Lecture 04

MEMS Biomedical applications

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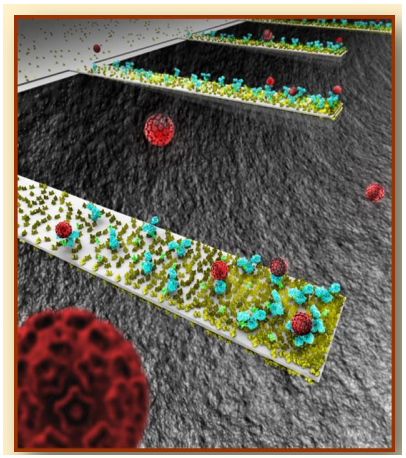
Biomedical MEMS

- MEMS pressure sensors are found in blood pressure monitors, infusion pumps, catheters, and intracranial probes
- Some of the MEMS are unique as it incorporate biological molecules as an integral part of the device.
- BioMEMS are MEMS that have biological and/or biomedical functions or applications.



A microcantilever transducer (left) may be coated with antibodies (green spheres) that capture a virus (red sphere) in a blood sample while ignoring the other components in the sample.

BioMEMS usually contains sensors, actuators, mechanical structures and electronics. Such systems are being developed as diagnostic and analytical devices.

BioMEMS in Biomedical Field

BioMEMS encompasses all interfaces and intersections of the life sciences and clinical disciplines with microsystems and nanotechnology.

MEMS	BioMEMS
Silicon based Material	Biocompatible Material
Electrical & Mechanical interface integration	Biomolecular & physical parameter (electrical,mechanical optical) transducer integration
Moving part in micromachining system (active component)	Motion medium in passive substrate (microfluidic driving force)

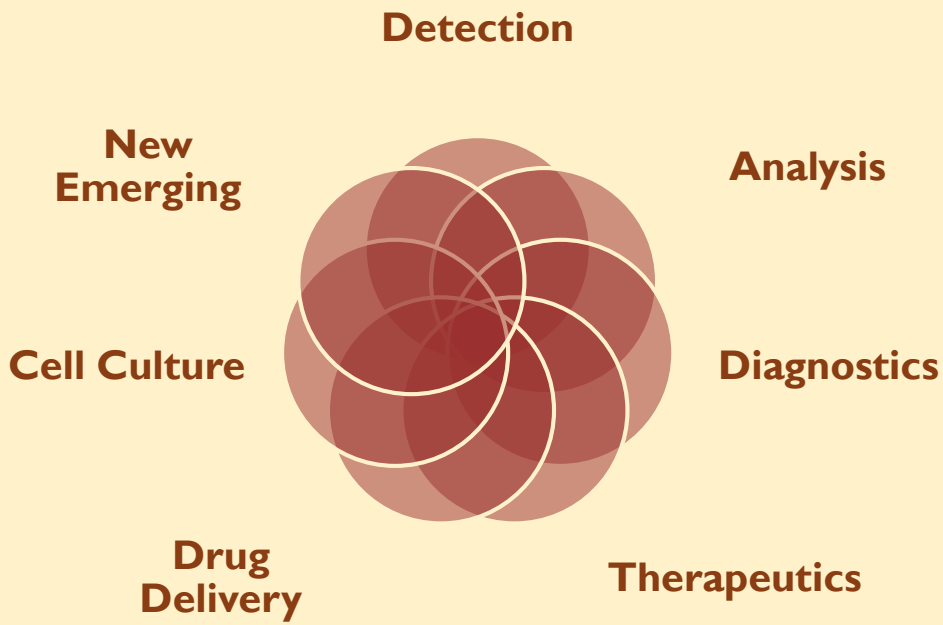
Why MEMS are exciting for medical applications

(1) Compatible size scales, especially with cells (2-100 micron-sized features are easy to make) (2) Many materials used in MEMS are biocompatible - (Gold, titanium, Polymers, Silicon) (3) Ease of electronics integration enables sophisticated capabilities in small form factor (Signal processing and analysis, Wireless capability)

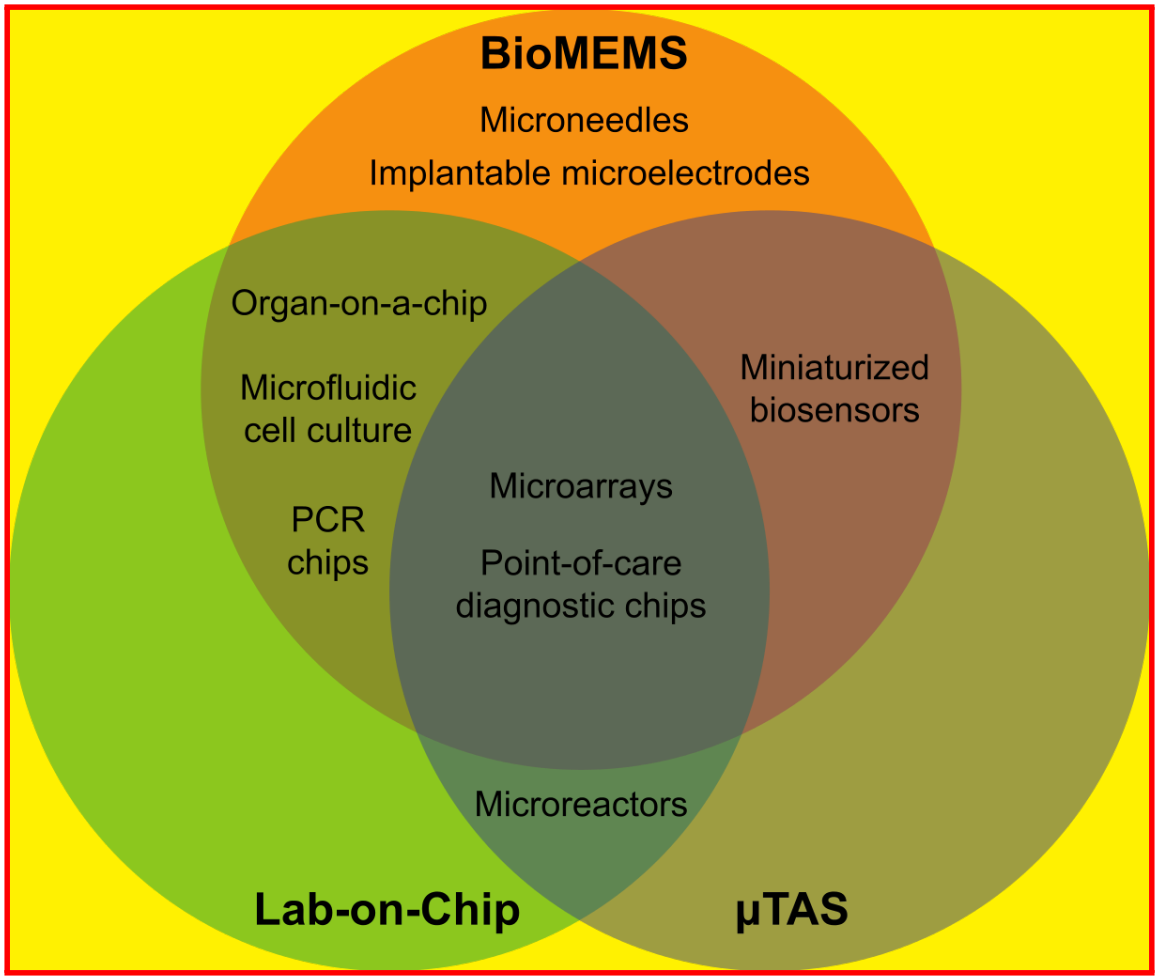
BioMEMS areas of applications

BioMEMS are being researched for possible applications in a variety of areas, but have already led to multiple applications in the following areas:

- Detection
- Analysis
- Diagnosis
- Therapeutics
- Drug delivery
- Cell culture



A Venn diagram



A Venn diagram outlining and contrasting some aspects of the fields of bio-MEMS, lab-on-a-chip, μTAS.

Constraints of BioMEMS

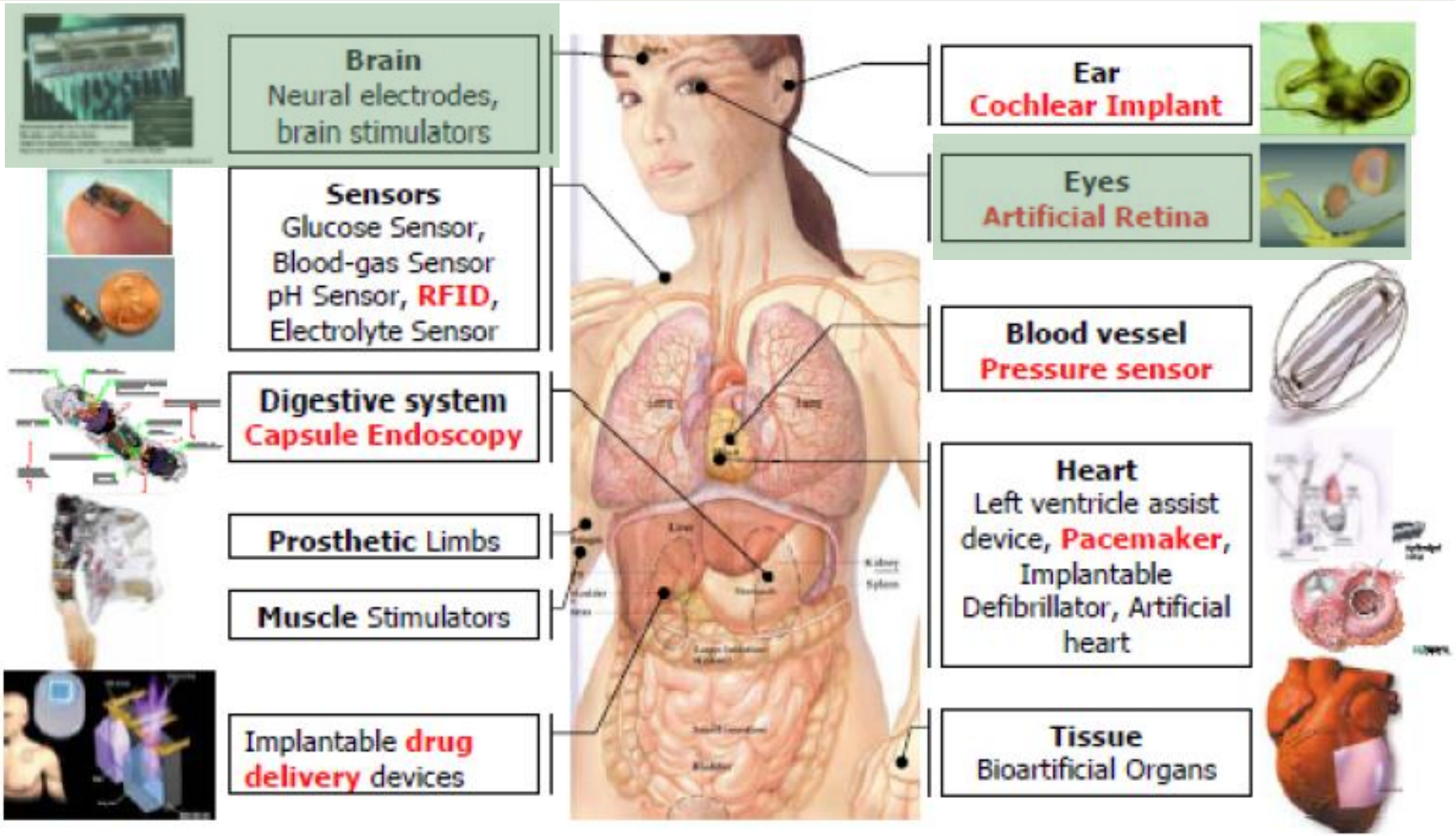
Material requirements

- Biocompatibility
- Mechanical compatibility
- Chemical resistance

Polymer MEMS

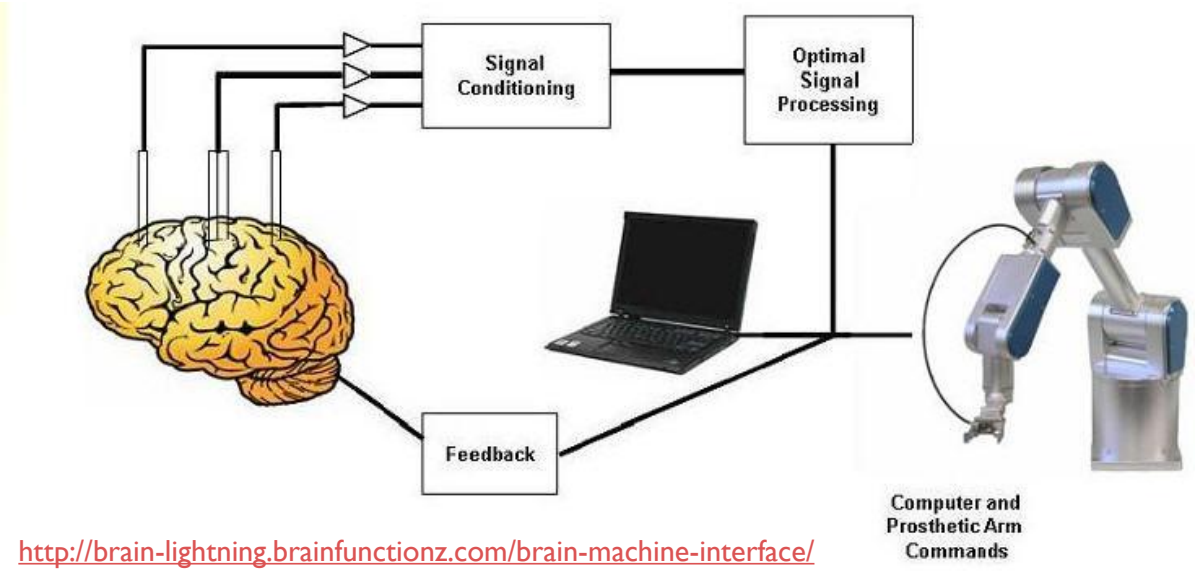
- Advantage
  - Biocompatible and biodegradable
  - Better mechanical shock tolerance
  - Low cost
- Disadvantage
  - Mechanical properties change dramatically over a narrow temperature range
  - Gas/moisture permeable, will need hermetic packaging

BioMEMS Applications



Brain Machine Interface (BMI)

- BMI forms a direct communication pathway between the brain and an external device
- Neural communication through
  - Electrical signal
  - Chemical signal



http://brain-lightning.brainfunctionz.com/brain-machine-interface/

Dynamic Data-Driven Brain-Machine Interface (DDDBMI)

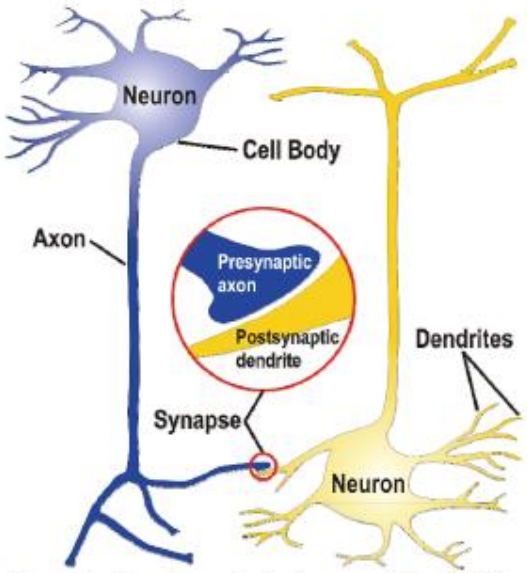
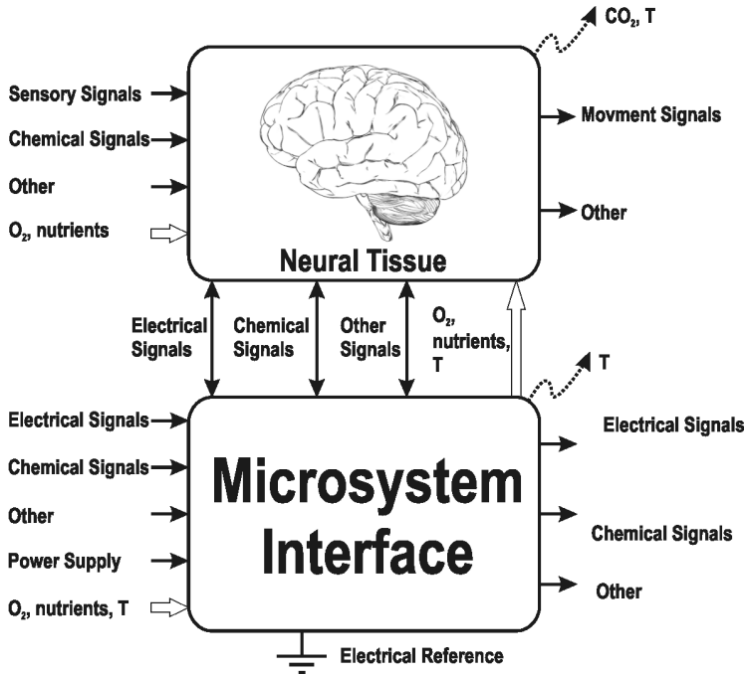
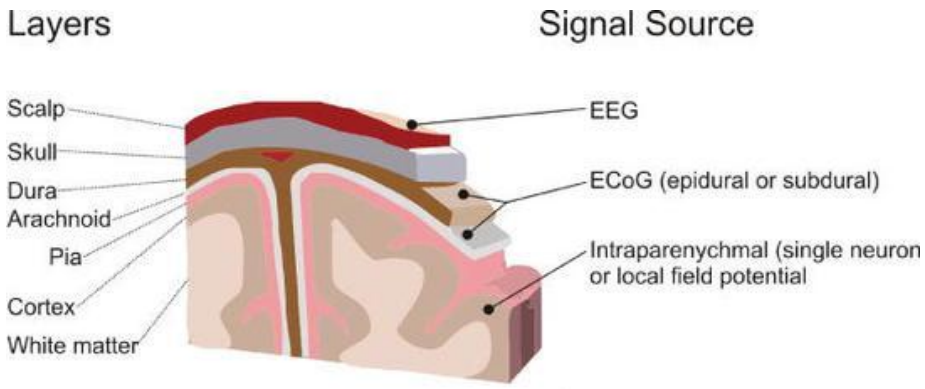


Figure 1 Structure of a basic neural circuit. The signal from the presynaptic axon is transmitted to the postsynaptic dendrite at a synapse.

Electrical/Chemical BMI

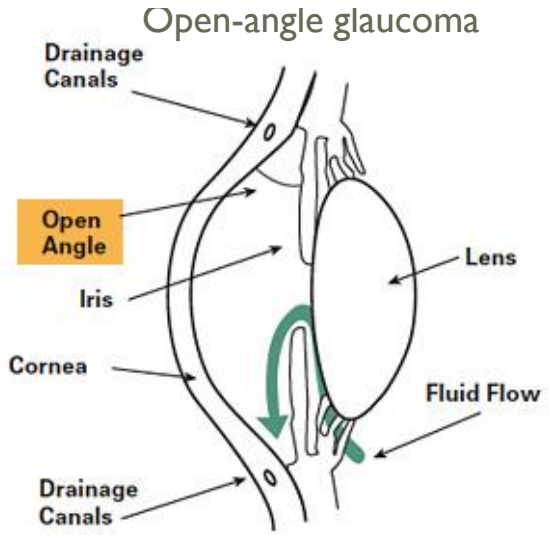
- Artificial BMI
  - Electrical stimulation/recording
  - Chemical stimulation/recording
  - Combined approach
- Several types
  - Surface type
    - Electroencephalography (EEG)
    - Electrocortigography (ECoG)
  - Penetration type

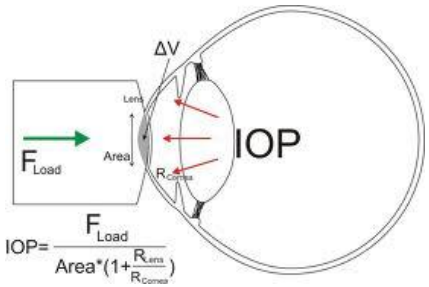


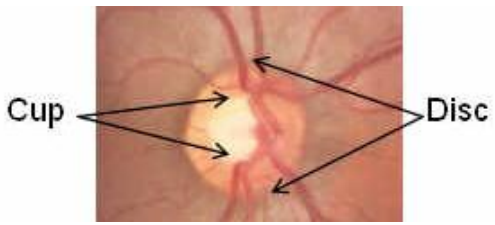


BioMEMS for Glaucoma Management

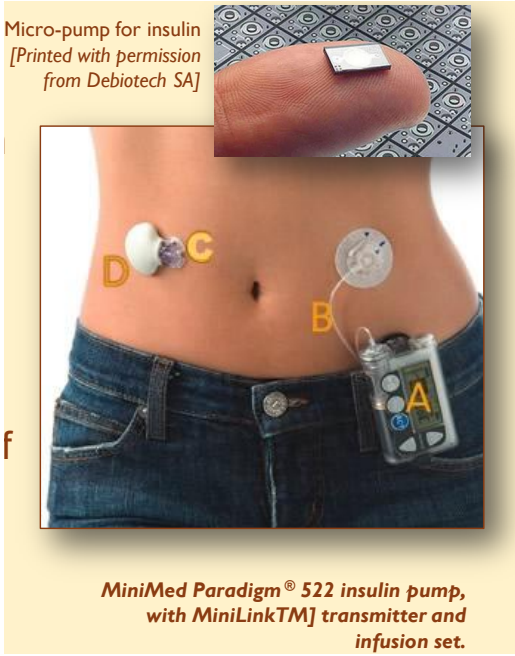
- Glaucoma
  - The second leading cause of blindness (WHO)
  - ~ 67 million worldwide
  - Over 4 million Americans have glaucoma but only half of those know they have it
  - ~10% of people with glaucoma become blind
- Types of Glaucoma
  - Open-angle glaucoma
  - Close-angle glaucoma
  - Normal-tension glaucoma
  - Congenital glaucoma
  - Other types
- Clinical Interventions
  - Applanation tonometry
  - Shape and color of the optic nerve
  - The complete field of vision







BioMEMS for Diabetics

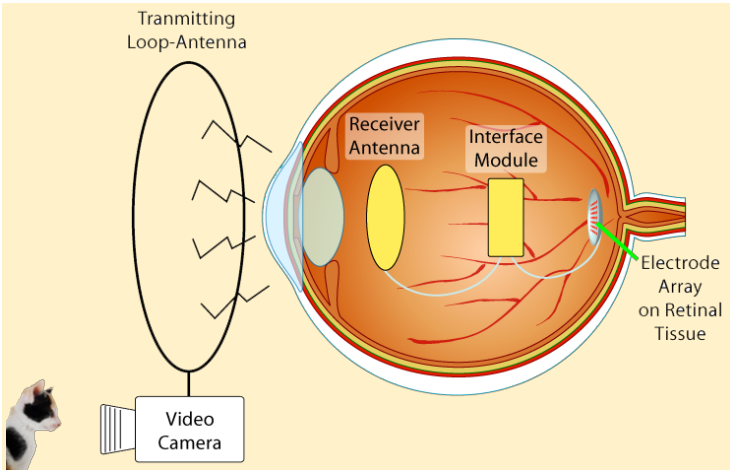


- The MiniMed Paradigm 522® insulin pump, with sensor, transmitter and infusion line is one of a few devices on the market that can not only monitor a persons glucose levels 24/7, but can deliver insulin on an as needed basis. Its components are
  - an external pump and computer,
  - a soft cannula that delivers the insulin
  - an interstitial glucose sensor
  - a wireless radio device that communicates with the computer

- The sensor (C) is placed under the skin.
- The sensor continuously measures glucose levels in the interstitial fluid
- Sensor measurements are received in real time by the wireless radio device (D).
- This device sends the readings to the computer (A) which determines the amount of insulin needed.
- The pump (A) administers that amount into the patient via the cannula (B).

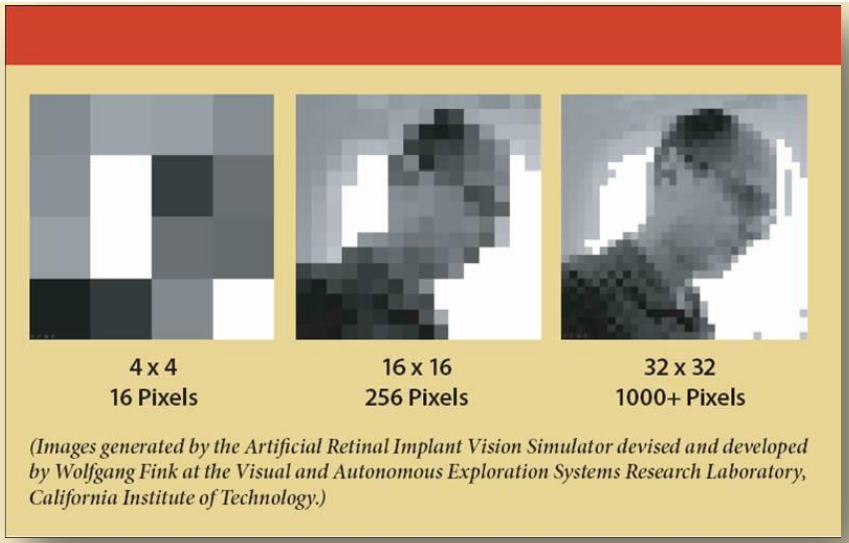
Artificial Retinal Prosthesis

- A therapeutic BioMEMS device currently being tested is the artificial retinal prosthesis called the ArgusTM Retinal Prosthesis System.
- The heart of the system is an artificial retina - an electrode array placed directly on the retina at the back of the eye. This array duplicates the task of the photoreceptor cells in the retina.
- These cells are destroyed in retinal diseases such as age-related macular degeneration and retinitis pigmentosa (RP).
- This device consists of a camera (in one's eyeglasses), microprocessor and transmitter (on a belt), receiver and interface module (the side of the eye) and an artificial retina implanted onto the retina of the eye.



Images from the camera, are converted to electronic signals and transmitted to the receiver. These signals activate specific electrodes in the array which become impulses along the retinal neurons, through the optic nerve and to the brain. The patient sees flashes of light, which the brain uses to make the equivalent of low- resolution images.

Recent Results from Artificial Retina



(Images generated by the Artificial Retinal Implant Vision Simulator devised and developed by Wolfgang Fink at the Visual and Autonomous Exploration Systems Research Laboratory, California Institute of Technology.)

(Left) Simulated images produced by the artificial retina prosthesis.
Argus I is the 4x4 array of 16 pixels. Argus II (used in the current clinical trial) has 60 pixels. Argus III, currently being developed by Lawrence Livermore National Lobs will have over 200 pixels and will transmit data wirelessly from the camera. [Images generated by the Artificial Retinal Implant Vision Simulator]

On May 4, 2011, Argus reported the results of the Phase II clinical trial of Argus II. All of the 30 patients being test showed significant improvements in visual ability – from finding doorways to identifying up to eight different colors. One patient was able to read at a rate of 10 wpm. *Medical News Today*

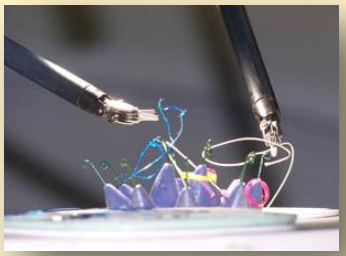
This device has now been approved for commercialization in Europe and an application has been submitted to the FDA for commercialization in the U.S.

Minimally Invasive Surgery

The da Vinci System

Surgeon operates from a seated position at the console with a large monitor.

Eyes and hands are positioned in line with the instruments.

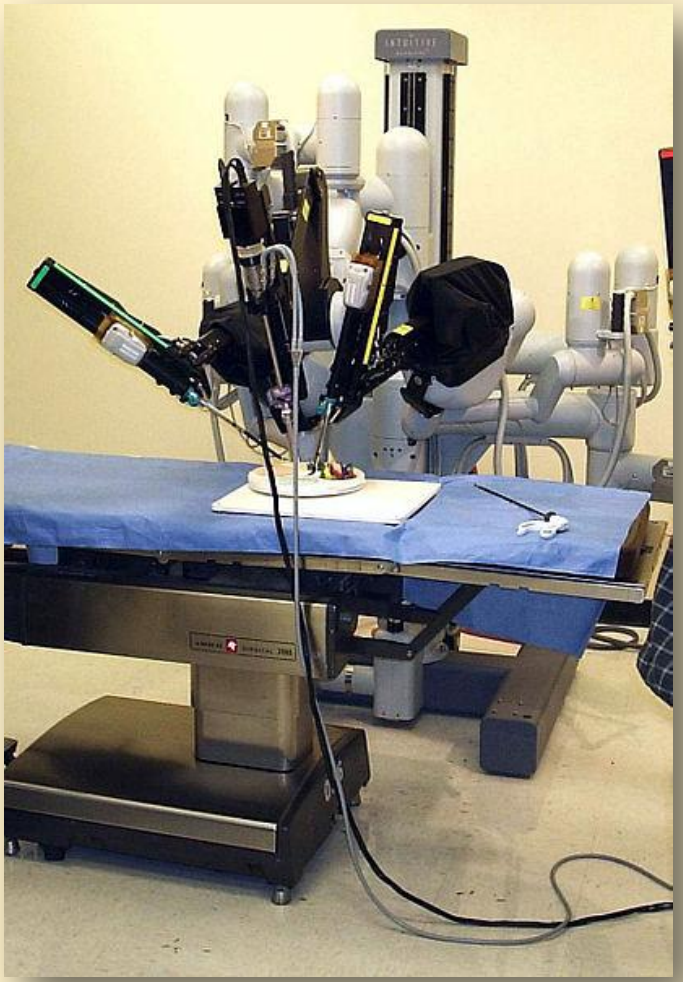


Each instrument has a specific task (e.g., clamp, suture, move tissue, cut, camera)

To move the instruments or to reposition the camera, the surgeon simply moves his/her hands. Seven degrees of motion are available.

<u>Con</u>

No sense of touch (haptic)

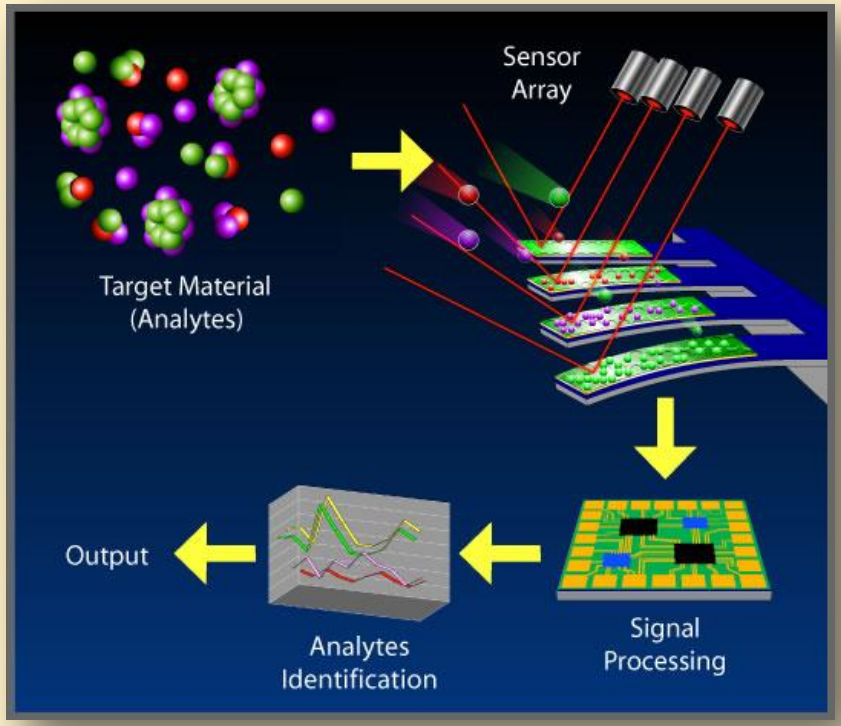


Chemical sensor arrays

The MEMS device used for many diagnostic tools is the chemical sensor array (CSA). These devices are used for

- disease identification,
- for gathering the biomolecular information needed to prescribe appropriate drugs for personalized medicine, and
- antibody identification (just to name a few).

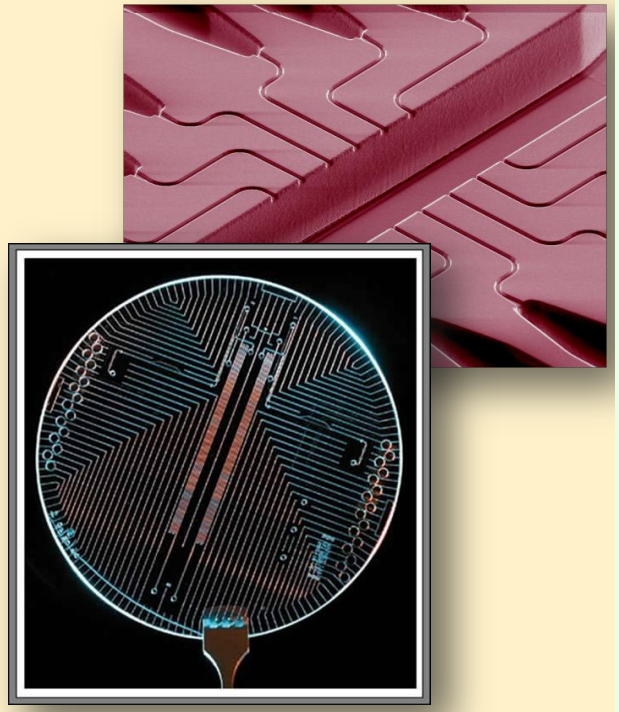
CSA are found in many lab-on-a-chip (LOC) devices.



Chemical Sensor Arrays (Can detect, identify and determine the amount of an analyte in solution for the purpose of diagnosis)

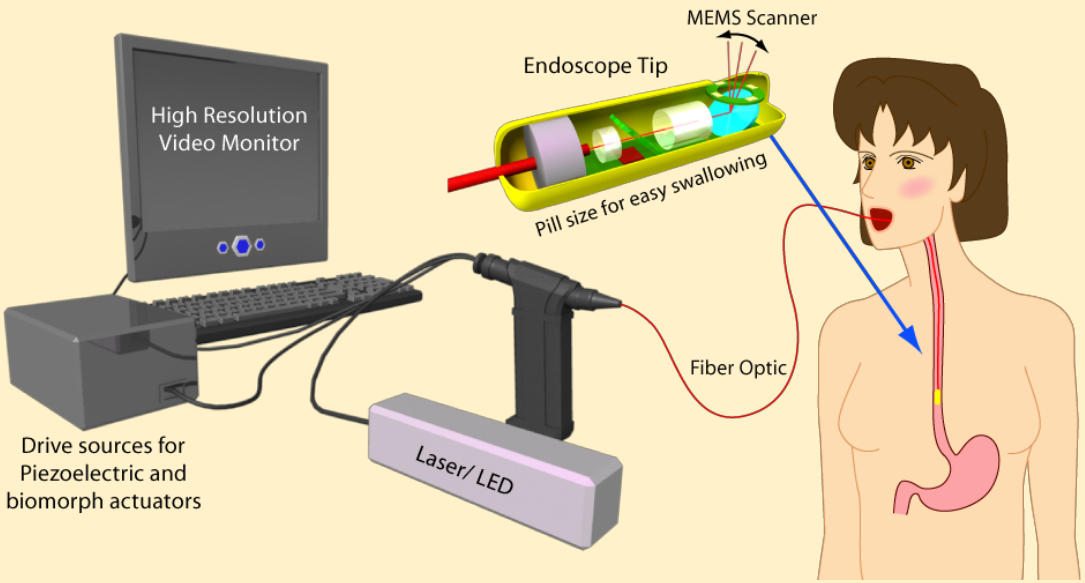
BioMEMS Microfluid

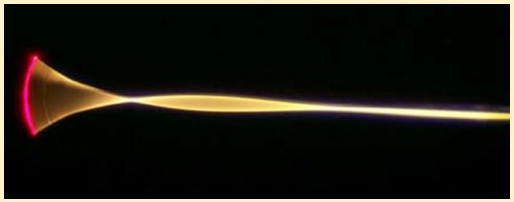
- Microfluidics are integrated microchips that allow separations, chemical reactions, and calibration-free measurements to be directly performed with minute quantities of complex samples (blood, environmental gases).
- Microfluidics applications are used in remote locations for clinical diagnostics and environmental sensing.
- Lab-on-a-Chip (LOC) systems enable the design of small, portable, rugged, low-cost, easy to use, yet extremely versatile and capable diagnostic



MicroFluidic Channels (Top)
Lab-on-a-chip (LOC) (bottom)
[Printed with permission from

BioMEMS in Endoscope

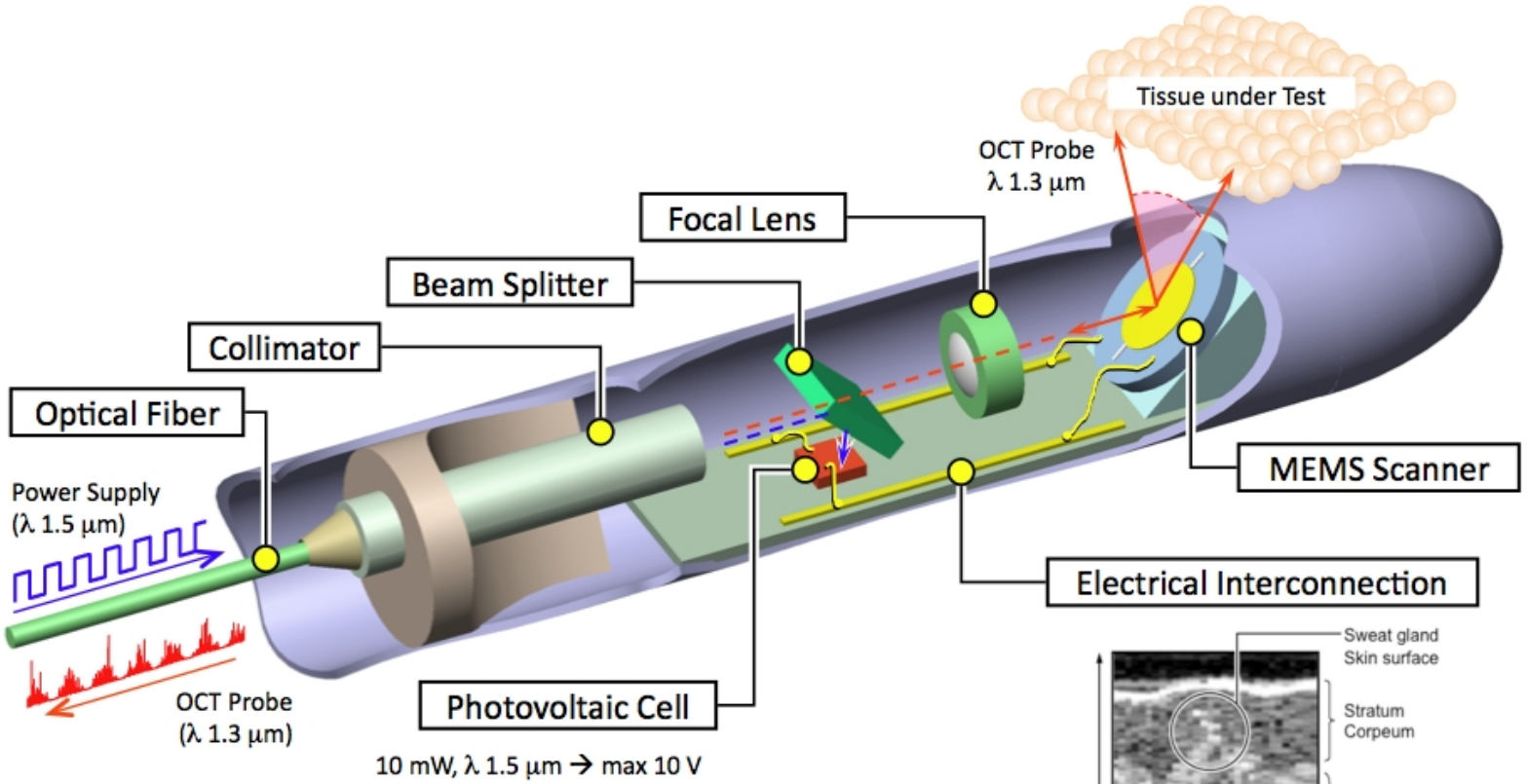


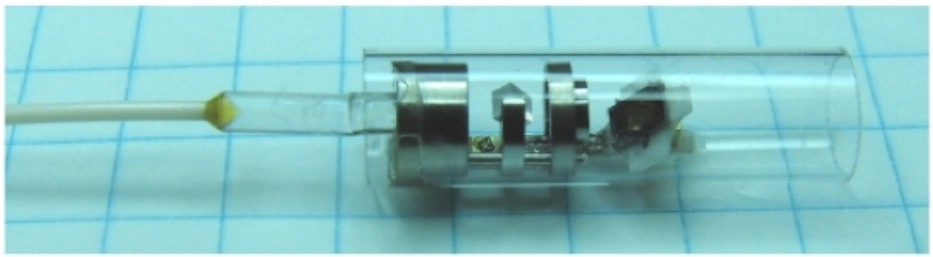


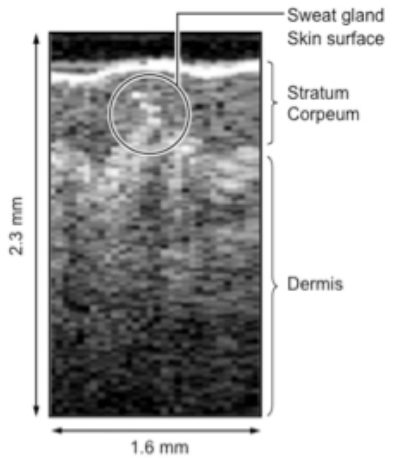
Scanner: 124 micron diameter micro-machined fiber vibrating at 40.4 KHz with an angular displacement of 80 degrees.
A piezoelectric actuator drives the fiber tip.

Single-fiber Micro-optical scanner for endoscopies.
UPDATE: No fiber optic cable is used. The patient swallows the pill!

BioMEMS in Endoscope





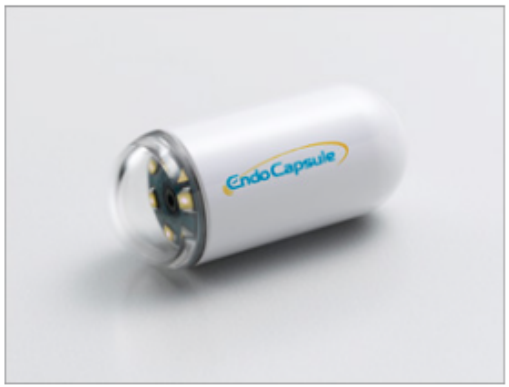


Endoscopic Pills

- **Given Imaging, Olympus: optical detection only**
- **SmartPill: pH measurement**
- **MEMS possible for in-situ measurements, navigation**

- www.givenimaging.com
- www.smartpillcorp.com
- www.olympus.co.jp/en/news/2005b/nr051013capsle.cfm

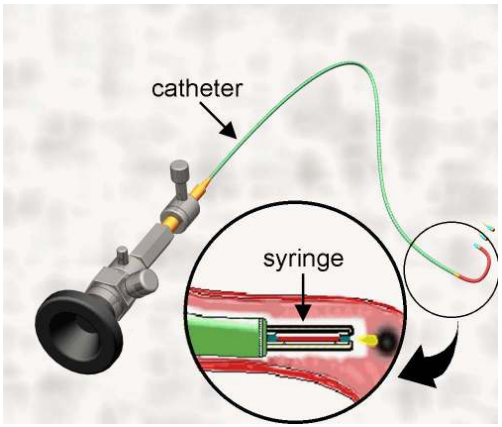
Source: Given Imaging



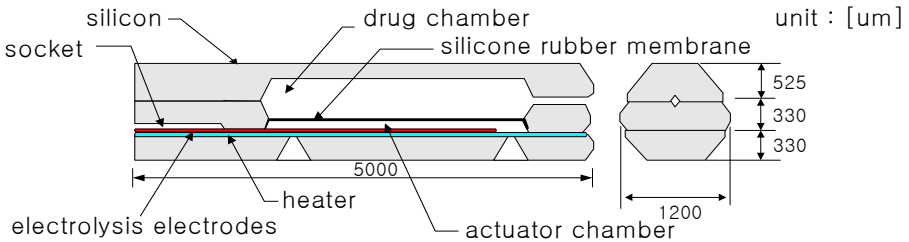
Source: Olympus

Source: SmartPill

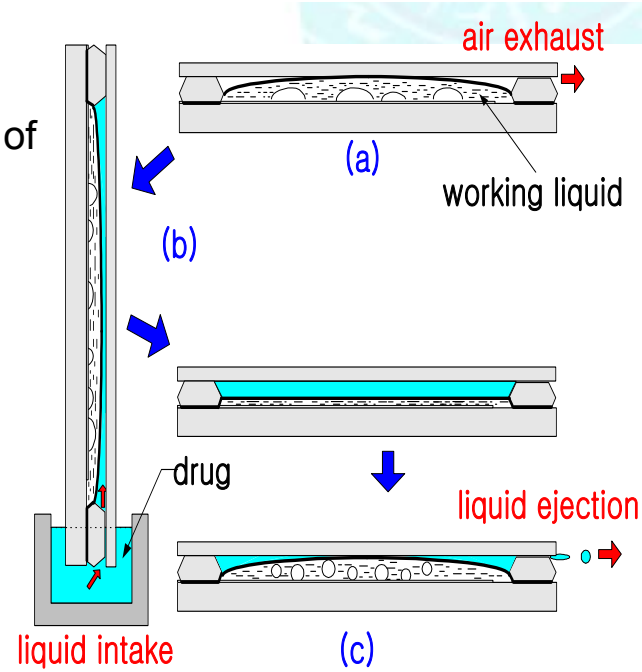
Micro syringe (1)



- Local medication
  - Attachable to the end of intravascular catheter
- Size: 1.2 ~ 1.5 mmϕ
- Volume: a few μl or less
- Evaporating / electrolysis actuation
- Disposable

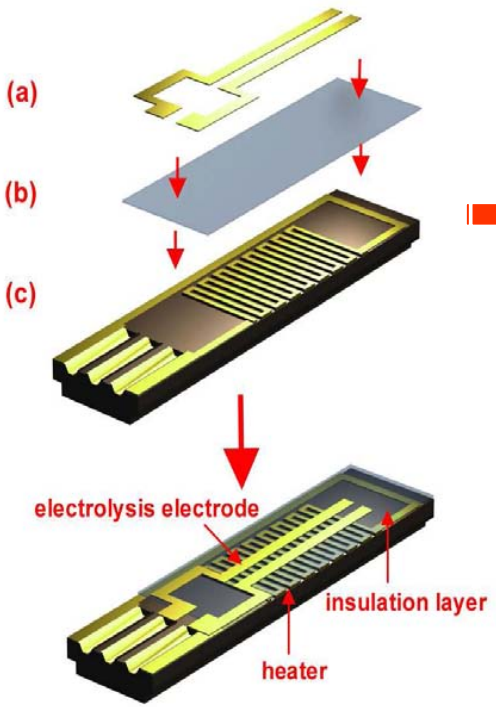


Structure of the micro syringe

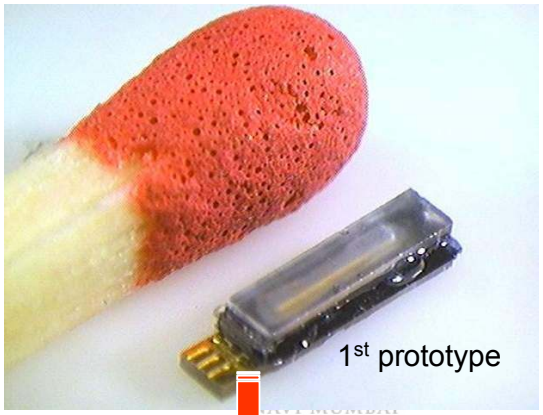


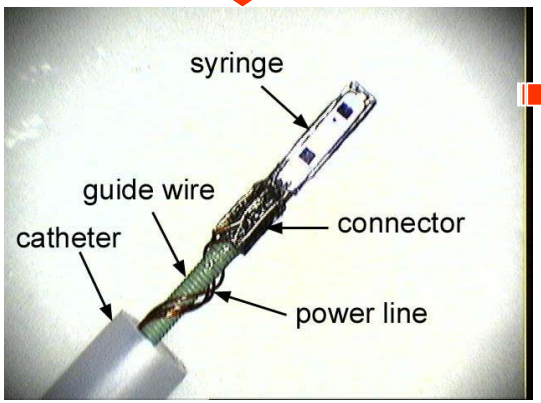
Operation of the micro syringe
(a) vaporization by heating
(b) condensation by cooling
(c) gas generation by electrolysis

Micro syringe (2)

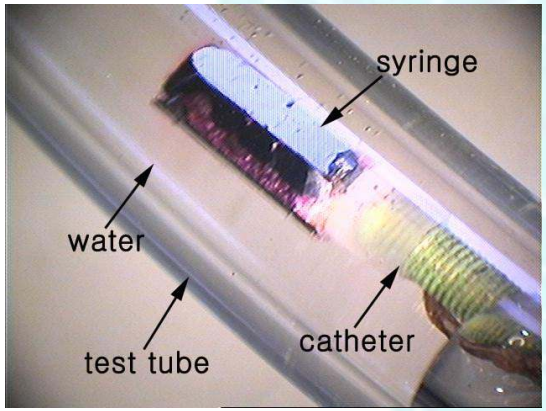


Layout of electrodes





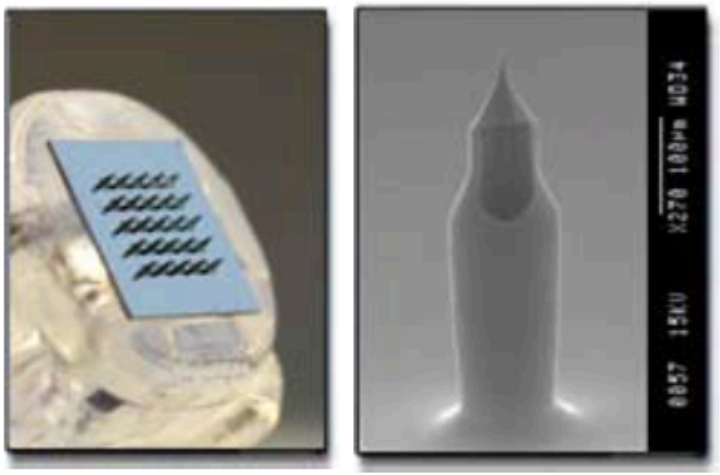
The photograph of the micro syringe attached to the catheter



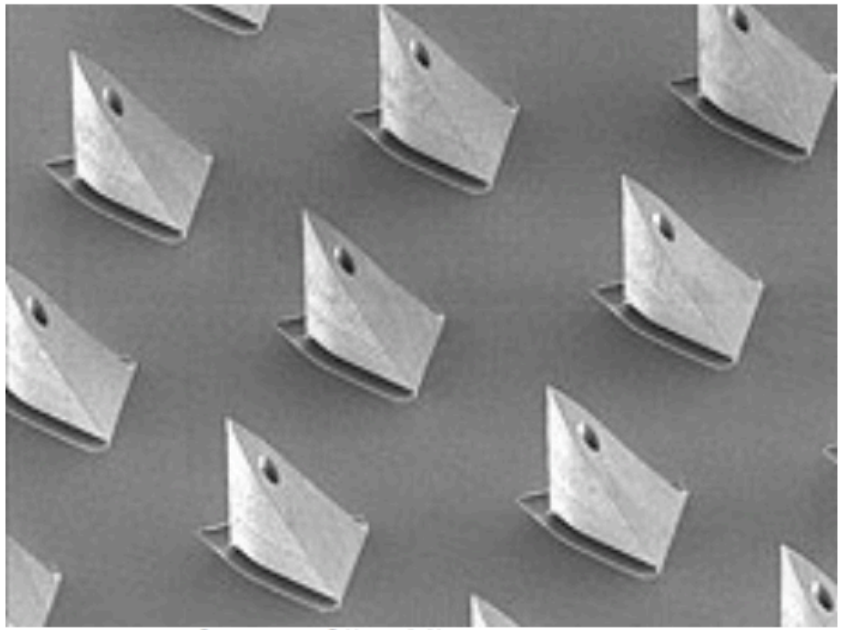
In-vitro test
(successful injection)

Microneedles

- **Pain-free blood sampling and drug delivery**



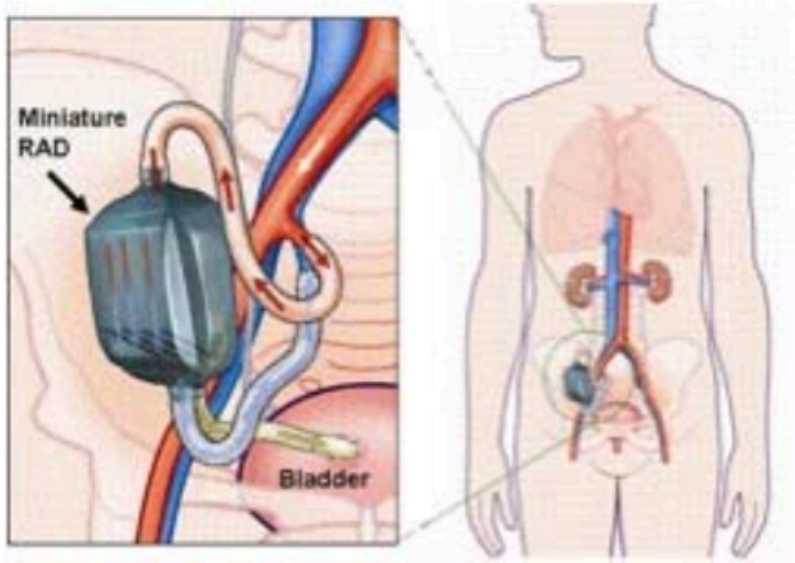
Source: Debiotech SA

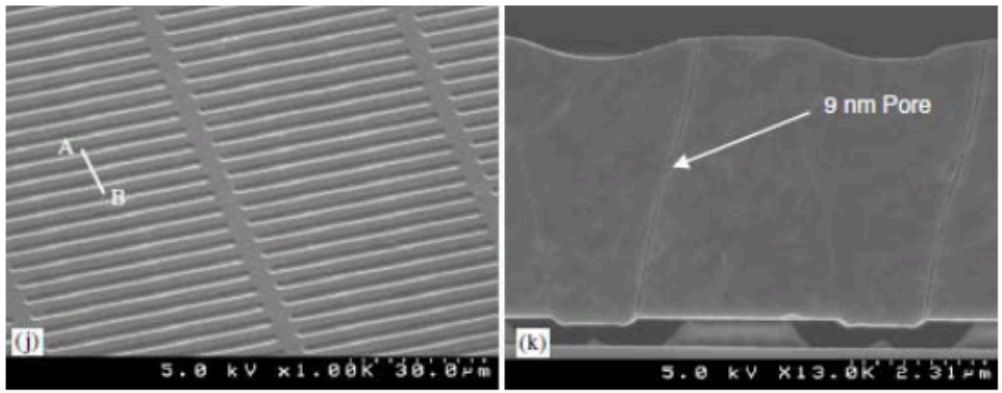


Source: Silex Microsystems

Artificial Kidney

- A bioartificial kidney has been developed by clinical collaborators at the University of Michigan, called the extracorporeal Renal Assist Device (RAD).
- The Biomedical Microdevices Laboratory at UCSF is investigating the feasibility of MEMS technology to miniaturize the RAD to a size appropriate for implantation.
- Principal investigator: Dr. Shuvo Roy, UCSF





Challenges in MEMS for medical applications

- **Packaging, packaging, packaging**
  - **MEMS chip often needs ASIC**
  - **Electrical interconnect**
  - **Mechanical stress management**
  - **Small form factor**
  - **Hermeticity (for both MEMS function and biocompatibility)**
- **Sterilization**
  - **Gamma, e-beam (damaging to electronics and some plastics)**
  - **Ethylene oxide (can be absorbed by plastics)**
  - **Steam 121-134C (creates problems with material CTE mismatch, glass transition temperature)**