MEMS for Medical Applications

Presented to IEEE-EMBS

Alissa M. Fitzgerald, Ph.D. | 17 November 2010

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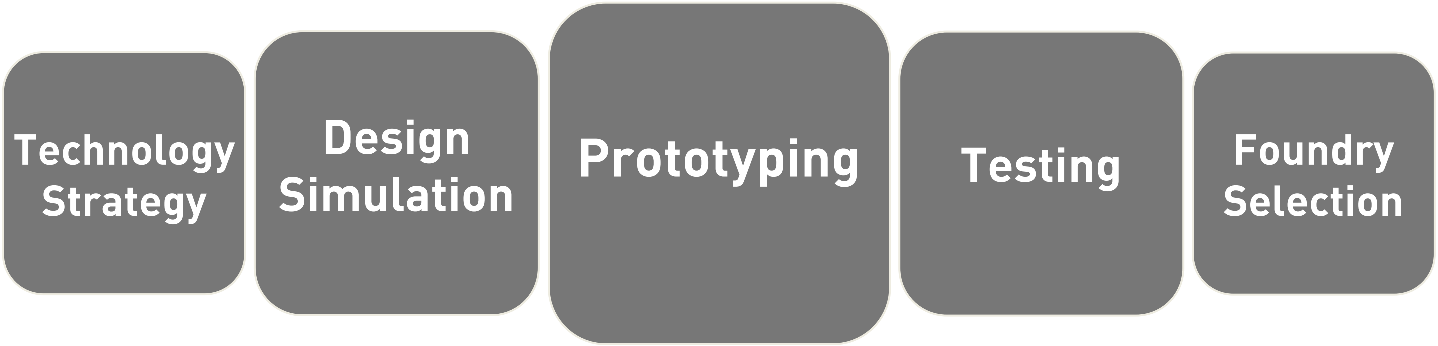
Outline

- About AMFitzgerald
- What are MEMS?
- Research applications
- Diagnostic applications
- Medical devices
- Packaging challenges
- MEMS development timeline and budget

Mission

We turn your ideas into silicon.

Fully integrated services: concept to foundry



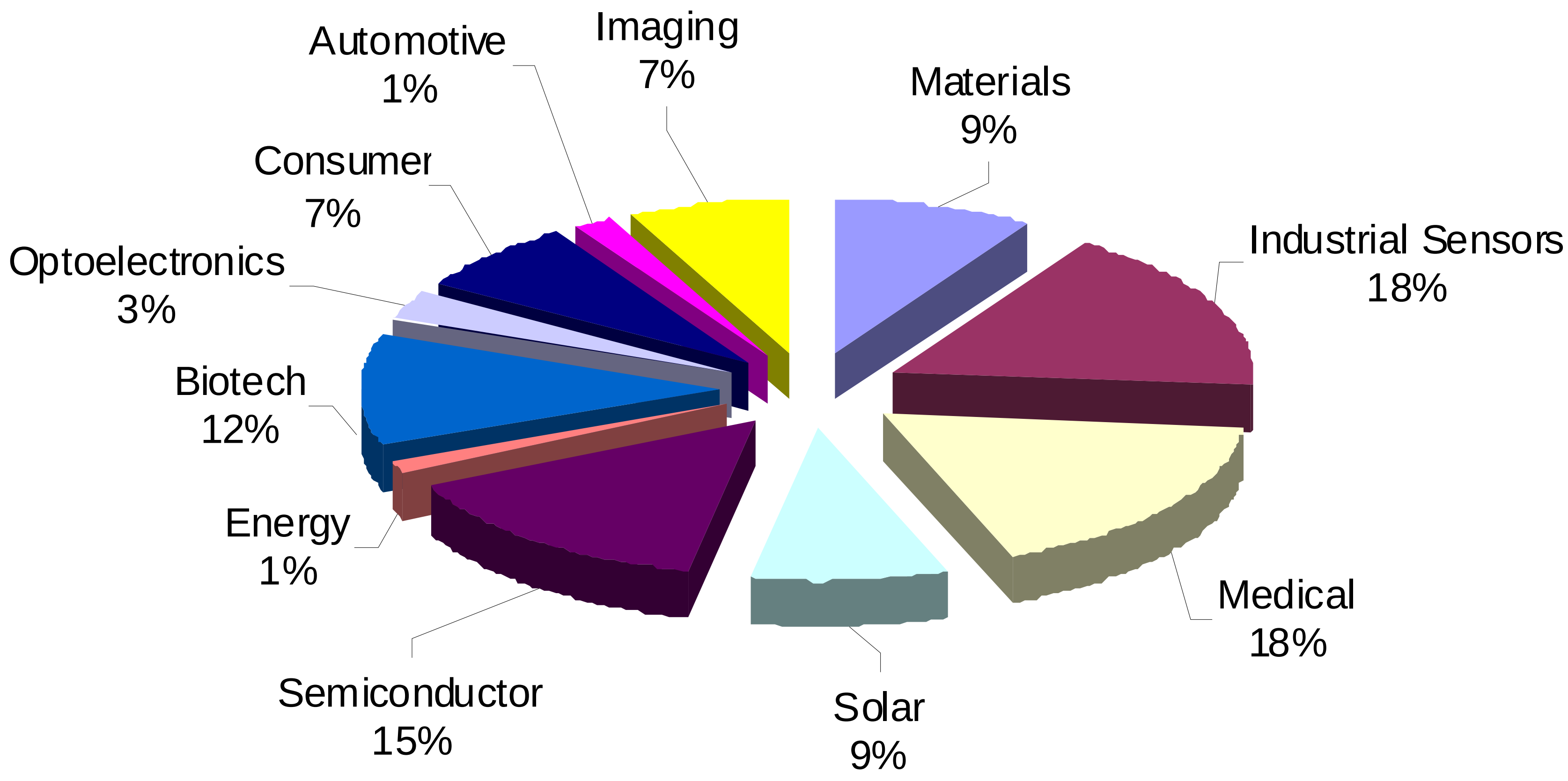
- Complete design and project management
- Feasibility and cost analysis
- Design optimization using simulation
- Process development on 100 mm or 150 mm wafers
  - Prototype fabrication with own staff engineers at UC Berkeley’s Microlab
- Test system development
- Packaging, system integration
- Technology transfer to foundries for production

Primary value to clients

- Risk reduction during all phases of technology development
  - Idea evaluation without major funding or staffing commitment
  - Fast prototyping cycles enable accelerated development
  - Critical system design and manufacturability issues addressed early
  - Streamlined transition from R&D to foundry production

- On-demand, expert engineering team
  - Use as needed to bridge gaps
  - Real-world MEMS knowledge: all staff have at least three years of hands-on fab experience

Our diverse customer base



MEMS design and process expertise

Technologies we have developed:

- Piezoresistive devices
- Piezoelectric
  (AlN and ZnO) devices
- Electrostatic structures
- Solar cells
- Passive microfluidics
- Electrophoretic pumps
- Mold masters
- Gratings, phase shift lenses etc.
- PDMS, SU-8 structures
- Mechanical dummies for package reliability testing
- Custom test systems

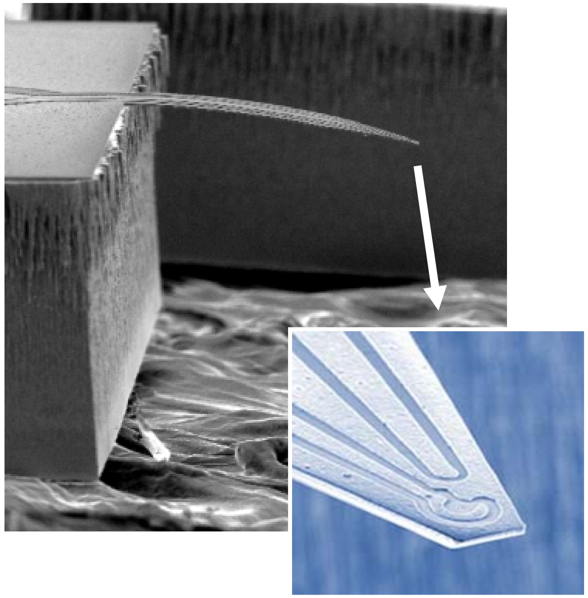
Over 70 clients served

Application areas:

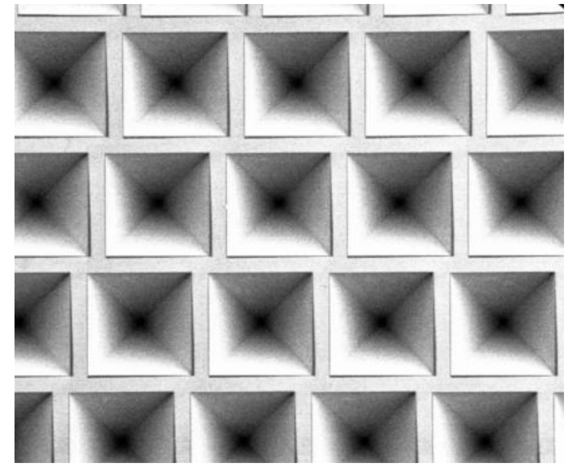
- Chemical sensing
- Materials characterization
- Medical implant
- Medical diagnostics
- Pressure sensing
- Filtration products
- Laser/ Infrared/ Visible optics
- Chip cooling
- Cell culture
- Radiation sensing
- Microphones
- Gas flow metering
- Multi-chip modules
- Solar

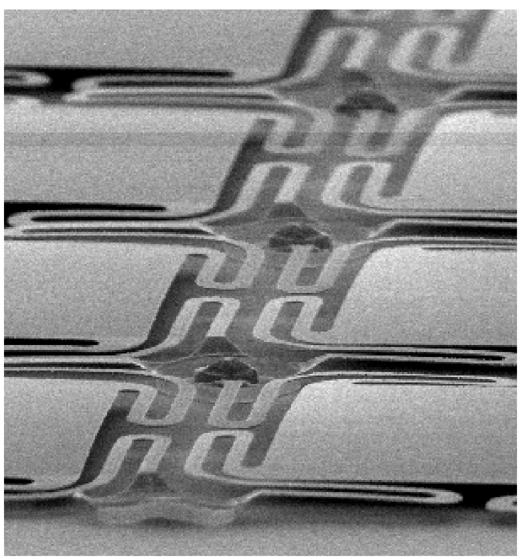
Product development gallery: some examples

Customized micro-cantilevers

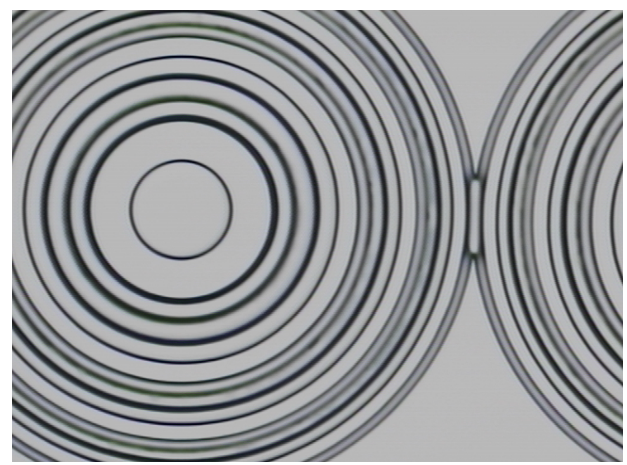


Pyramidal crystal planes left by KOH etch





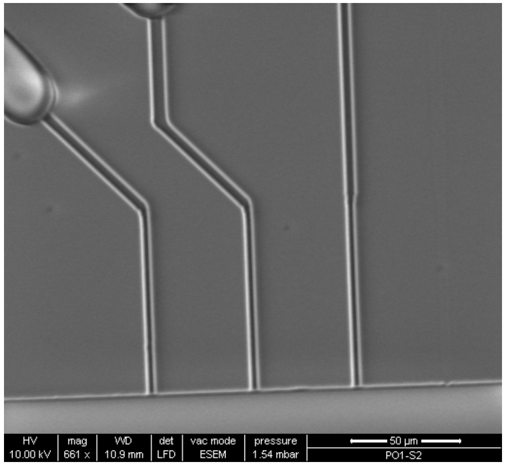
Infrared imaging pixels: MEMS over CMOS

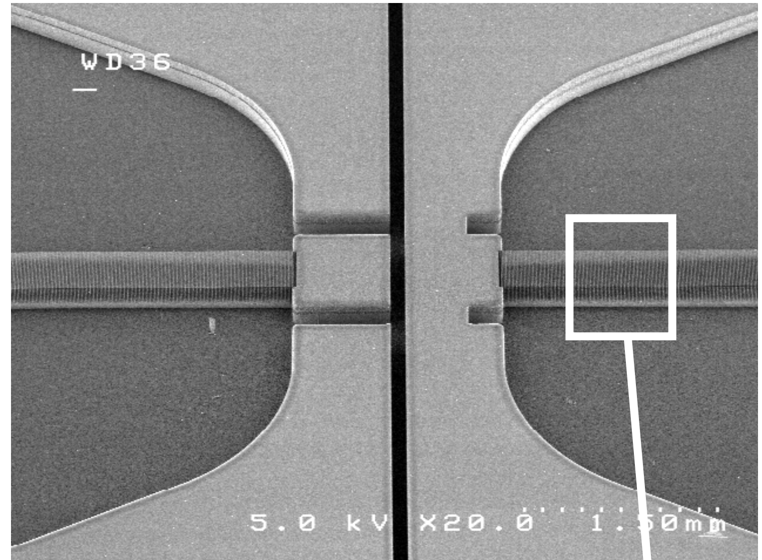


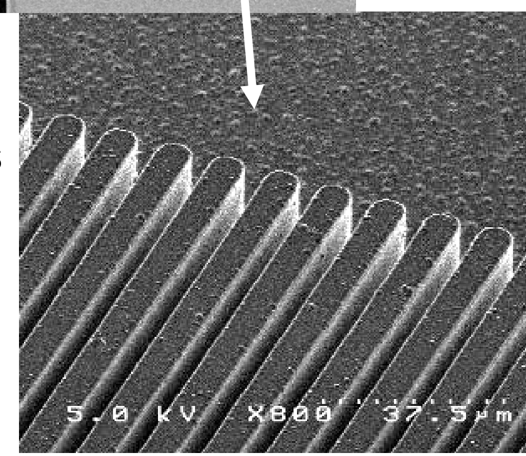
Silicon acoustic lenses

Product development gallery: some examples

Fluxion Biosciences: Micro-channels for cell patch clamping

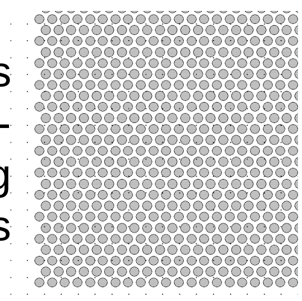






Wave80 Biosciences: Microfluidic chip for rapid HIV analysis

Mold masters for micro-texturing polymers



MIT/Bhatia Lab: cell culture platforms

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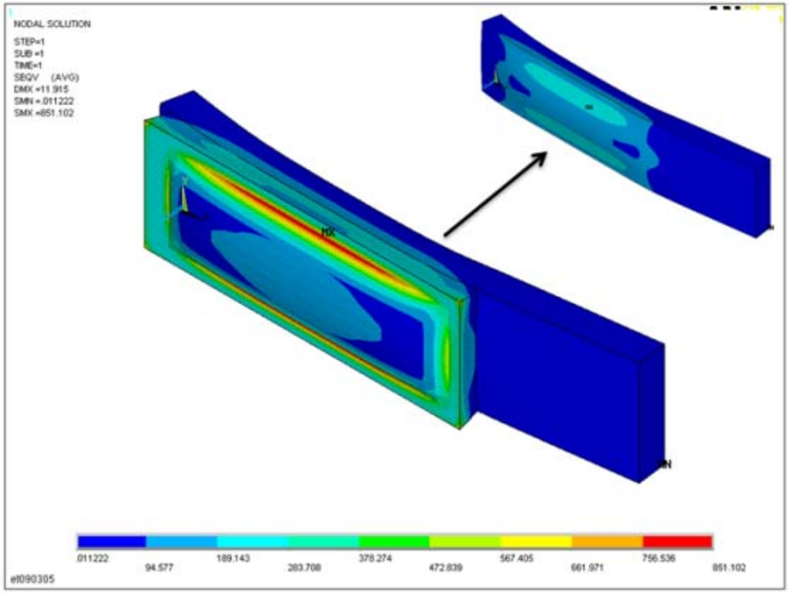
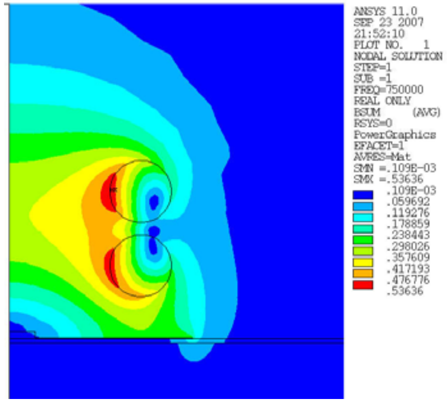
Modeling and design optimization

- ANSYS Multiphysics R12
- Matlab
- Proprietary fracture prediction

- Intelligent use of simulation to minimize risk and reduce fab cycles
  - Management of uncertainty in MEMS material properties
- Design exploration and performance optimization



Package-induced stresses

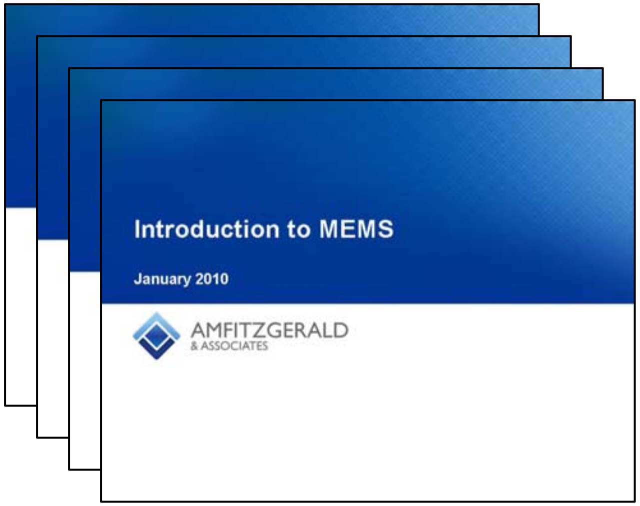


Magnetic field of inductor coils

Technology strategy

- Device feasibility
- Manufacturing cost models
- Technology readiness
- Patent landscapes
- Development roadmaps
- Due diligence

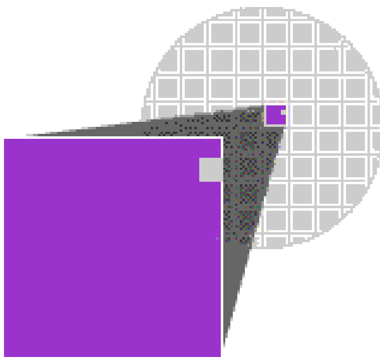
Customized workshops on MEMS



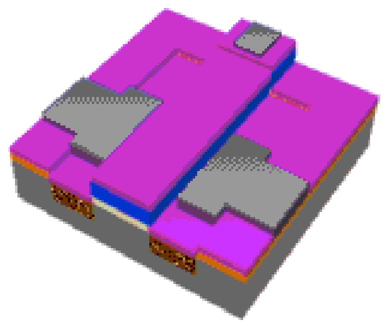
What are MEMS?
MicroElectroMechanical Systems

MEMS are an offspring of the IC Industry

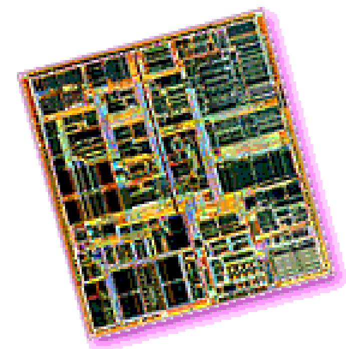
- **Uses techniques originally developed to make transistors and integrated circuits**



Silicon wafer



Material deposition
Lithographic patterning
Material etch back
Repeat for multiple layers

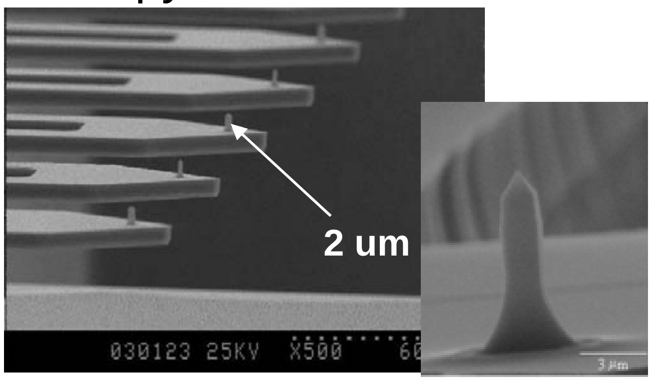


Pentium chip

Images from: http://www.intel.com/education/chips/index.htm

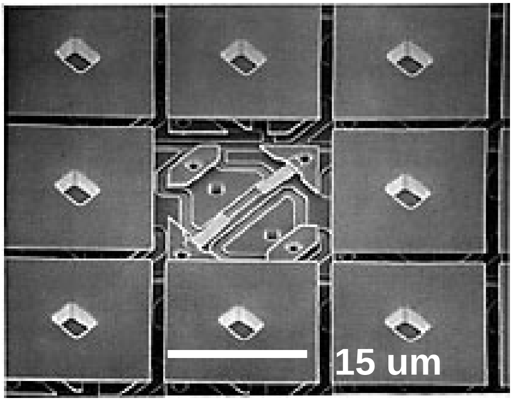
Many Shapes and Functionalities are Possible

Cantilevers for atomic force microscopy



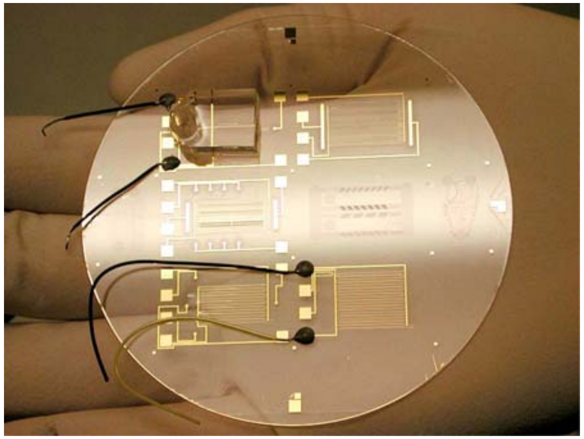
E. Chow, Stanford Univ.

TI Digital Display Chip



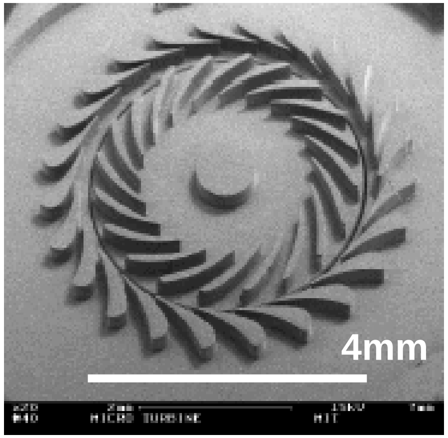
the diameter of a human hair ~ 100 μm

Microfluidics on glass



U. of Washington

MIT Microengine



the length of an ant ~ 3 mm

An evolving manufacturing technology

Courtesy HTE Lab
Santa Clara, CA

Stanford Nanofabrication Facility

MEMS belong where miniaturization is needed

- **Applications in many industries:**
  - **Silicon sensors (traditional): pressure, inertial**
  - **RF: components, switches, inductors**
  - **Optical: components, displays, switches**
  - **Medical devices: needles, cell scaffolds, ultrasound**
  - **Microfluidics: lab-on-chip, drug delivery**
  - **Instruments: AFM, data storage**
- **More applications to be explored**

Why MEMS are exciting for medical applications

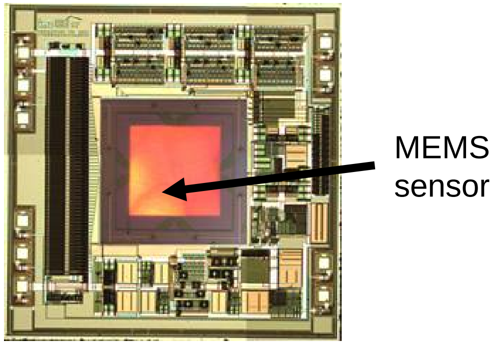
- **Compatible size scales, especially with cells**
  - **2-100 micron-sized features are easy to make**

- **Many materials used in MEMS are biocompatible:**
  - **Silicon (under study)**
  - **Silicon dioxide (glass, fused silica, quartz)**
  - **Precious metals: Gold, titanium**
  - **Polymers: Polydimethylsiloxane (PDMS), Parylene, etc.**

Why MEMS are exciting for medical applications

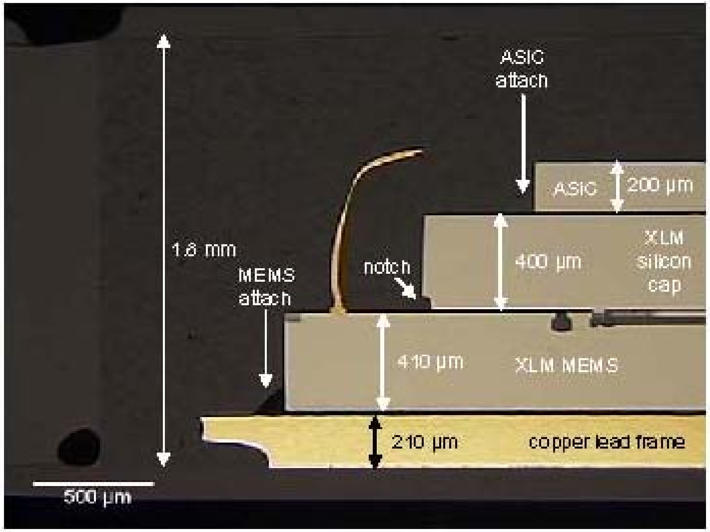
- **Ease of electronics integration enables sophisticated capabilities in small form factor:**
  - **Signal processing and analysis**
  - **Wireless capability**
    - **Battery-less operation (power/read)**
    - **Telemetry for medical sensor network (with cell phone)**

Integrated Pressure Sensor



Source: IMD

Stacked MEMS and ASIC chips, wirebonded



Source: Chipworks/Kionix

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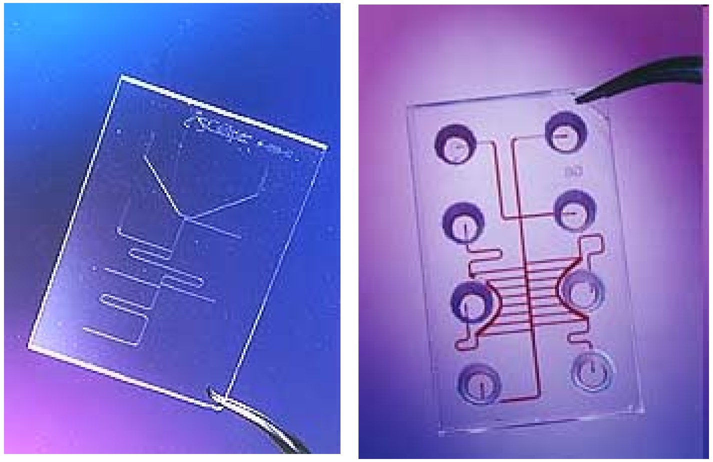
Research Applications

Microfluidics

- **Laboratory tools: genomics, proteomics, drug discovery**
- **Microfluidics enable:**
  - **Reduction of fluid sample size**
  - **Arrayed test sites – up to thousands of tests per chip**

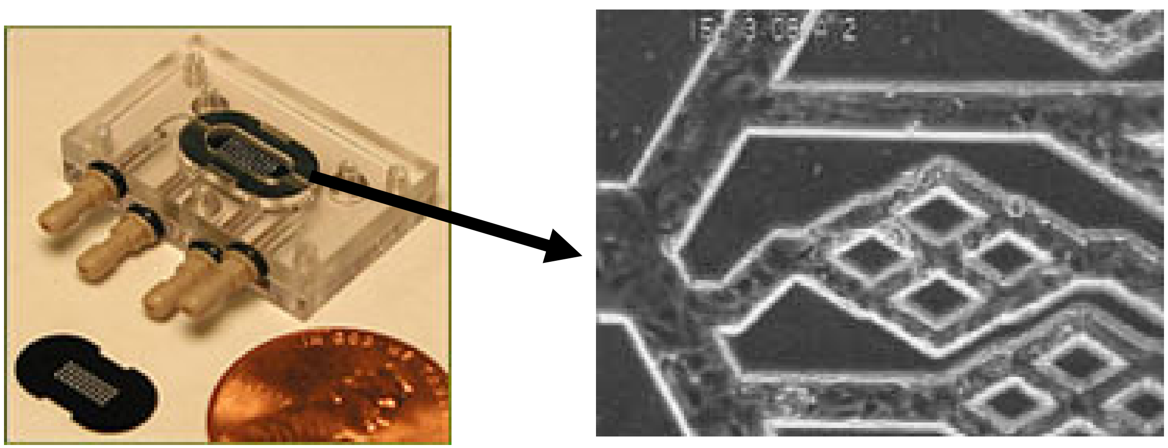
Affymetrix

Caliper LifeSciences



Cell Manipulation

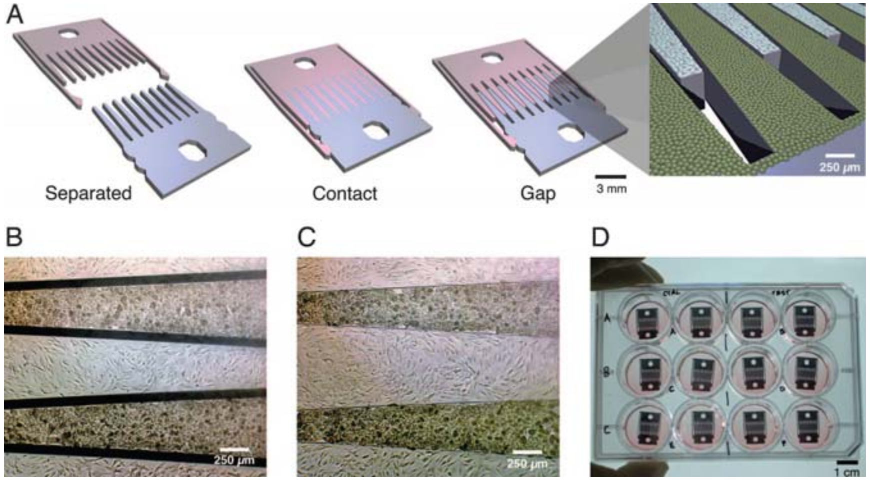
- **Flow cytometers and cell sorters**
- **Patch clamps for cell electrophysiology**
- **Cell scaffolds for artificial organs and tissue engineering**
  - **Liver, kidney**
  - **Working on biodegradable scaffolds**



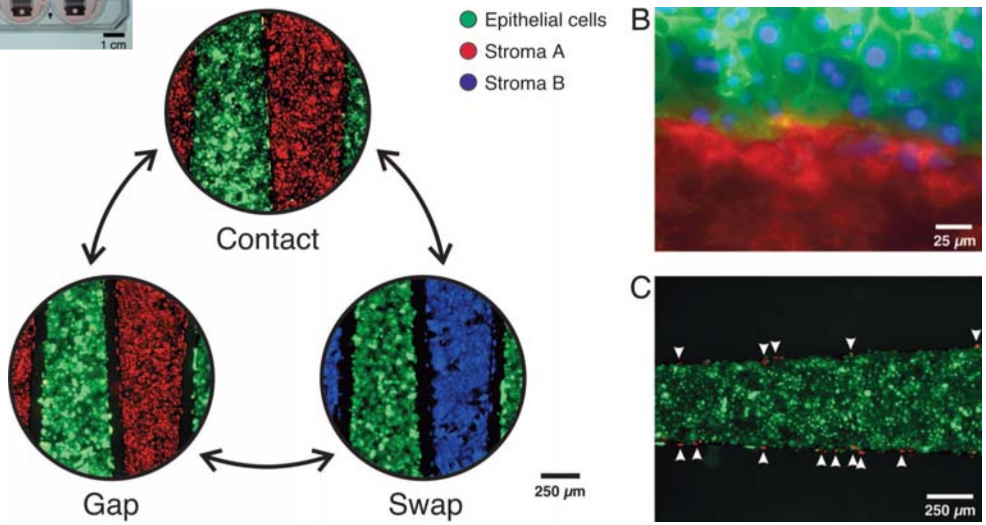
Dr. Joseph Vacanti, Harvard Medical School

Jeffrey Borenstein, Draper Laboratory

Hepatocyte and Stromal Cell Interactions



Hui and Bhatia (MIT), “Micromechanical control of cell-cell interactions,” PNAS vol. 104 (14), 2007.

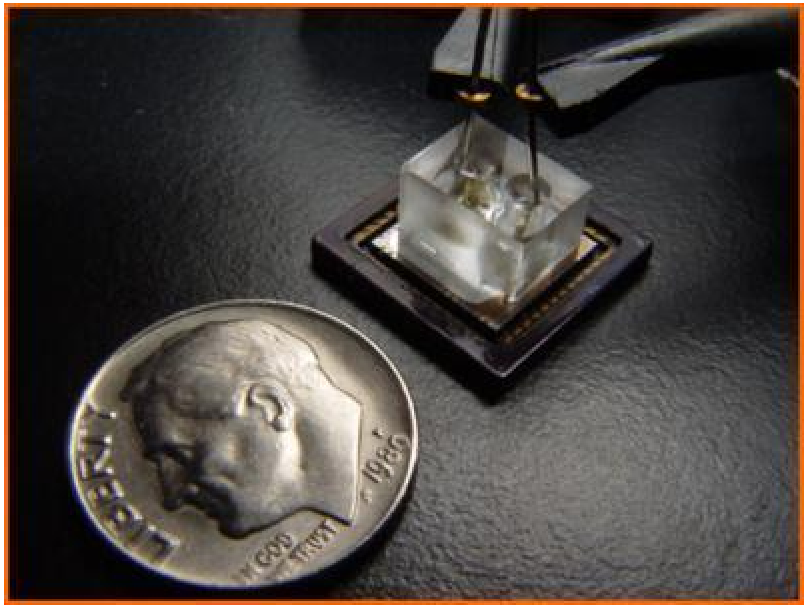


Diagnostic Applications

Microscope on a Chip

- **Sample contained in a microfluidic chip**
- **Lensless shadow imaging with pattern recognition algorithm**
- **Optofluidic microscope for imaging cell samples**
- **Pinhole apertures combined with CCD array**

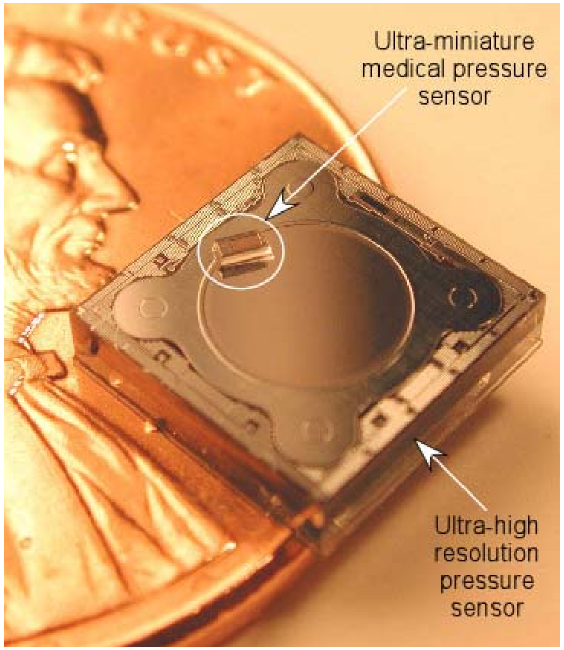
Source: Aydogan Ozcan, UCLA



Source: Changhuei Yang, California Institute of Technology

MEMS Pressure Sensors

- **Used in non-invasive medical equipment since 1980's**
  - **Respiratory equipment**
  - **Blood pressure cuffs**
- **Invasive uses increasing**
  - **Catheter tip sensors**
- **Many manufacturers:**
  - **GE Sensors**
  - **Measurement Specialties**
  - **Silicon Microstructures**
  - **ISSYS**
  - **RADI**

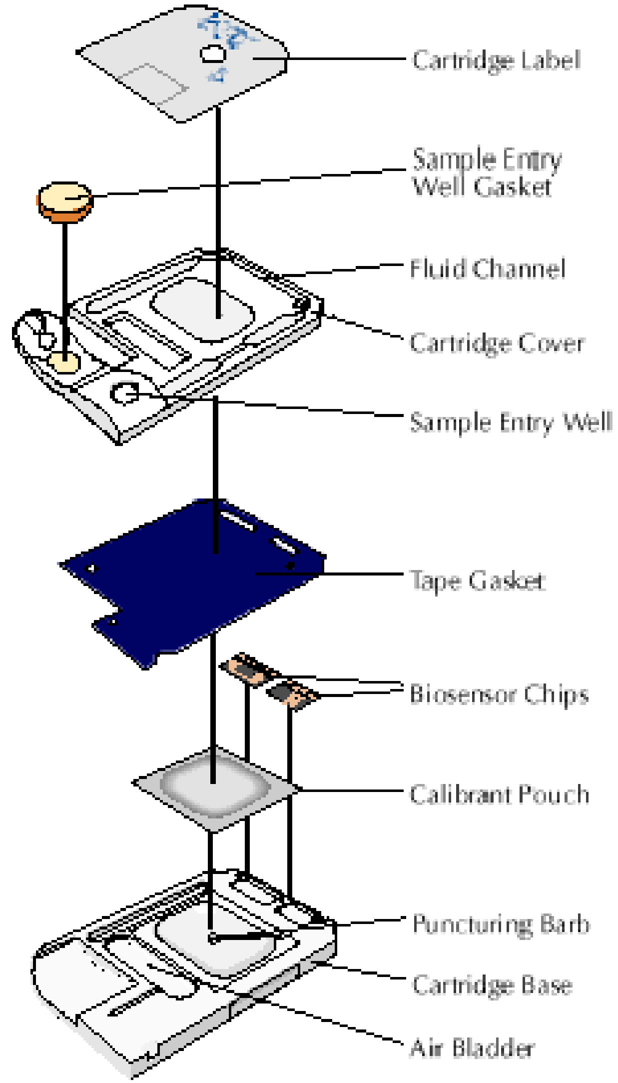


Source: ISSYS


Source: GE

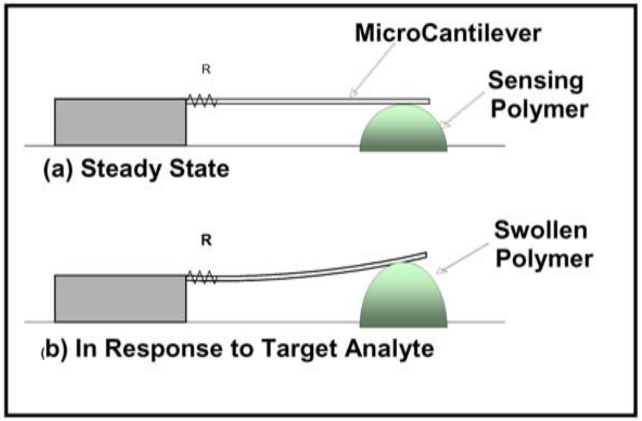
i-STAT/Abbott sensor arrays

- **Sample interacts with membranes and films containing reagents.**
- **Biosensor chip measures reaction output via:**
  - **Ion-selective electrode potentiometry: Na, K, Cl, Ca, pH**
  - **Current measurements: Glucose, oxygen**
  - **Conductivity: Hematocrit**

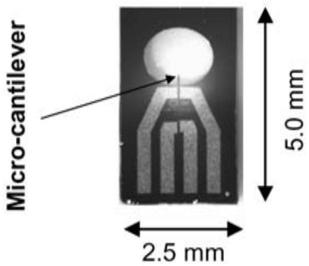


Source: i-STAT/Abbott

Cantimer Dehydration Sensor

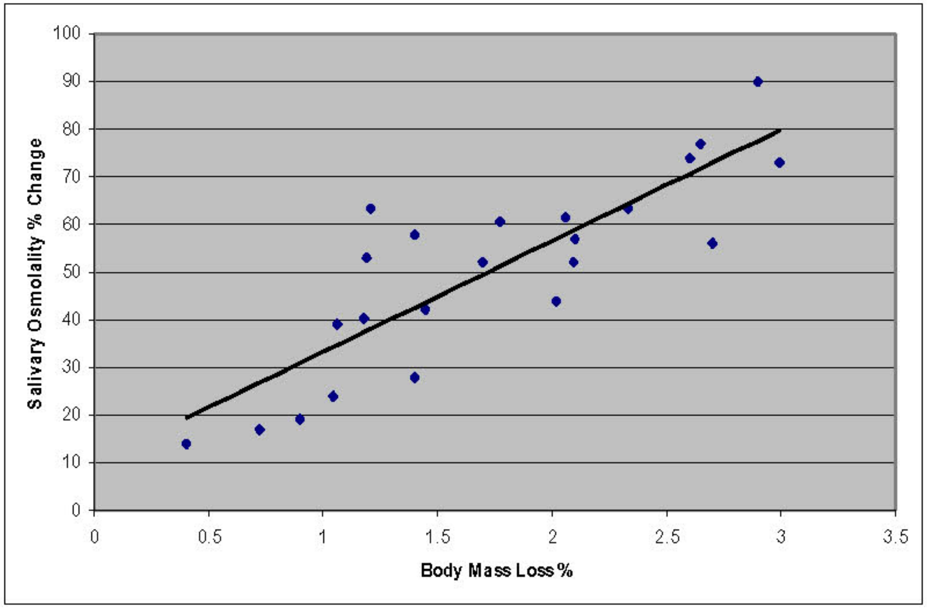


Principle of Operation
(Side View)



Fabricated Sensor
(Viewed From Above)

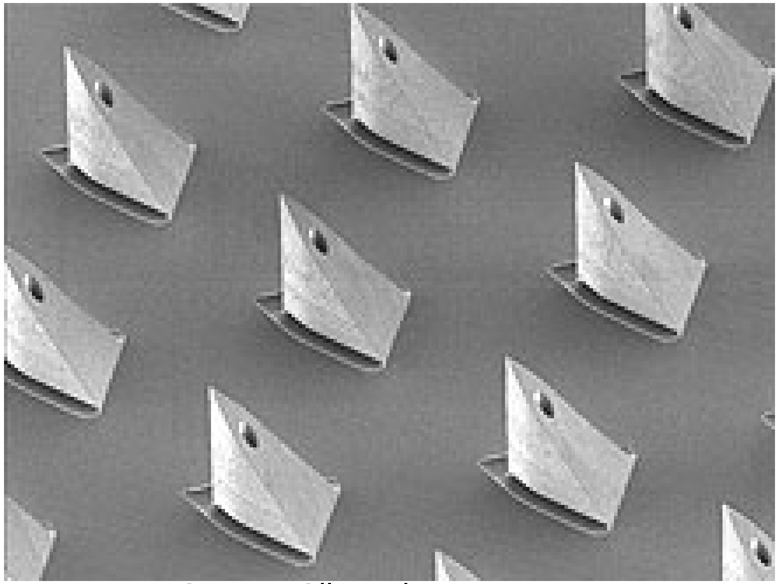
Disposable sensor and reader for home or lab use



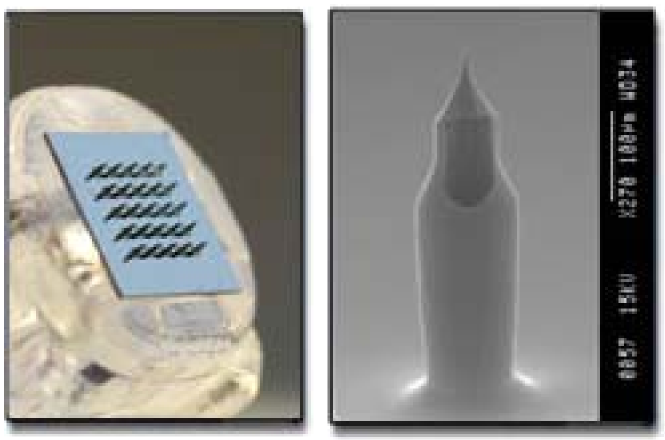
Source: Cantimer, Menlo Park, CA

Microneedles

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



Source: Silex Microsystems



Source: Debiotech SA

Medical Devices

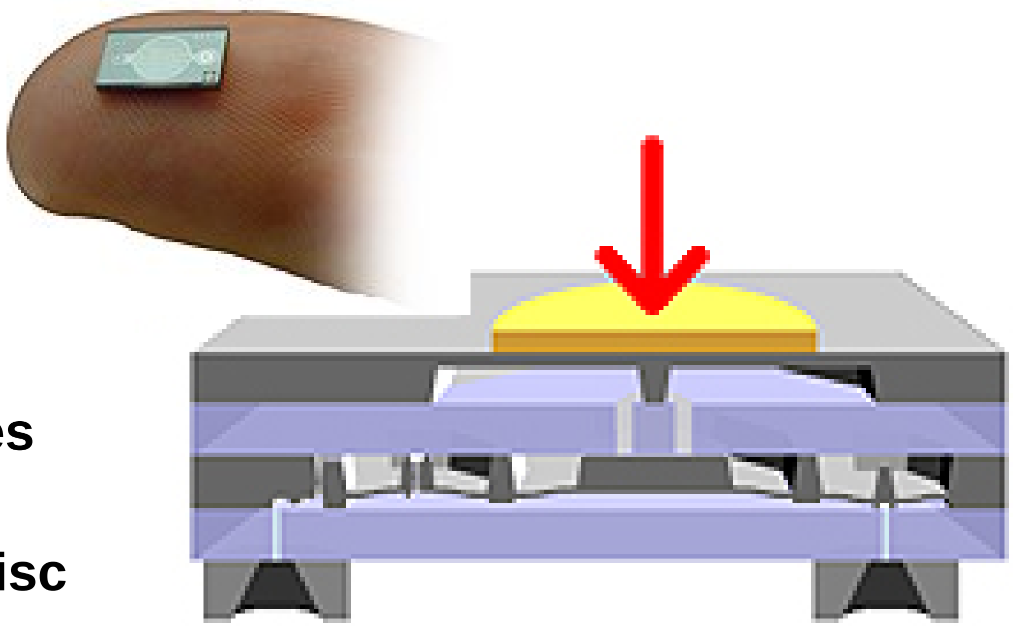
CardioMEMS: Aneurysm Pressure Sensor

- Aorta stent graft monitoring, FDA-approved
- Pressure on the membrane of a micro-cavity result in changes to the sensor's resonant frequency.
- Powered by RF-energy provided by an external antenna
- Encapsulated in fused silica and silicone, and surrounded by a PTFE-coated nickel-titanium wire.
- www.cardiomems.com

Source: CardioMEMS

Debiotech: Insulin Micropumps

- Volumetric pump for drug delivery (insulin)
- The device is a stack of four layers bonded together:
  - Silicon plates with micromachined pump structures (gray)
  - Glass with through-holes (blue)
  - Piezoelectric actuator disc (yellow)
  - Two titanium fluid connectors (gray)
- www.debiotech.com



Source: Debiotech SA

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

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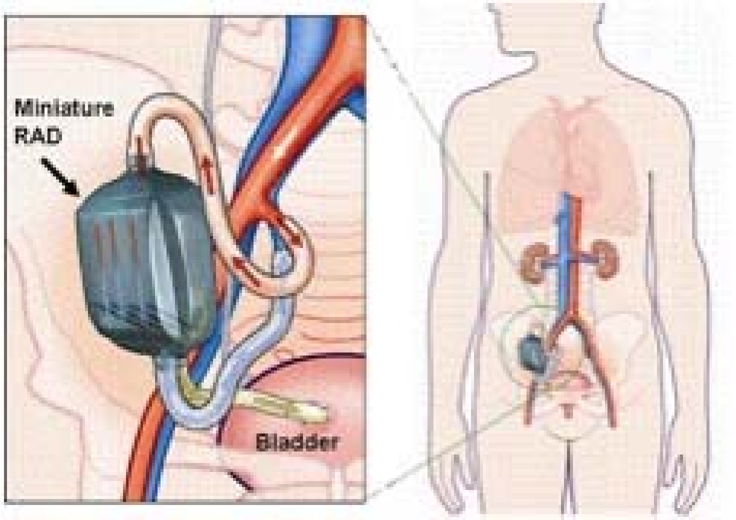
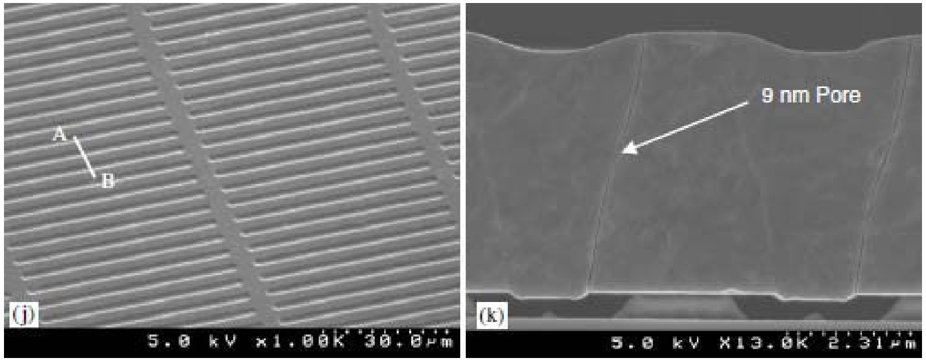
Artificial Kidney

- 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





Source: Shuvo Roy, UCSF

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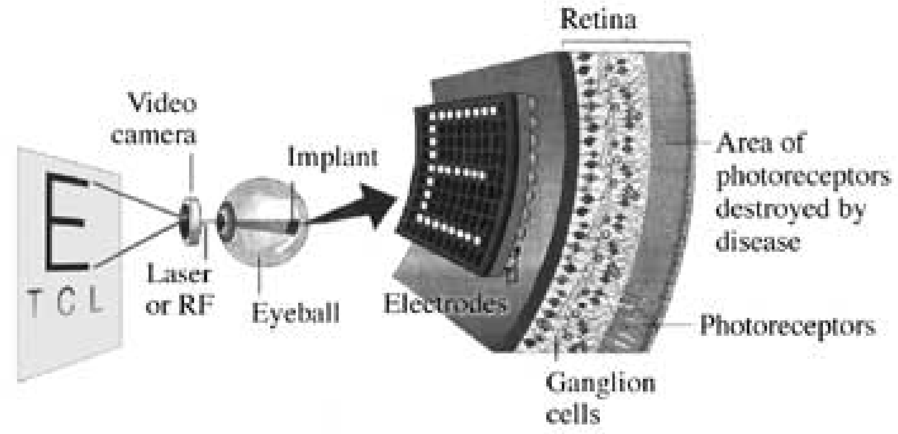
Second Sight: Retinal Prosthesis

- **First phase of development of a retinal prosthesis, with FDA approval to conduct two clinical trials**



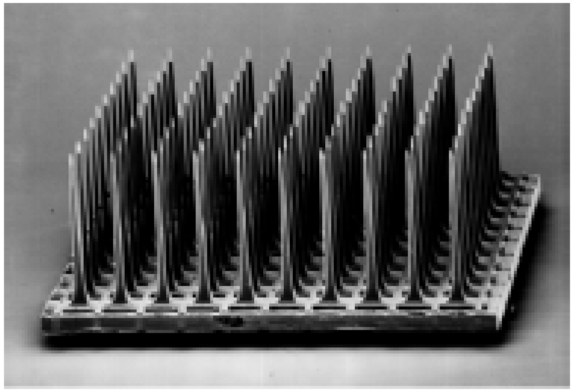
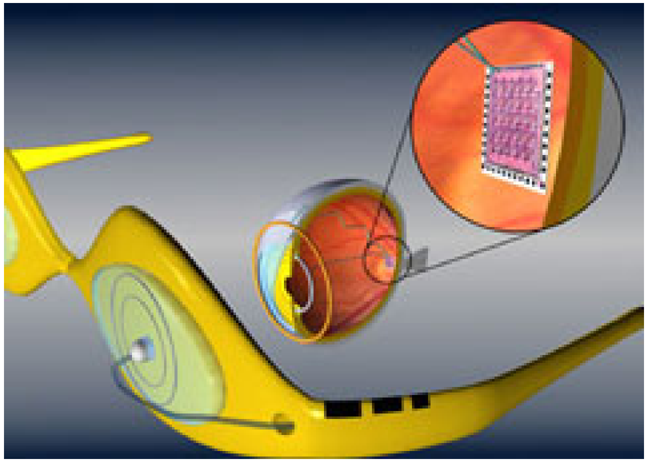


Fig. 1. Visual cortex electrode array courtesy of Dick Normann at the University of Utah.



Source: Second Sight

Neural Prosthesis

- **Neural microsystems for neuroscience research**
- **Systems for control of Parkinson's tremors and epilepsy**
- **Electronics select probe, detect, signal processing, and wireless telemetry**

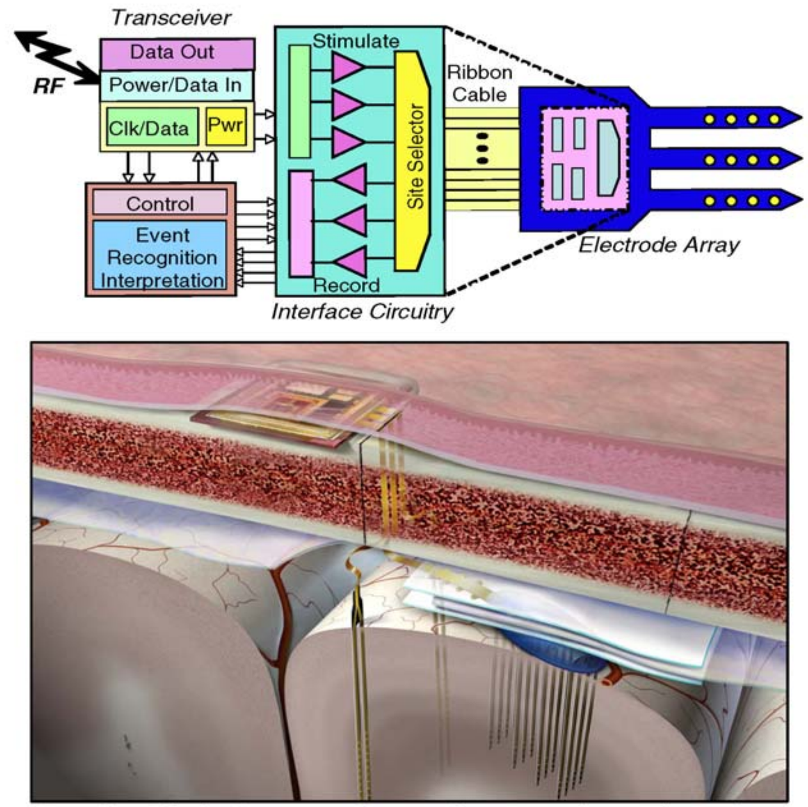


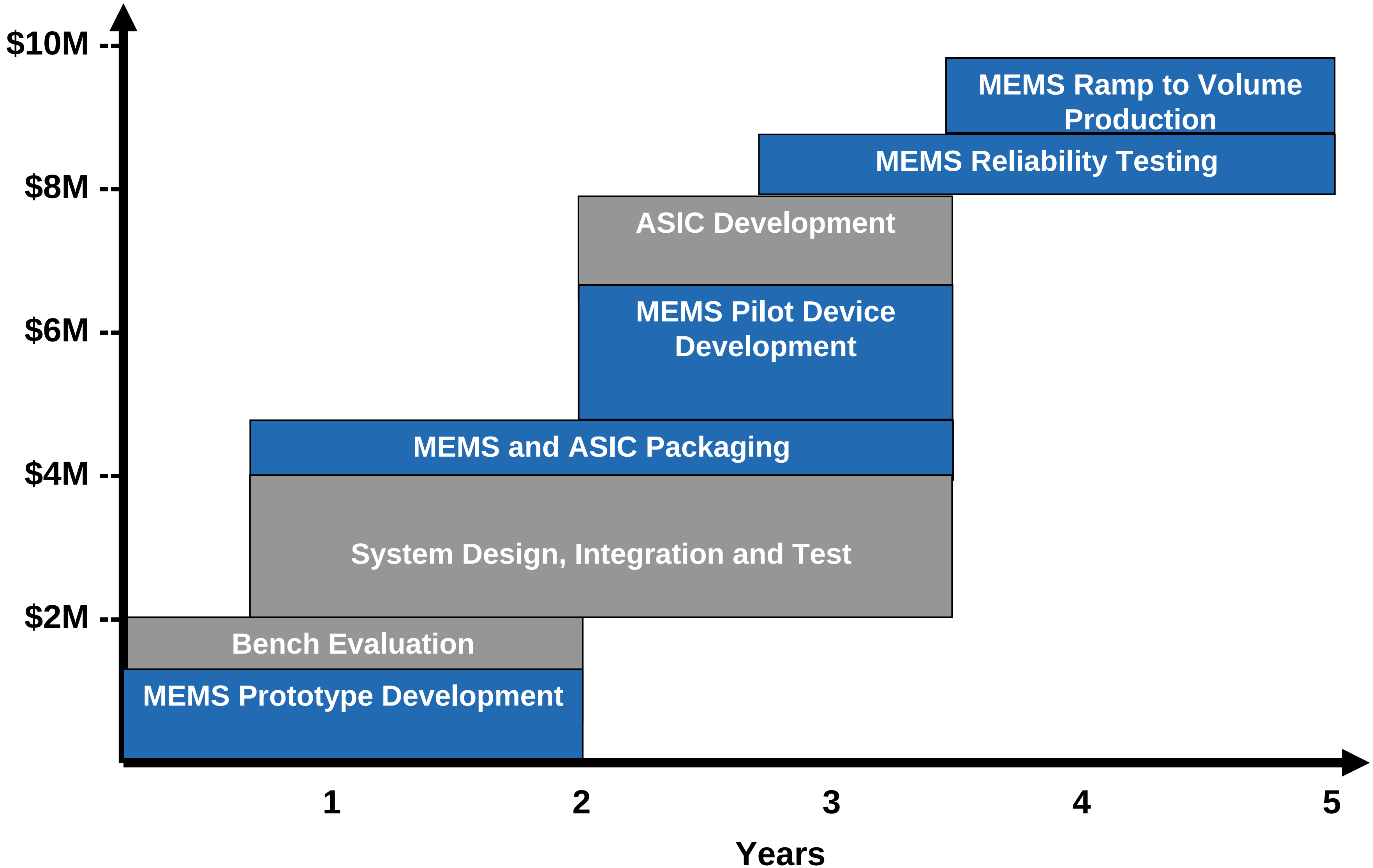
Fig. 9: Block diagram of a wireless neural interface along with a possible implant configuration in which the signal-processing module is positioned subcutaneously.

Source: K. Wise, "Wireless Integrated Microsystems: Wearable and Implantable Devices for Improved Health Care," Transducers 2009.

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)

New MEMS Device (Fabless) Development: Cost and Timeline Minimums



Summary

- **MEMS is a growing suite of manufacturing tools and techniques**
  - **Newest frontier: flexible (and biodegradable) materials**
- **Huge opportunity in medical and biotech applications**
  - **Compatible materials and sizes**
  - **Electronics integration**
- **Challenges remain in packaging**
  - **Hermeticity**
  - **Sterilization**

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