Introduction to BioMEMS & Medical Microdevices, BMEn 5151

Course Introduction

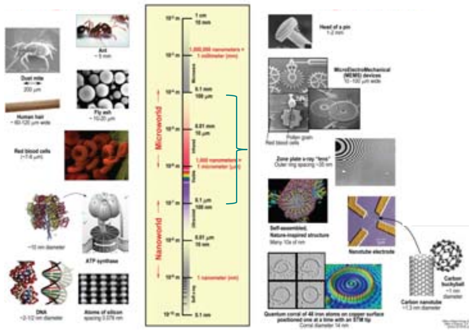
Prof. Steven S. Saliterman, http://saliterman.umn.edu/

Topics

1) Nano- *and* Microfabrication of Silicon & Polymers.
2) Microfluidics - Design, Transport, and Electrokinetics.
3) Biosensors, Microsensors and Nanotechnology.
4) Lab, Organ and Body-on-a-Chip Systems.
5) Microactuators & Drug Delivery.
6) Clinical Laboratory Medicine & Micro Total Analysis Systems.
7) Genomics and Proteomics - Gene and Protein Chips.
8) Clinical Applications & Point-of-Service Devices.
9) Biocompatibility, FDA & ISO 10993.

BioMEMS…

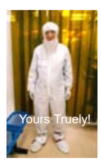
- Biomedical Micro Electro-Mechanical Systems.
- Devices or systems, constructed from nano or microfabrication, that are used for processing, delivery, manipulation, analysis or construction of biological and chemical materials.
- At least one dimension is from ~100 nm to 200 µm.
- Incorporating new materials and an understanding of the nano- microenvironment, and biocompatibility.
- Harnessing any phenomenon that accomplish work at the microscale.
- Includes research and laboratory tools, and point-of-service, therapeutic and implantable devices.



Micro-Nano Realm
~100 nm to 200 µm
100 nm to 0.078 nm

US Department of Energy, Office of Science 2019

Silicon Nano- and Microfabrication



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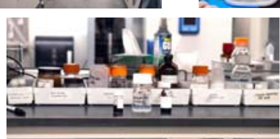
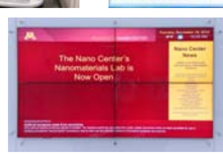
Nano-Bio Lab Facility…





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Polymer Microfabrication

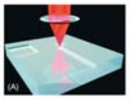


Image courtesy of Marco, CD

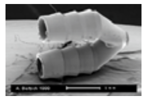

Image courtesy of Bertsch A.

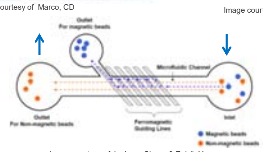

Image courtesy of Jaehoon Chung & Euisik Yoon

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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

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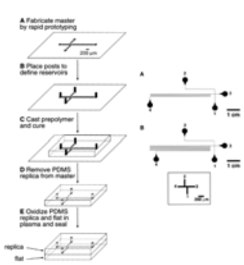
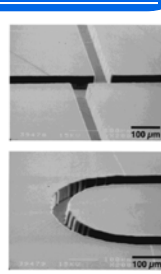
Rapid Prototyping Systems in PDMS…

Image courtesy of Sylgard





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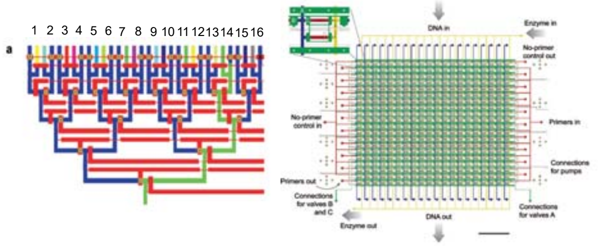
Duffy DC, McDonald JC, Schueller OJA, Whitesides GM. Rapid prototyping of microfluidic systems in poly(dimethylsiloxane). *Analytical Chemistry.* 1998;70(23):4974-4984.

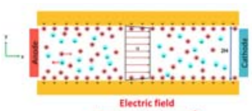
Large-Scale Integration…



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

Electrokinetics…

- Electrokinetic phenomenon:
  - Electroosmosis
  - Electrophoresis
  - Dielectrophoresis

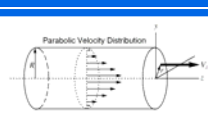


- An important tool for moving, separating and concentrating fluid and suspended particles.

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

Transport Processes…

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



- Mixing by diffusion, special geometries and mechanical means.
- Effects of increased surface area-to-volume as dimensions are reduced in microfluidic channels.

Biosensors & Nanotechnology

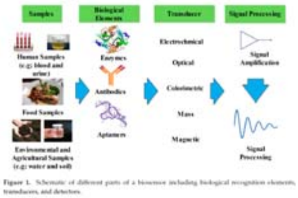


Figure 1. Schematic of different parts of a biosensor including biological recognition elements, transducers, and detectors.

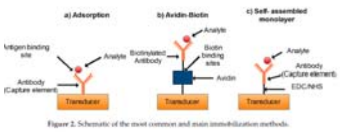


Figure 2. Schematic of the most common and main immobilization methods.

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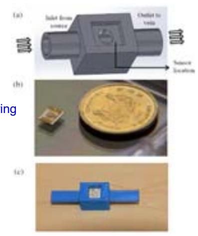
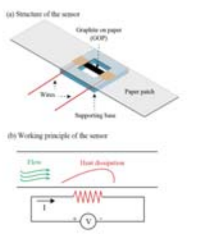
Luka G, Ahmadi A, Najjaran H, et al. Microfluidics Integrated Biosensors: A Leading Technology towards Lab-on-a-Chip and Sensing Applications. *Sensors.* 2015;15(12):30011-30031.

Microsensors…

Flow Monitoring



Thermal Flow



Kottapalli AGP, Shen Z, Asadnia M, et al. Polymer MEMS sensor for flow monitoring in biomedical device applications. 2017 IEEE 30th International Conference on Micro Electro Mechanical Systems (MEMS); 22-26 Jan. 2017, 2017.

Dinh T, Phan H, Qamar A, et al. Environment-friendly wearable thermal flow sensors for noninvasive respiratory monitoring. 2017 IEEE 30th International Conference on Micro Electro Mechanical Systems (MEMS); 22-26 Jan. 2017, 2017.

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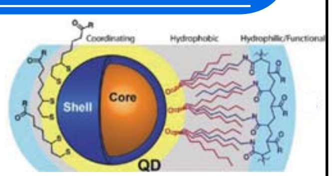
Nanotransducers…

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.



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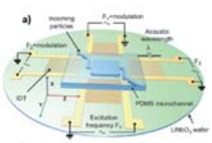
Hildebrandt N, Spillmann CM, Algar WR, et al. Energy Transfer with Semiconductor Quantum Dot Bioconjugates: A Versatile Platform for Biosensing, Energy Harvesting, and Other Developing Applications. *Chemical Reviews.* 2017;117(2):536-711.

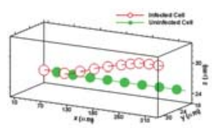
Lab-on-a-Chip

Surface Acoustic Waves

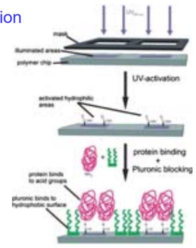


Tran, S.B.Q., Marmottant, P., Thibault, P., 2012. Appl. Phys. Lett., 101.

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

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Detection Strategies…

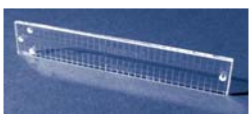
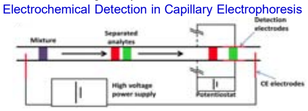
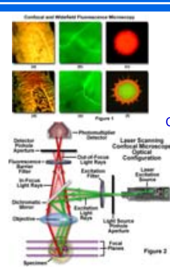


Image courtesy of Micronit

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

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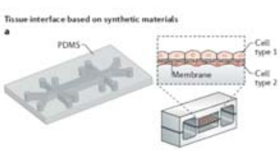
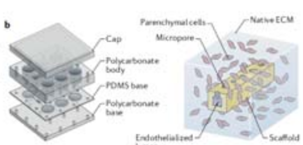
Organ-on-a-Chip…

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).

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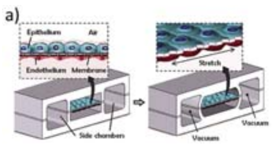
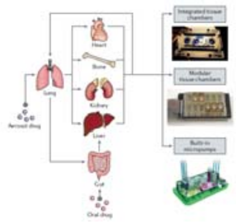
From Organ to Body-on-a-Chip…



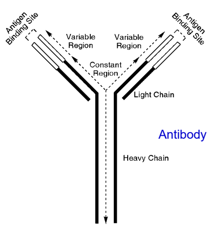
Lung-on-a-Chip



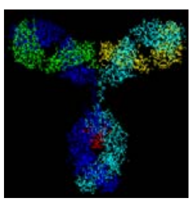
Body-on-a-Chip - "Organ Coupling"

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

Clinical Laboratory Medicine

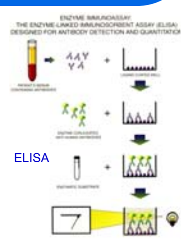


Antibody



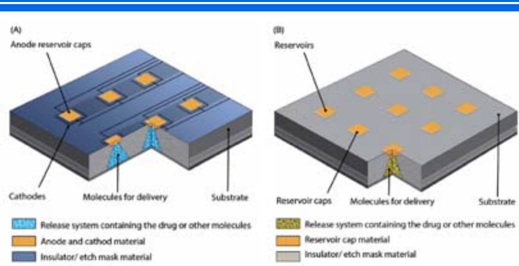
http://www.umass.edu/microbio/rasmol/padlan.htm

ELISA



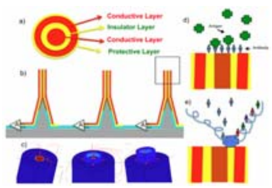
Laposata M, *Laboratory Medicine, Clinical Pathology in the Practice of Medicine*, ASCP Press, Chicago (2002).

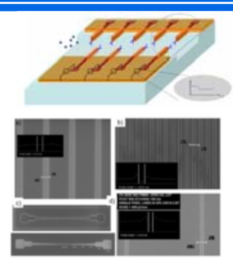
Microactuators and Drug Delivery



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

Genomics, Proteomics and µTAS





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Esfandyarpour R, Esfandyarpour H, Harris JS, Davis RW. Simulation and fabrication of a new novel 3D injectable biosensor for high throughput genomics and proteomics in a lab-on-a-chip device. *Nanotechnology.* 2013;24(46):465301-465301.

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.

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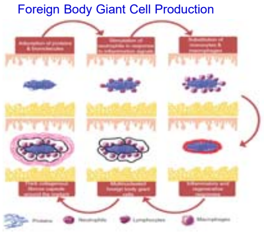
Biocompatibility, FDA & ISO 10993

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

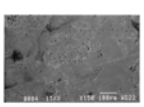
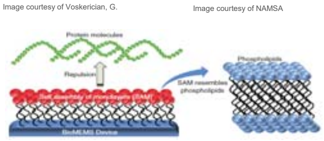


Image courtesy of Voskerician, G.

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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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.

Examples of Past Projects…

- A BioMEMS Implant to Treat Spinal Cord Injuries
- A Mobile Neurostimulation Electrode
- Assay of Testicular Germ Cell Tumors
- COVID-19 High Throughput Serology Chip
- Detection of the SARS-COV-2 Using SPR
- Heart-on-a-Chip
- Microfluidic Device for Cancer Diagnosis & Monitoring of Metastasis
- Organ-on-a-Chip Model for COVID-19
- Piezoelectric Patch & Pump for Drug Delivery in Tumors
- Quantum Dots for Auditory Brainstem Prosthesis
- Real Time Drug Monitoring Peritoneal Dialysis

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