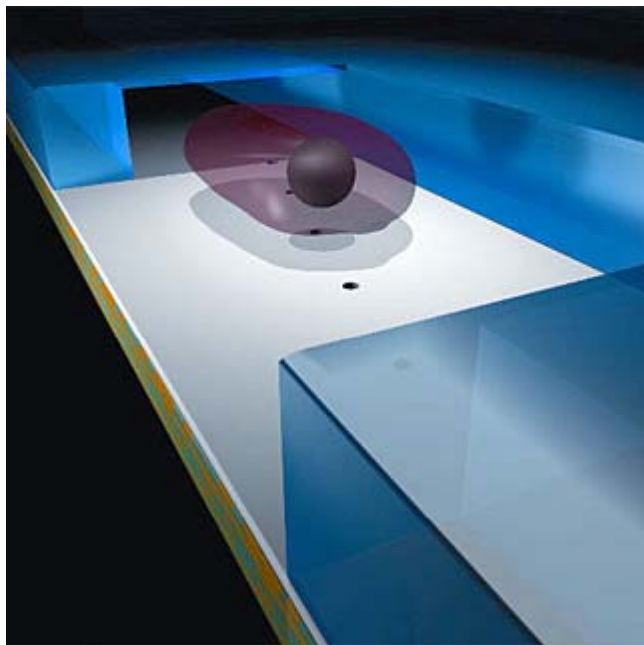


Presented at the evening meeting of the
Santa Clara Valley Chapter, CPMT Society, IEEE
January 14, 2009 www.cpmt.org/scv/



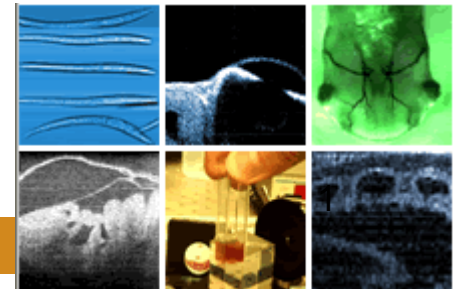
A Highly Compact Lensless High-Resolution Optofluidic Microscope (OFM)



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Caltech Biophotonics Laboratory

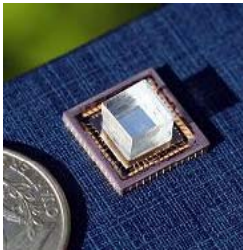
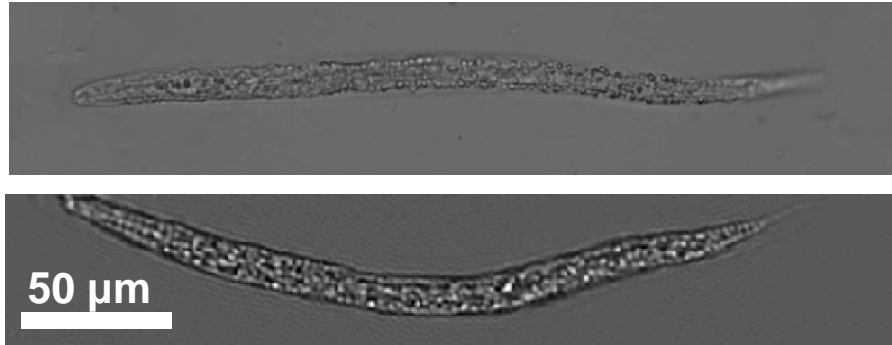


Redesigning the microscope

We abandon the conventional microscopy design and use a novel aperture array for high resolution cell-level imaging.

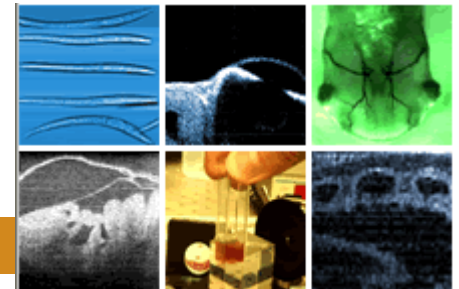


Images of *C. elegans*



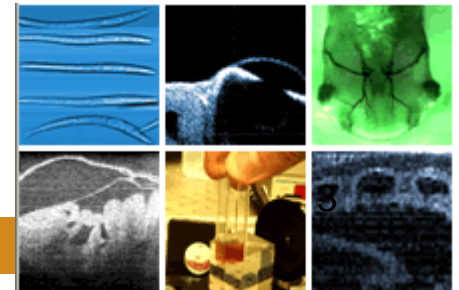
- compact (~ the size of a dime)
- potentially cheap (\$10's)

X. Cui et. al, PNAS, **105**, 10670 (2008)

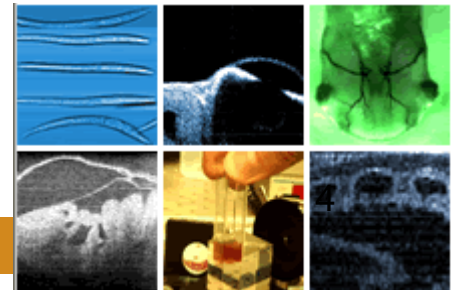


Overview

- **Motivation**
- **Intensity contrast OFM**
 - (a) **Gravity driven OFM (GD OFM)**
 - Automated and quantitative OFM microscopy
 - Phenotype characterization of *C. elegans*
 - Resolution issue
 - (b) **Electrokinetic OFM (EK OFM)**
 - Spherical/ellipsoidal cells imaging
- **Conclusions and future directions**



Motivation



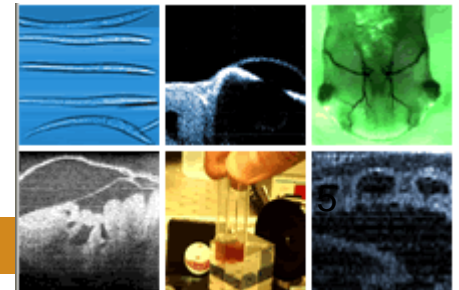
Conventional optical microscopy

Advantages:

- Noninvasive
- High resolution
- Comprehensive microscopy information
- Gold diagnosis standard

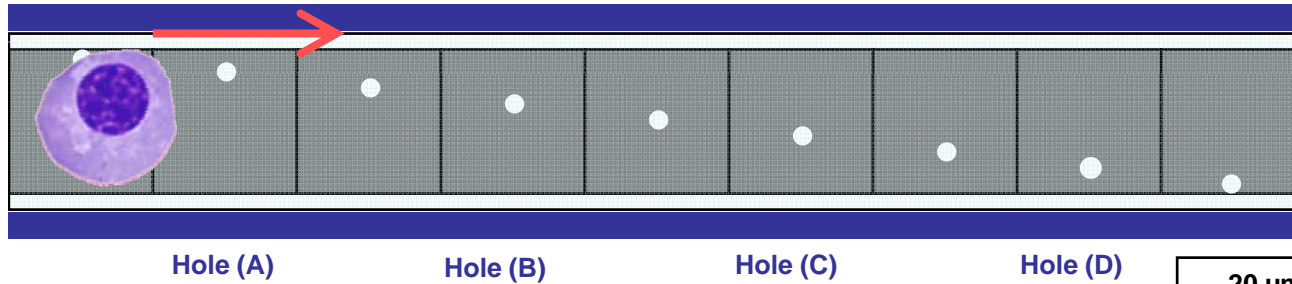
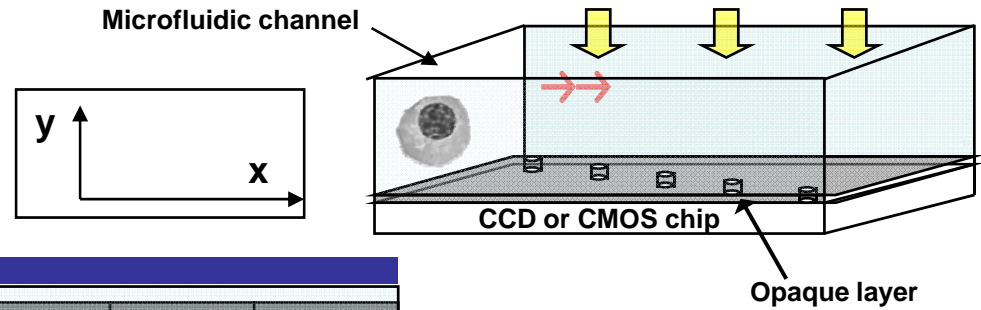
Disadvantages:

- Bulky
- Expensive

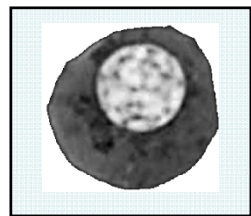


Optofluidic microscopy (OFM)

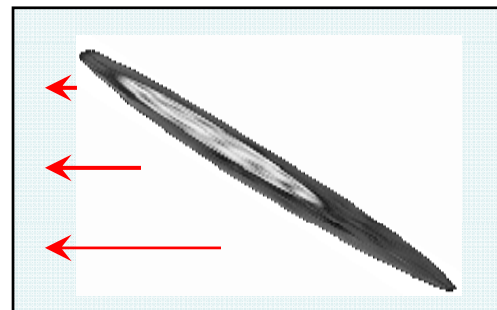
Top view



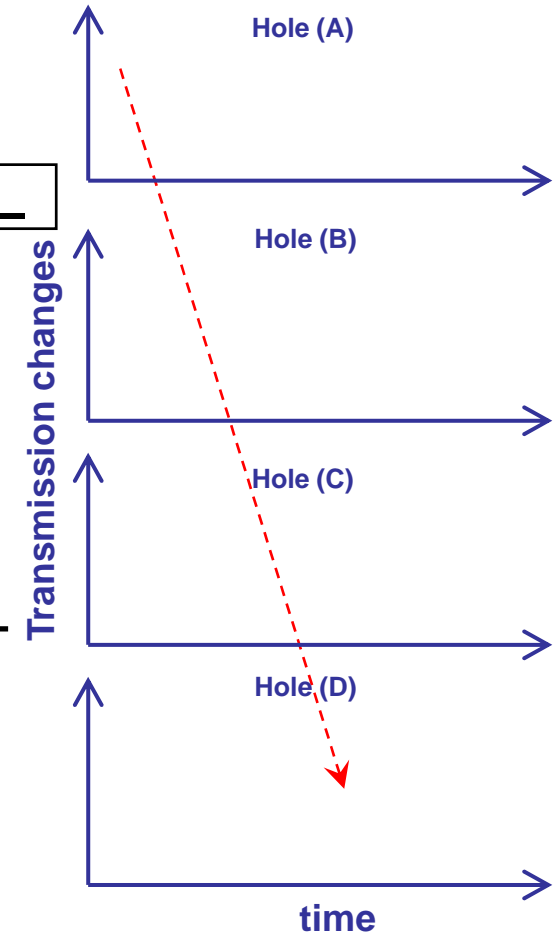
Slanted nanohole 1D array
Improve resolution in both x and y direction



Final !!!



Linear shifting factor



Nucleated blood cell image is from http://www.wadsworth.org/chemheme/heme/glass/slide_011_nrbc.htm

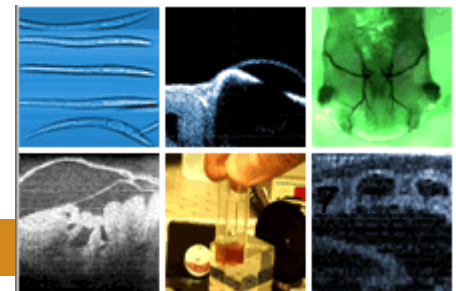
X. Heng, *Lab on a Chip*, **6**, 1274 (2006)

Advantages of OFM

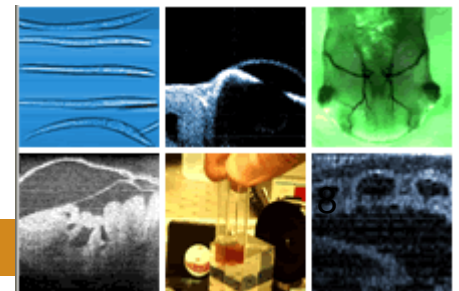
- **On-chip high resolution imaging**
 - Compact
 - Low cost
- **Microfluidics**
 - Sharp projection
 - Bio-friendly
 - High efficiency and throughput
 - Automatic operation



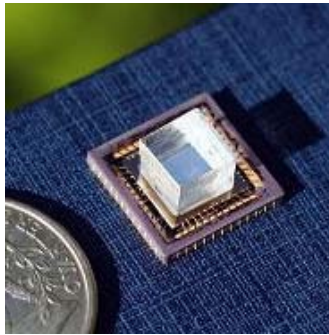
C. elegans images



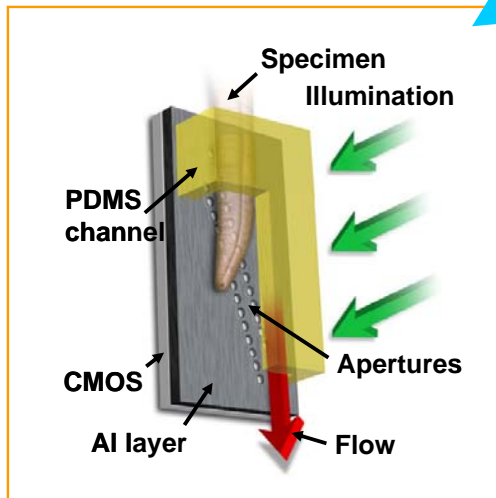
Intensity contrast OFM



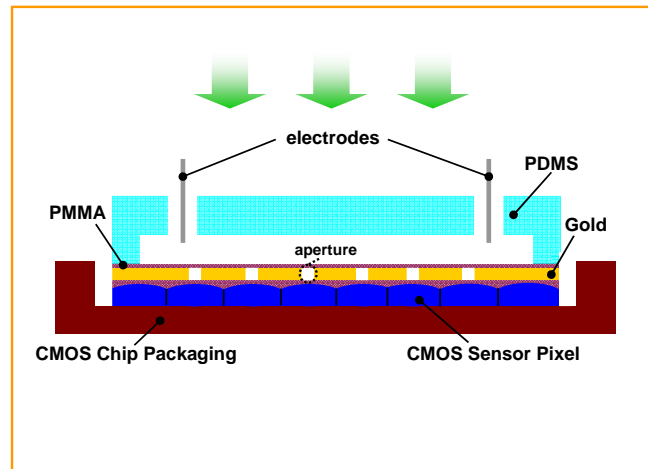
Complete on-chip OFM



- Small as a dime
- High resolution ($\sim 1\mu\text{m}$)
- Imaging & pump are all on chip

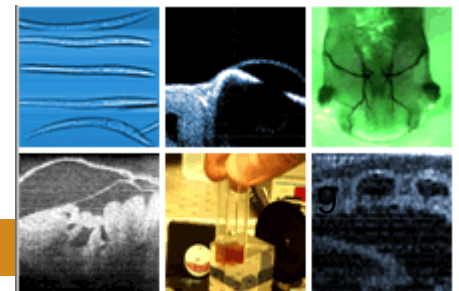


Gravity driven OFM
(GD OFM)

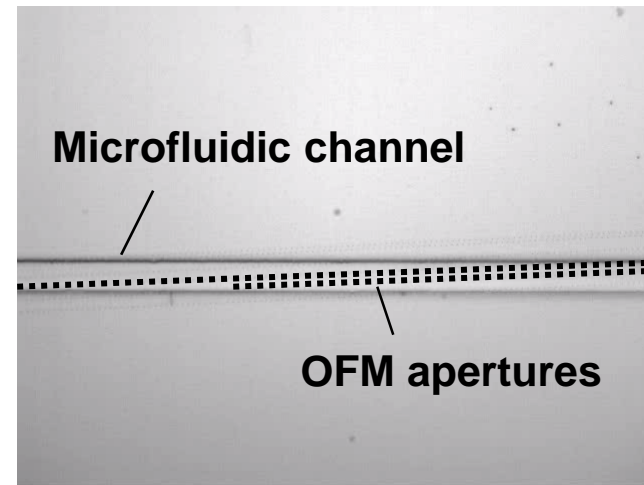
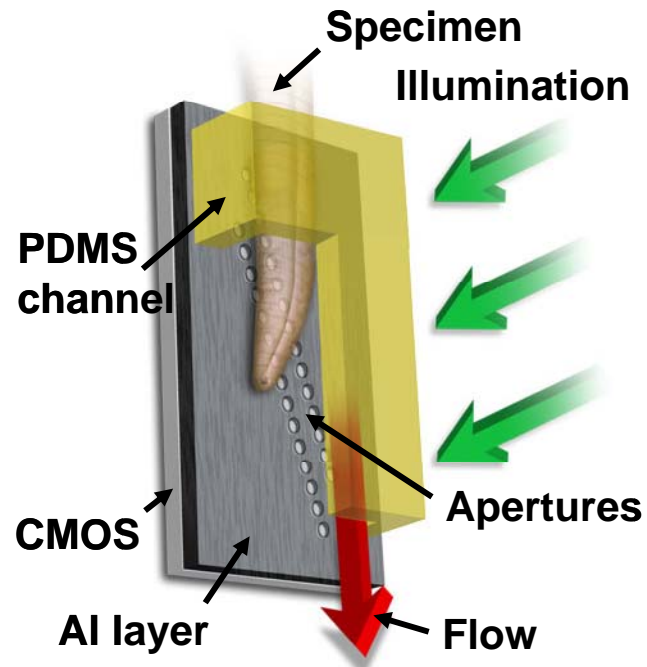


Electrokinetic OFM
(EK OFM)

X. Cui et. al, PNAS, **105**, 10670 (2008)

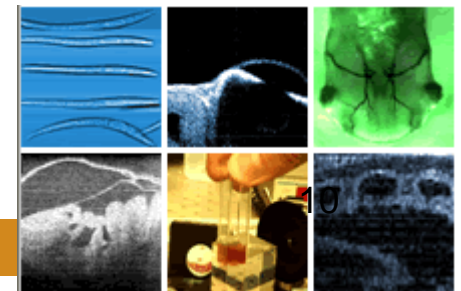


Gravity driven OFM (GD OFM)

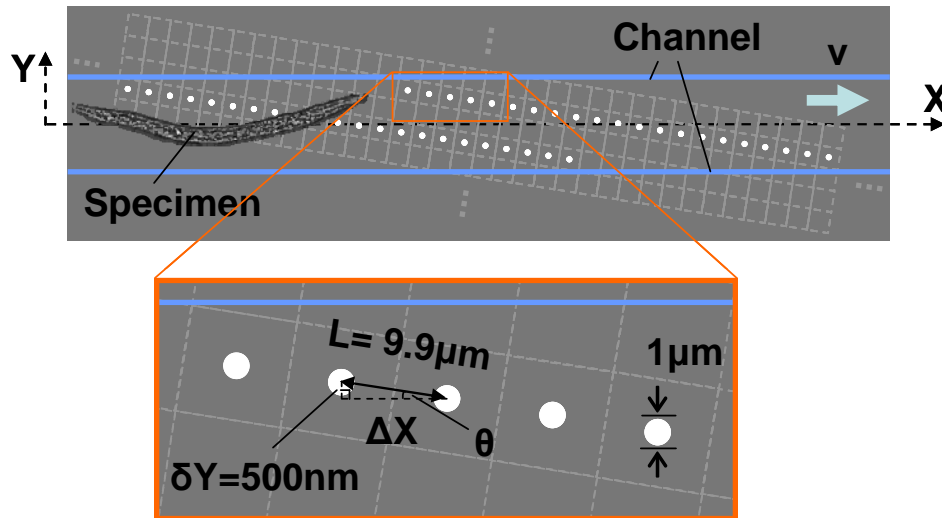


C. elegans flowing in OFM
(top view)

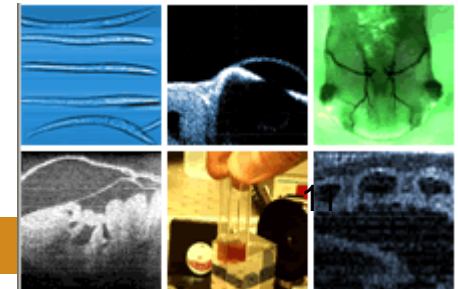
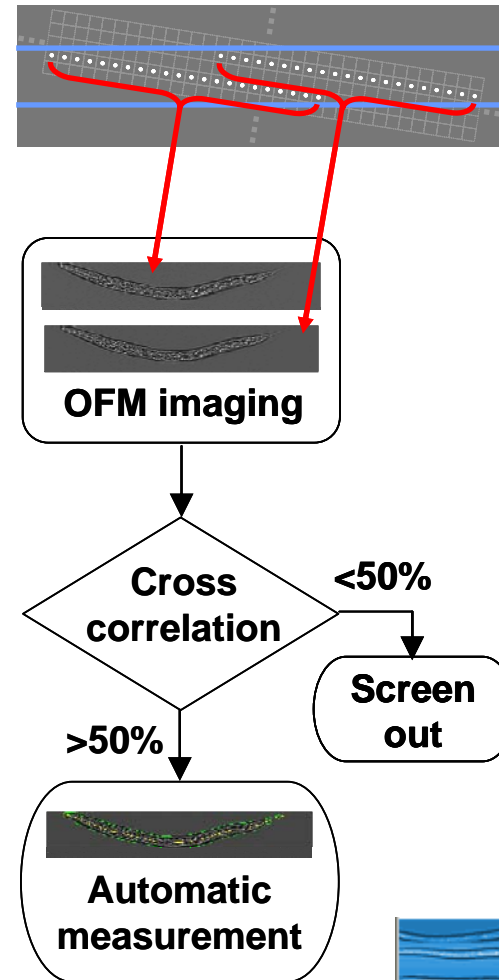
- Complete on-chip device
- Self-sustained flow
- Bio-compatible



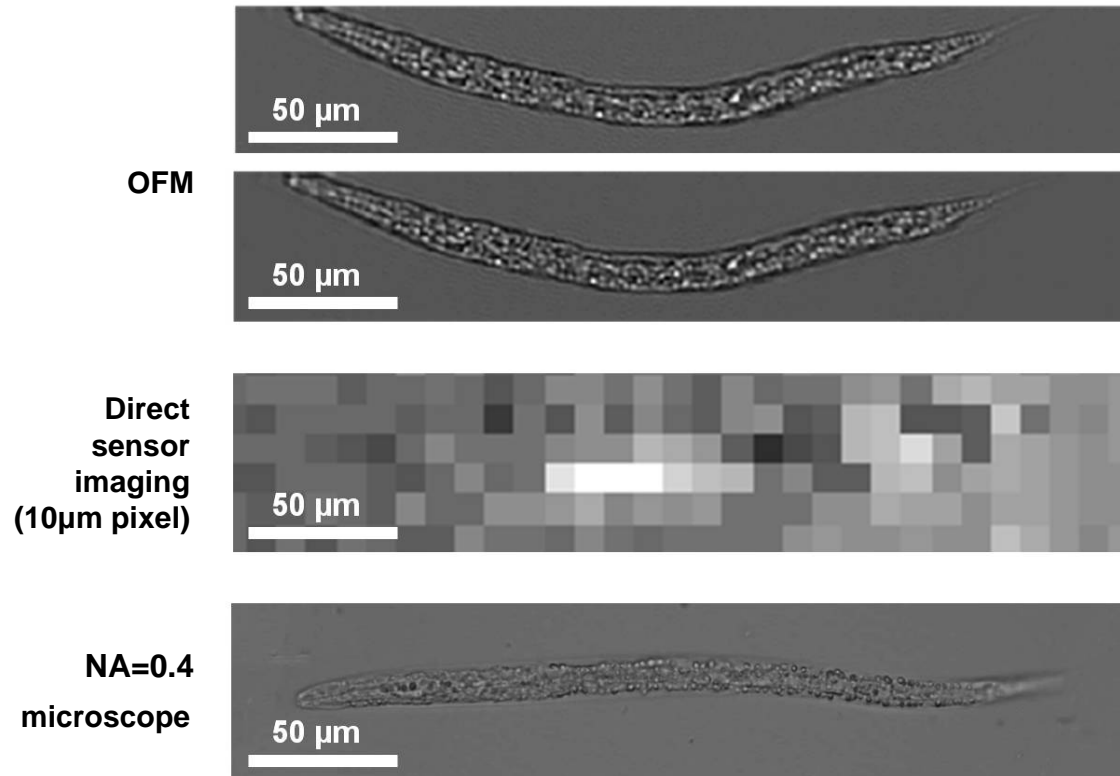
Automated and quantitative OFM microscopy



- Automated operation
- Digitized image
- Quantitative evaluation



Resolution comparison

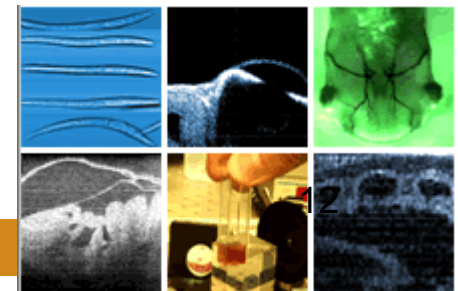


C. elegans

OFM imaging parameters:

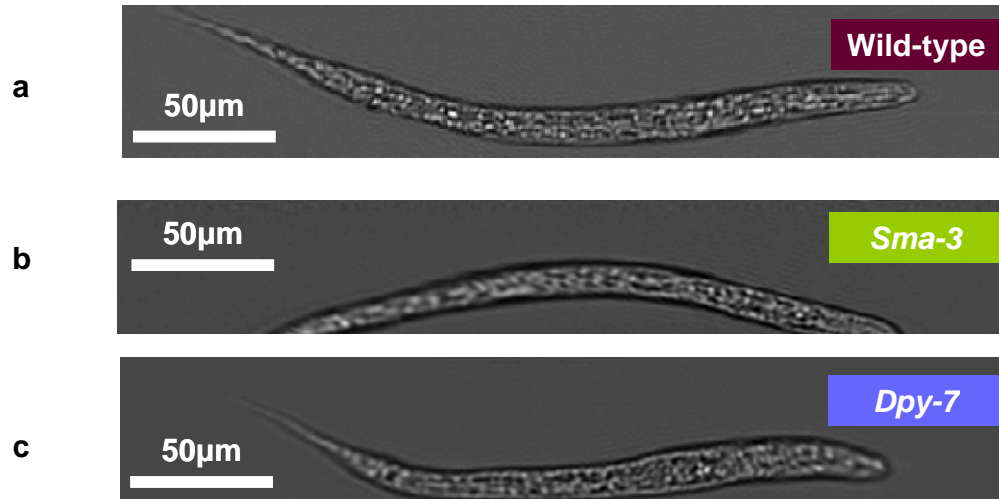
- **Illumination:**
~ 20 mW/cm² white light, the intensity of sunlight
- **CMOS sensor line rate:**
1k fps
- **Specimen velocity (V):**
~500 μ m/s
- **Sampling grid:**
 $\delta X = \delta Y = 0.5 \mu$ m
- **Aperture size (D):**
1 μ m
- **Microfluidic channel:**
width 50 μ m, height 15 μ m

OFM has comparable resolution as a conventional microscope.



Phenotype characterization of *C. elegans*

Performed automated
phenotype characterization

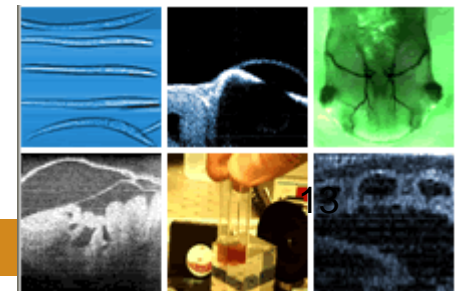
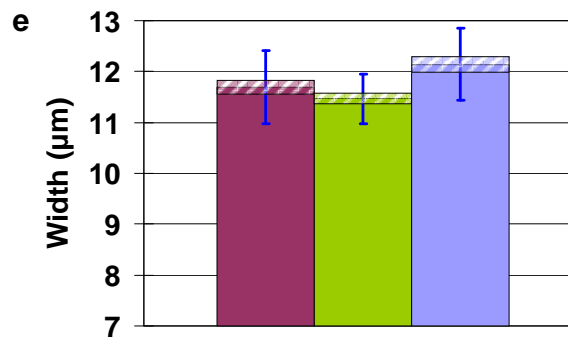
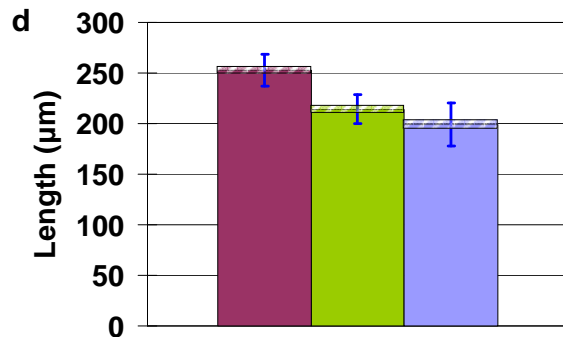


a) Automated

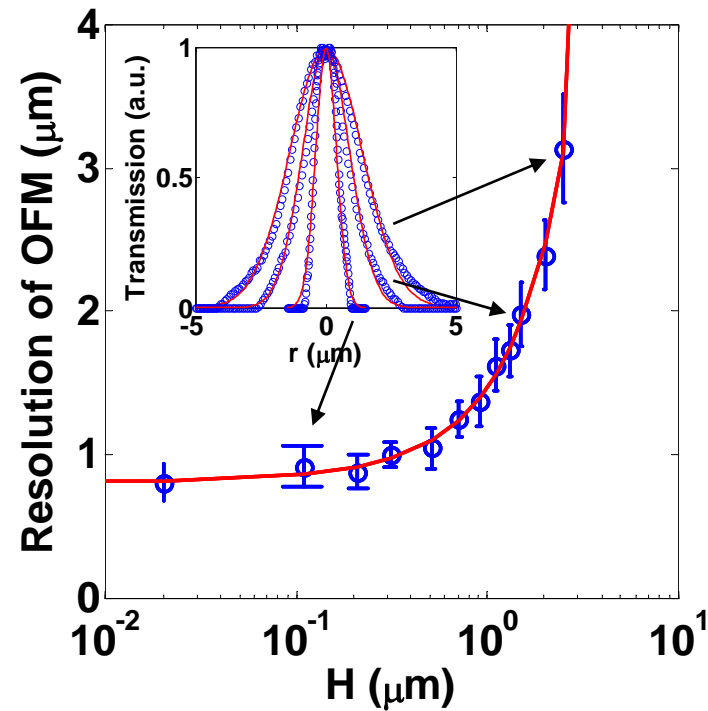
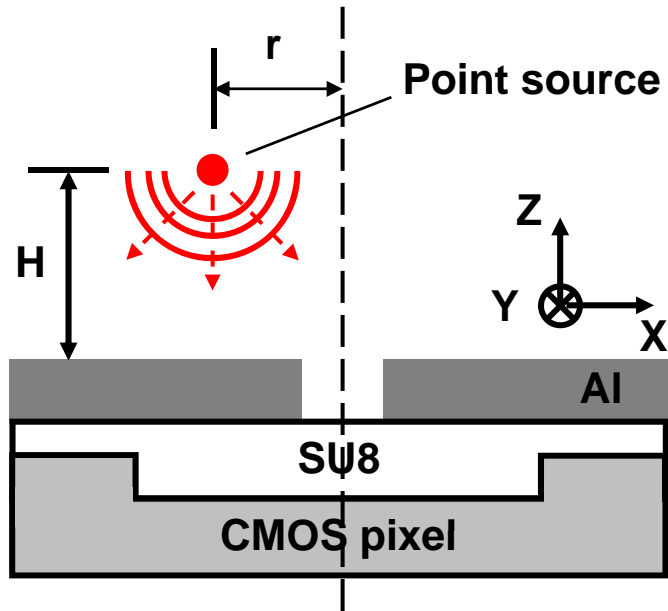
b) Image 1 worm / 2.5 sec

c) Computerized worm length
and area measurement

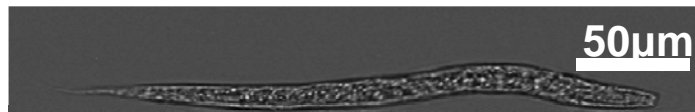
d) Drop and go



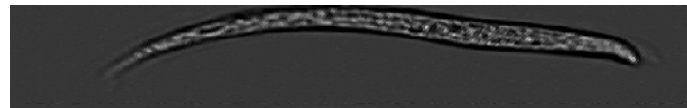
Resolution Issues



Prototype resolution = 0.9 microns (Sparrow's Criterion)

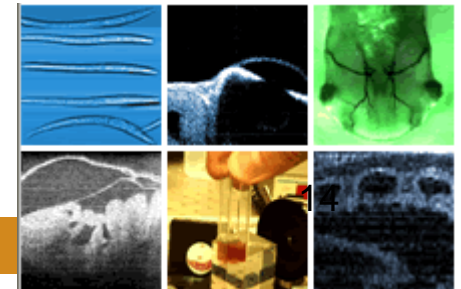


15 micron tall channel



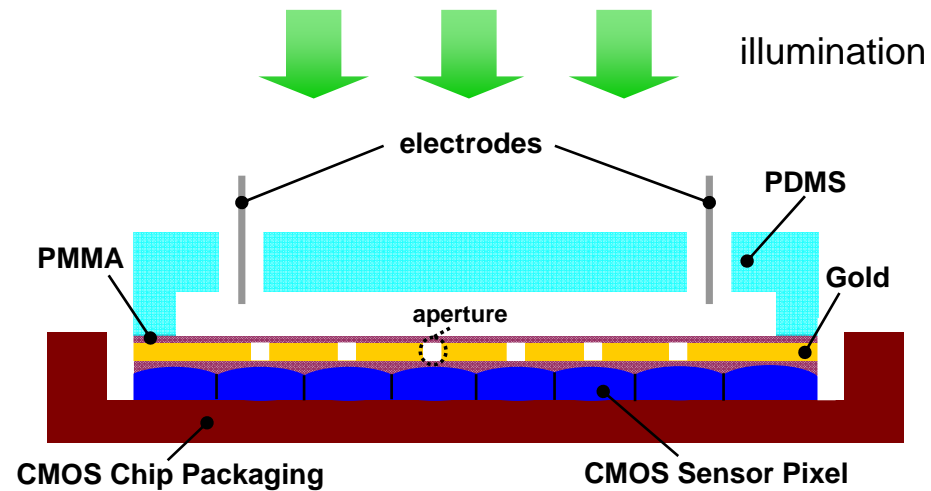
25 micron tall channel

Shallow channels give better images.

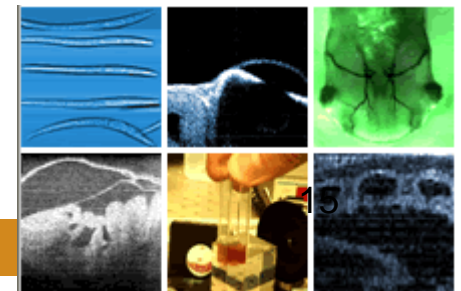


Electrokinetic OFM (EK OFM)

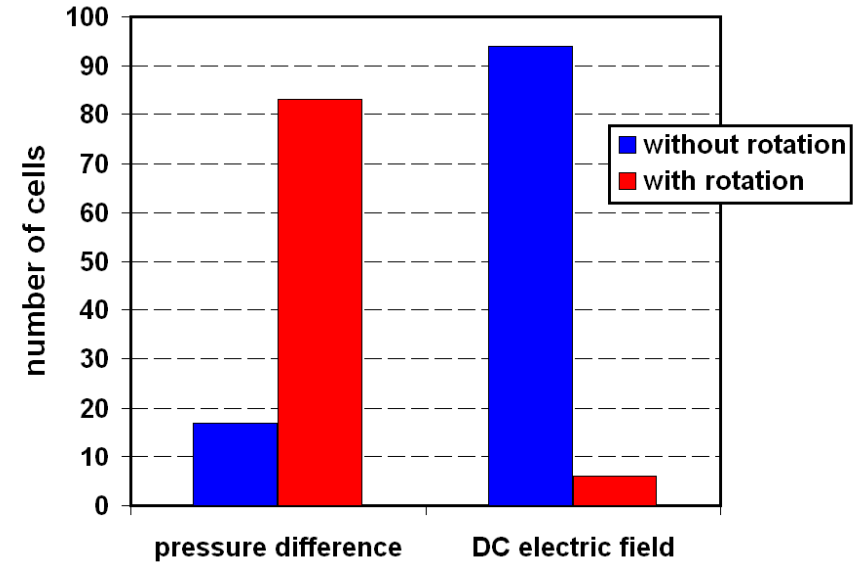
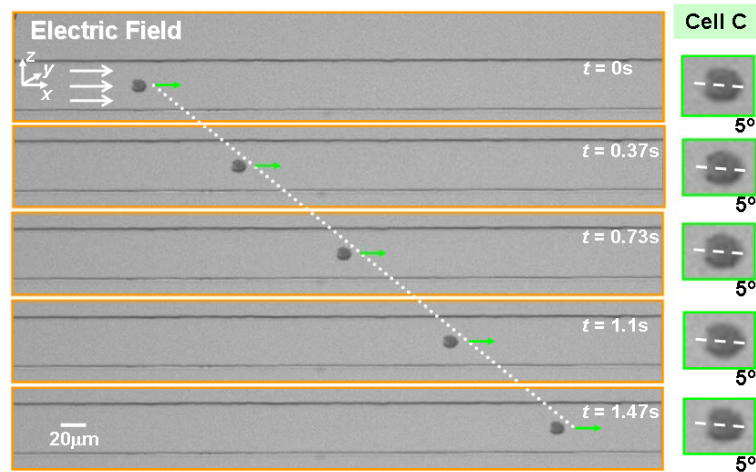
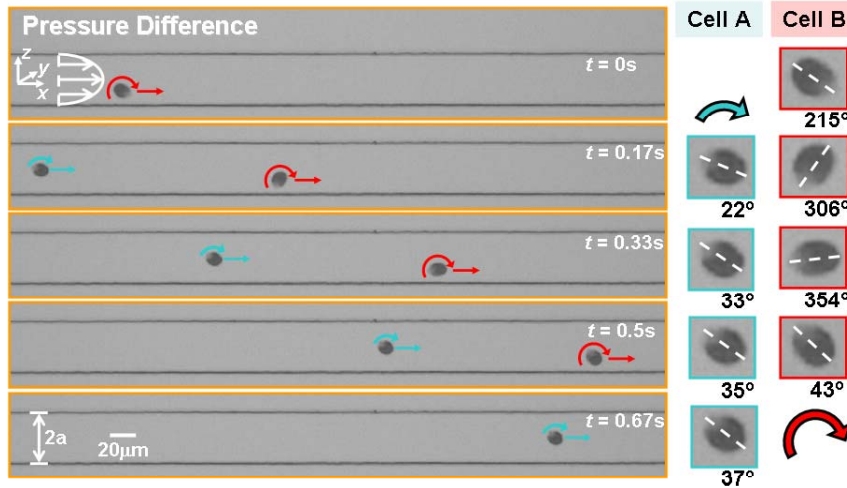
(Collaborated with Lap Man Lee)



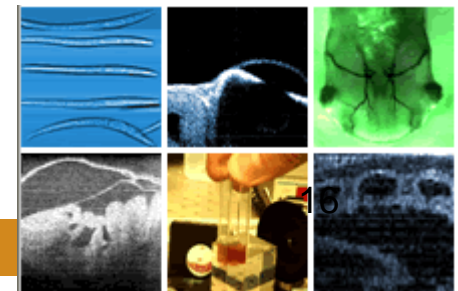
- Spherical/ellipsoidal cells imaging
- Easy to be integrated on a chip



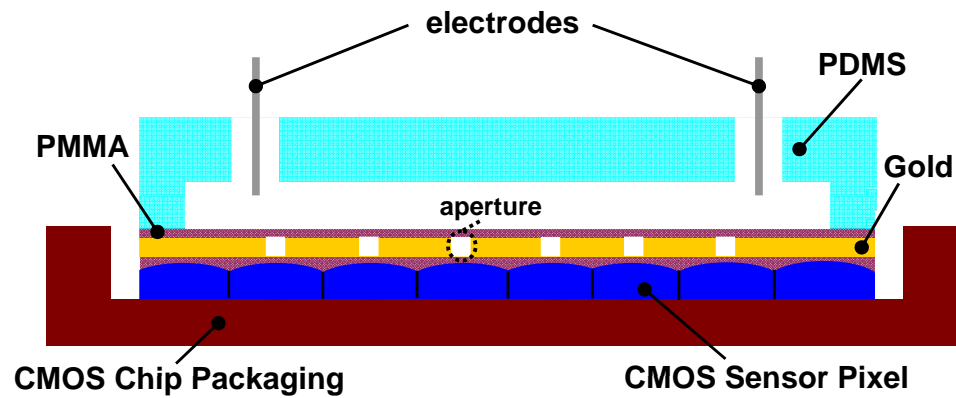
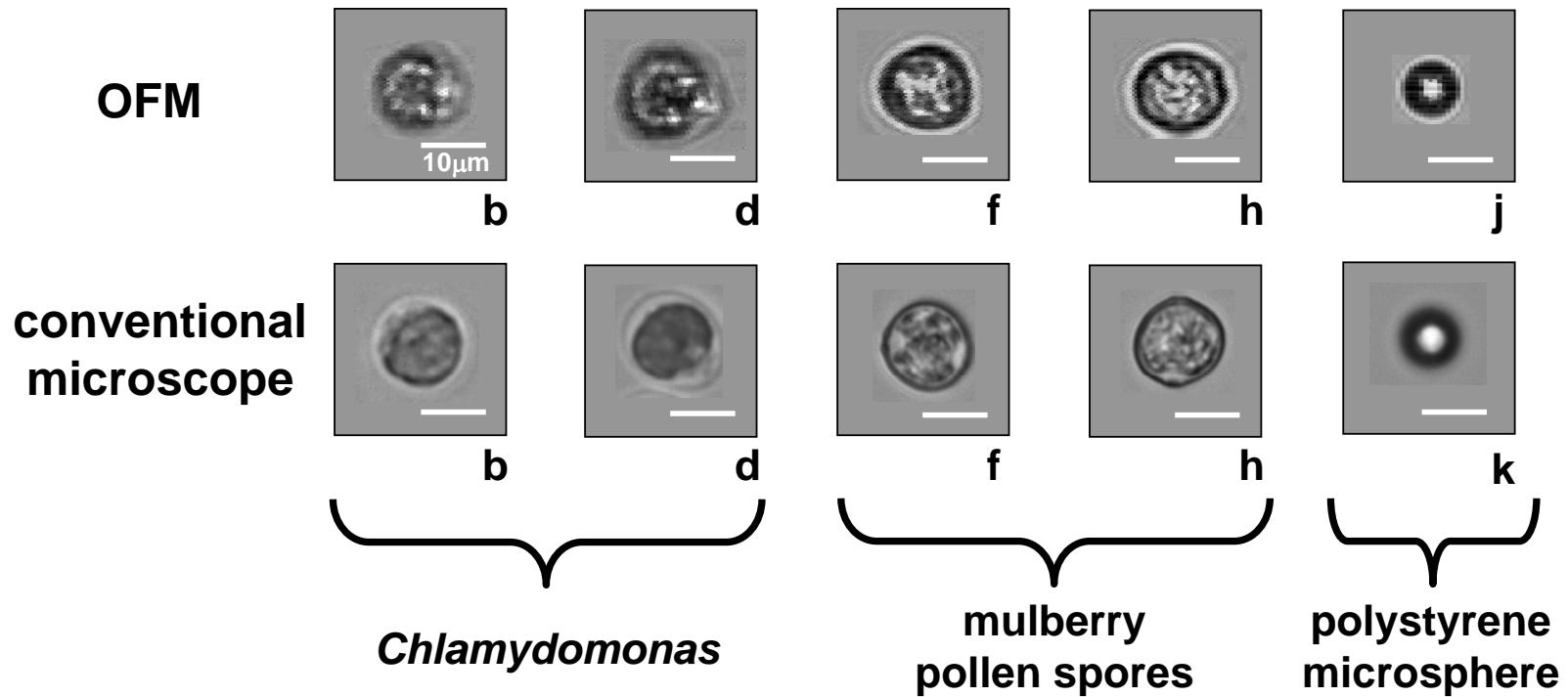
Electrokinetic Drive: Why?



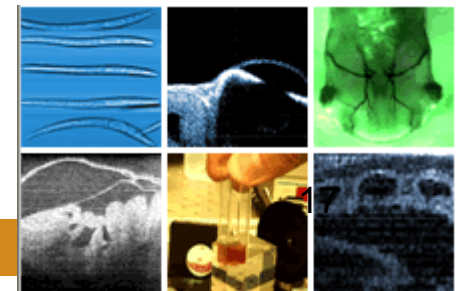
1. EK enables uniform cell transportation.
2. Electroorientation aligns cells.



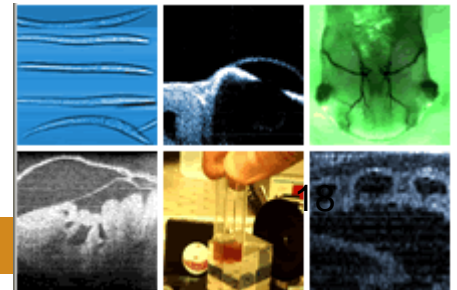
On-chip EK OFM



Uniform motions of samples yield perfect EK OFM images.

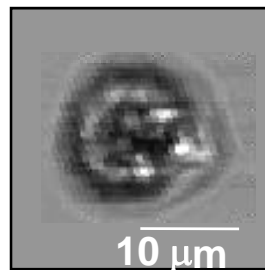
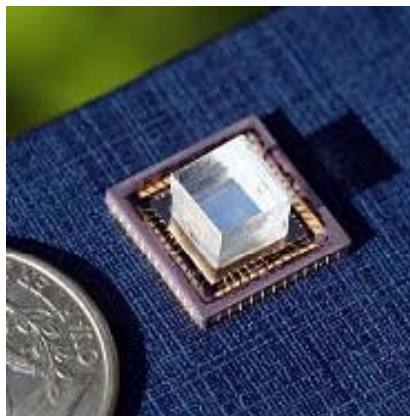


Conclusions and future directions



Conclusions

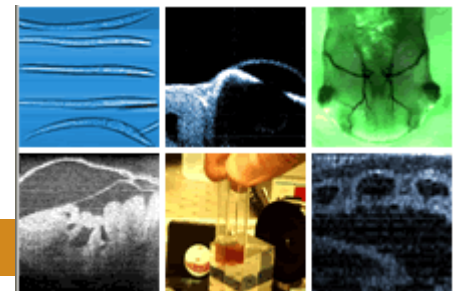
- Created world's smallest high resolution microscope on a single chip
- Automated & parallelizable on-chip cell microscopy method
- The low cost and compactness of OFM can change the way we use microscopes



Chlamy



C. elegans



Acknowledgment

Biophotonics group:

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Arthur Chang
Jose Pacheco
Edward Hsiao

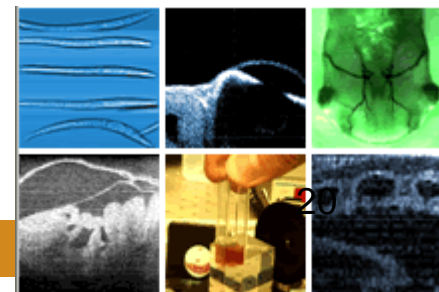


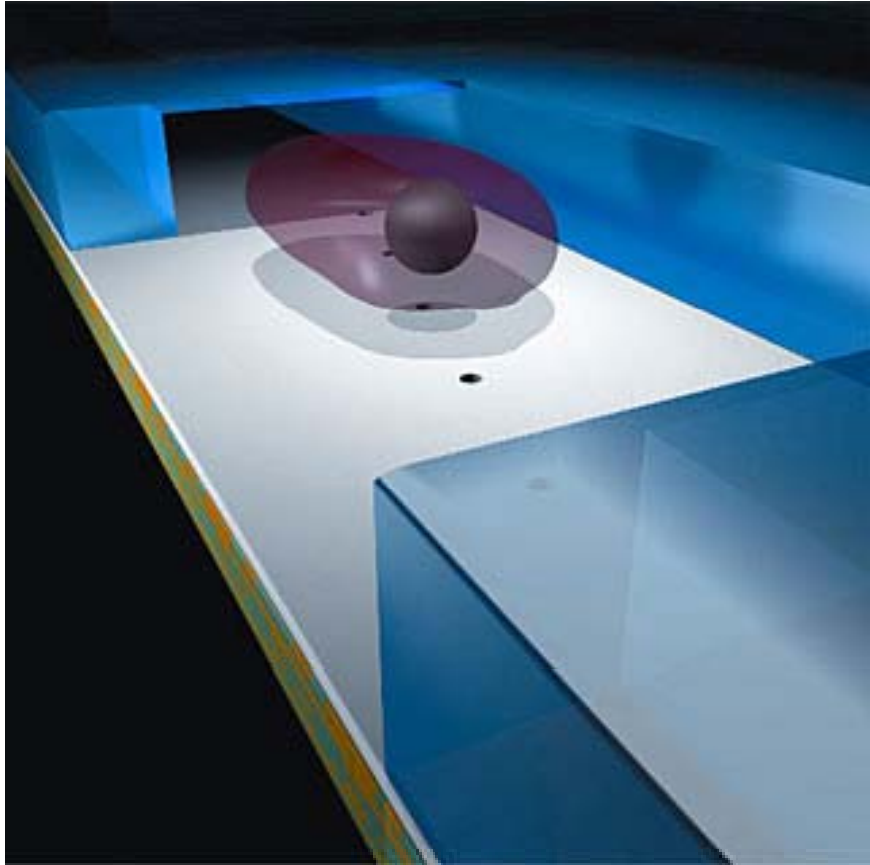
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Dr. Weiwei Zhong
Prof. Axel Scherer
Prof. David Erickson (Cornell)
Dr. L. Ryan Baugh

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Thank you!

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