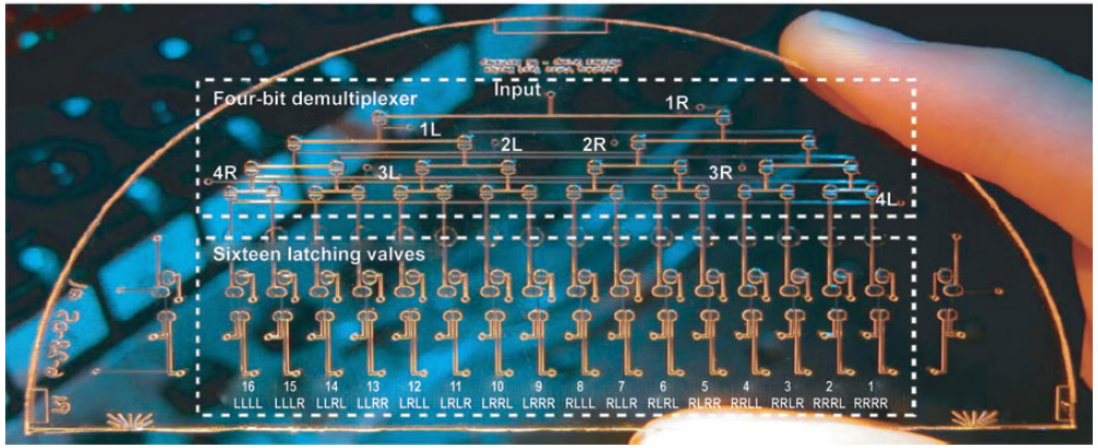
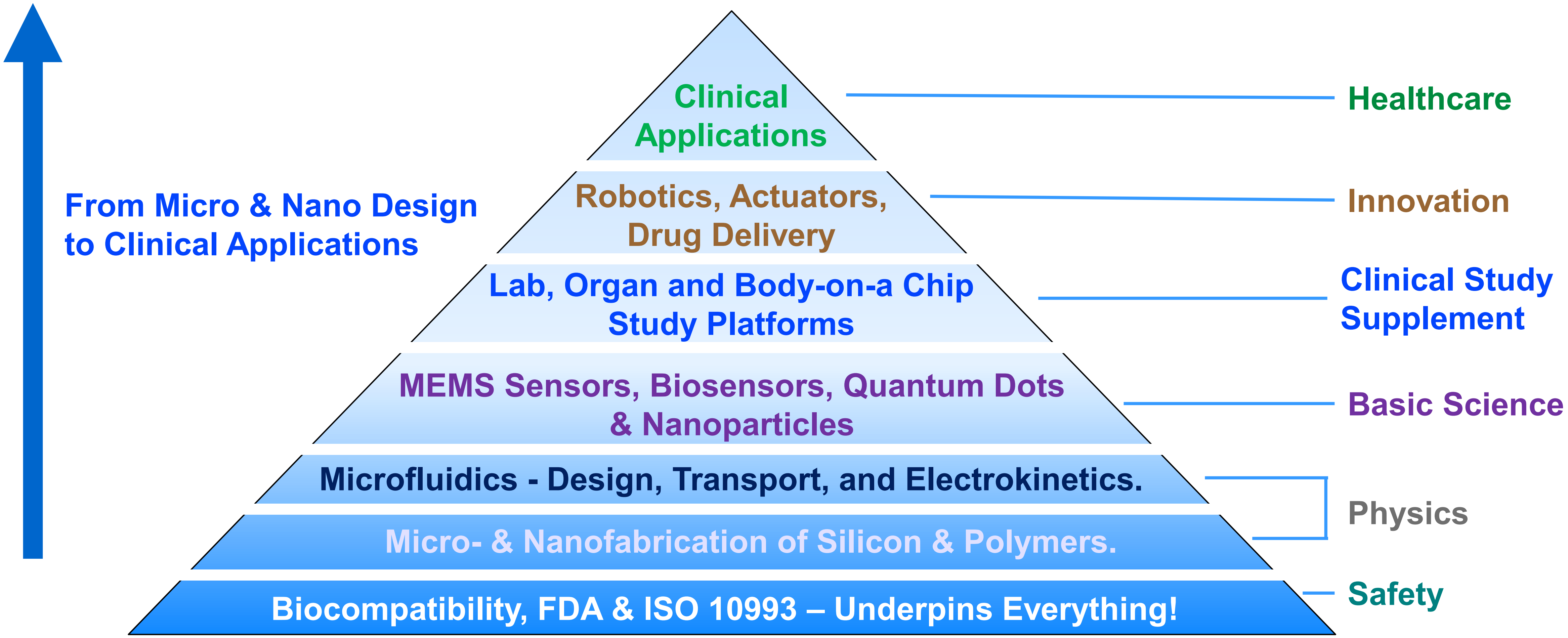
Introduction to BioMEMS & Medical Microdevices, BMEn 5151

Course Introduction

Prof. Steven S. Saliterman, http://saliterman.umn.edu/



BMEN 5151 Course Content



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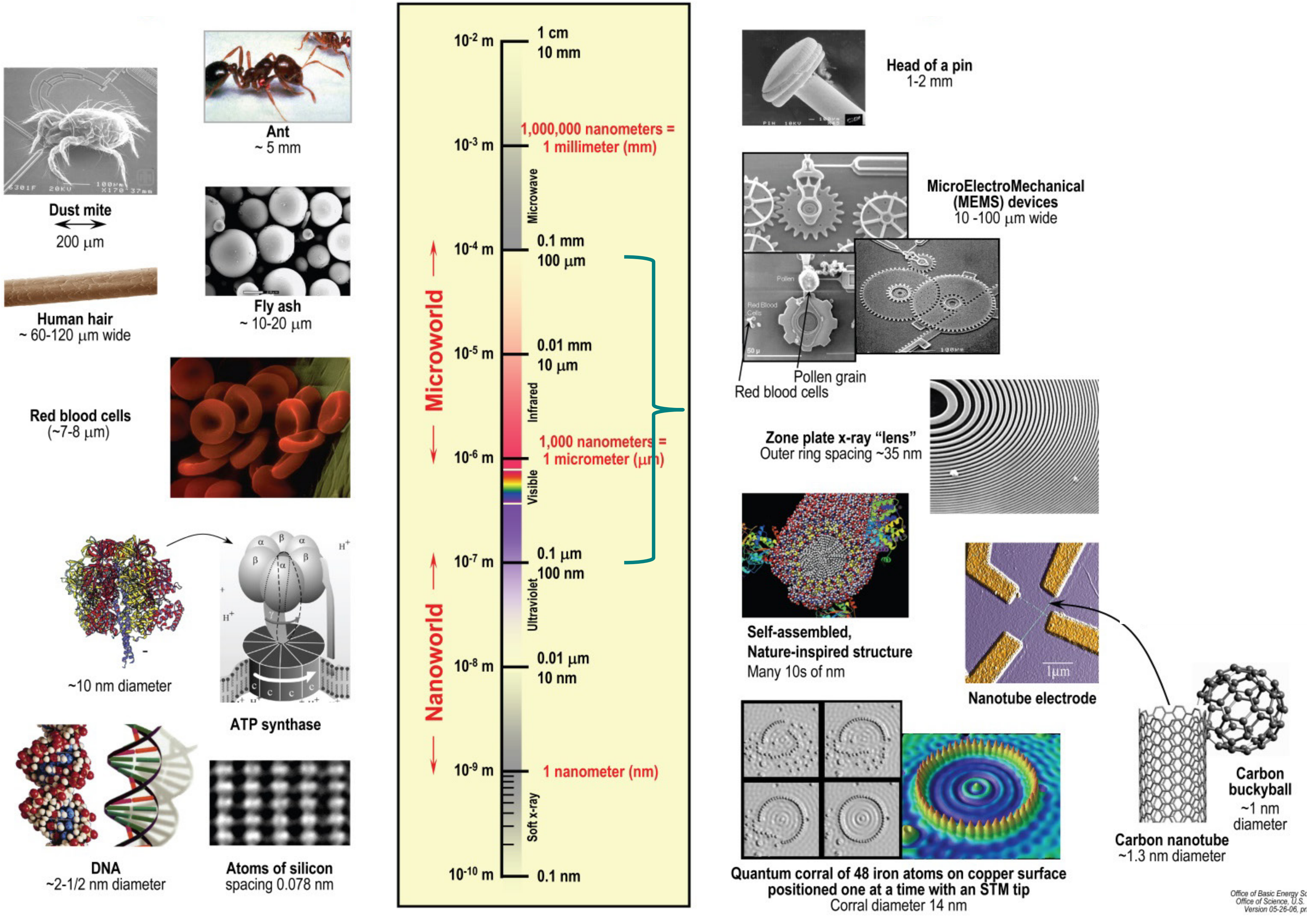
Micro & Nano Realms…

- Devices or systems, constructed from micro- & nanofabrication, that are used for processing, delivery, manipulation, analysis or construction of biological and chemical materials.
- *Micro* - At least one dimension is from ~100 nm to 200 µm.

  Nano - ~0.1 nm to 100 nm
- Incorporating new materials and an understanding of the micro & nano environments, and biocompatibility.
- Harnessing any phenomenon that accomplish work at the micro & nano scale. For example, micro- & nanorobotics include driving, sensing, grasping, loading, releasing, signal transmission, and information processing.
- Includes research and laboratory tools; and point-of-service, therapeutic and implantable devices.

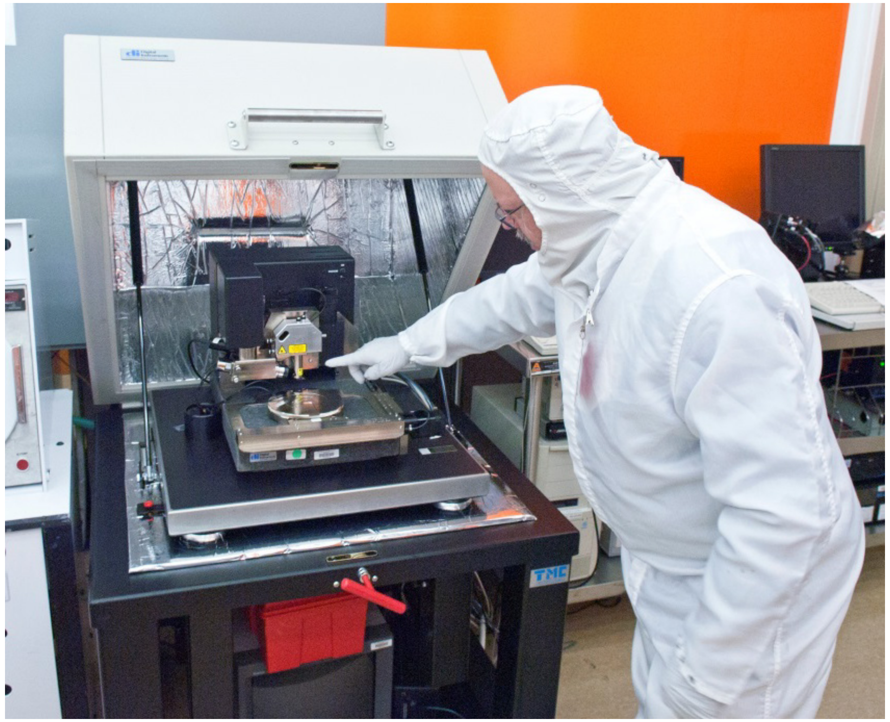
Micro Realm
~100 nm to 200 μm

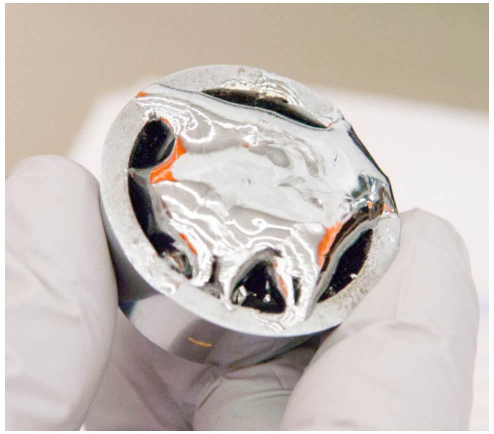
Nano Realm
~0.1 nm to 100 nm



US Department of Energy, Office of Science 2019

Silicon Micro- and Nanofabrication





Polymer Microfabrication

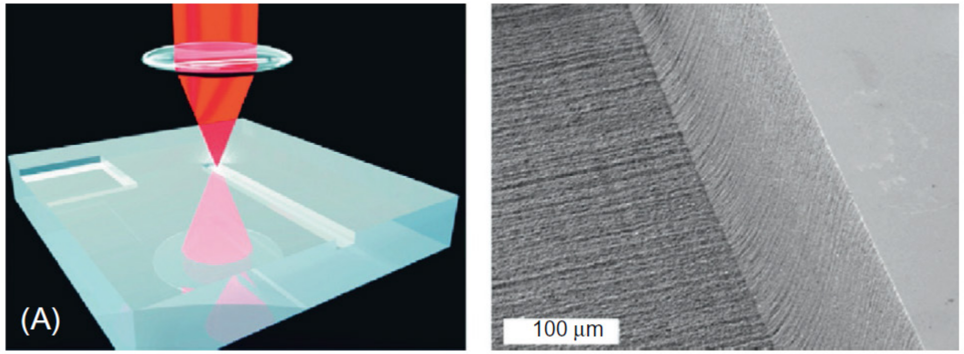


Image courtesy of Marco, CD

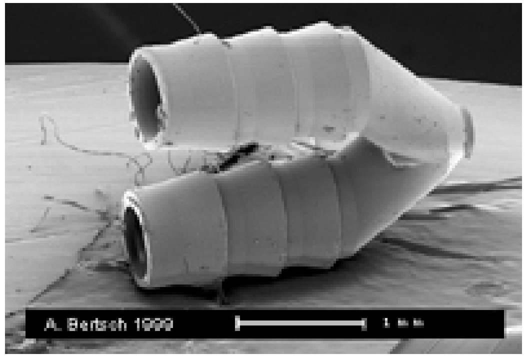


Image courtesy of Bertsch A.

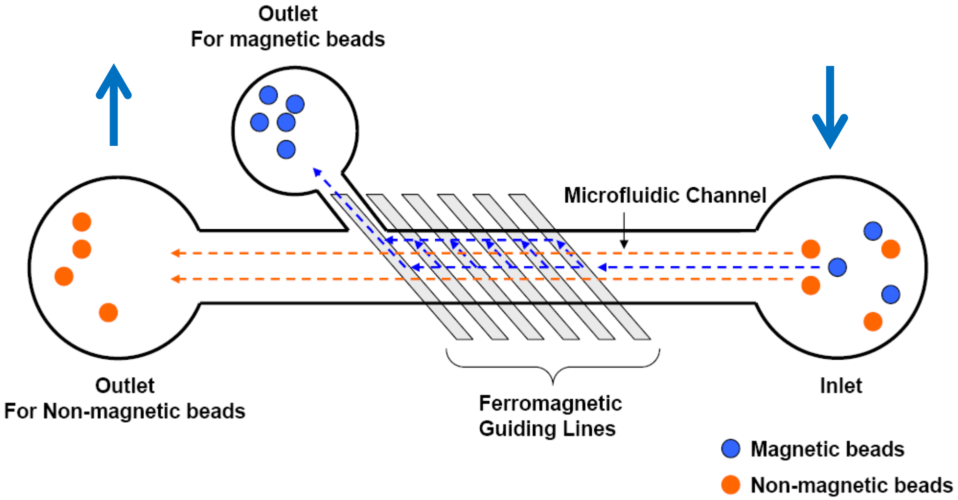


Image courtesy of Jaehoon Chung & Euisik Yoon

Microfluidics

- Science of fluid behavior in microchannels.
- In lab-on-a-chip and μTAS devices, the following features are often seen:
  - Microchannels,
  - Microfilters,
  - Microvalves,
  - Micropumps,
  - Microneedles,
  - Microreserviors,
  - Micro-reaction chambers.

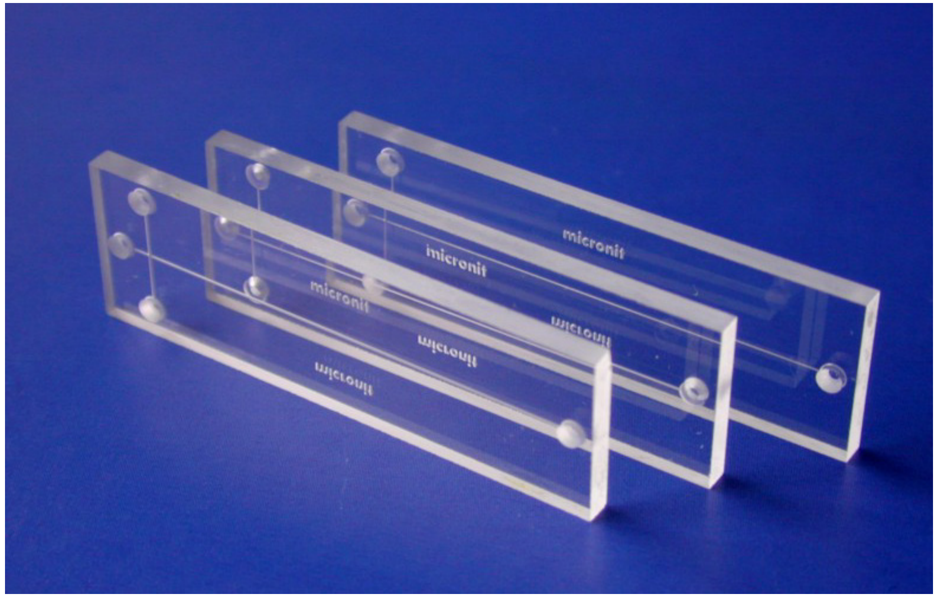
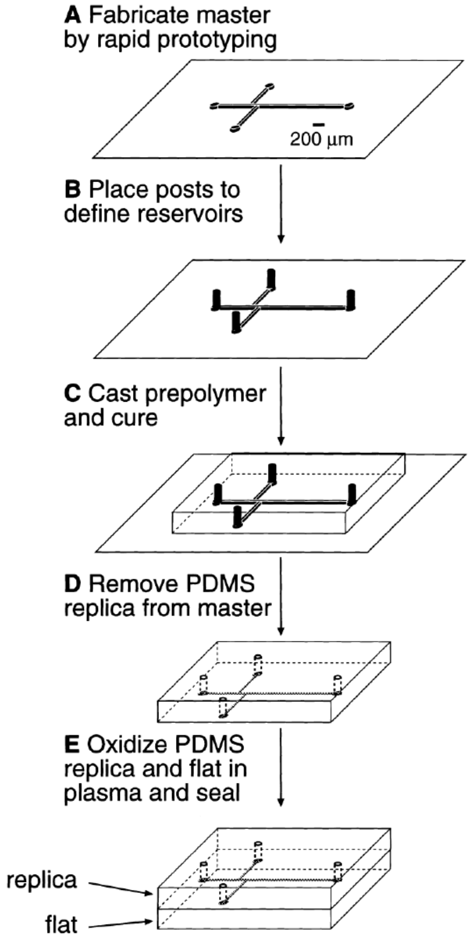
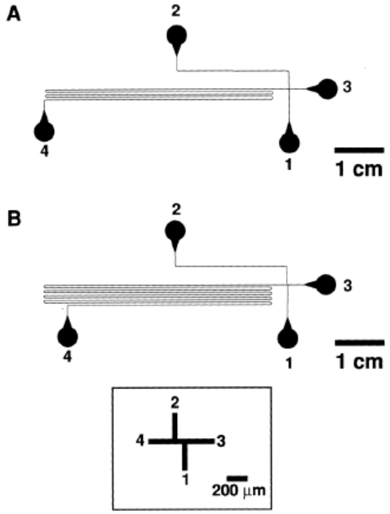


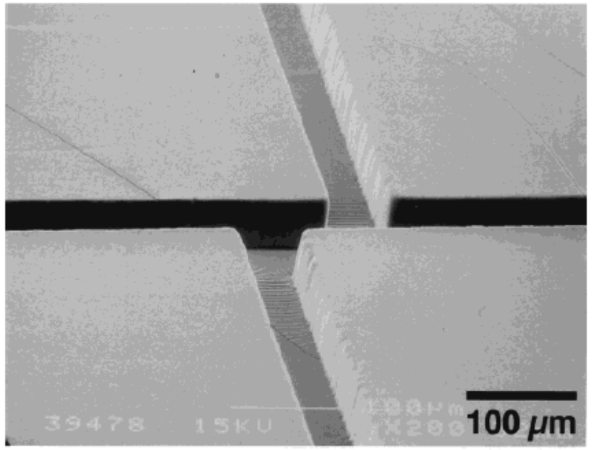
Image courtesy of Micronit

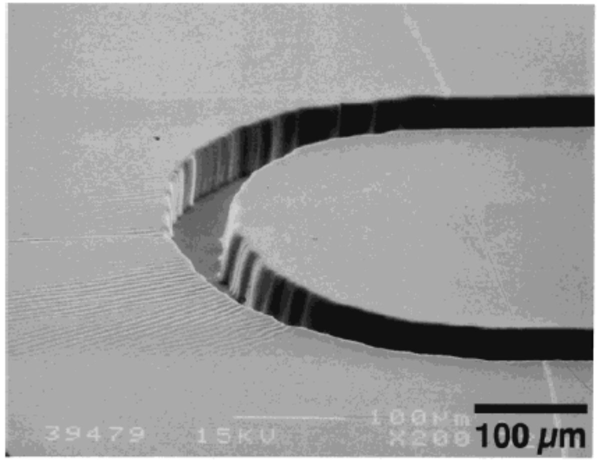
Rapid Prototyping Systems in PDMS…

Image courtesy of Sylgard









Duffy DC, McDonald JC, Schueller OJA, Whitesides GM. Rapid prototyping of microfluidic systems in poly(dimethylsiloxane). *Analytical Chemistry.* 1998;70(23):4974-4984.

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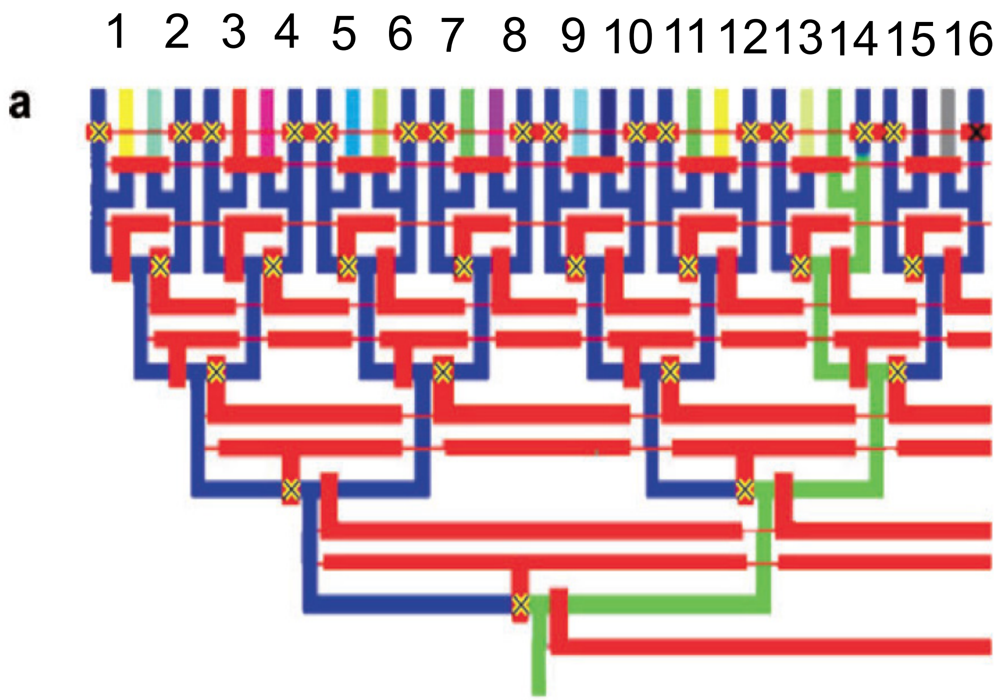
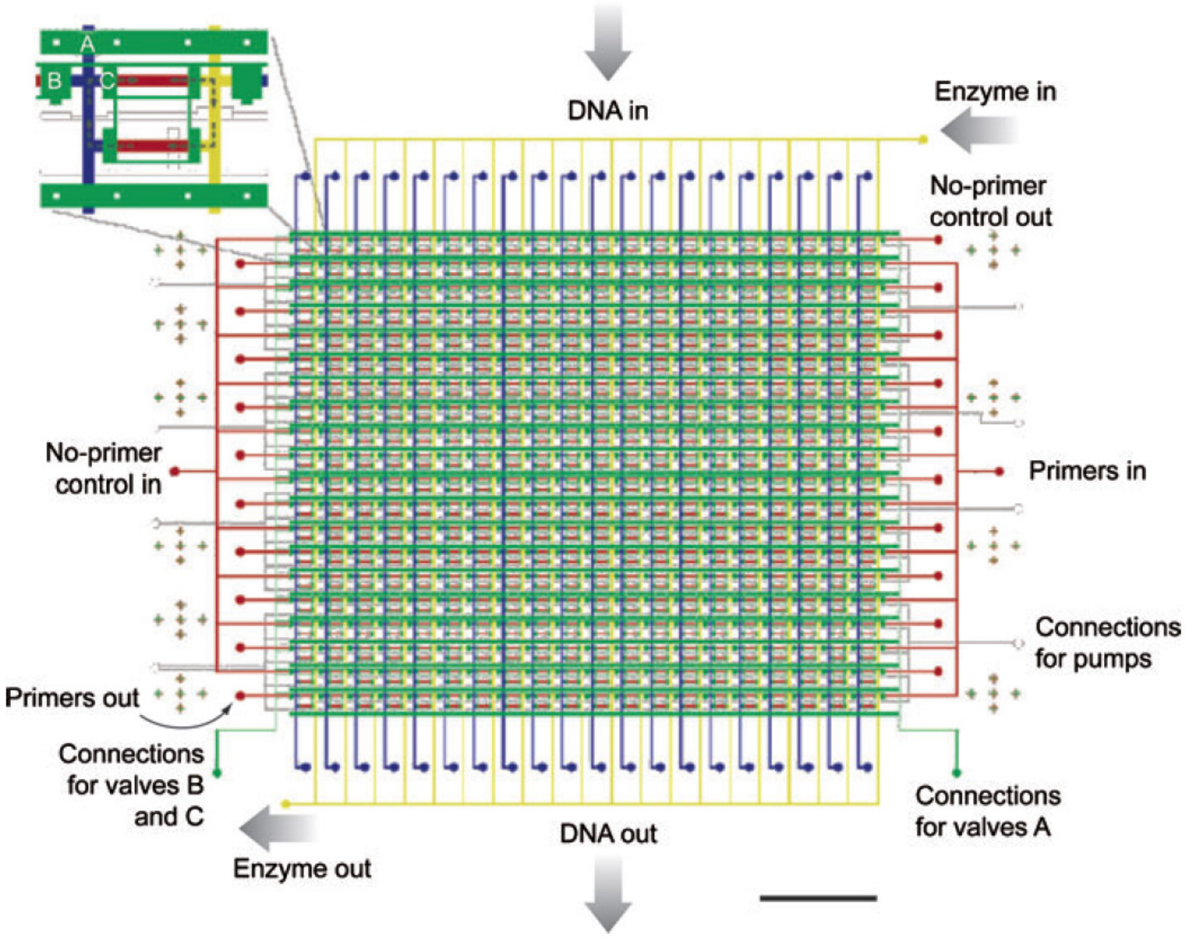
Large-Scale Integration…

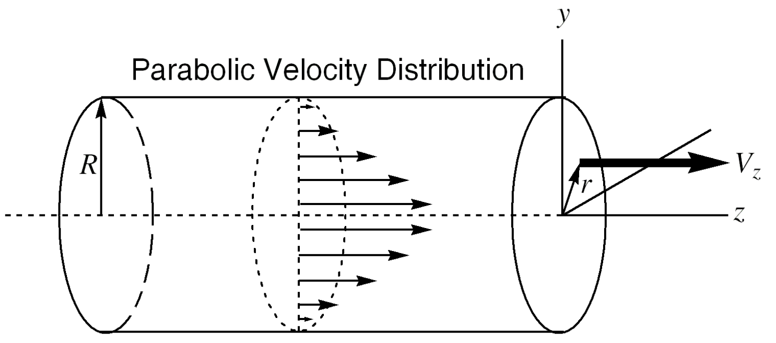




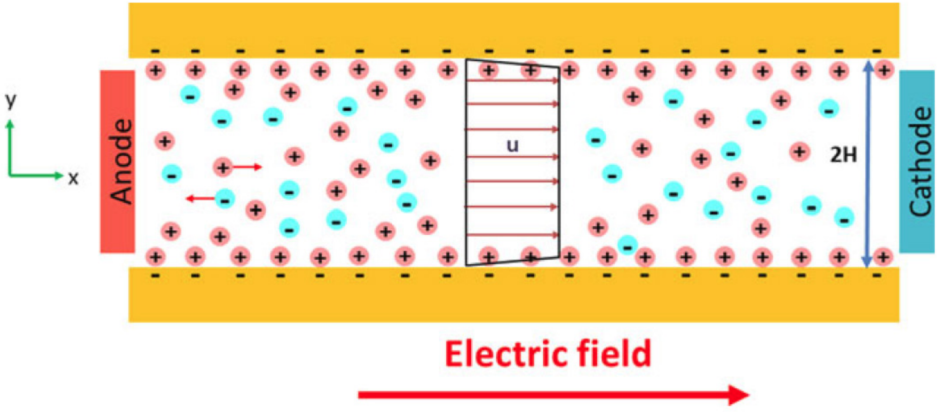
Left) Melin J, Quake SR. Microfluidic large-scale integration: The evolution of design rules for biological automation. In: *Annual Review of Biophysics and Biomolecular Structure.* Vol 36.2007:213-231.
Right) Liu J, Hansen C, Quake SR. 2003. Solving the “world-to-chip” interface problem with a microfluidic matrix. Anal. Chem. 75(18):4718–23

Transport Processes & Electrokinetics…

- Fluid mechanics:
  - Laminar vs turbulent flow,
  - Fluid kinematics.

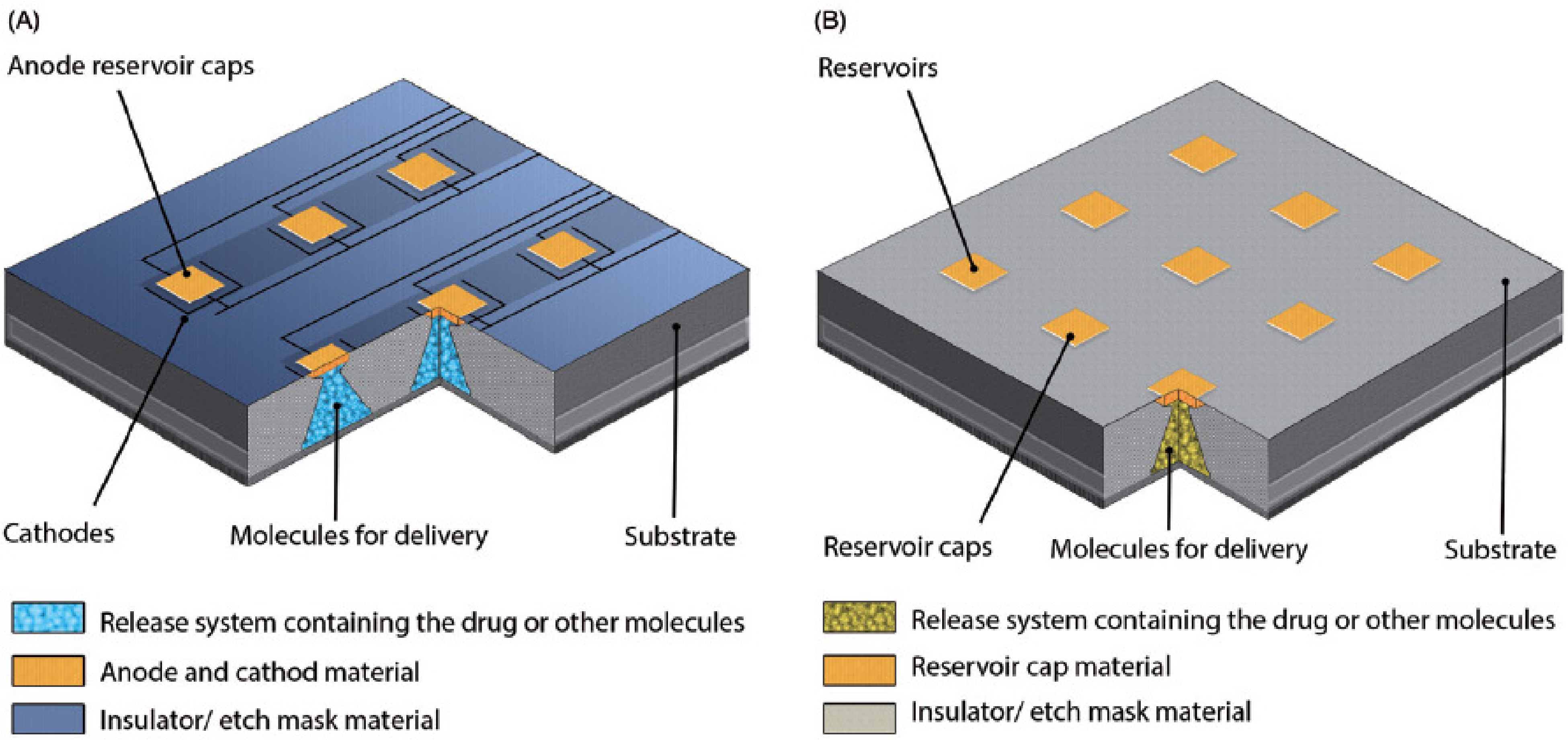


- Electrokinetic phenomenon:
  - Electroosmosis
  - Electrophoresis
  - Dielectrophoresis



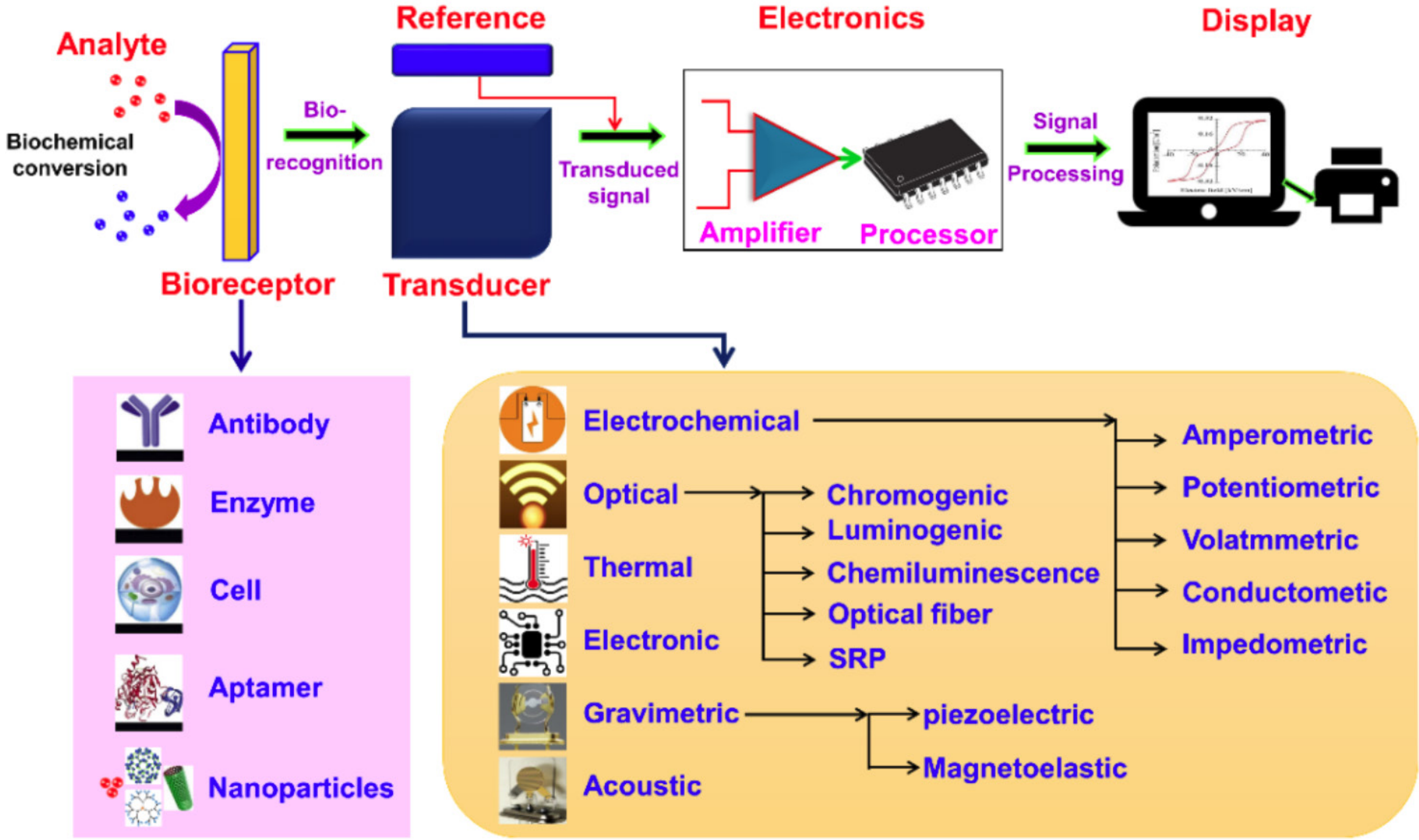
Hossan MR, Dutta D, Islam N, Dutta P. Review: Electric field driven pumping in microfluidic device. *Electrophoresis.* 2018;39(5-6):702-731.

Micro- & Nanosensors and Actuators.



Sutradhar KB, Sumi CD. Implantable microchip: the futuristic controlled drug delivery system. *Drug Deliv.* 2016;23(1):1-11.

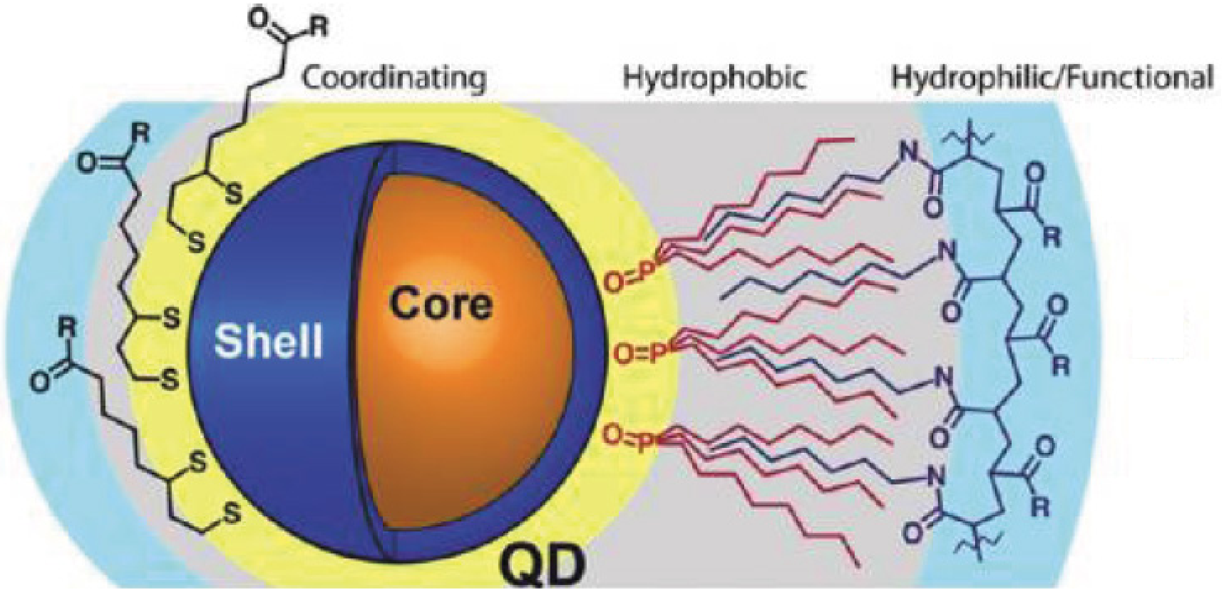
Biosensors, Quantum Dots & Nanoparticles



Naresh V, Lee N. A Review on Biosensors and Recent Development of Nanostructured Materials-Enabled Biosensors. *Sensors*. Feb 2021;21(4)1109. doi:10.3390/s21041109

Nanotransducers…

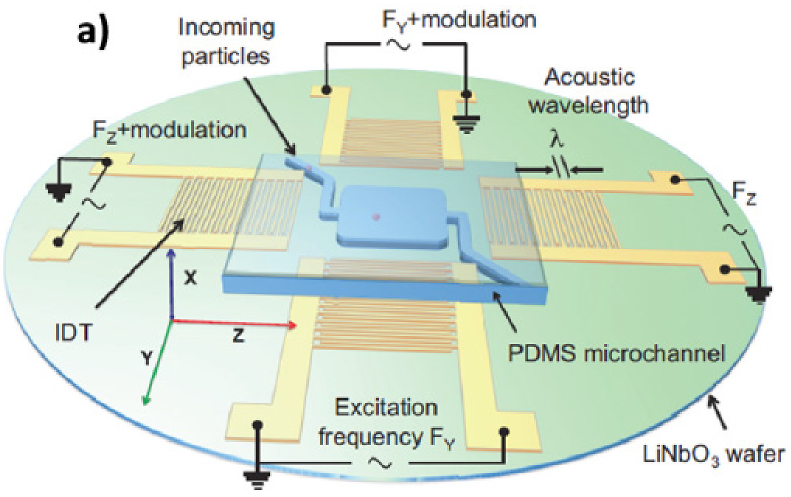
1. Nanoparticle transducers:
    1. Quantum dots.
    2. Carbon dots.
    3. Nobel metal nanoparticles.
    4. Lanthanide nanoparticles.
2. Label free transducers - rather than relying on attachment to reporter labels for signal transduction:
    1. Nanowires
    2. Nanotubes
    3. Nanocantilevers
    4. Mesoporous membranes.



Hildebrandt N, Spillmann CM, Algar WR, et al. Energy Transfer with Semiconductor Quantum Dot Bioconjugates: A Versatile Platform for Biosensing, Energy Harvesting, and Other Developing Applications. *Chemical Reviews.* 2017;117(2):536-711.

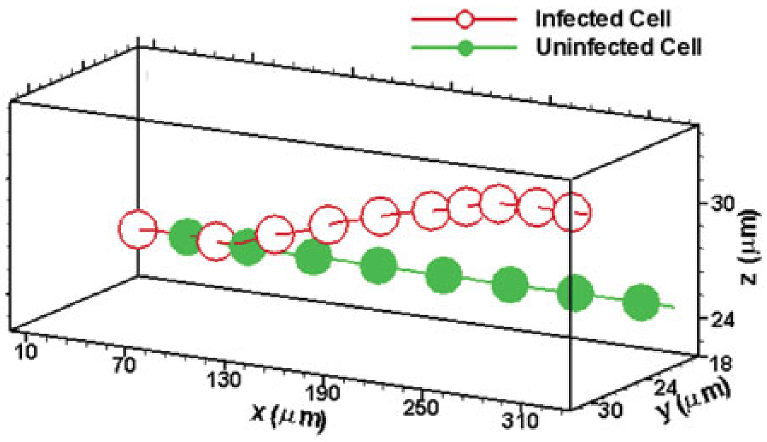
Chip-Level Technologies: *Lab-on-a-Chip*

Surface Acoustic Waves

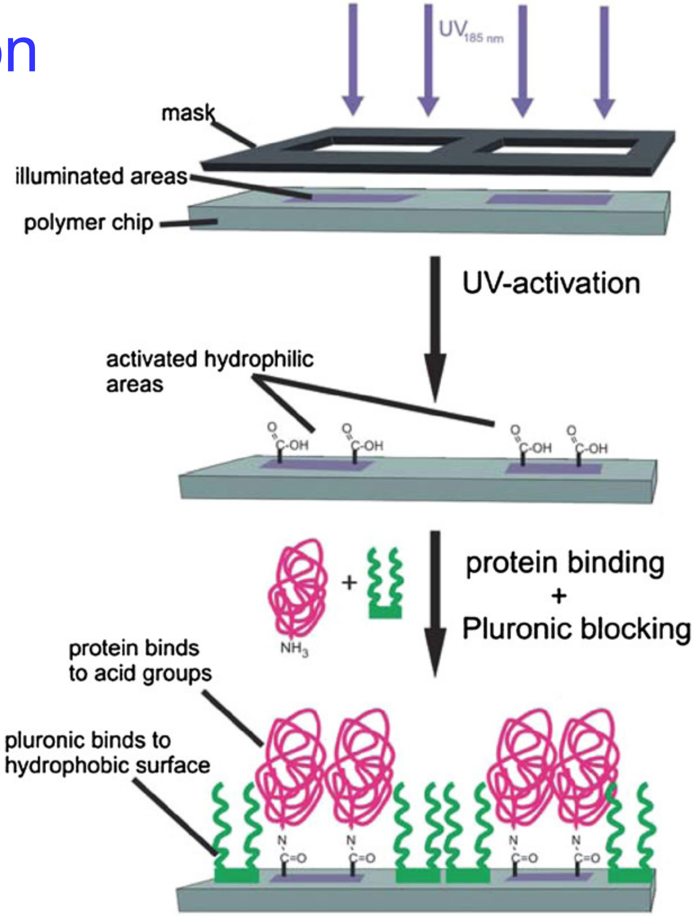


Tran, S.B.Q., Marmottant, P., Thibault, P., 2012. Appl. Phys. Lett., 101.

Dielectrophoretic Separation



Jubery, TZ and P. Dutta. A new design for efficient dielectrophoretic separation of cells in a microdevice . *Electrophoresis* 2013, 34, 643–650



Schutte J, Freudigmann C, Benz K, Bottger J, Gebhardt R and Stelzle M 2010 A method for patterned in situ biofunctionalization in injection-molded microfluidic devices Lab Chip 10 2551–8

Detection Strategies…

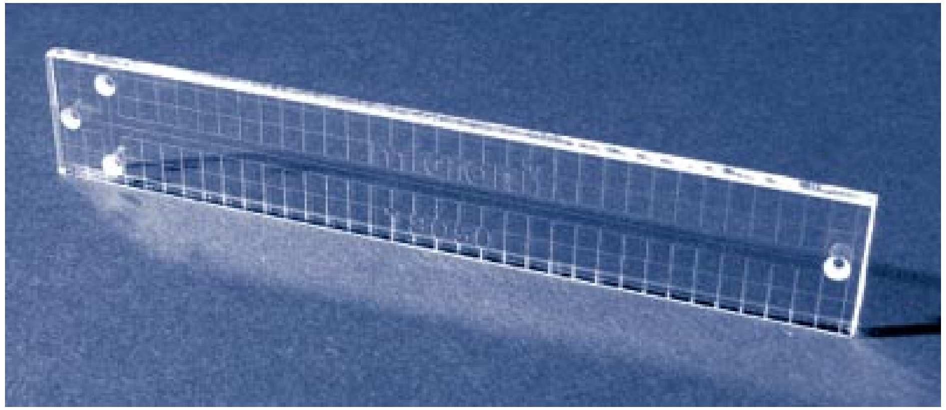
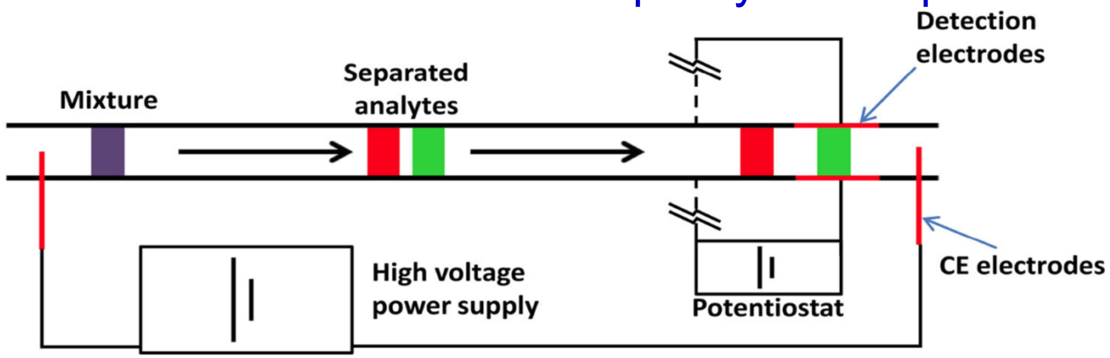
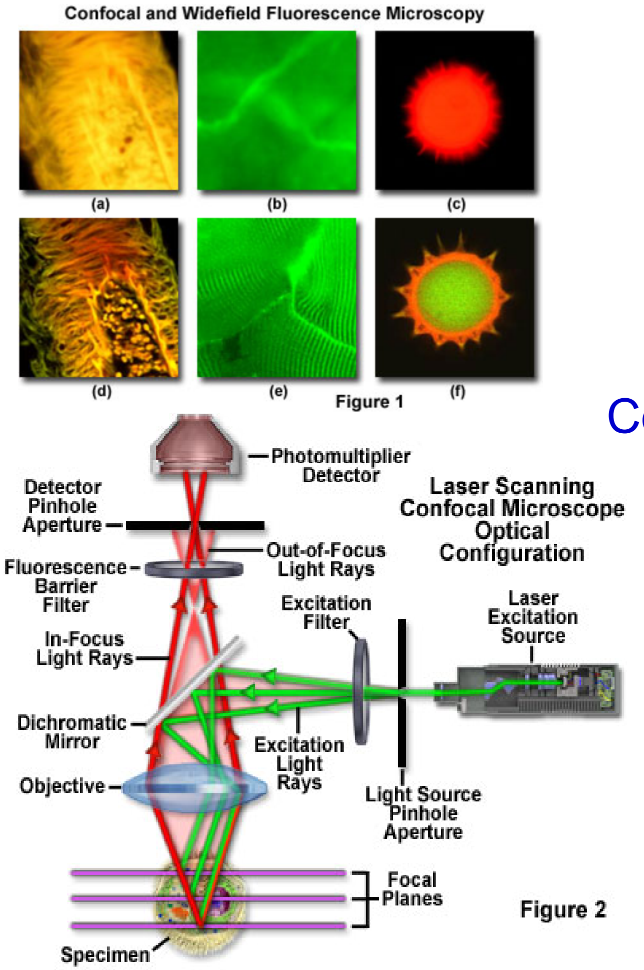


Image courtesy of Micronit

Electrochemical Detection in Capillary Electrophoresis



Gencoglu, A and Adrienne R. Minerick . Electrochemical detection techniques in micro- and nanofluidic devices. *Microfluid Nanofluid* (2014) 17:781–807

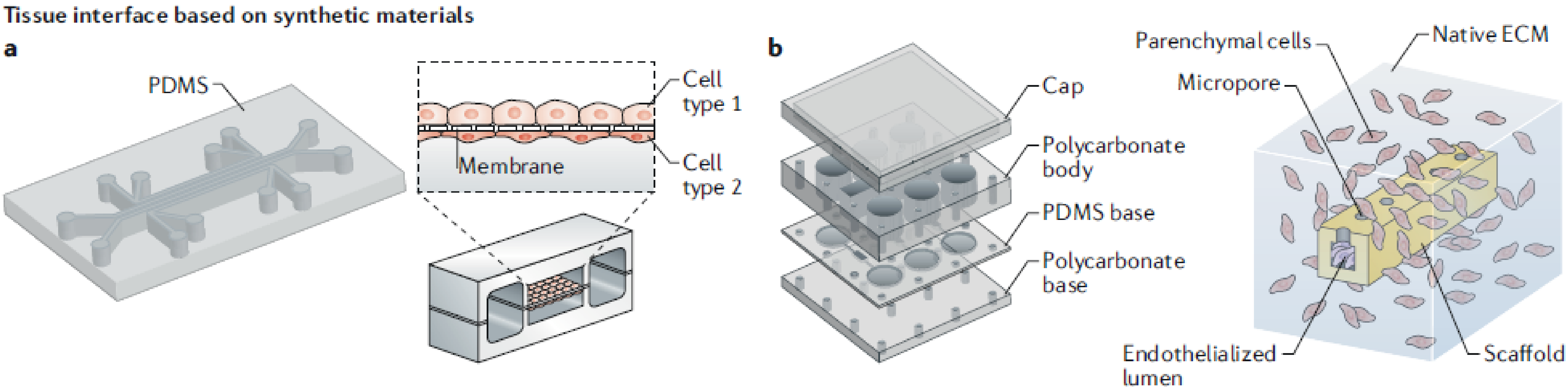


Confocal Fluorescence Microscopy

Image courtesy of Olympus

Organ-on-a-Chip…

Reproducing the Tissue Barrier Function

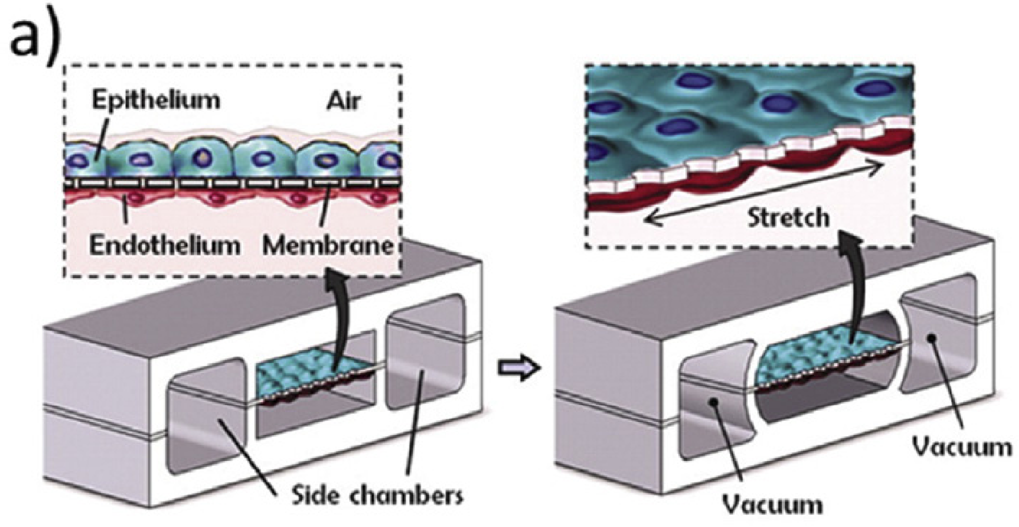


PDMS membranes.

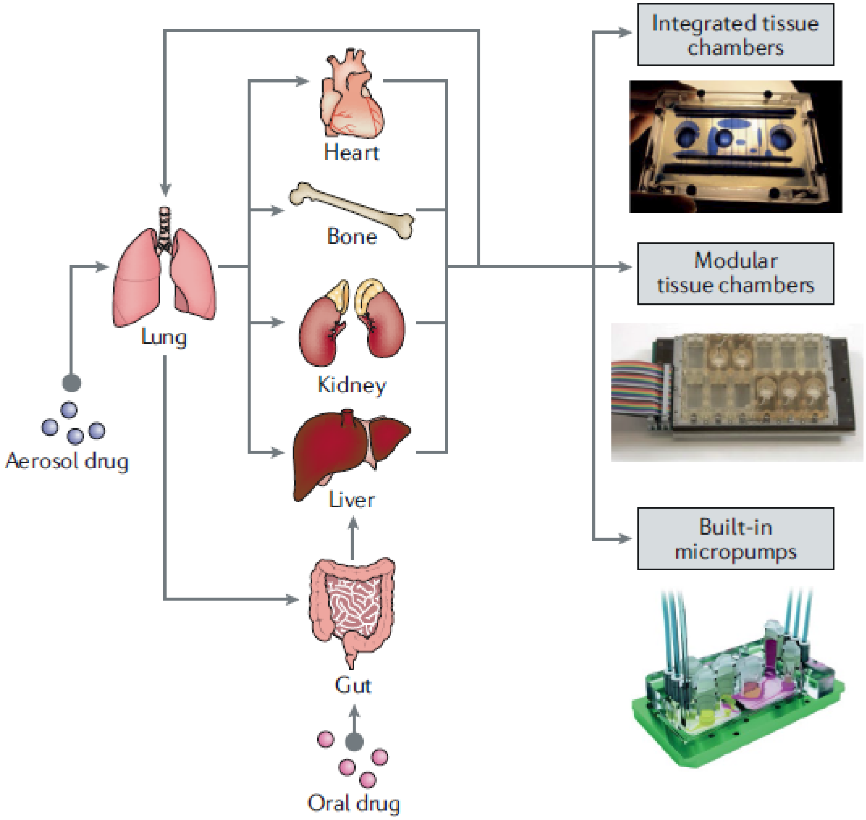
Perfusion bioreactor and synthetic microfabricated scaffold.

a) Huh, D. et al. Reconstituting organ- level lung functions n a chip. Science 328, 1662–1668 (2010).
b) Zhang, B. et al. Biodegradable scaffold with built- in vasculature for organ- on-a- chip engineering and direct surgical anastomosis. Nat. Mater. 15, 669–678 (2016).

From Organ to Body-on-a-Chip…



Lung-on-a-Chip



Body-on-a-Chip - "Organ Coupling"

Zhang B, Korolj A, Lai BFL, Radisic M. Advances in organ-on-a-chip engineering. *Nature Reviews Materials.* 2018;3(8):257-278.

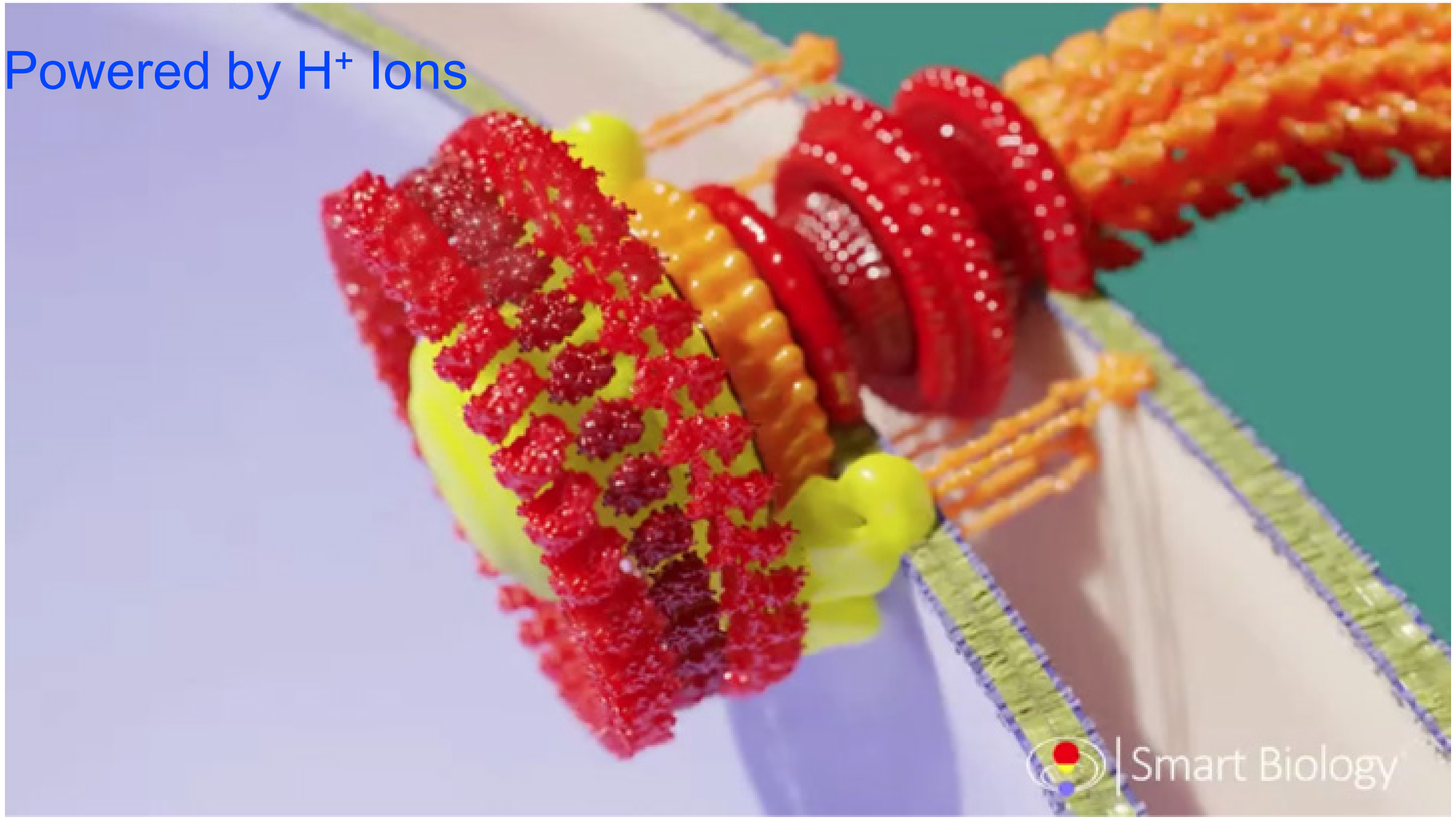
Micro- & Nanorobotic Classifications

- The composition, structure, size, and biodegradability of micro- and nanorobots.
- The driving mode of micro- and nanorobots (such as magnetic, optical, ultrasonic, chemical reaction, and other different energy forms) and the type of driving source.
- The different functions of micro- and nanorobots, such as treatment, surgery, diagnosis, and medical imaging.
- The diagnosis and treatment of different diseases by different micro- and nanorobots.

Maochun, Wan M. *Biomedical micro- and nanorobots in disease treatment*. Wiley-VCH; 2023. p. 14

Example of Propulsion…

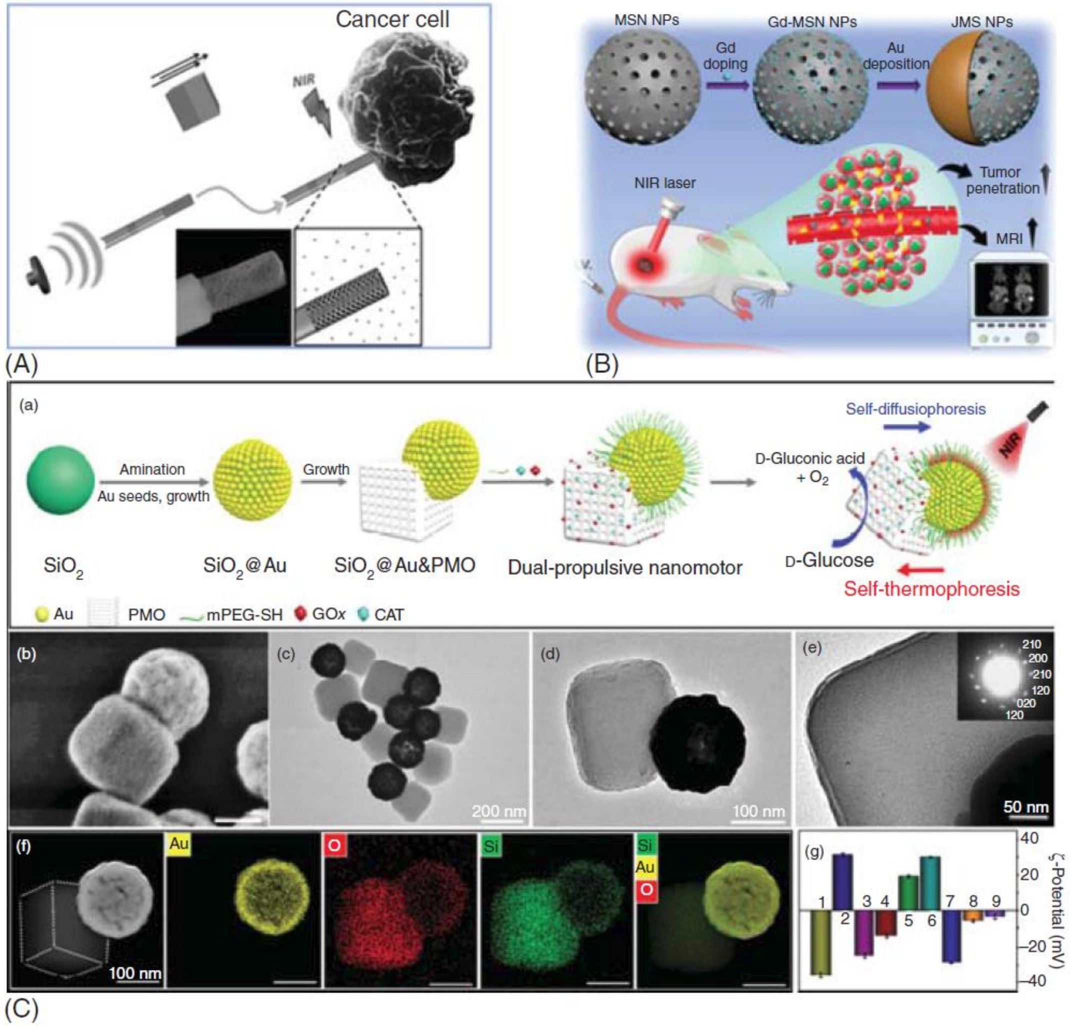
Molecular Engine Powered by H^+ Ions



The flagellum of an E coli cell is a molecular engine powered by the flow of hydrogen ions across the inner membrane. Spinning at an incredible speed, the flagellum here is shown only in slow motion.
Bacterial Flagellum by Smart Biology
https://youtu.be/dYt5135_0bs?feature=shared

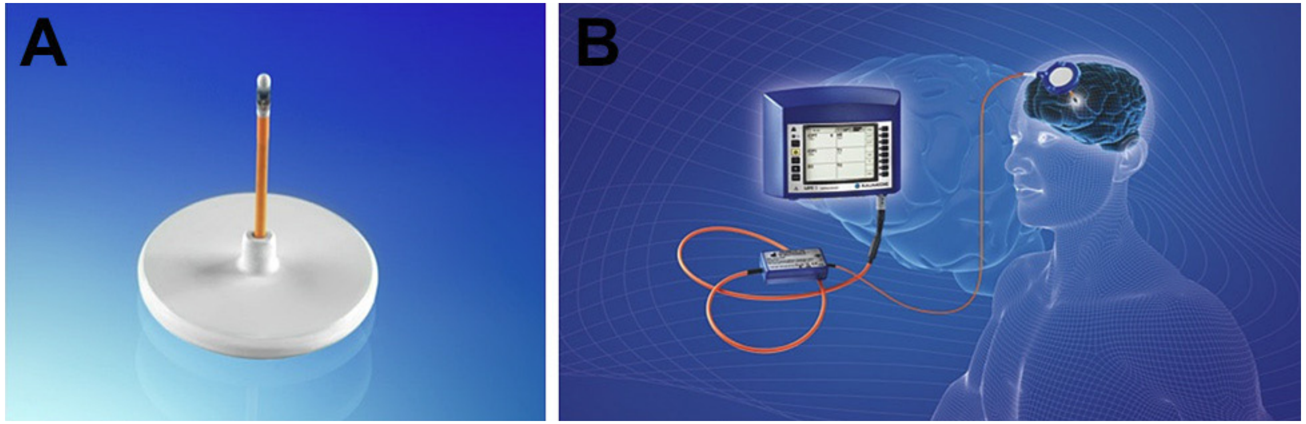
Other Examples…

A. Ultrasound-propelled tubular porous drug-loaded gold wire nanorobot for efficient drug loading and release.
B. Enzyme-based mesoporous nanorobots with NIR optical brakes.
C. NIR light-driven Janus mesoporous silica nanorobot to promote magnetic resonance imaging.



Maochun, Wan M. *Biomedical micro- and nanorobots in disease treatment*. Wiley-VCH; 2023, Fig. 2.3 p 15.

Clinical Applications

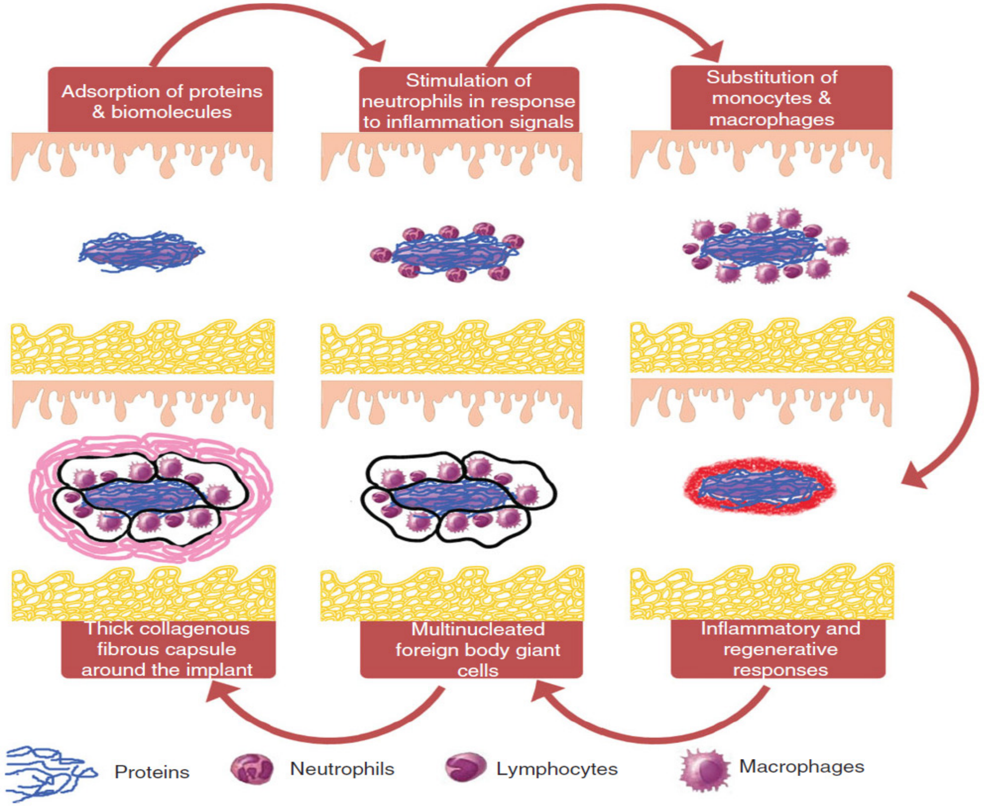


Neurovent P-tel implantable piezoresistive ICP monitoring sensor. Telemetric reader is placed over intact skin and collects intracranial pressure readings. Image courtesy of Raumedic, Inc.

iSTAT cartridge and handheld system. Image courtesy of Abbot Laboratories.

Biocompatibility, FDA & ISO 10993

Foreign Body Giant Cell Production



Barkam, S, et al. Fabricated micro-nano devices for in vivo and in vitro biomedical applications. WIREs Nanomed Nanobiotechnol 2013, 5:544–568

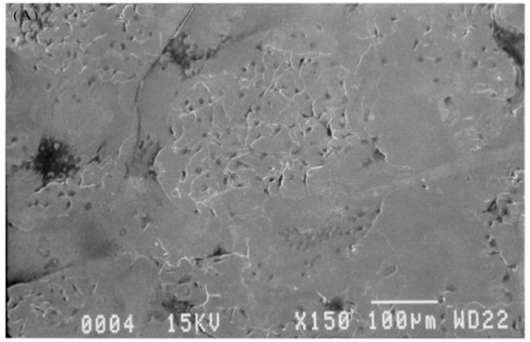


Image courtesy of Voskerician, G.

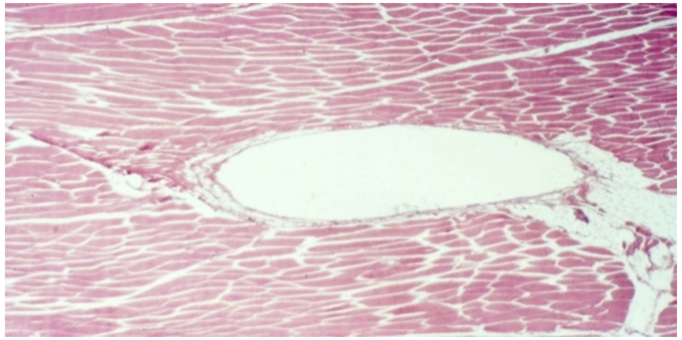
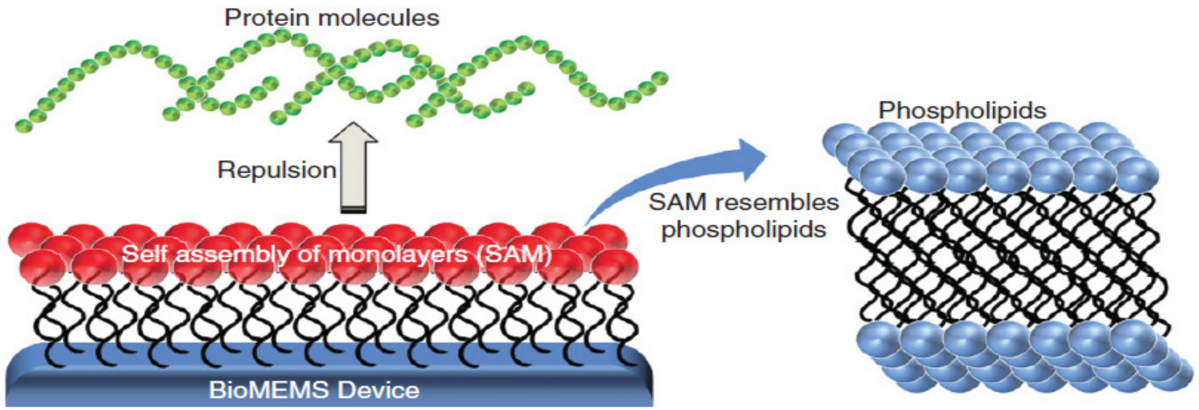


Image courtesy of NAMSA



Barkam, S, et al. Fabricated micro-nano devices for in vivo and in vitro biomedical applications. WIREs Nanomed Nanobiotechnol 2013, 5:544–568

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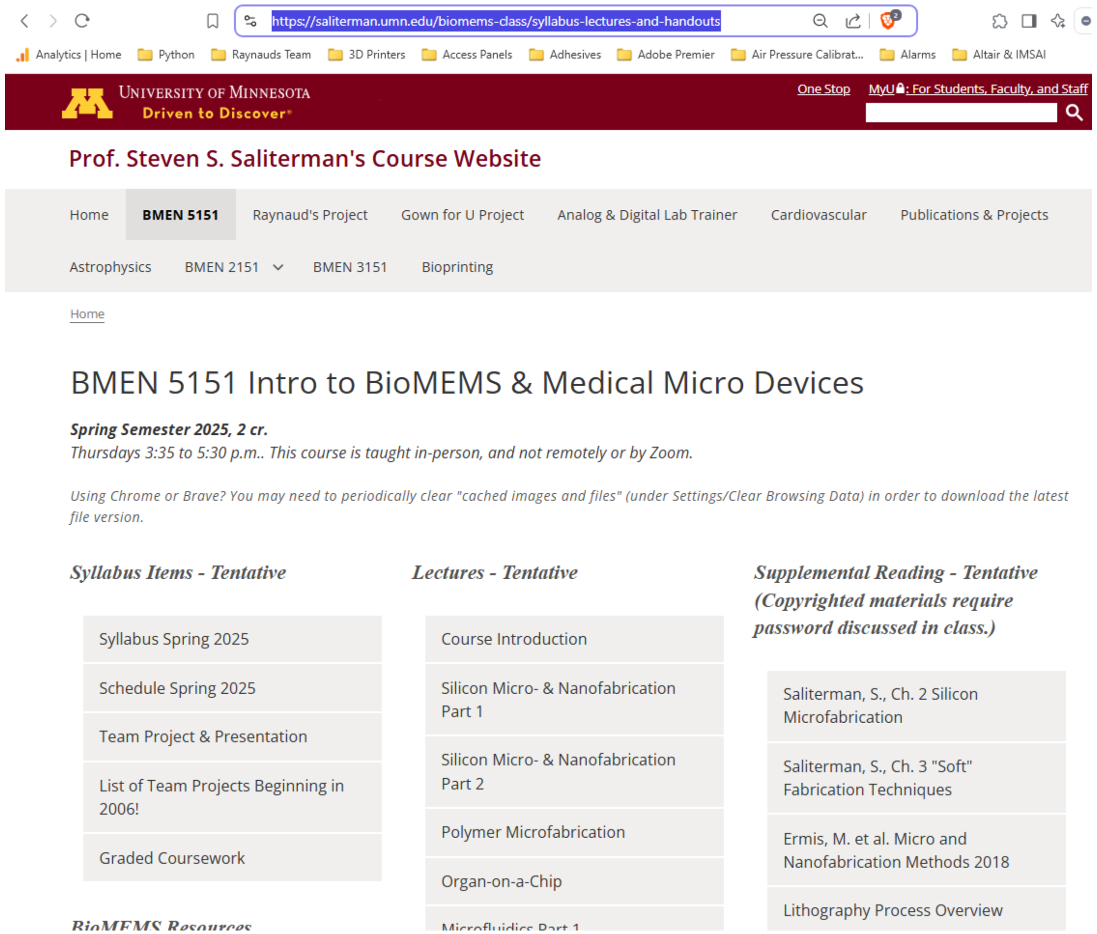
Course Website



- Course Website Link

Important

- Mari Hanchi is our Teaching Assistant.
- The class schedule contains recommended reading for each week.
- The midterm and final examination questions will be "essay" style. Your understanding of the material and ability to complete essays questions will be benefitted by the supplemental reading.
- The most successful students have kept their computers off and closed during the lectures, using the time to read the slides, listen to the discussion, and attempting to memorize as much as possible at the time.

Team Projects

- Purpose: To study further a particular bioMEMS concept or device that you are interested in.
- Format: Team presentation of 4 students as a 20-minute Power Point® presentation at the end of the semester. Submitting a paper is not required, although you may wish to distribute a handout. A brief class discussion will follow each talk.
- Description: Propose a new bioMEMS device or expand upon a previously published device or useful methodology. Discuss the purpose of your concept, and if appropriate, the theory (what principles are at work), fabrication (materials and techniques), testing, limitations, and biocompatibility of your device.

Projects Continued…

- Undergraduate Students: You will want to expand upon concepts presented in class and envision new methods and applications.
- Graduate Students: You should take a more technical, mathematical, and modeling approach to your team projects.
- Everyone: The course webpage includes updated lists of dozens of current and highly cited articles grouped by areas of interest; and library links to some excellent books.

Key Points

- *Have an awareness of the environment and related physics:*
  - *Micro* - At least one dimension is from ~100 nm to 200 μm.
  - *Nano* - ~0.1 nm to 100 nm.
- Explore and understand micro- & nanofabrication, including methods and materials.
- Understand microfluidics, chip-level design, and the incorporation of biological sensors & materials.
- Appreciate the emergence of biomedical robotics.
- Pursue a novel design or application of the techniques learned, as a team project.