Virginia Tech
Wake Forest University
School of Biomedical Engineering and Sciences

Why can't humans walk on water and climb walls with their fingertips like spiders?

Rafael V. Davalos

- How many of you like to be creative or use your imagination?
- How many people like math or science?
- Who likes art or likes to draw?

All of you could be engineers!

What do Engineers do?

- Many different types of Engineers:
  - Mechanical Engineers (Design Spaceships!)
  - Electrical Engineers (Fast computers)
  - Chemical Engineers (Nanotechnology)
  - Civil Engineers (Build Skyscrapers!)
  - Bio Engineers: Engineering with biology- design and build a hip bone to put inside a body

All engineering needs teamwork!

I am a Bioengineer

(As a professor, I work with my students in a lab, doing all sorts of things...)

What is at the micro level?

- Microelectromechanical systems (MEMS)

What are MEMS?

- Miniature devices that enable the operation of complex systems (e.g., air bags, printers)
- Needs teamwork (every type of engineer/scientist)

Why do we need things so small?

- Computer chips
- Treat diseases
- Cells, bacteria, Fred…

1 m | 1 mm | 1 µm | 1 nm

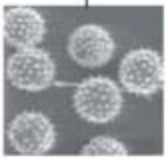
Wafer (10 cm)

Chip (~1 cm)

Hair
(~100 µm)

Cells (~10 µm)

Most MEMS
(1 µm - 1 mm)

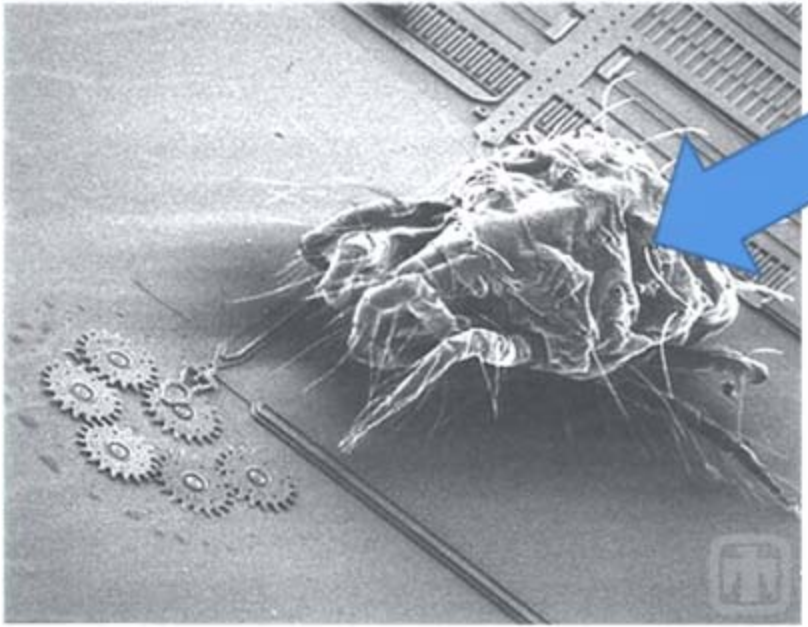


Virus (~10 nm)

Transistor
(~1 µm)

Molecules
(~1 nm)

How many of you would like a pet?



It's a dust mite- you all have many of them right now! Dust mites are even bigger than what we can make at the microscale.

Why can't humans walk on water and climb walls with their fingertips like spiders?

Answer: Because the physical laws that dominate are different at such a small level! And things just sometimes don't make sense when we look at things from the microscale.

When you jump off a diving board, what happens when you hit the water?

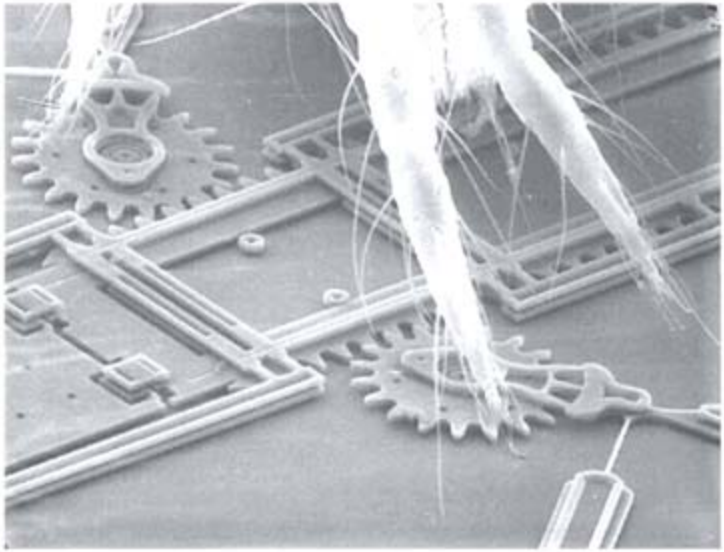
Splash! Sink... and swim up to the surface.

If you were the size of a microparticle, do you know what would happen if you jumped off a diving board?

It would be like jumping on top of Jello!

Birthday at Microscale!

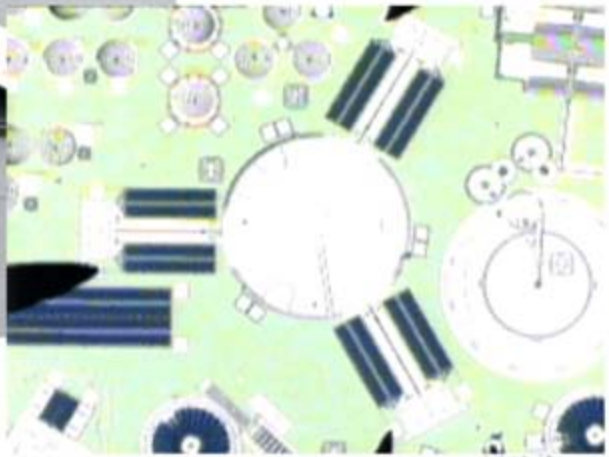
Complex Gearboxes



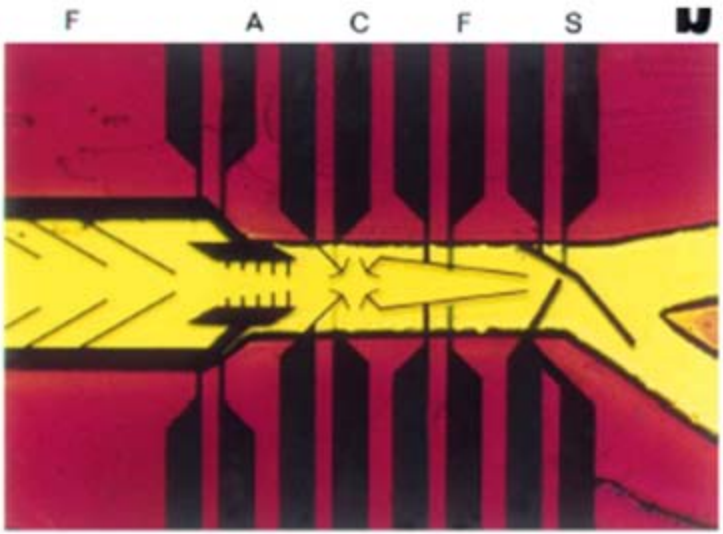
Fred on a MEMS Device

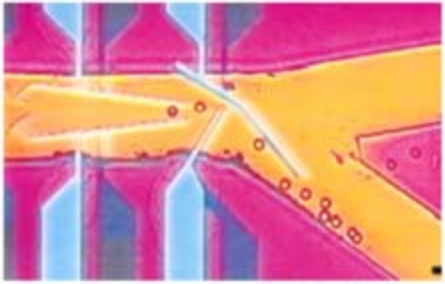
Micro tweezers

Micro mirrors



Microfluidics
(Cell Sorter, Muller 1998)

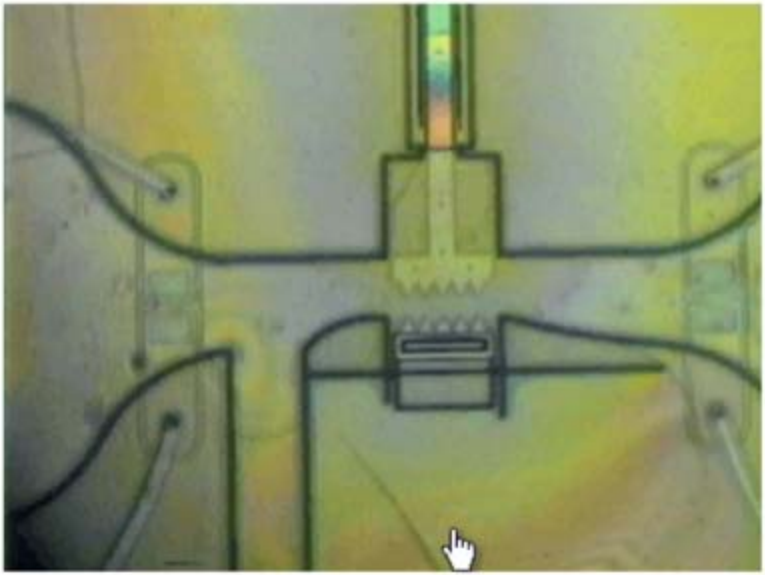




Field Cage

Slide

Microfluidics

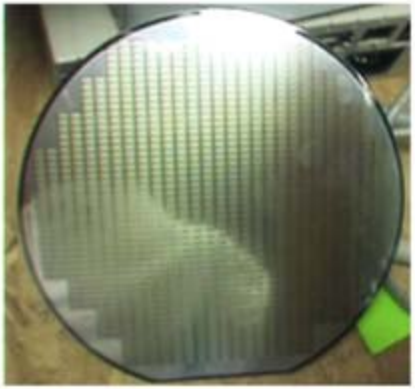


RBC cell sorter and microinjector

Basic Materials

You can't use micro nails or hammers to build something this tiny!

Building block approach: One layer on top of another- then use special techniques to add or subtract materials



Silicon Wafers
10cm dia. / 525um thick

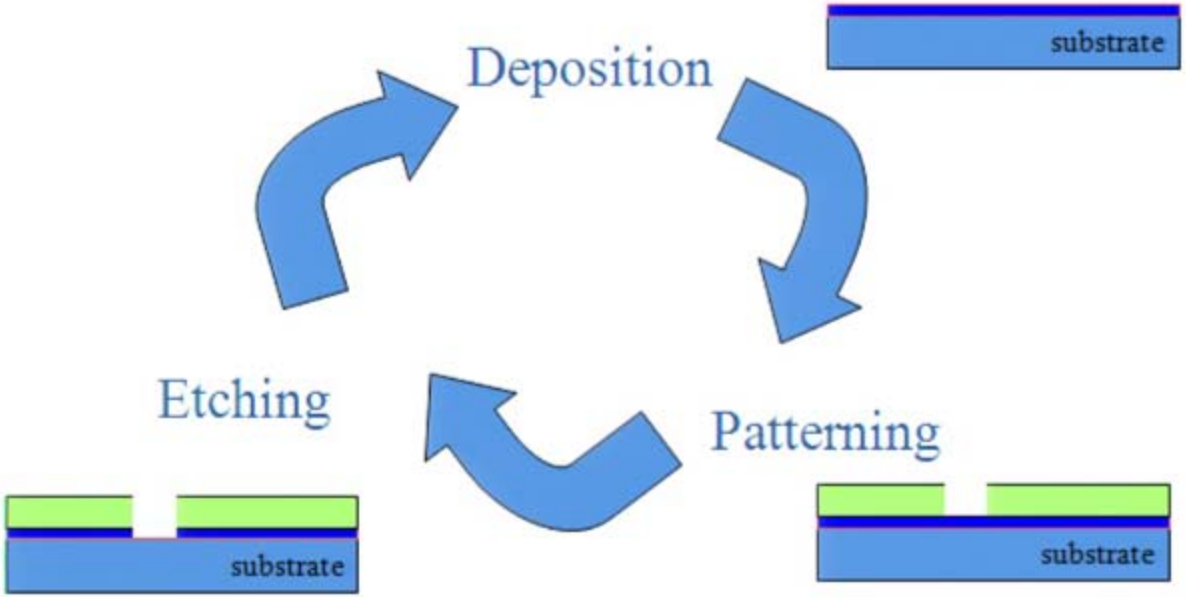
Thin Films ~2um

Sacrificial, Insulative (Silicon Dioxide & Nitride)

Structural (Polysilicon)

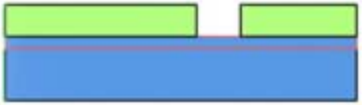
Electrical Contact (Metals: Al/Ti/Copper)

Basic Process Flow



Example: How to make a beam

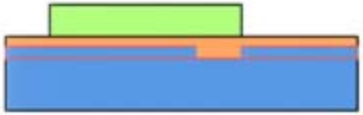
1. Deposit Sacrificial Layer (SiO2)



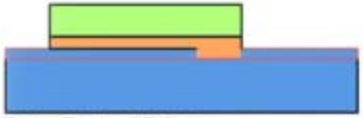
2. Deposit/Expose/Develop Photoresist

3. Oxide Etch (HF)

4. Deposit Polysilicon



5. Deposit/Expose/Develop Photoresist



6. Poly Etch (HNA)

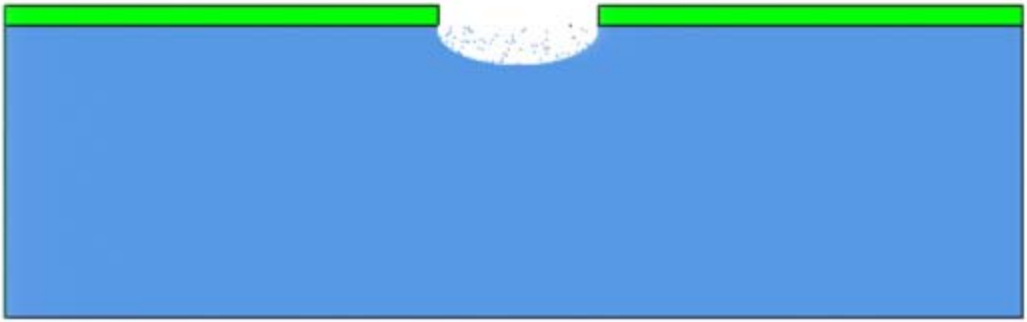
7. HF Release

Sometimes we cut right into the chip!

Virginia Tech
Wake Forest University
Bioelectromechanical Systems Lab.

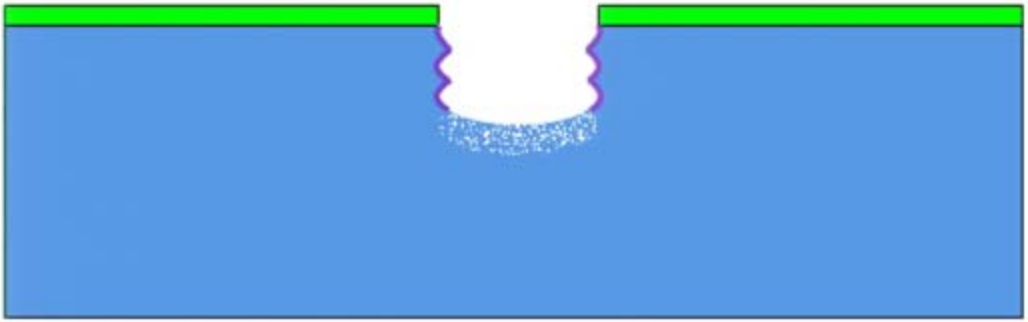
Sometimes we cut right into the chip!

Virginia Tech
Wake Forest University
Bioelectromechanical Systems Lab.



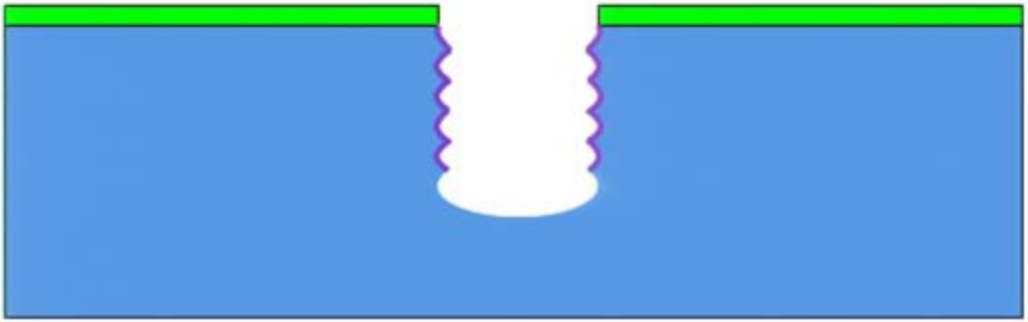
Sometimes we cut right into the chip!

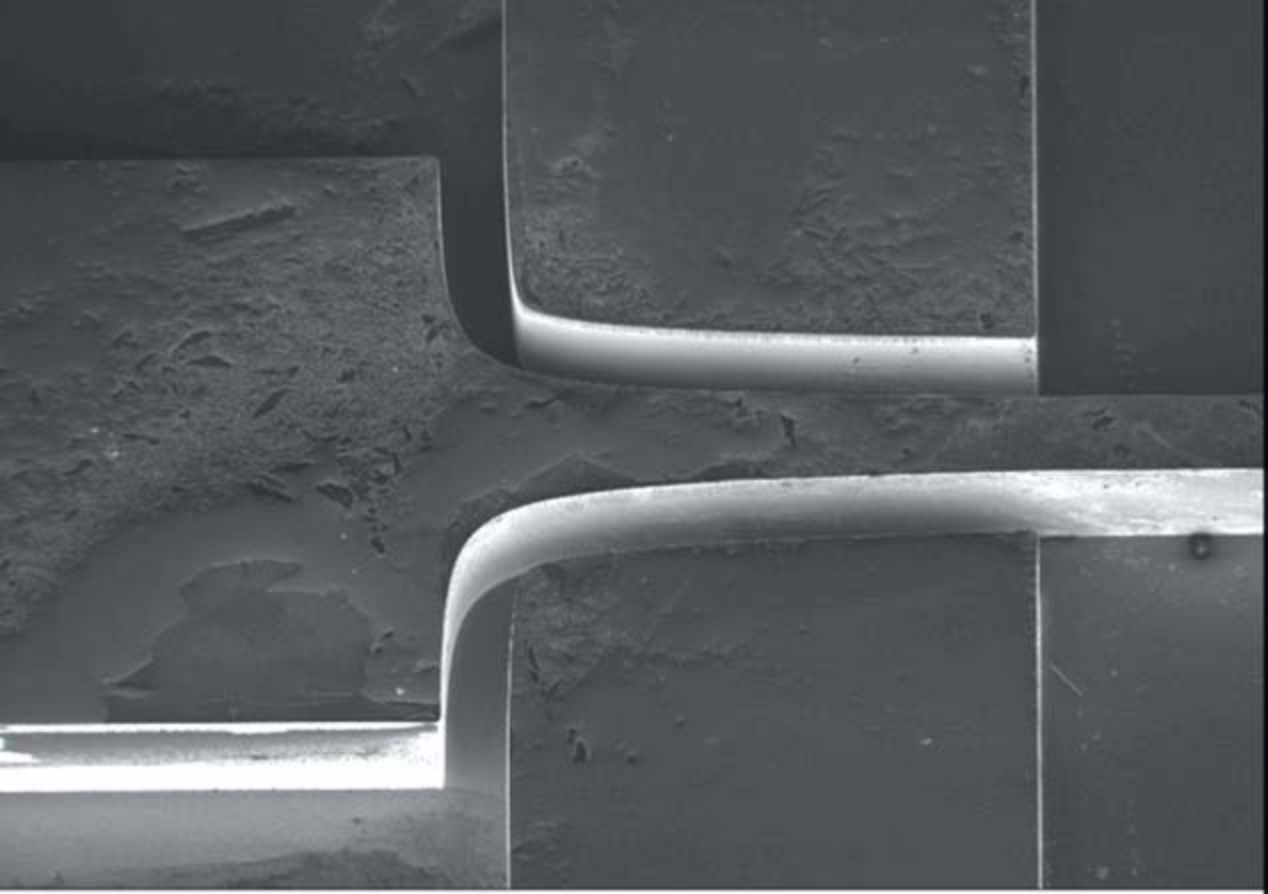
Virginia Tech
Wake Forest University
Bioelectromechanical Systems Lab.

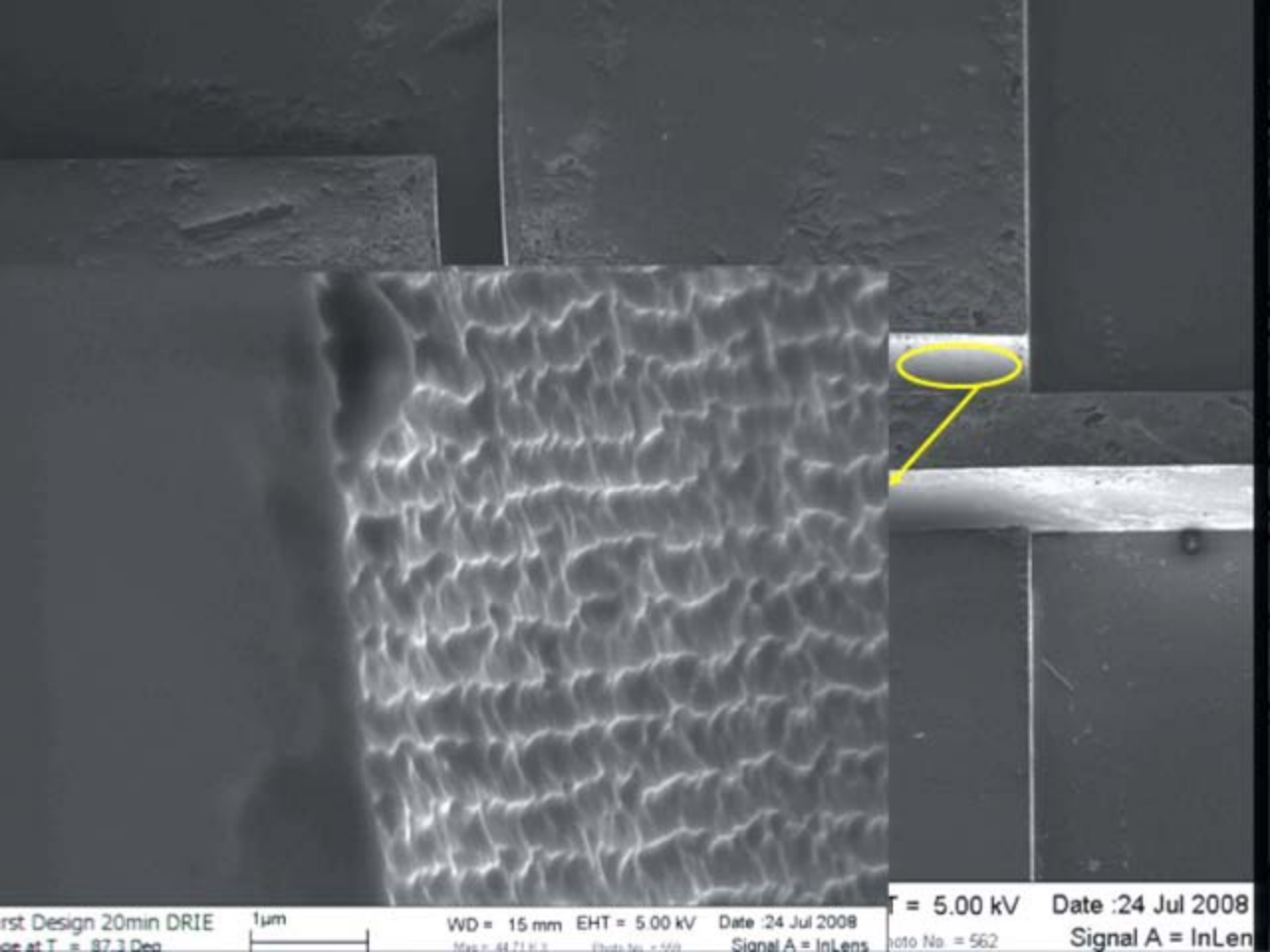


Sometimes we cut right into the chip!

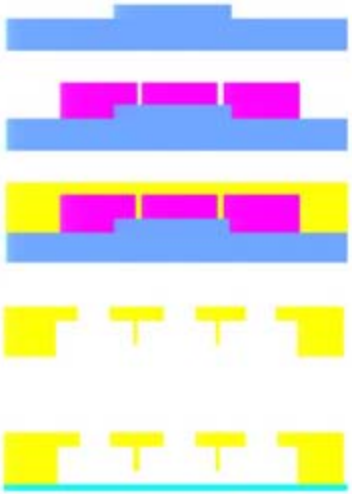
Virginia Tech
Wake Forest University
Bioelectromechanical Systems Lab.




First Design 20min DRIE
Stage at T = 27.0 Deg
30µm
WD = 8 mm
EHT = 5.00 kV
Date :24 Jul 2008
Mag = 801 X
Photo No. = 562
Signal A = InLen


rst Design 20min DRIE
1µm
WD = 15 mm EHT = 5.00 kV
Date :24 Jul 2008
Signal A = InLens
T = 5.00 kV
Date :24 Jul 2008
Signal A = InLen

You can use the chip as a mold



(a) 3.1 μm height patterns were made using deep reactive ion etching

(b) 50 μm high patterns were added for wide regions using SU-8 negative photoresist

(c) PDMS poured on top and cross linked

(d) Via holes punched to interface with world

(e) Oxygen plasma bond to substrate

Silicon
SU-8
PDMS
glass

Repeating unit of PDMS

UCSF & UCB joint graduate group in BIOENGINEERING

Sandia National Laboratories

BSAC

You can use the chip as a mold

(a) 3.1 μm height patterns were made using deep reactive ion etching

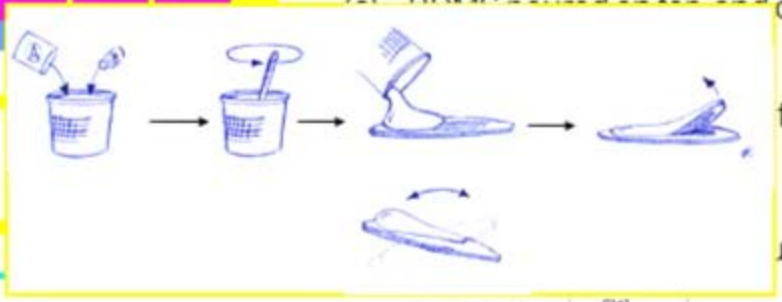
(b) 50 μm high patterns were added for wide ng SU-8 negative photoresist

cross linked

face with world

ubstrate

Easy as baking a cake!

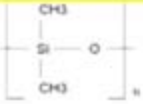


Silicon

SU-8

PDMS

glass

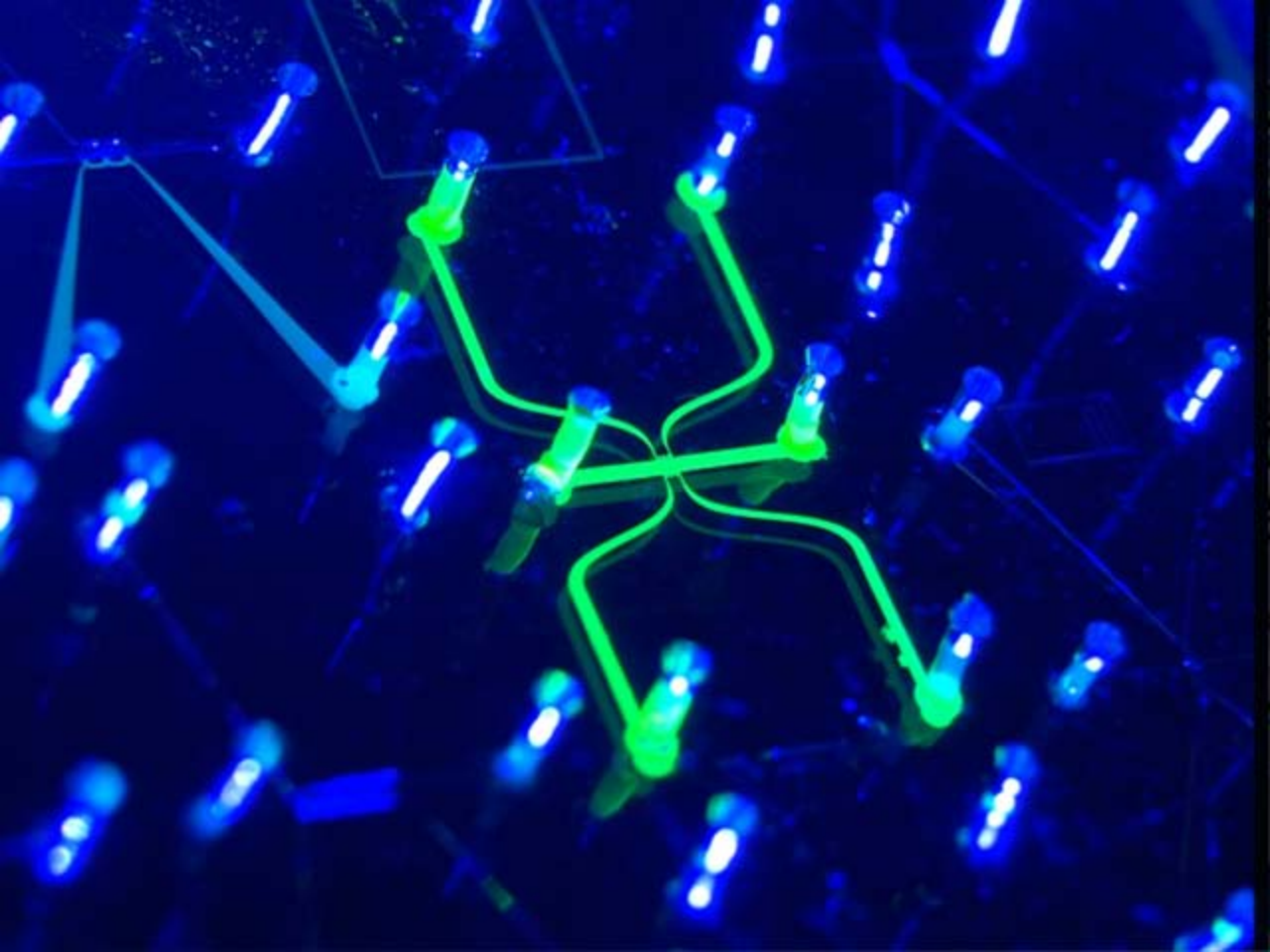


Repeating unit of PDMS

BIOENGINEERING

Sandia National Laboratories

BSAC



What might you consider when designing a MEMS device?

Not intuitive Science

- Usual assumptions go out the window
  - –Surface Tension
  - –Friction
  - –Capillary Forces
  - –Electrostatic Forces

} Dominating factors at the microscale

$$\mathrm{Re} = \frac{\text{inertial forces}}{\text{viscous forces}} = \frac{\rho L^2 V^2}{\mu L V} = \frac{\rho L V}{\mu} << 1$$

As if swimming in mud...

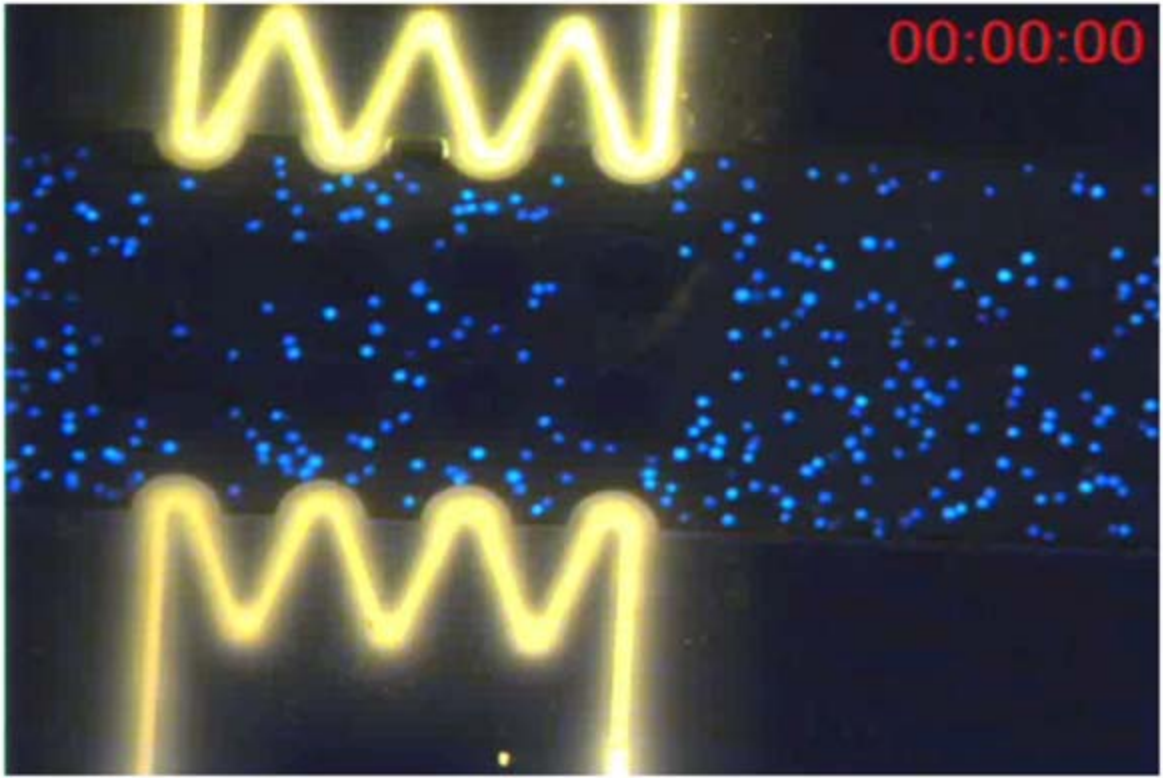
Scaling Laws

- Muscles ~L*L
- Weight ~L*L*L
- Jumping = Muscles / Weight
  - Human (L=2m) ~ 0.5
  - Spider (L=0.01m) ~ 100

Peter Parker
should be a wimp!

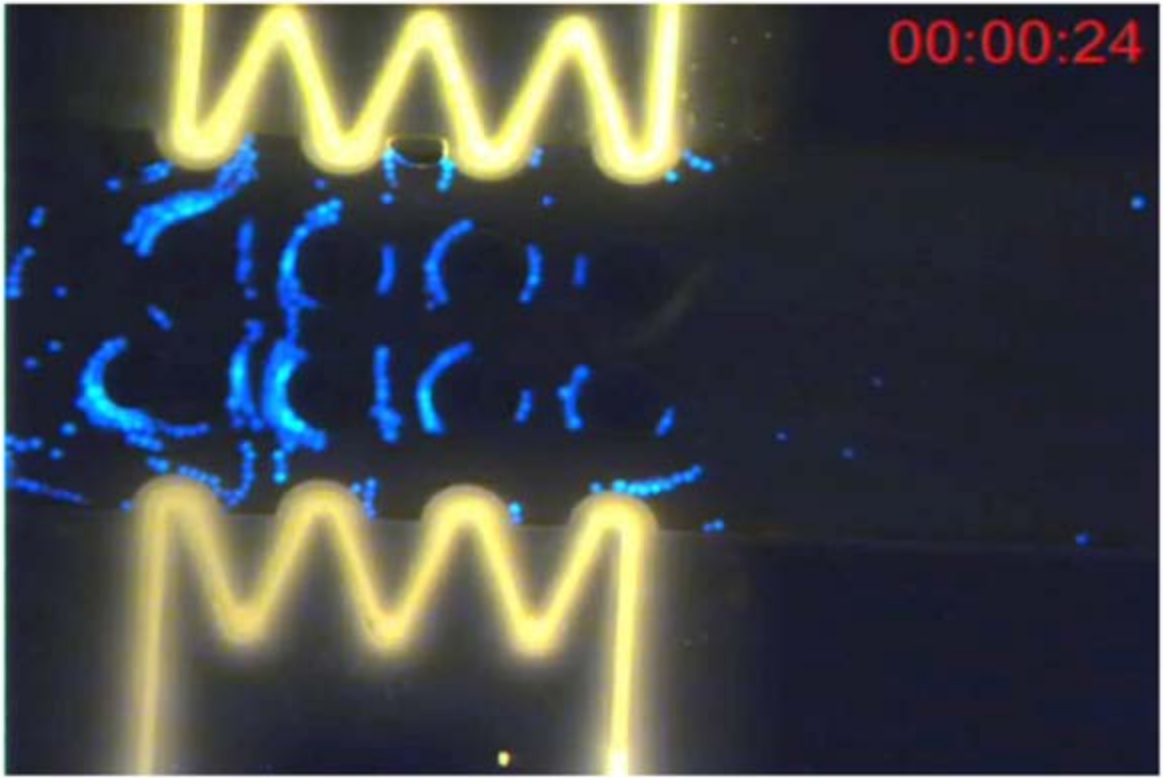
My lab traps cancer cells

Virginia Tech
Wake Forest University
School of Biomedical Engineering and Sciences



My lab traps cancer cells

Virginia Tech
Wake Forest University
School of Biomedical Engineering and Sciences



Who has heard of cancer, the disease?

Right now, if someone goes to the doctor, they recognize cancer when:

- A patient doesn't "feel right".
- Nurses and doctors collect simple measurements.
- Follow-up clinical tests (blood, saliva).
- Internal examinations using "non-invasive" imaging (x-rays, CAT, MRI).

Doctors compare results with ranges of normal people thought to not be diseased.

How Today's Medicine Works for Treatment of Disease

- Stabilization of the patient so that the patient can repair himself/herself
- Surgical repair of injuries or removal or diseased tissues or organs
- Treatment with chemical drugs that are delivered locally
- Treatment with chemical drugs that are delivered systemically

James F. Leary, Ph.D., Professor of Basic Medical Science and Biomedical Engineering, Purdue Cancer Center.

Future Medicine: Nanomedicine

- Medicine performed at the single cell level –advanced targeted drug therapy
- Possible repair, rather than just elimination, of diseased cells at the single cell level (regenerative medicine)
- Sufficiently early diagnosis and treatment of disease that the distinction between prevention and treatment is blurred
- Portable and inexpensive diagnostic devices.

Nanomedicine is an area my students and I work on in my lab. Now, we're going to talk about some of the devices we have designed and some experiments we have done.

James F. Leary, Ph.D., Professor of Basic Medical Science and Biomedical Engineering, Purdue Cancer Center.

HOSPITAL REPORTS.

MELBOURNE HOSPITAL.

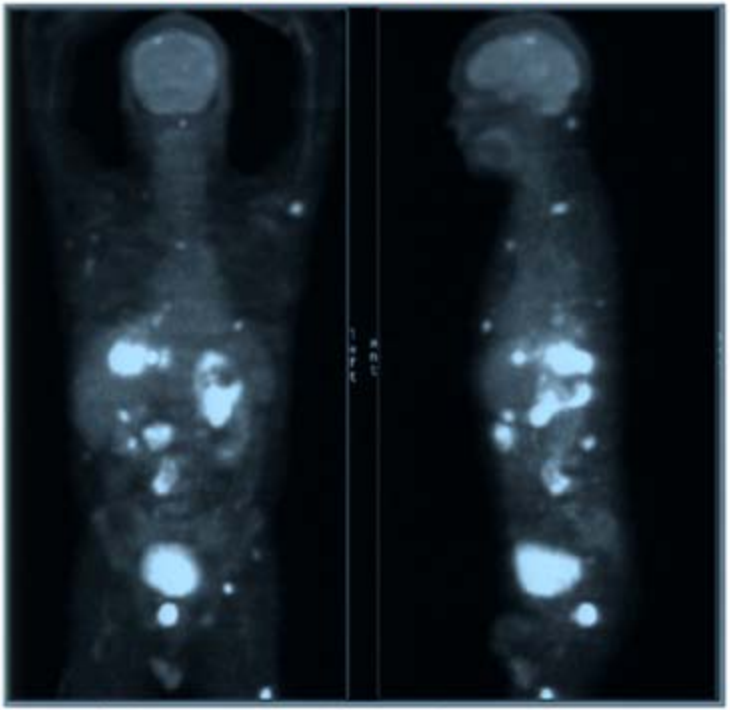
A case of Cancer in which cells similar to those in the Tumours were seen in the blood after death. Reported by THOMAS RAMSDEN ASHWORTH, Resident Physician.

(WITH ENGRAVING.)

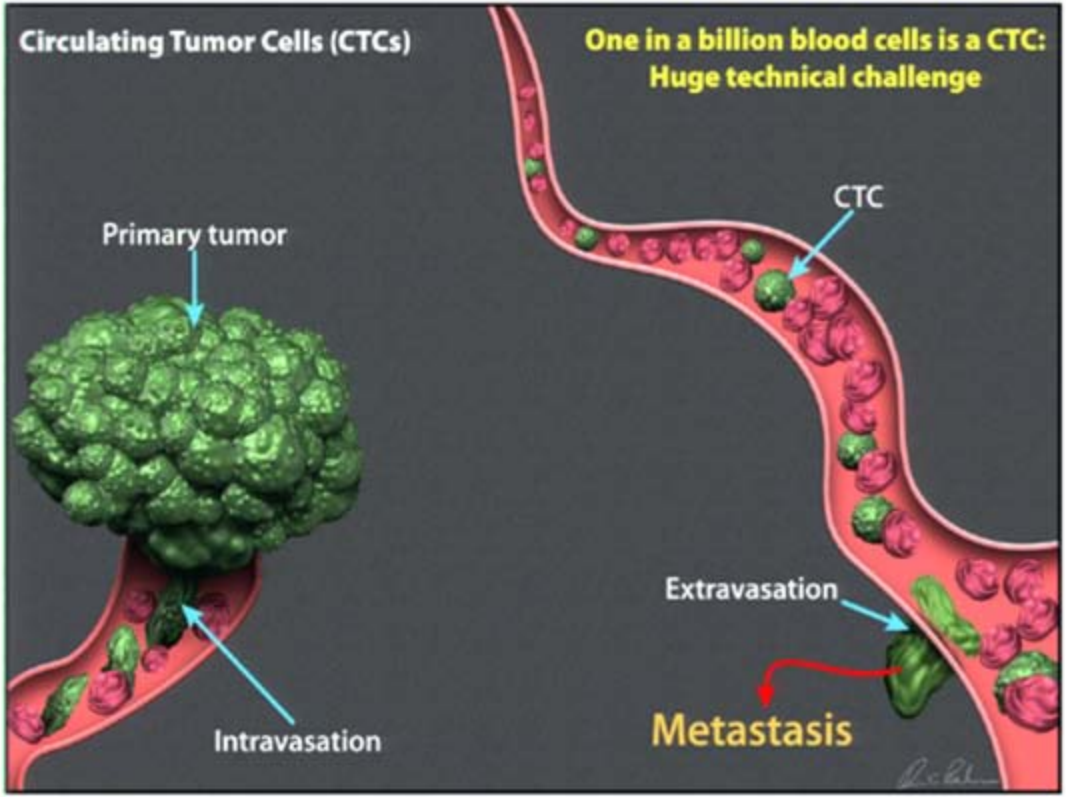
Richard J——, æt. 38, was admitted on Oct. 9th, 1868, suffering from what was understood to be "Rheumatism and Debility." He died of Marasmus on the 10th of the following March.

certain, that if they came from an existing cancer structure, they must have passed through the greater part of the circulatory system to have arrived at the internal saphena vein of the sound leg.

Metastatic Cancer



9 out of 10 cancer deaths are due to the metastasis


Circulating Tumor Cells (CTCs)
One in a billion blood cells is a CTC:
Huge technical challenge
CTC
Primary tumor
Extravasation
Intravasation
Metastasis

Our Vision: Early Cancer Detection

Virginia Tech
Wake Forest University
School of Biomedical Engineering and Sciences

The earlier you know cancer is in the body, the better the results will be for treatment.

With our micro devices, we can trap cancer cells from the blood before the patient feels any symptoms.

This means we can detect cancer before the patient has organ or tissue damage.

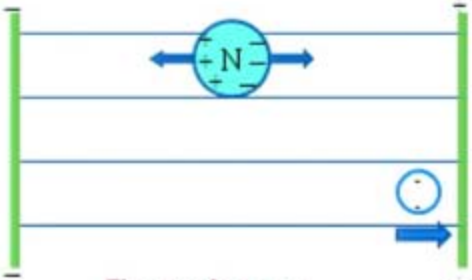
This means the patient can get treated and will be able to heal.

Here's how it works...

Dielectrophoresis (DEP)

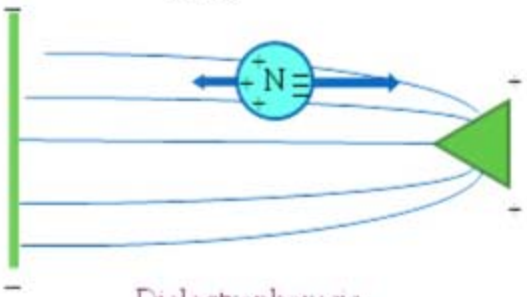
Dielectrophoresis: Motion of a particle due to a nonuniform electric field

Uniform Electric Field



Electrophoresis

Nonuniform Electric Field



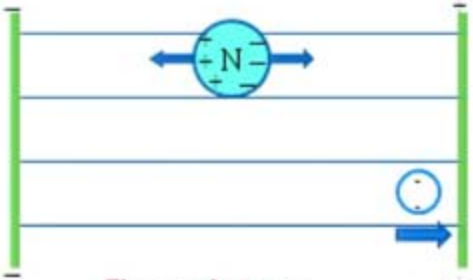
Dielectrophoresis (DEP)

Pohl, H.A. (1978) Dielectrophoresis, Cambridge University, Press Cambridge, U.K.).

Dielectrophoresis (DEP)

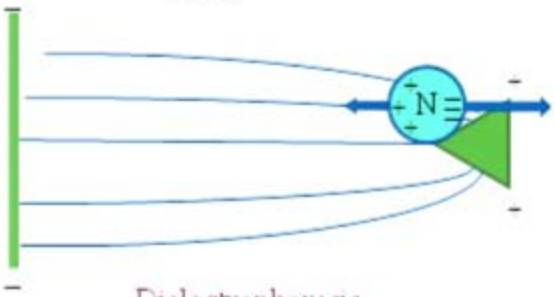
Dielectrophoresis: Motion of a particle due to a nonuniform electric field

Uniform Electric Field



Electrophoresis

Nonuniform Electric Field



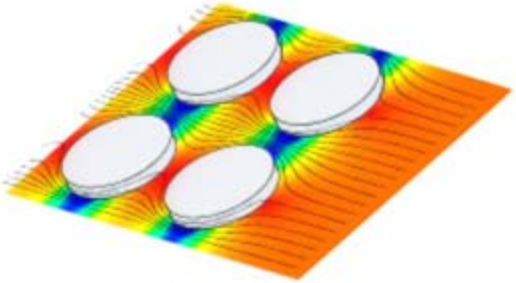
Dielectrophoresis (DEP)

Pohl, H.A. (1978) Dielectrophoresis, Cambridge University, Press Cambridge, U.K.).

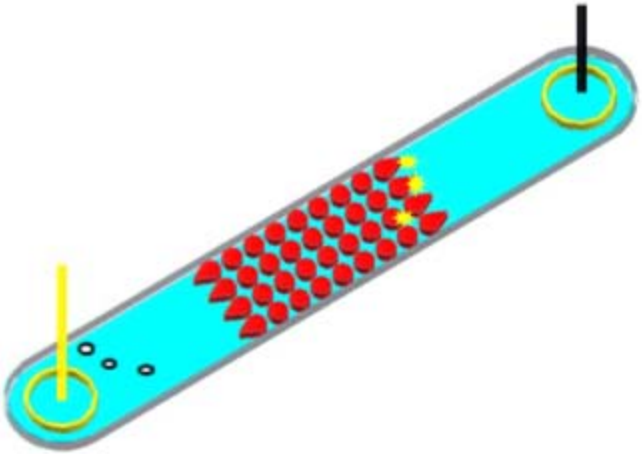
Dielectrophoresis

Virginia Tech
Wake Forest University
School of Biomedical Engineering and Sciences

- Integrated arrays of insulators used to create a nonuniform electric field
- Separates cells based on their unique electrical fingerprints
- Simple fabrication process
- DC or AC electric fields



Non-uniformities in E-field generated by insulating posts.

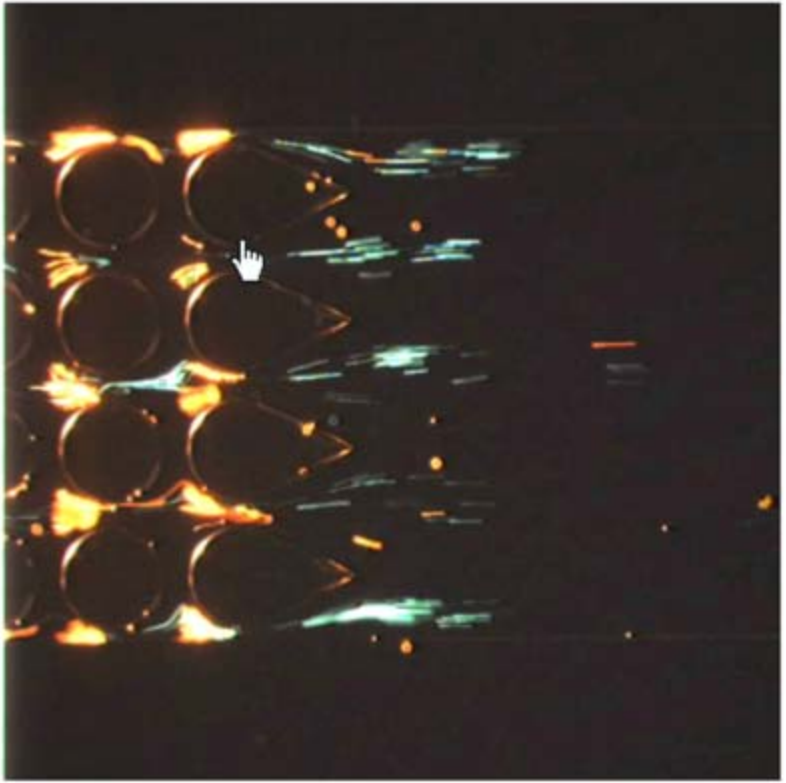


Red Blood Cell
Cancer Cell
Electrodes

apizco-Encinas, B. et al (2004) Analytical Chemistry

DEP separation in 'batch' mode

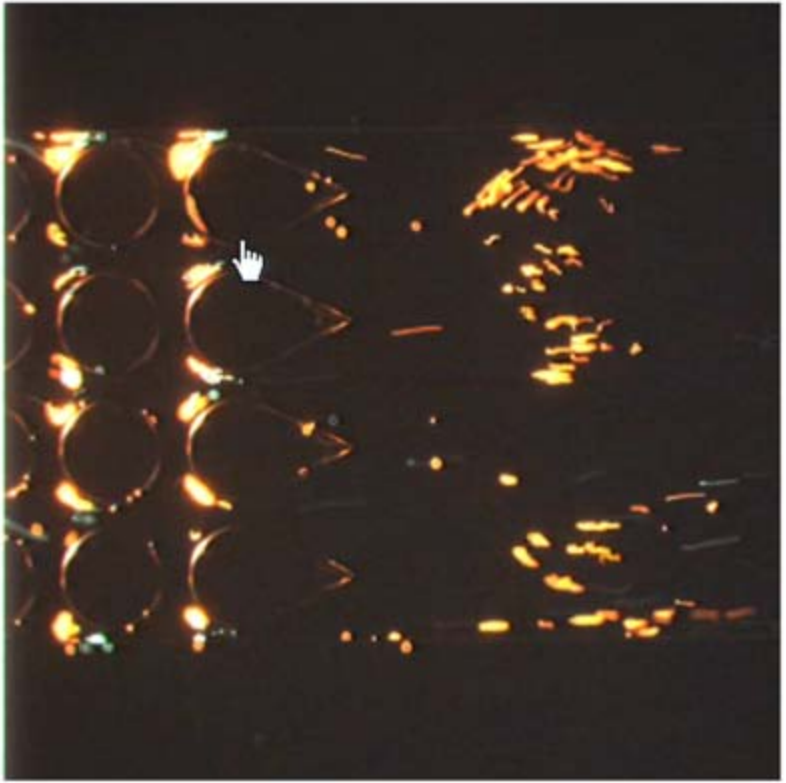
Virginia Tech
Wake Forest University
School of Biomedical Engineering and Sciences



2-μm red beads
1-μm green beads

DEP separation in 'batch' mode

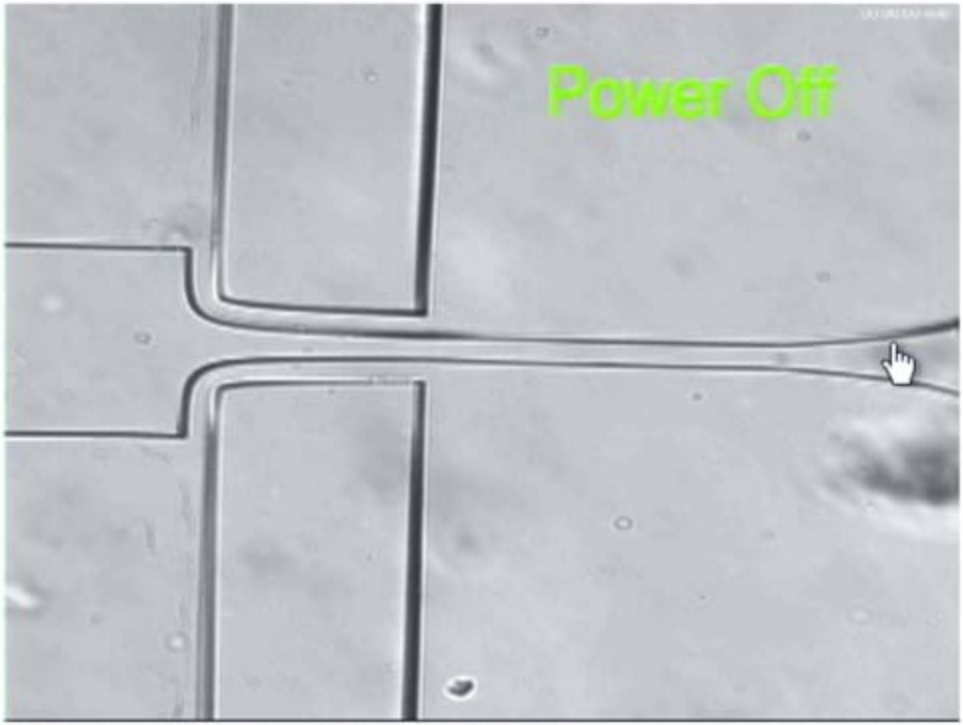
Virginia Tech
Wake Forest University
School of Biomedical Engineering and Sciences



2-μm red beads
1-μm green beads

Proof of Concept DEP

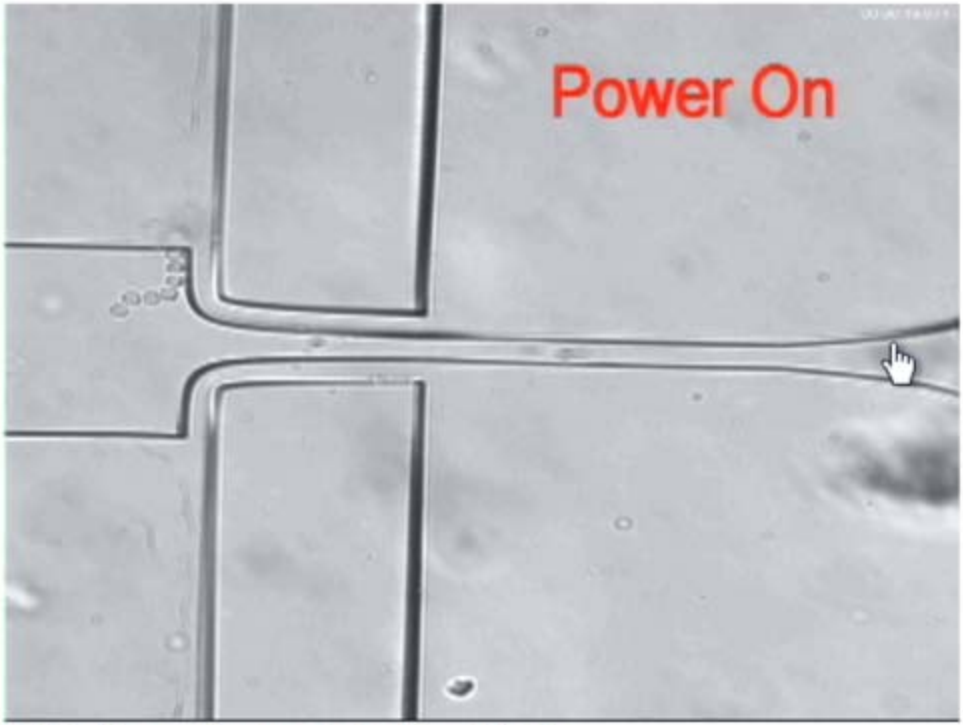
Virginia Tech
Wake Forest University
School of Biomedical Engineering and Sciences



THP-1 Human Leukemia 250V_{rms} 85kHz

Proof of Concept DEP

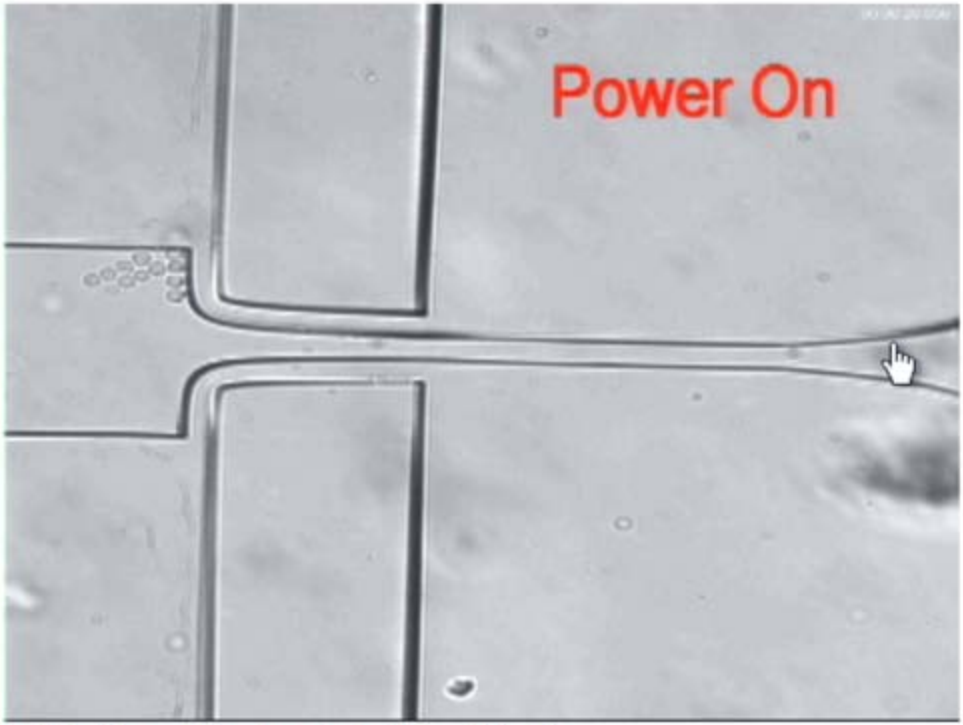
Virginia Tech
Wake Forest University
School of Biomedical Engineering and Sciences



THP-1 Human Leukemia 250V_{rms} 85kHz

Proof of Concept DEP

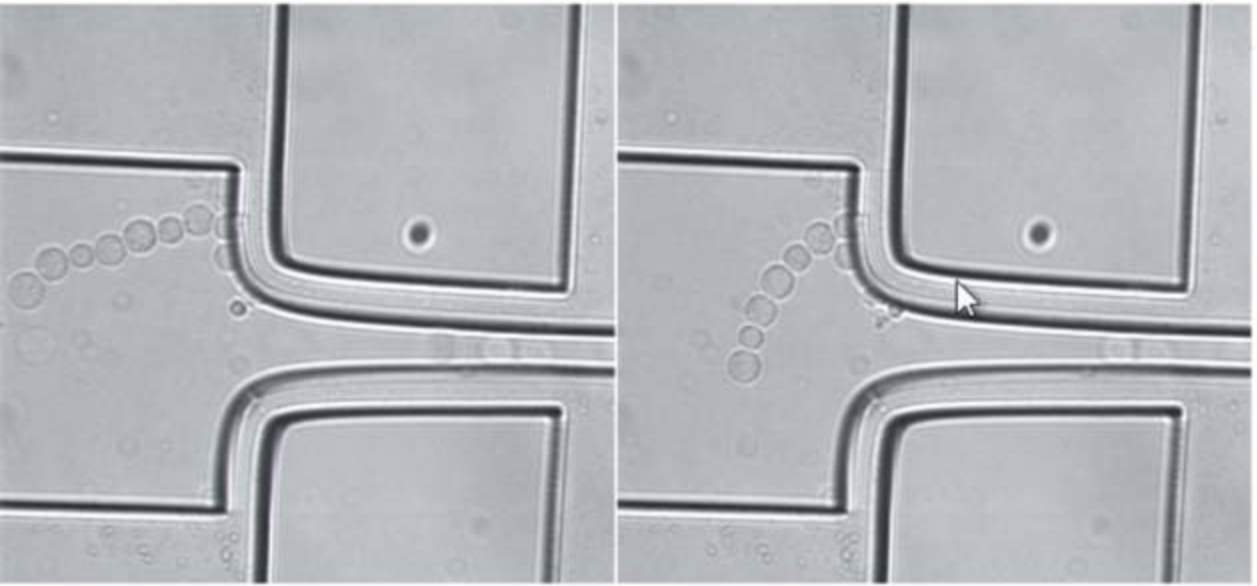
Virginia Tech
Wake Forest University
School of Biomedical Engineering and Sciences



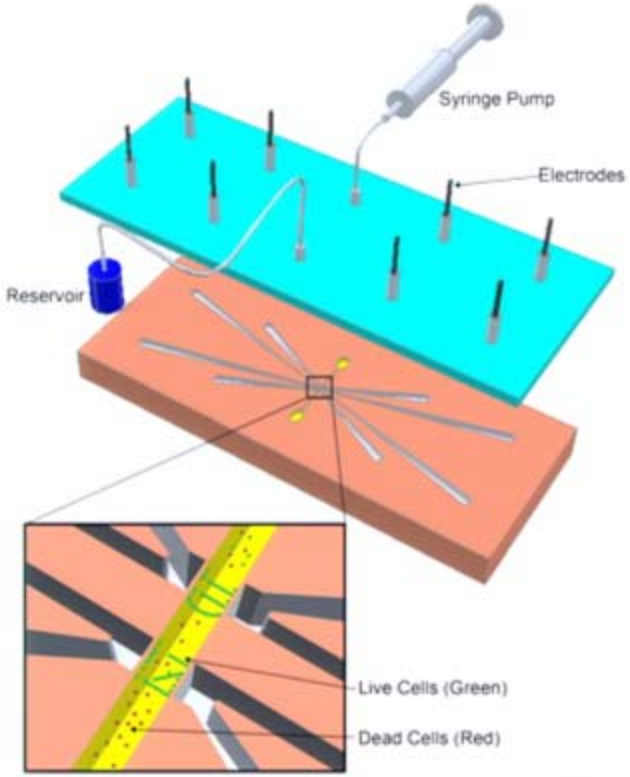
THP-1 Human Leukemia 250V_{rms} 85kHz

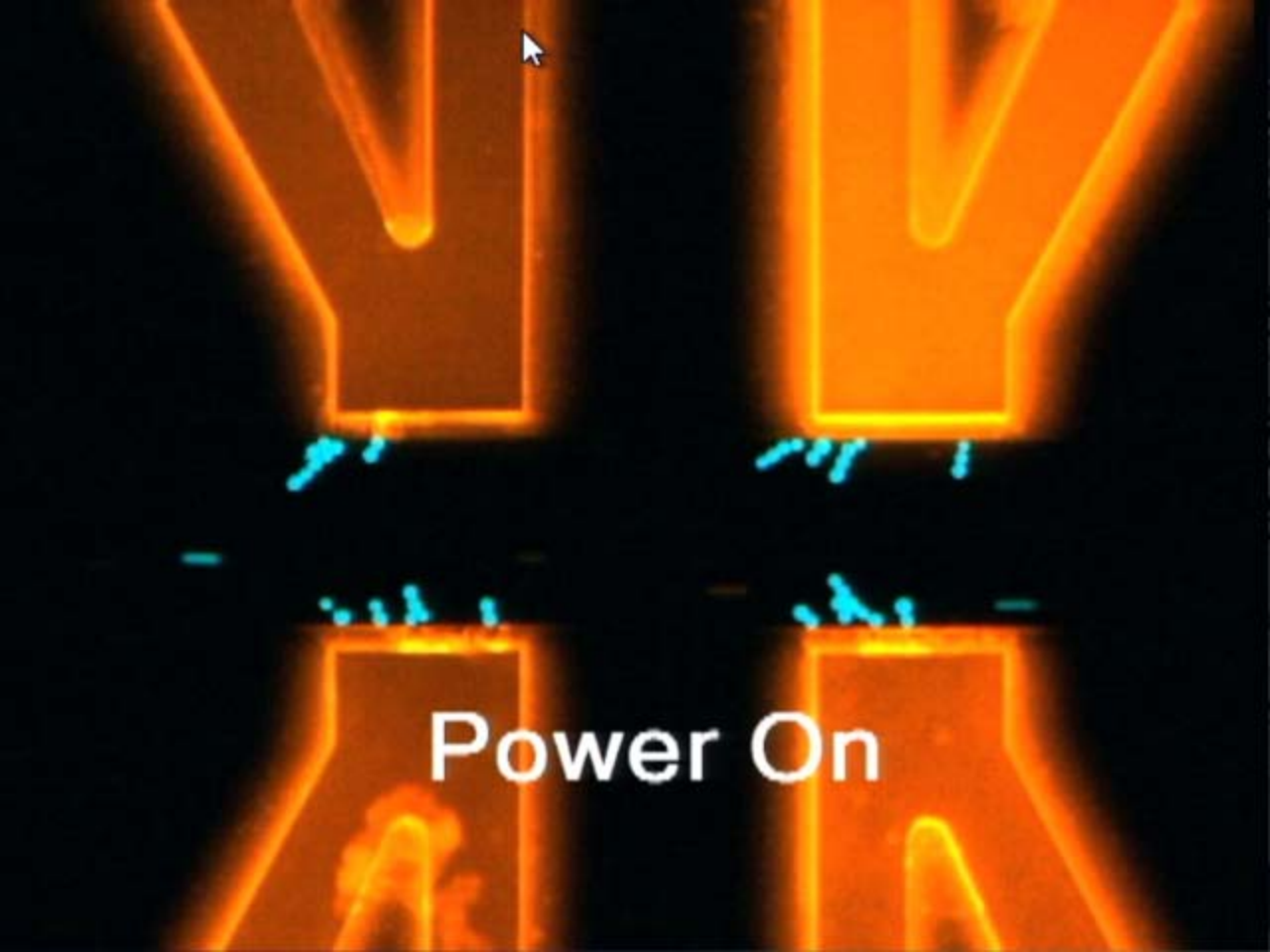
Polarized cells connect like magnets!

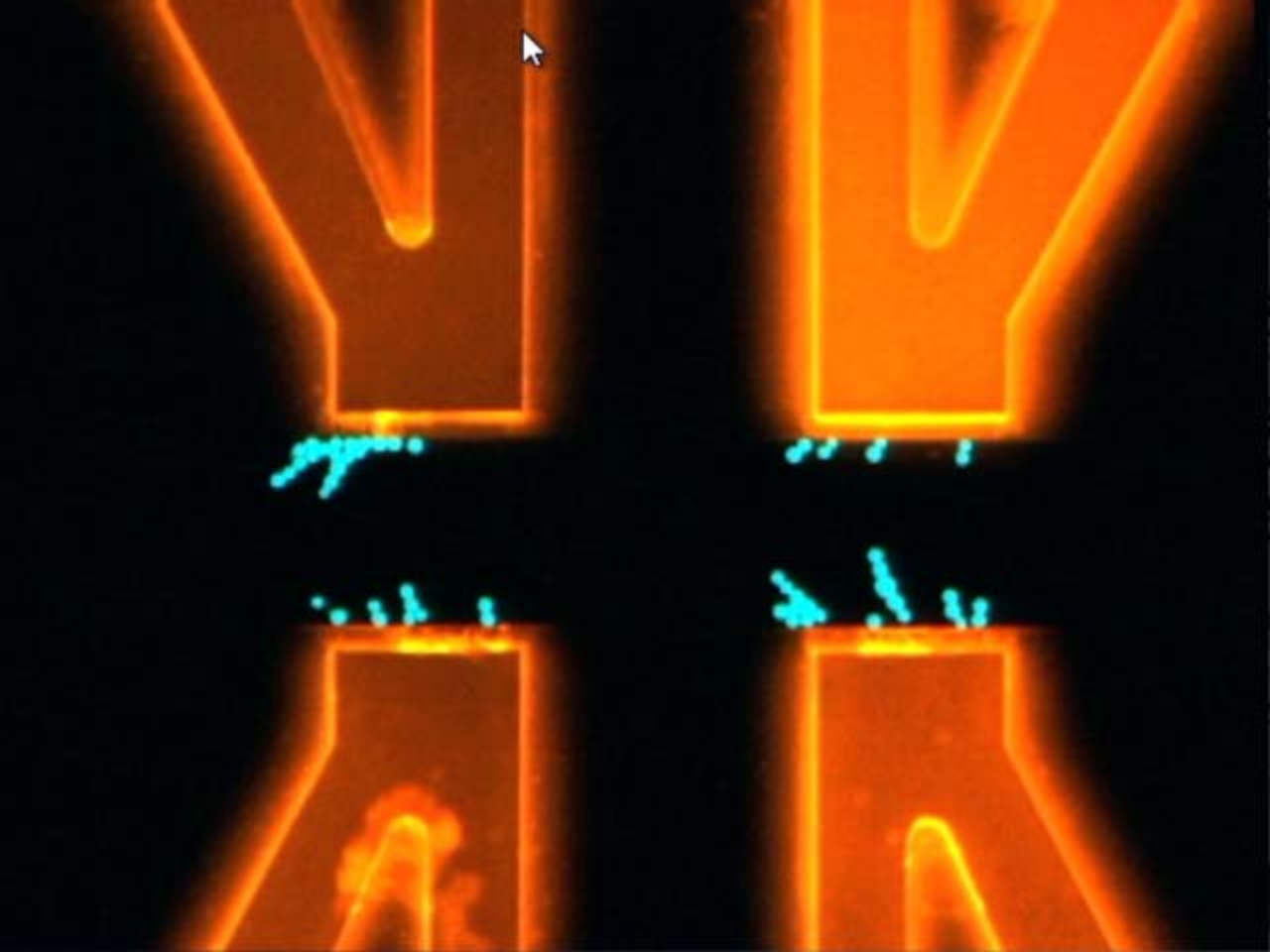
Virginia Tech
Wake Forest University
School of Biomedical Engineering and Sciences

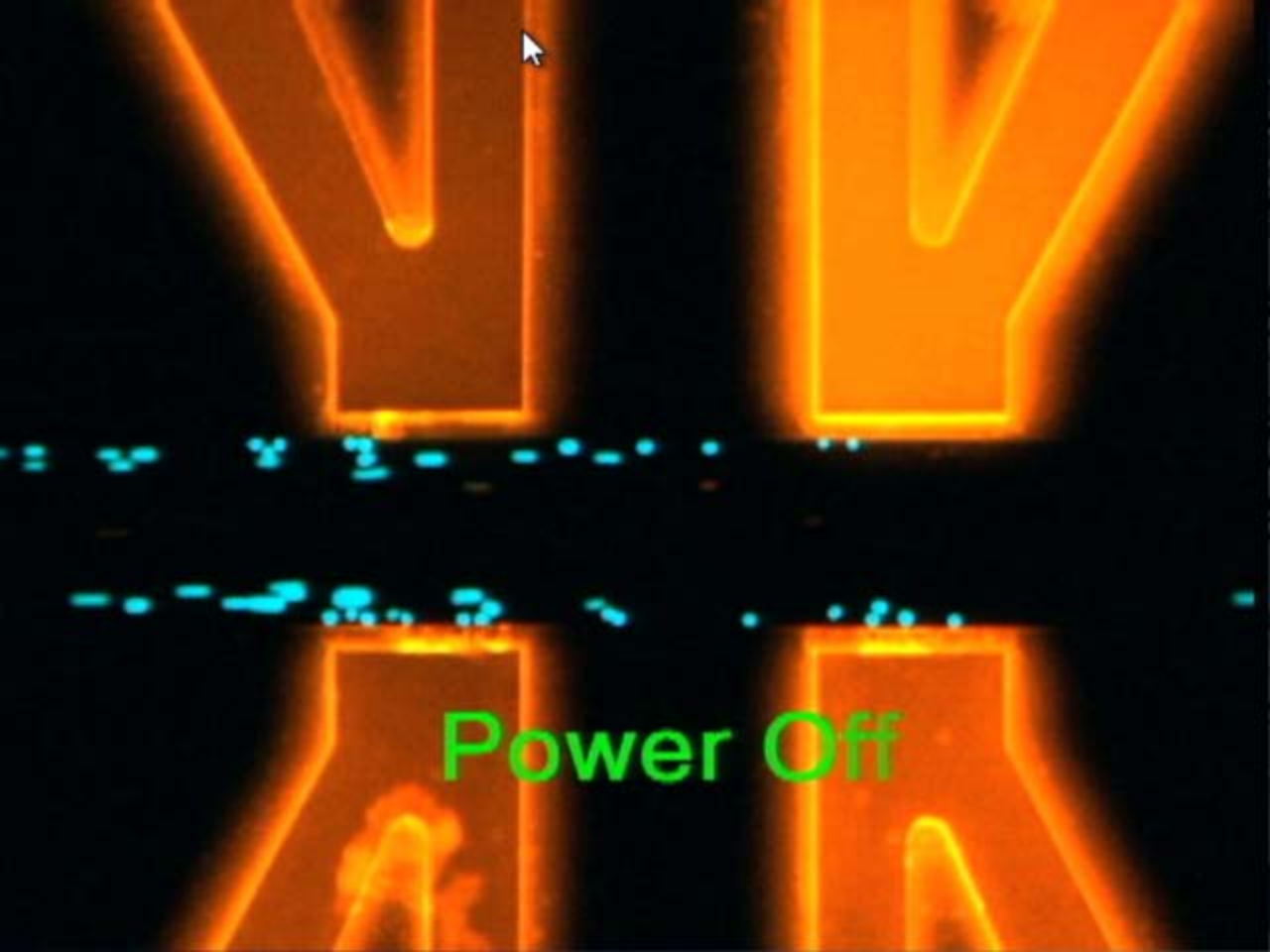


Experimental Set up



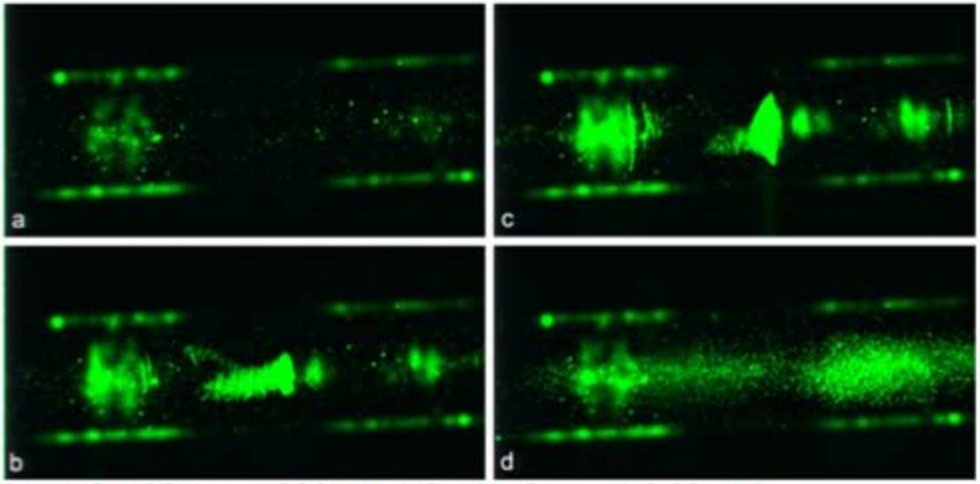

Power On



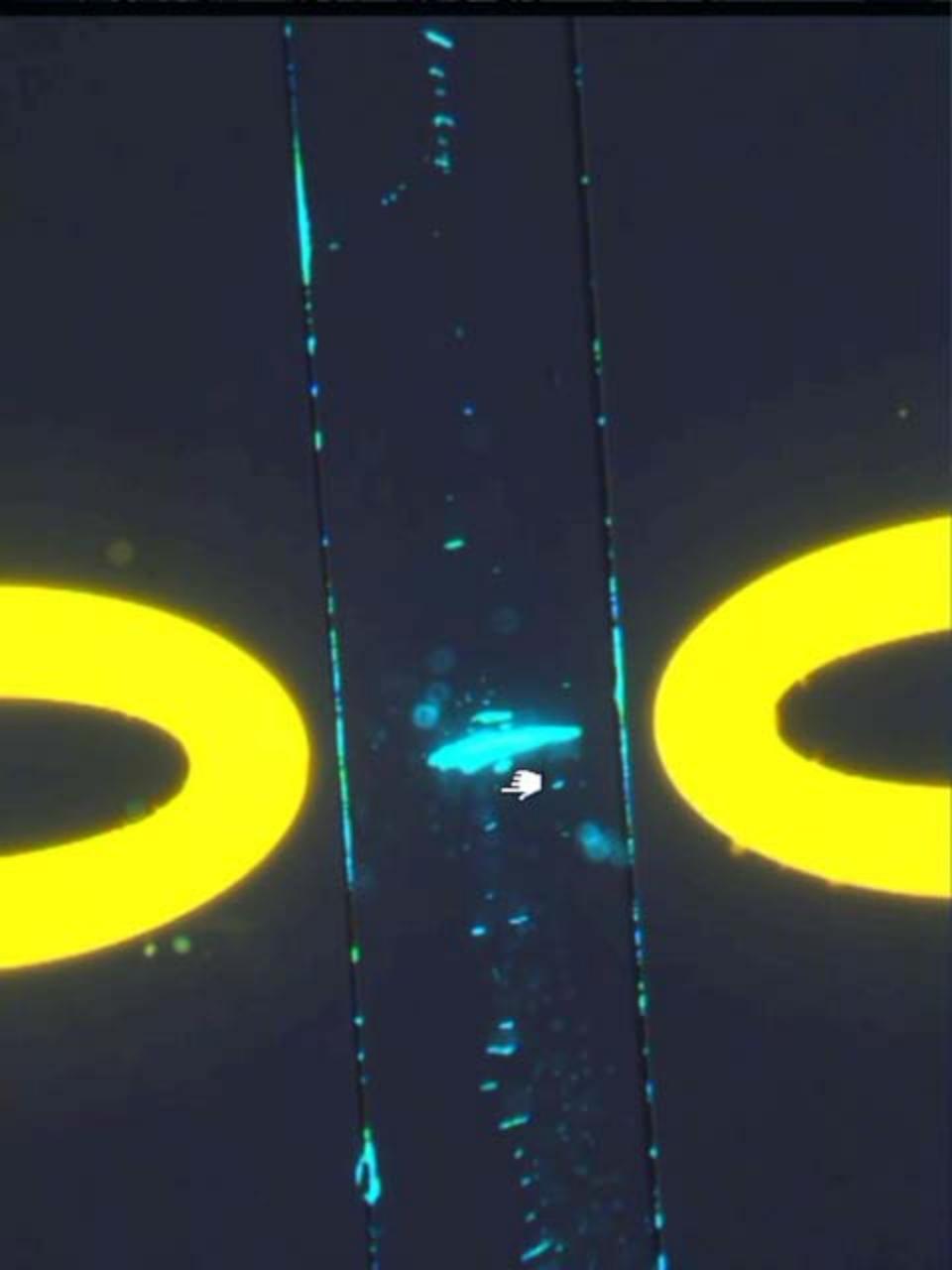

Power Off

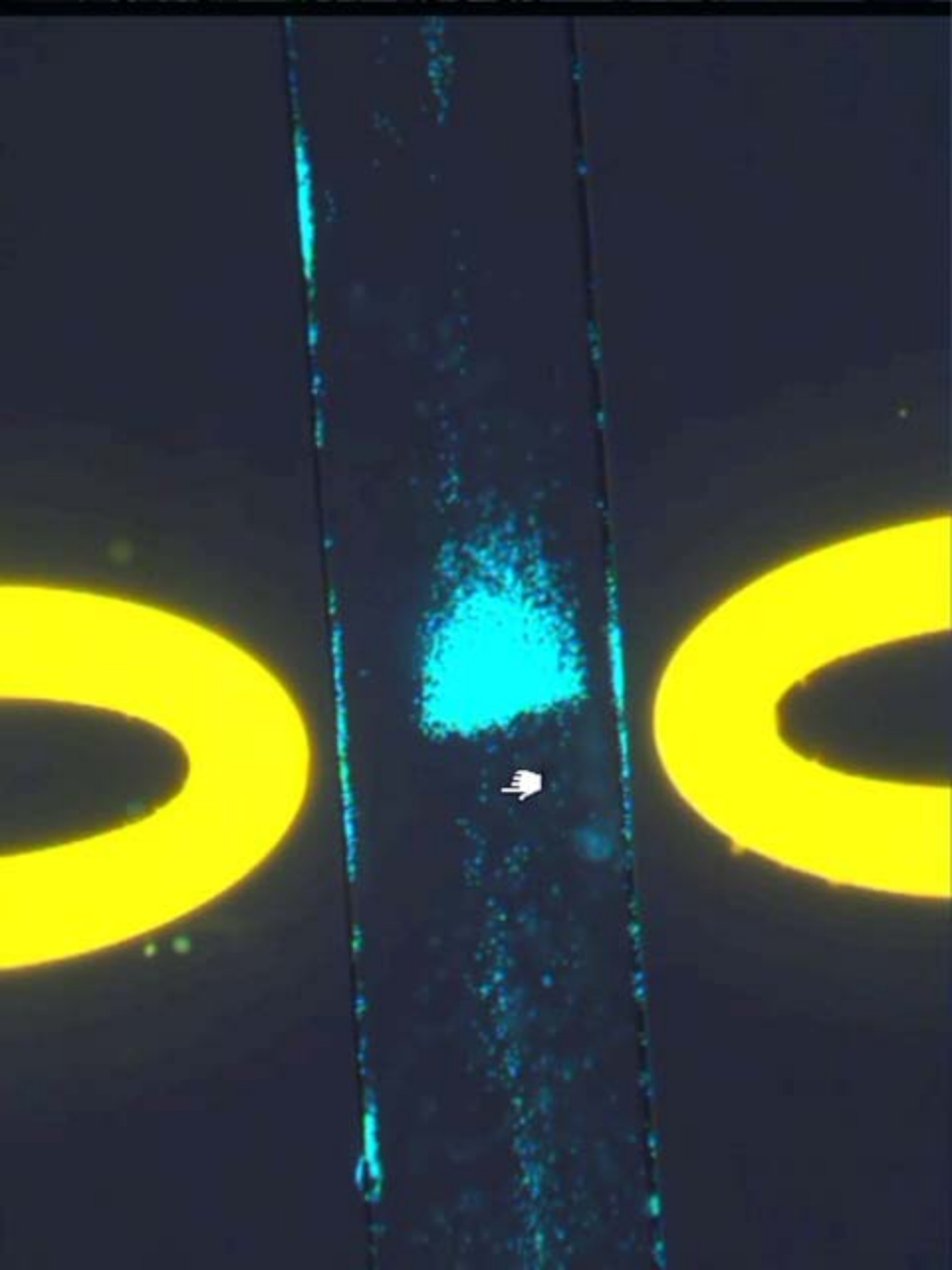
Negative DEP trapping of 2um beads

Virginia Tech
Wake Forest University
School of Biomedical Engineering and Sciences

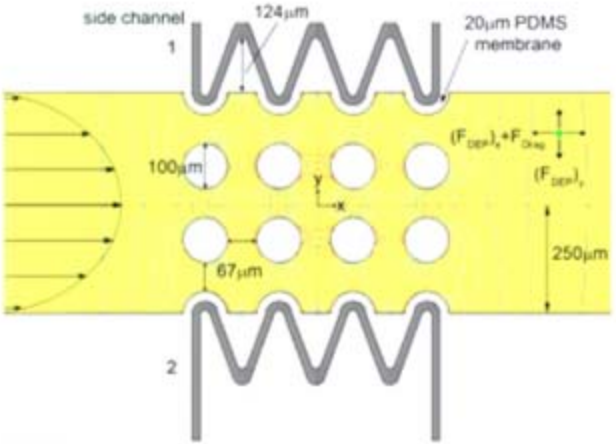


V1=V2=190V_{rms} at 300kHz V3=V4=Ground 0.02mL/hr





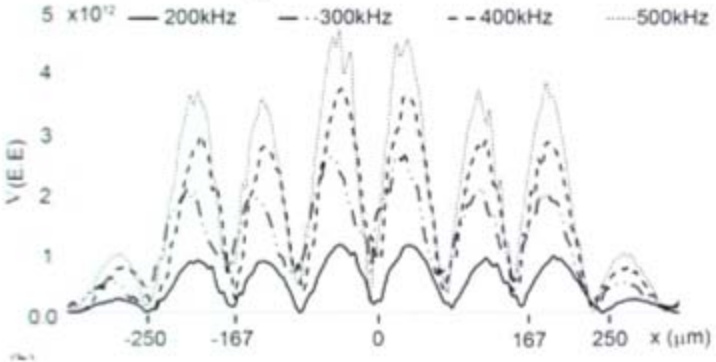
Customizable field patterns altering geometry

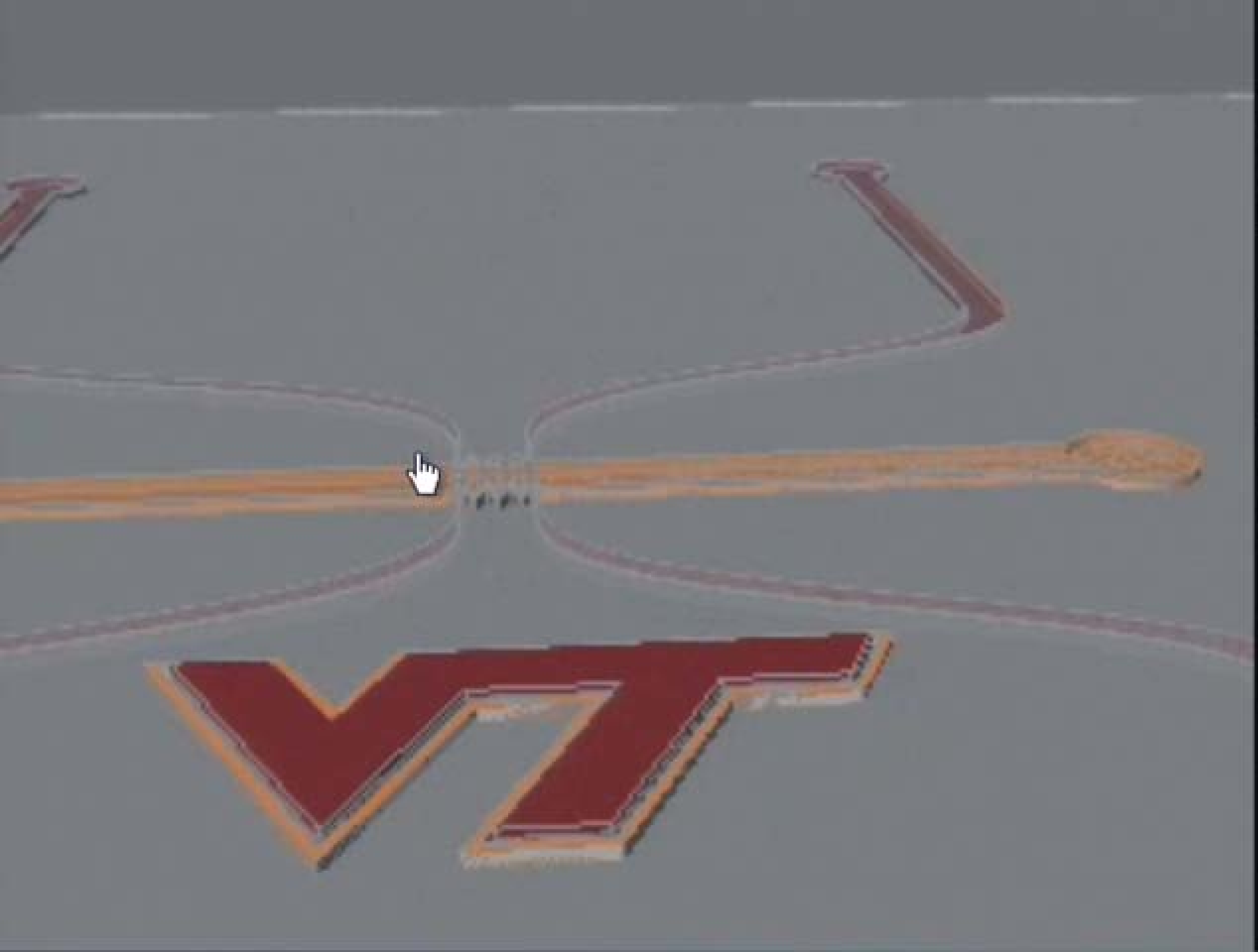


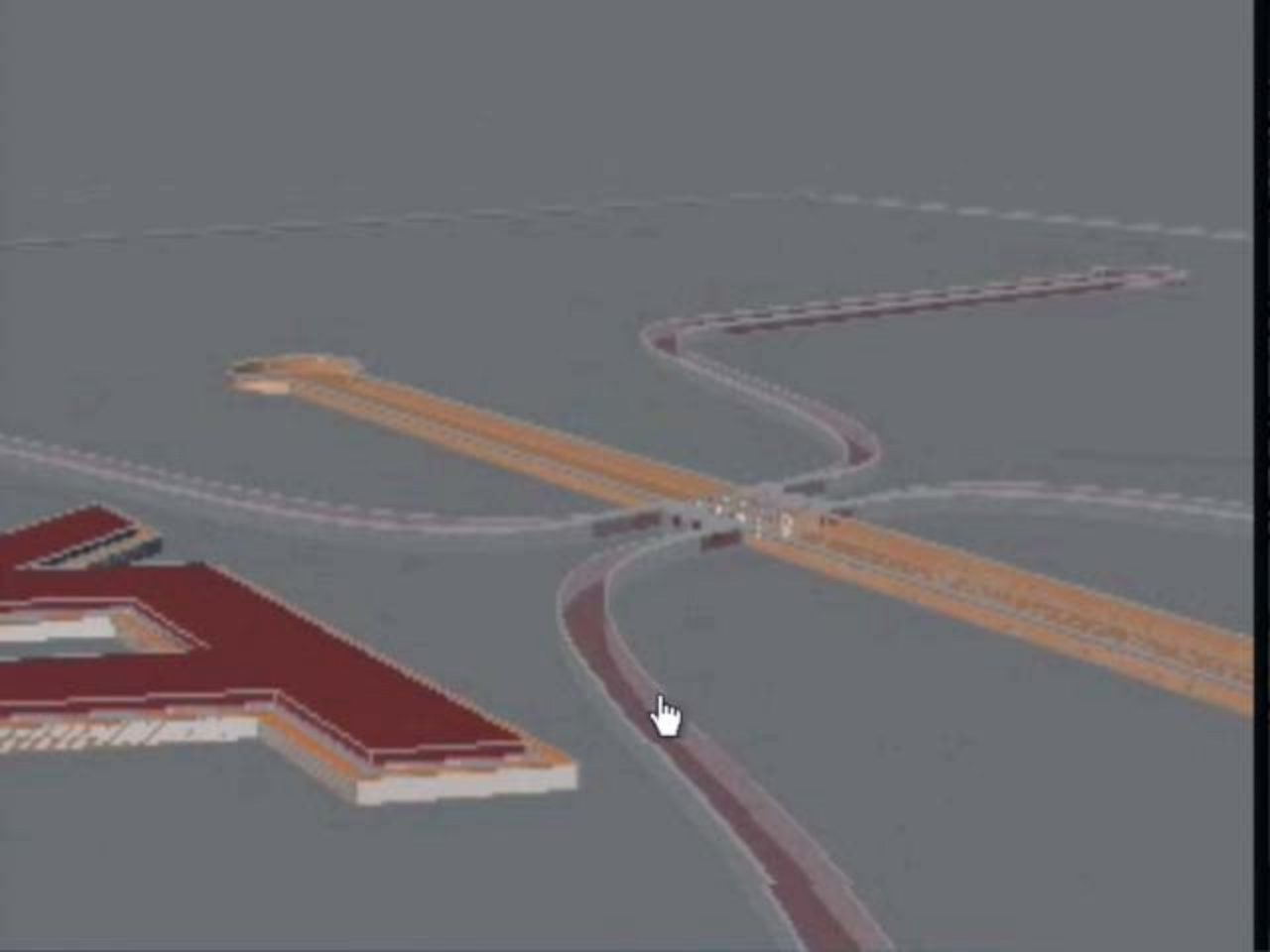
Designer Requirements:

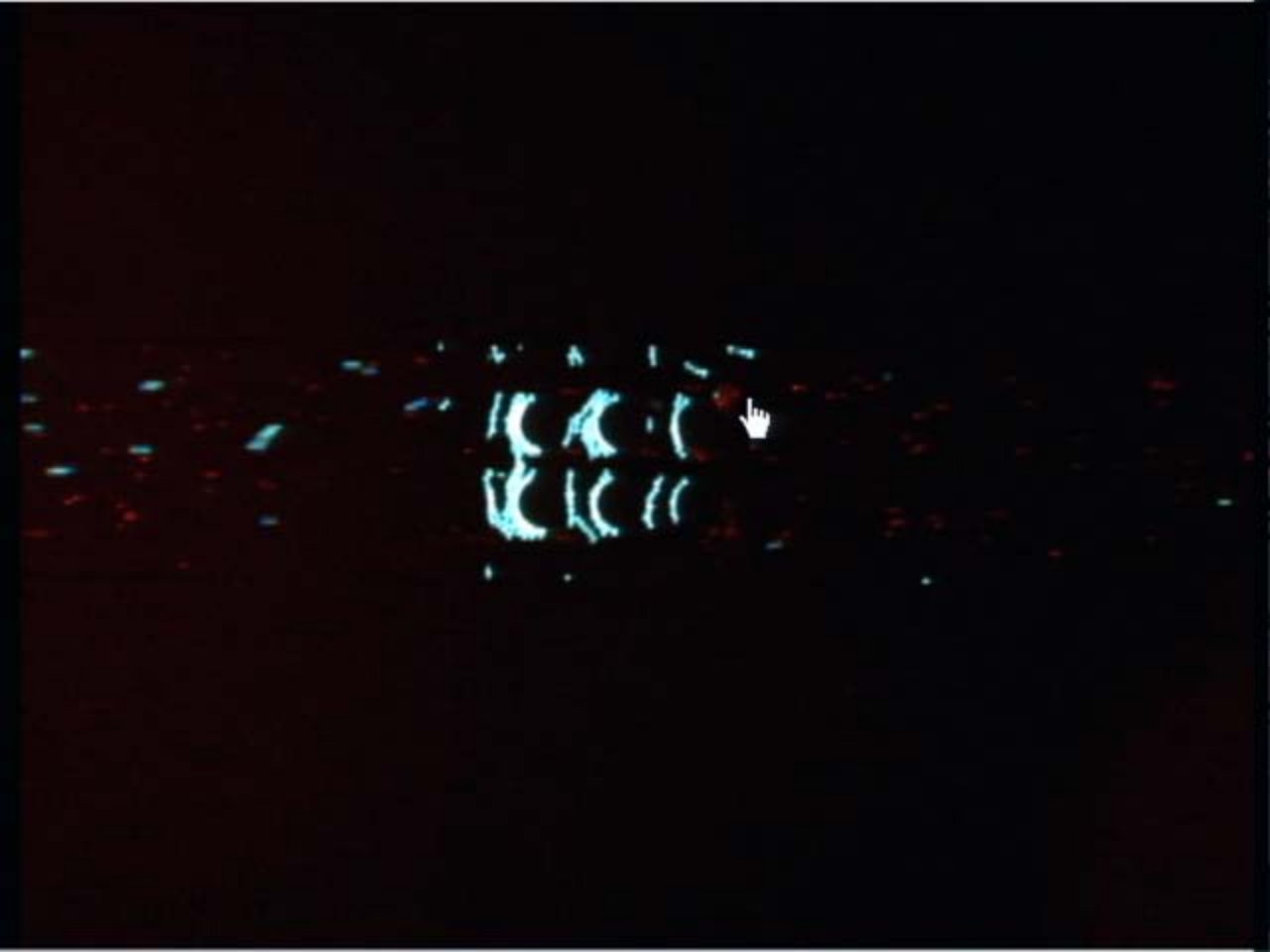
- Use math
- Be creative
- Use computers

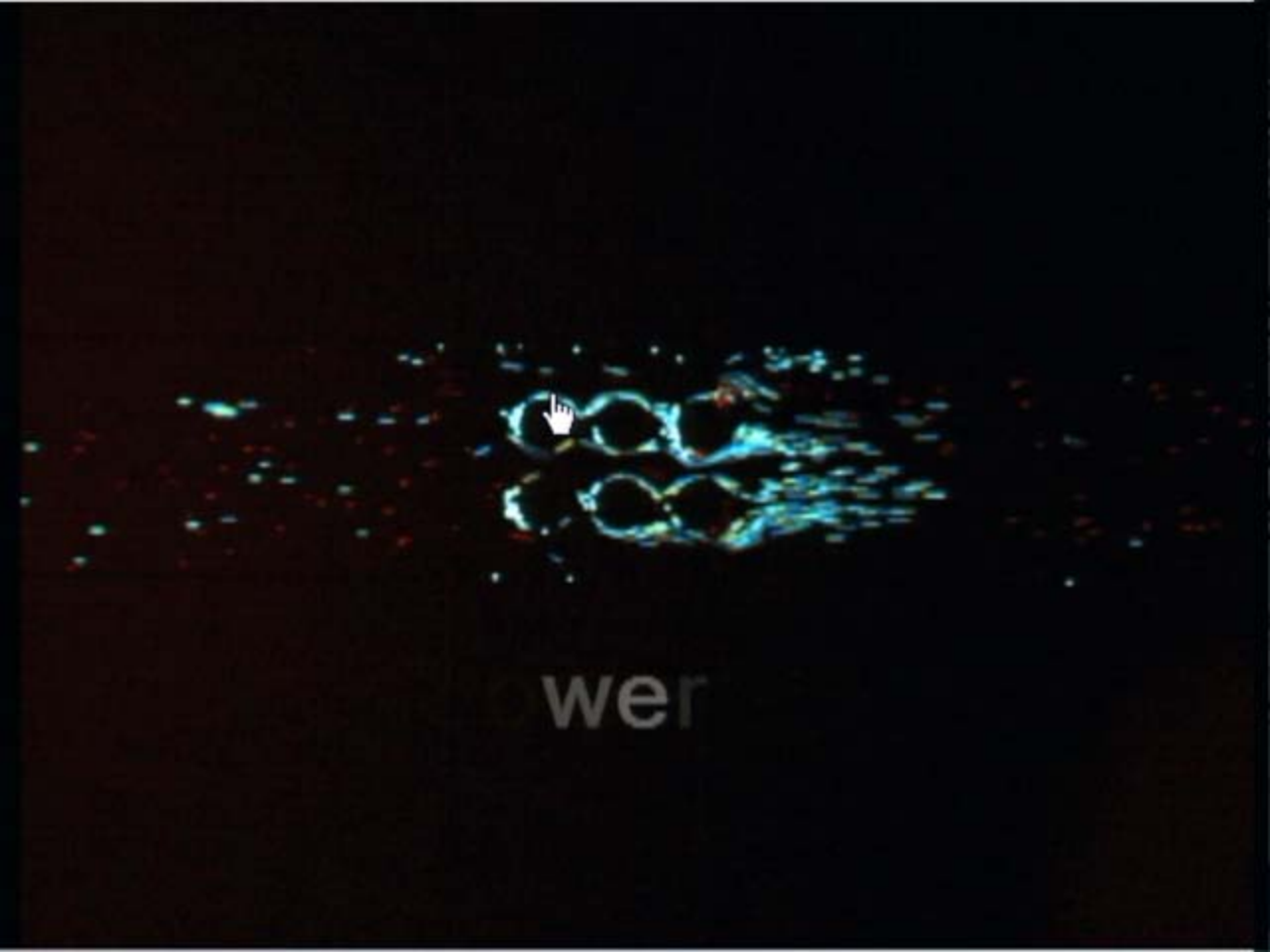
By the way—
These posts are the size of a hair!

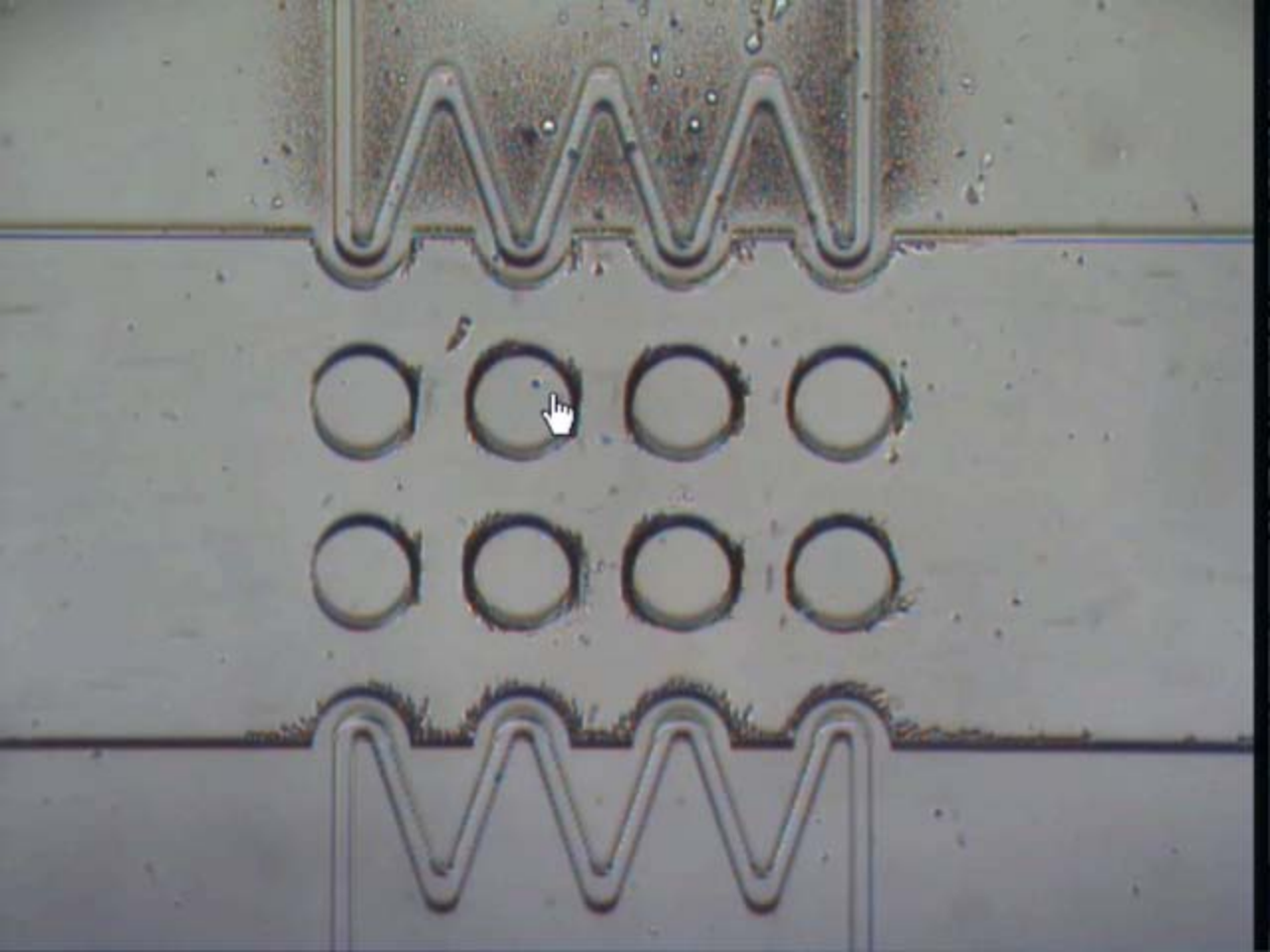






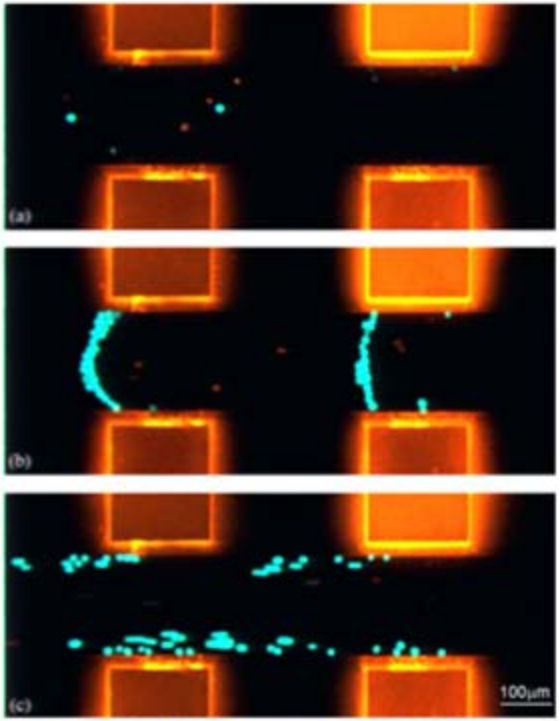



wer

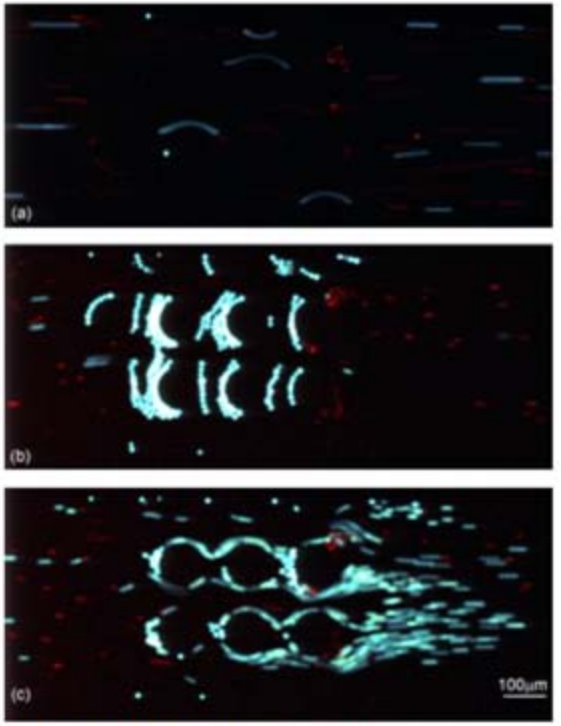


Live/Dead Separation of Cancer Cells

Virginia Tech
Wake Forest University
School of Biomedical Engineering and Sciences



Removal efficiency up to 99%



Removal efficiency >90%

Continuous separation using DEP

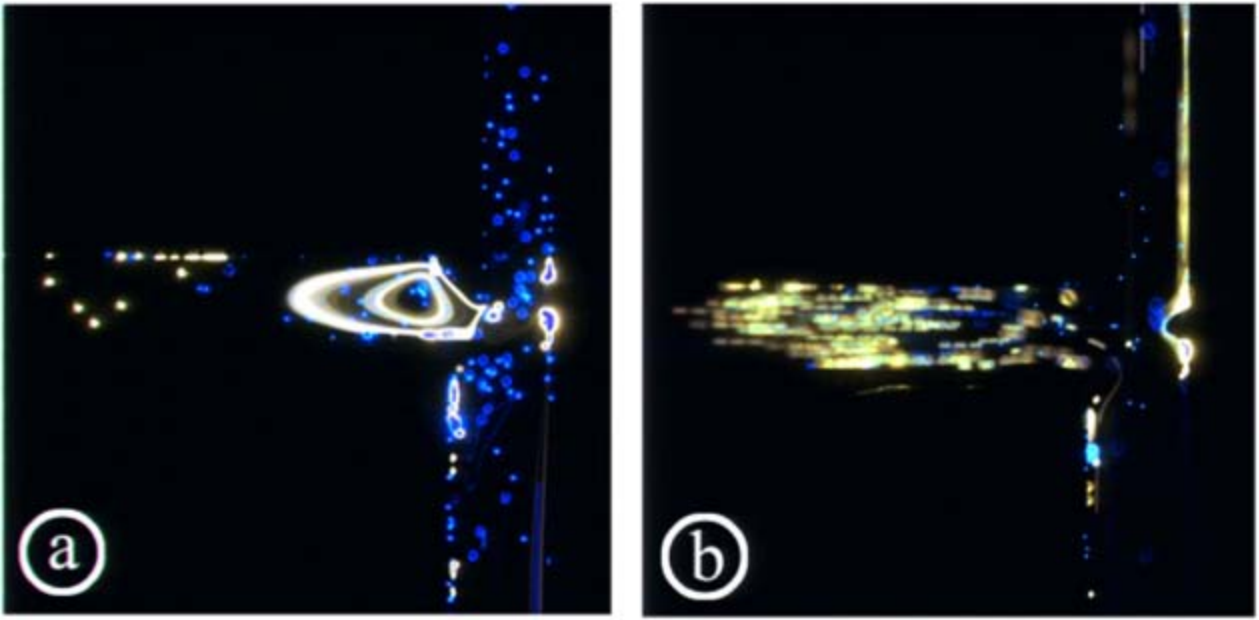
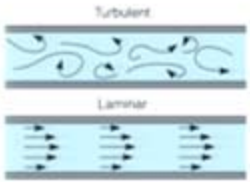


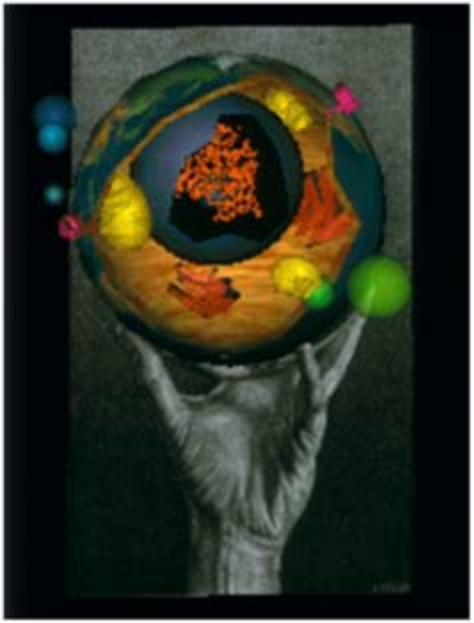
Figure 2: a) Enrichment of and b) release of 4μm beads (yellow) along the side channel while 1μm beads (blue) pass uneffected.

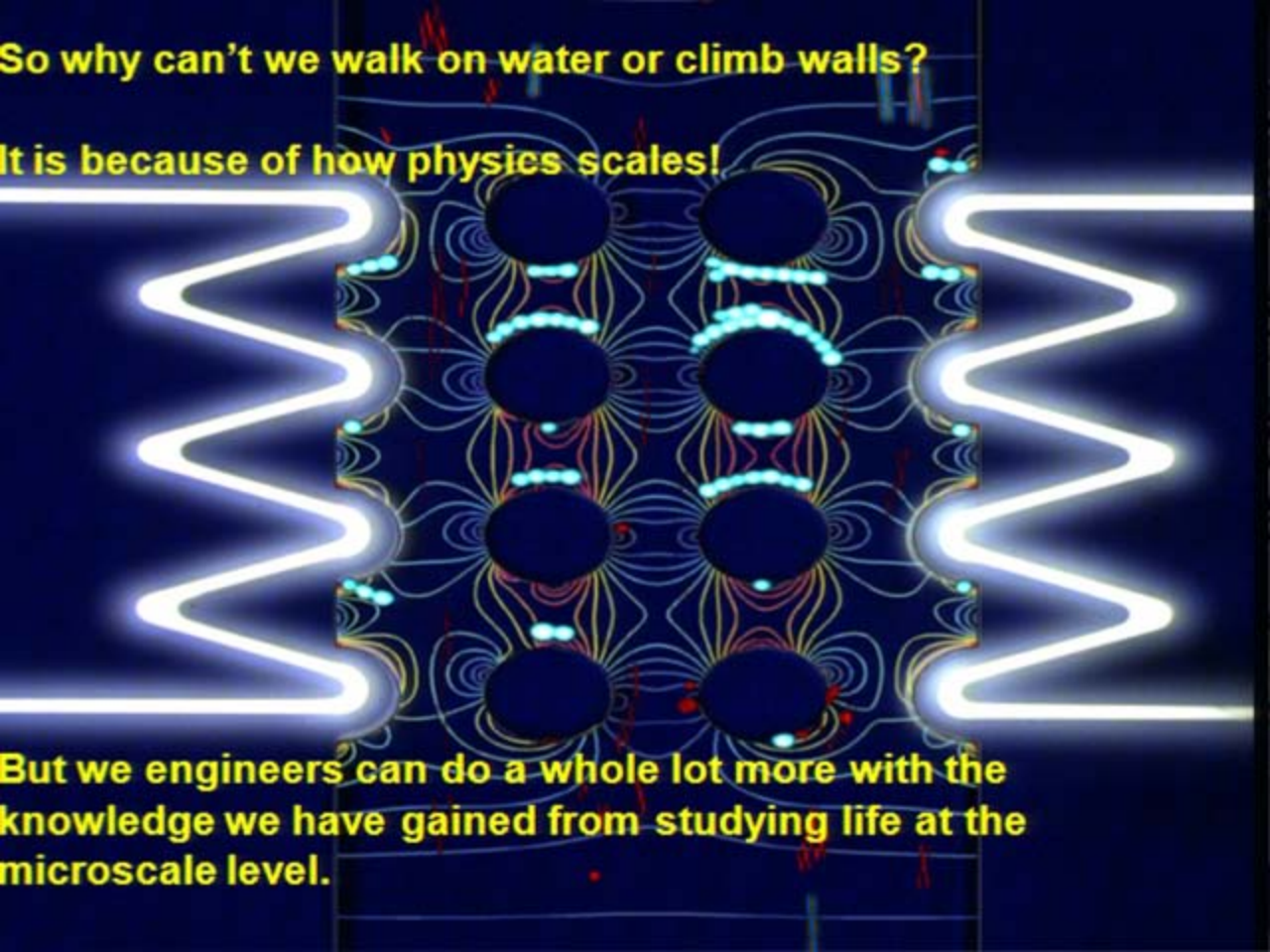
Advantages of being small

It's a small world…

- A world of smooth flow
- A world of diffusion motion
- A world where cell is king






So why can't we walk on water or climb walls?
It is because of how physics scales!
But we engineers can do a whole lot more with the knowledge we have gained from studying life at the microscale level.