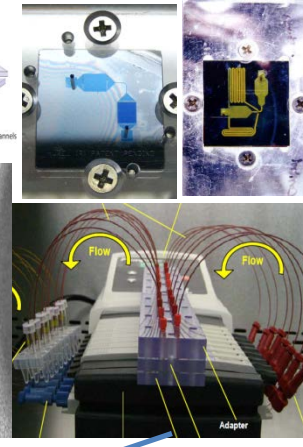
Spatiotemporal control



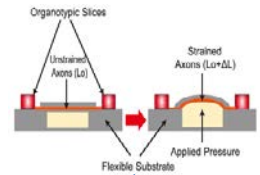
Organotypic systems



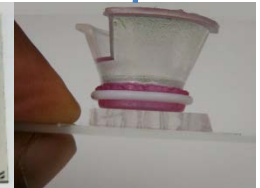
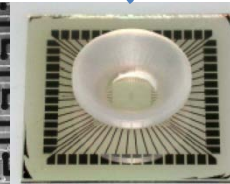
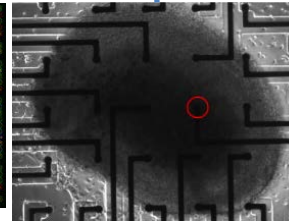
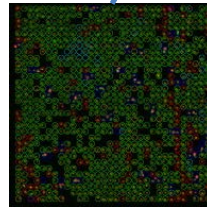
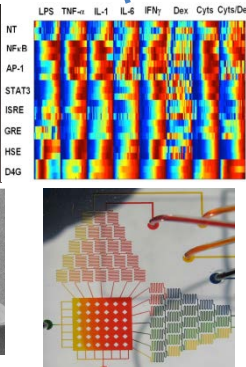
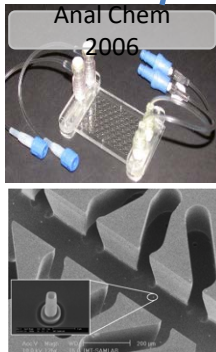
Multiple organ systems



Controlling forces

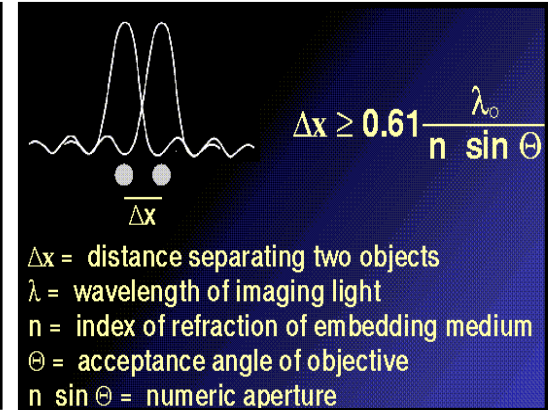
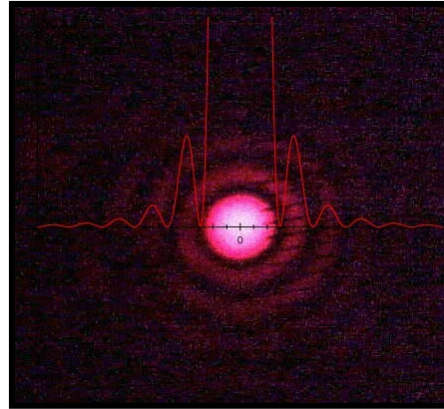
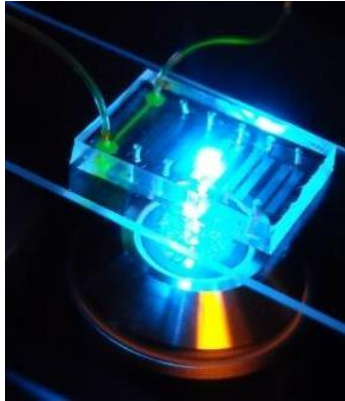


2004 2005 2006 2007 2008 2009 2010 2011 2012 2013

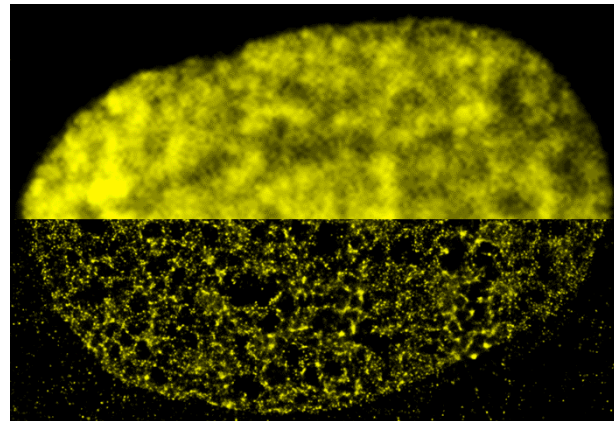
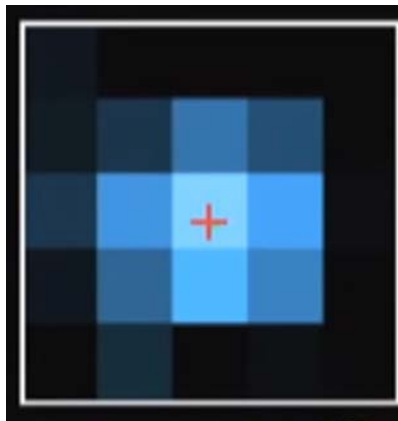




# Diffraction Limit in Optical Imaging



## Super-resolution microscopy



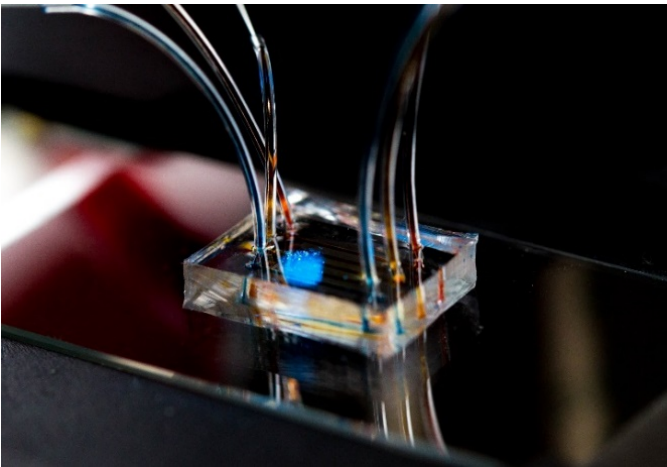
- Breaking diffraction limit through stimulation emission depletion or single molecule localization
- Fundamentally limited by the property of fluorophores (size, photo-switching, etc.)
- Compromised temporal resolution

- **Electron microscopy**

- Electrons as probes: much shorter wavelengths
- Reveals critical structural information at sub-nanometer scale
- Cryo-EM opens up new possibilities for ultra-resolution imaging of frozen biological samples

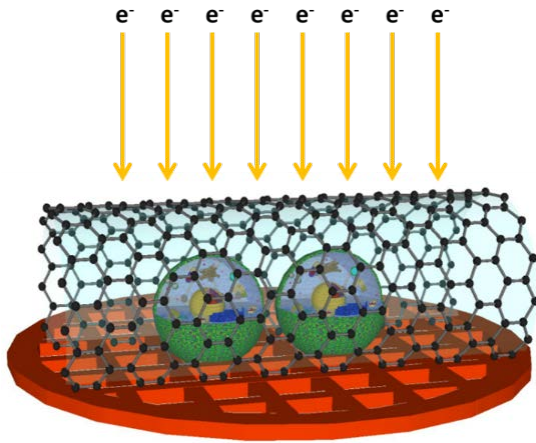


## **Microfluidics for dynamic bio-imaging under electron microscope?**



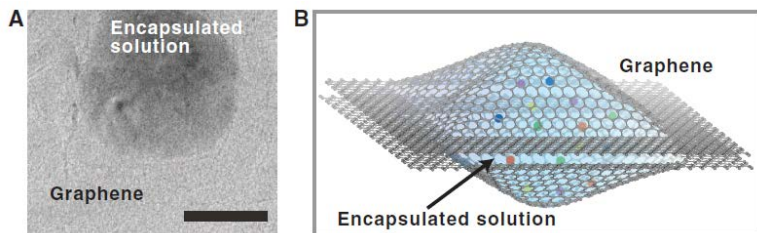
- Requires high-vacuum operation conditions: challenges in preserving the wet biological specimen
- Electron “transparency” issues: poor-contrast for biological samples, particularly under low electron dose conditions
- High-energy electron beams: generating radiolysis products (solvated electrons,  $H^+$  and  $OH^-$  radicals, etc.) that would damage biomolecules/kill cells

# Graphene as core material for microfluidics



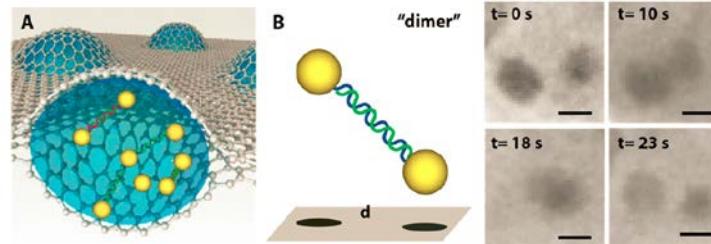
- Low atomic number
- Ultra thin with superior electron transparency
- Tight, covalently bonded carbon atoms are inherently impermeable to liquid or gas molecules
- Excellent mechanical properties
- Mitigate electron beam-induced damage (scavenging reactive radical species)
- Compared with the “sandwich”-type of graphene liquid cell:
  - more effective encapsulation
  - less-harsh imaging conditions
  - sophisticated microenvironment control
  - multiplexed device integration

## nanocrystal growth



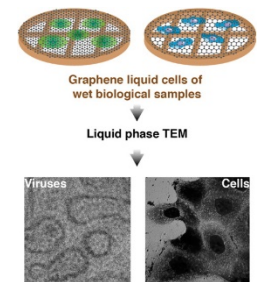
*Yuk et.al., Science, 2012*

## biomolecular transformations



*Chen et.al., Nano Lett, 2013*

## mammalian cells



- Encapsulating liquids between two graphene sheets on TEM grids
- Formation of separated liquid pockets throughout the grid