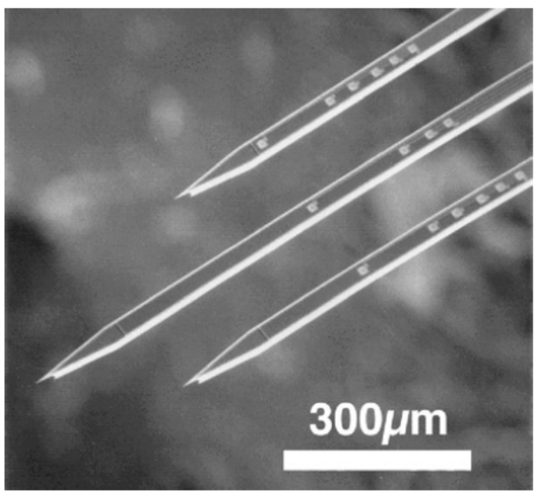
Biomedical applications of MEMS devices



Edmond Cretu

edmondc@ece.ubc.ca

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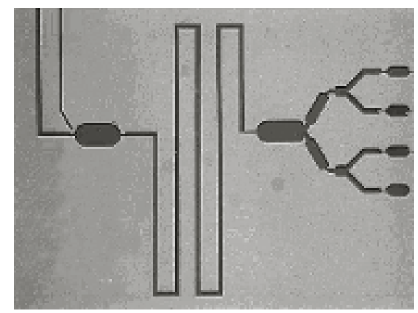
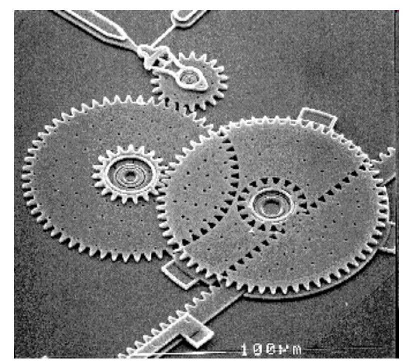
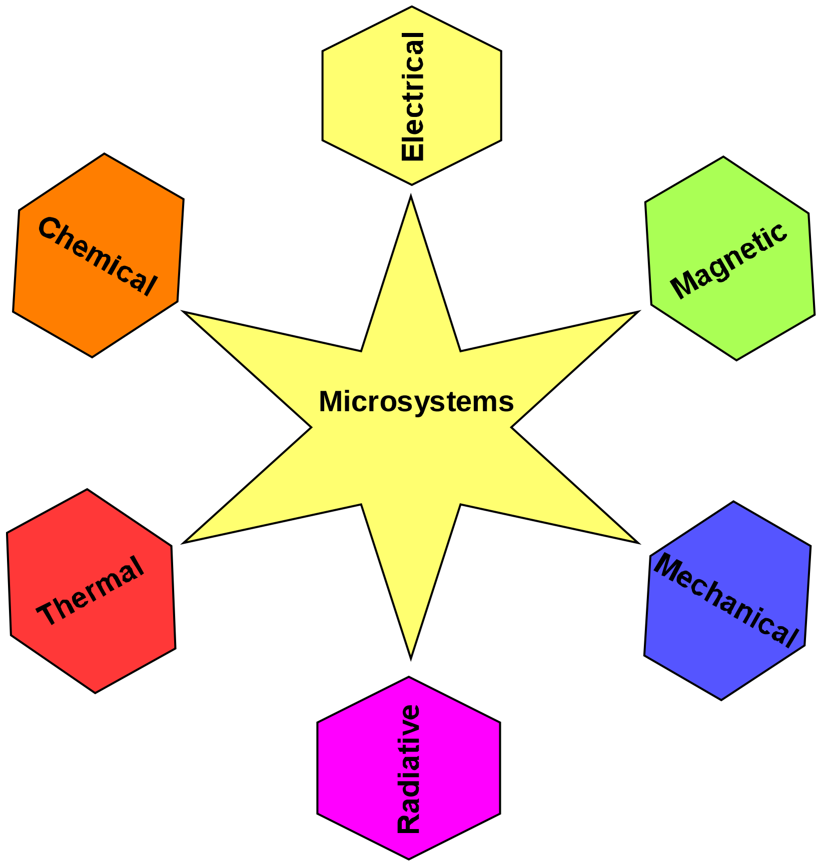




“Nothing is small, nothing is great. Inside us are worlds. What is small divides itself into what is great, the great into small.”

Edvard Munch (Norwegian artist)



What is a microsystem?

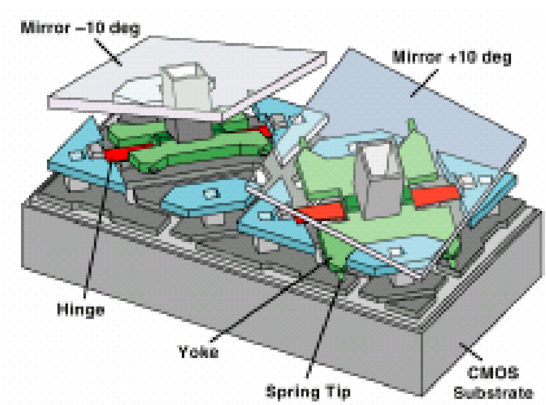
- MEMS=
  - **M**icro-**e**lectro**m**echanical **s**ystems (USA)
  - Microsystem Technology (MST) (Europe)
  - Micromechatronics (Japan)

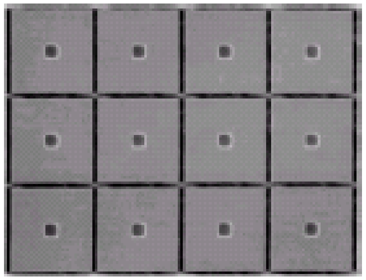
macro-engineering at microscale

Two main features:

1. Design structures/devices/systems at micro/nano scale
2. Typical microsystems involve multiple physical domains

Example: Texas Instruments – DLP (Digital Light Processor)





Top View of DMD

- Light-modulating chip
- >100000 individually addressable micromirrors ($10x10um^2$)
- Binary tilting: $\pm 7.5^0$
- 0.8um CMOS SRAM on the substrate, beneath the layer of mirrors

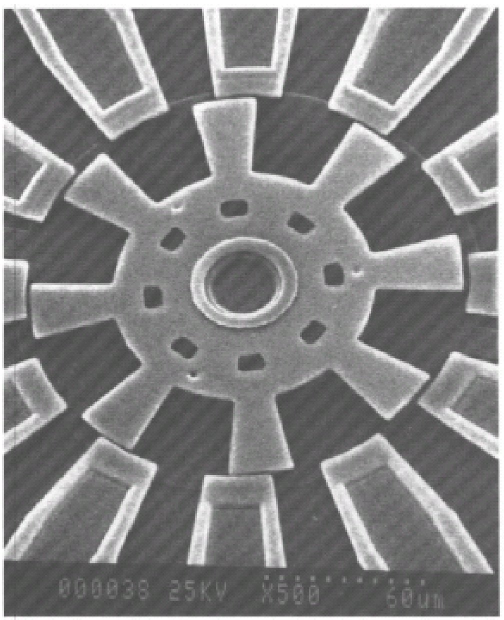
Scaling modifies the design process

- Water strider =>The bug can walk on water!

$$F_{surface\,tension} \sim (surface\,tension) \cdot perimeter \sim S^1 \cdot S^1 = S^2$$

$$\frac{F_{surface\,tension}}{F_{gravity}} \sim \frac{S^2}{S^3} = S^{-1}$$

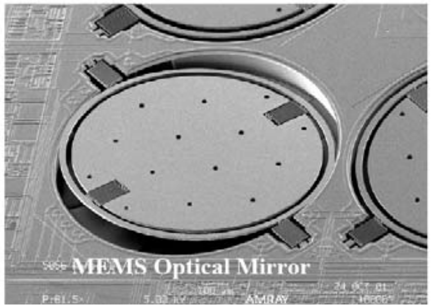
Exm 2: motors at microscale



Glucose-fueled umotor

Magnetic- actuated motor

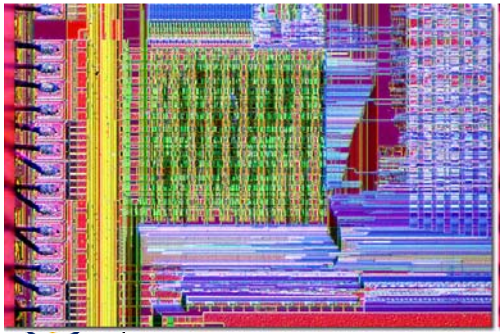
MEMS vs. IC



- Microelectronics
  - Few elementary structures
  - Complex system topologies and topographies
  - Huge number of interconnections
  - Electrical signal dominant

Microsystems

- MEMS
  - Growing no. of elementary structures
  - Generally simple topologies
  - Few complex components
  - Different energy domains, with no dominance



MEMS/Microsystems for biomedical applications

- Potential to revolutionize the medicine, from drug delivery methods to minimally invasive surgery, "Lab on a chip" or smart prosthesis
- Specific **advantages** of using microsystems in the medical field:

-Biocompatibility (Si is biocompatible)

-Greater reproducibility+reliability

-Miniaturized implants

-Ability to respond to short time scales

-Ability to provide electrical stimulus (neural interfaces)

-Chemical functionalization (tissue engineering)

-Low power, small size (non-invasive)

-Low cost (disposable drug delivery)

-Integrate sensor, actuators and electronics (precise adaptive control loops)

-Ability to interact with fluids (microfluidics TAS, biochemical sensors)

-Etc.

Market and challenges

- Medical applications of MST are growing at double-digit growth rates – **global market volume in 2007 > $2 billion** => relevant segment of the medical technology
- Specific challenges for the medical industry:
  - Technical barriers: packaging for bio-compatibility, fluidics
  - Stringent regulatory control (US food and Drug Administration approval process)
  - Inertia of the medical industry – skepticism of users (doctors, patients)
  - Testing, calibration and packaging difficulties
  - High entry and facilities development cost => difficult for small companies
  - Interdisciplinary work – engineers need to understand the health care needs and the health care environment

Categories of devices

- A large variety – difficult to classify
- Patient viewpoint:
  - **diagnostic microsystems**: rapid point-of-care, systems on a chip, cell and molecule sorting, DNA diagnostics
  - **surgical microsystems**: MIS (minimally invasive surgery), CAD-assisted surgery - microrobotics
  - **therapeutic microsystems + prostheses**: drug and gene delivery, tissue augmentation/repair, biocapsules, micro/minimally invasive surgical systems
- The scale of the application: body level (drug delivery, tools for microsurgery, pacemakers, neural probes), analysis of body fluids ("Lab-on-a-chip" for blood analysis, glucose monitoring, electrophoresis), tissue and cell analysis, genomics (DNA microarrays) and proteomics (protein identification and characterization)
- Biggest promise: better outcome for the patient and a lower overall health and cost

Interaction with the human body

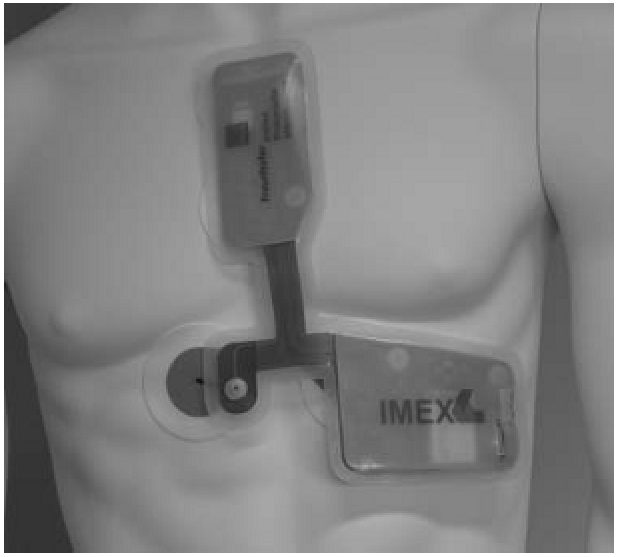
- Classification according to MEMS relationship with the anatomy (the kind and duration of interaction with the human body):

Classes of MST applications	Relationship to human body	Current examples	Future application examples
Class 1 – extra-corporeal	Used outside of the human body	• Telemetric blood pressure measurement devices • Wearable telemetric ECG foils • Point of care blood testing systems	• Wearable integrated physical activity and cardiovascular parameter monitoring
Class 2 – intra-corporeal	Used inside the human body, e.g. surgical instruments or interventional catheters	• Sensor-controlled ablation probes • Cardiovascular sensor-controlled monitoring catheters	• Tactile laparoscopic instruments for palpation • Smart scalpels
Class 3 – temporarily incorporated	Temporary incorporation, e.g. ingestion or injection or active placement with ancillary devices	• Capsule endoscopes • ph sensors temporarily fixed in the esophagus	• Endoscopic microrobots and smart capsules
Class 4 – implantable	Long-term implants	• Cardiac rhythm management devices with telemetric signal transfer • Intra-ocular lenses with pressure sensors (glaucoma monitoring) • Endovascular stent grafts for aneurysm repair with pressure sensors (leakage monitoring) • Cochlear implants • Brainstem implants	• Smart orthopedic joint implants with sensors for functional monitoring • Retina implants • Implantable glucose sensors

Extra-corporeal devices

- Probably the best established field for MST applications
- Exm: handheld diagnostic devices, smart textiles, wearable monitoring systems, blood pressure monitoring, portable drug delivery, etc.
- Relevant microtransducers: pressure sensor, acceleration sensors, angular rate sensors

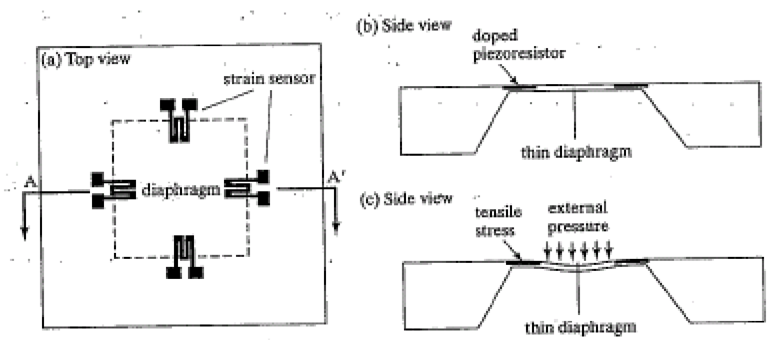
Telemetric pacemaker for remote patient monitoring (Biotronik, Germany).

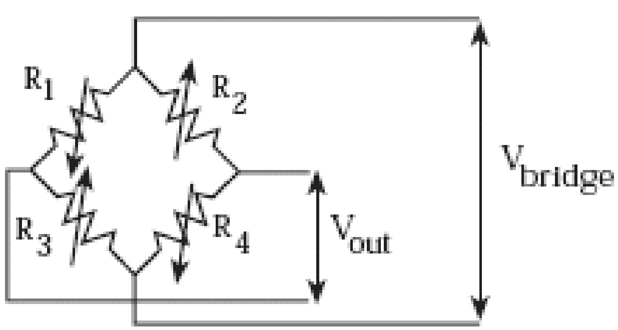


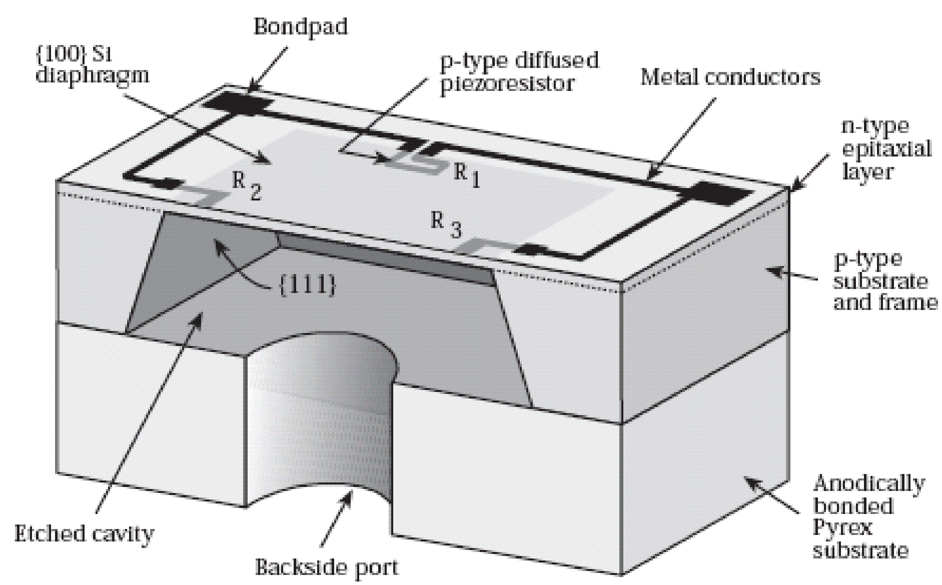
3-channel ECG system (Fraunhofer, Germany).

Pressure sensors

- Most of the pressure sensors detect the stress in a thin Si diaphragm in response to a pressure load - using the piezoresistive effect
- Alternative detection mechanism: capacitance change between the deformable membrane and the substrate
- Applications: blood pressure control, monitoring intra-ocular pressure in surgical interventions, etc.

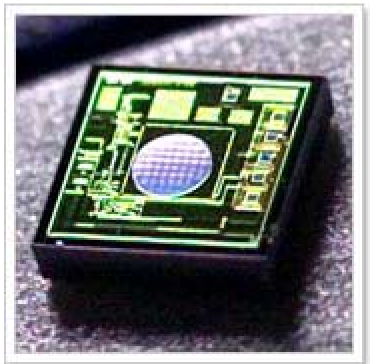




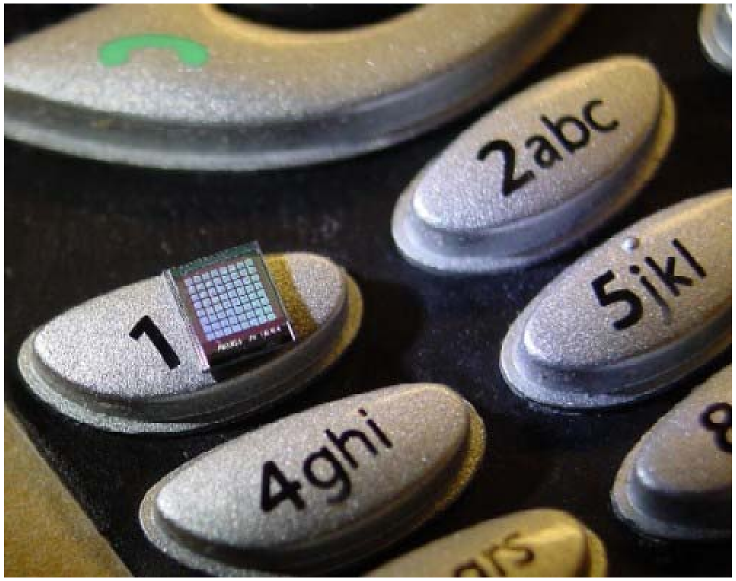


Exm: hearing aids

- MEMS array of microphones, integrated with electronics => acoustic array processing for better directivity and sensitivity
- The power of integration: acoustic system-on-chip

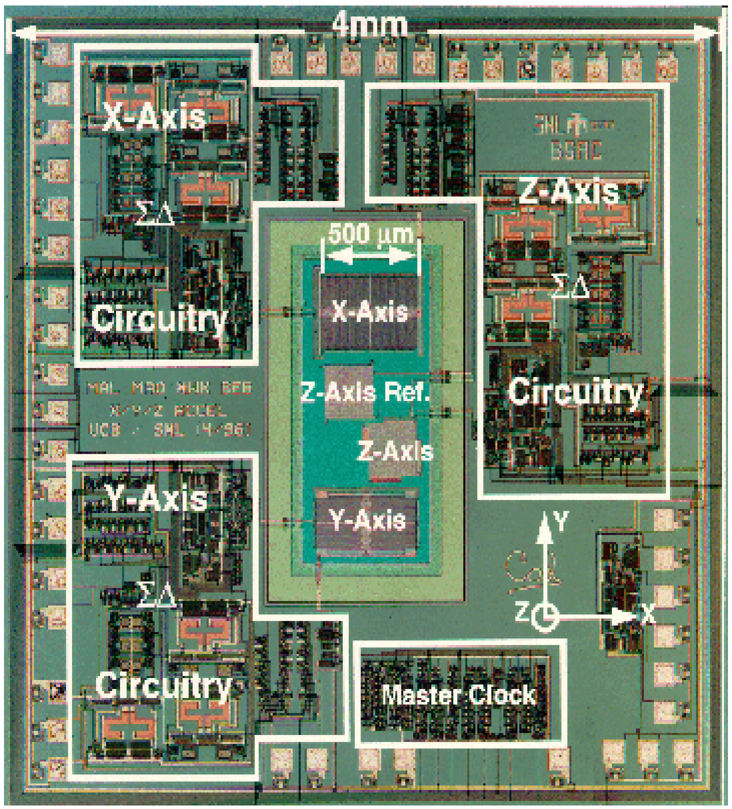


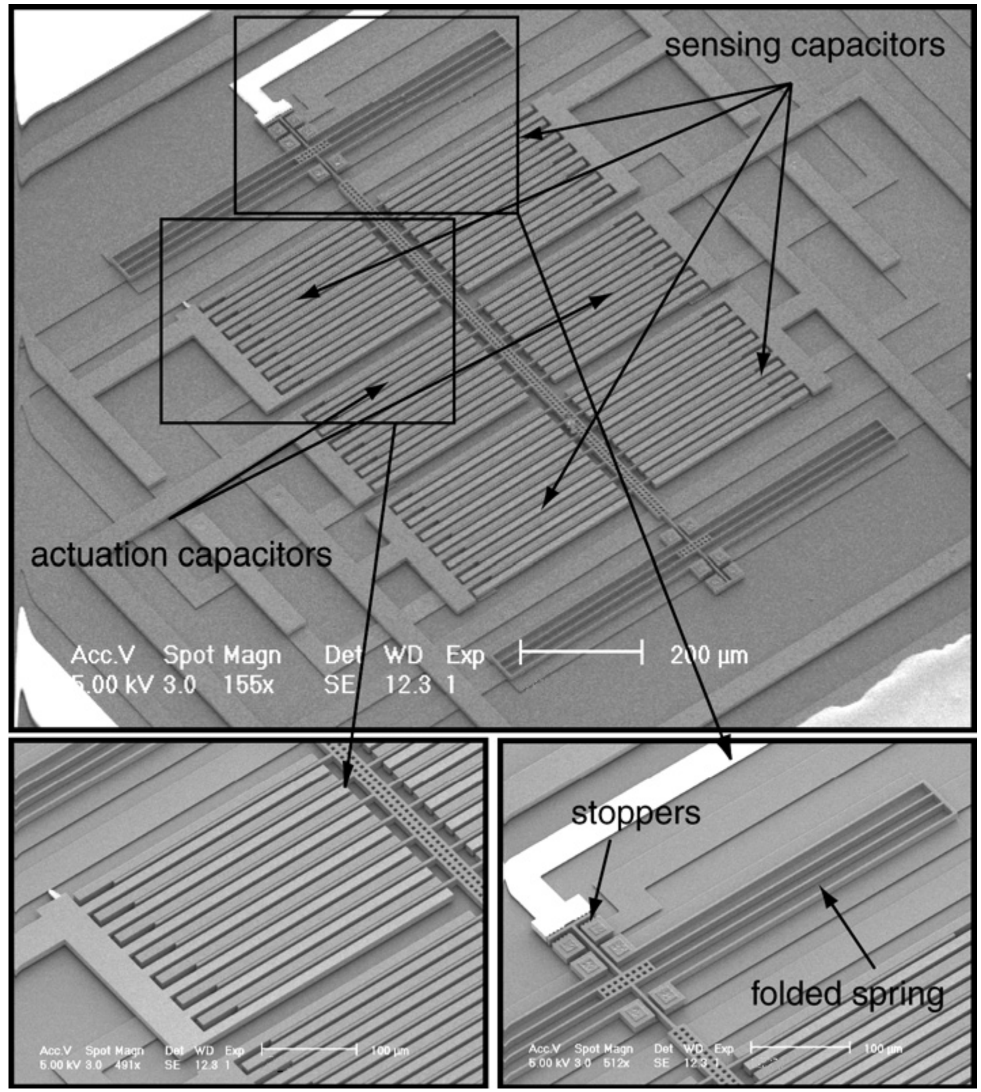
Akustica's digital microphone



Accelerometers

- Operating principle: a movable micromass (ug) senses a_{ext}; readout electronics for sensing the induced stress or the displacement





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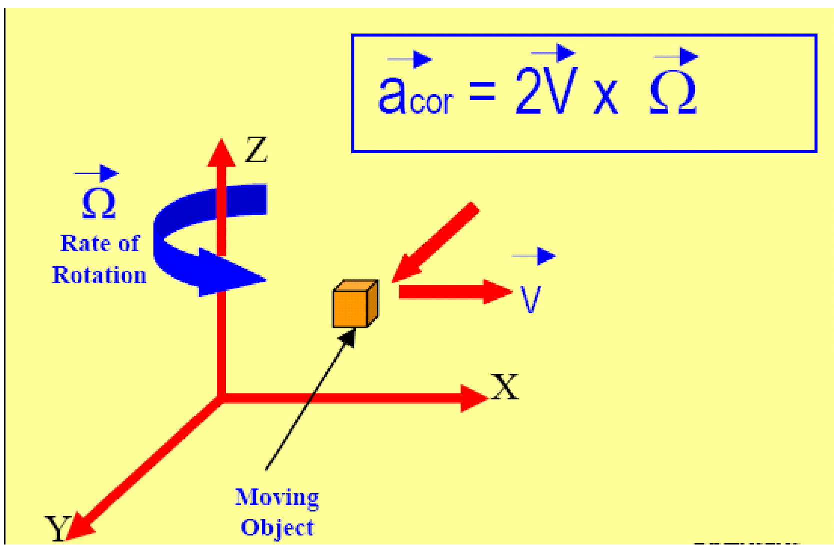
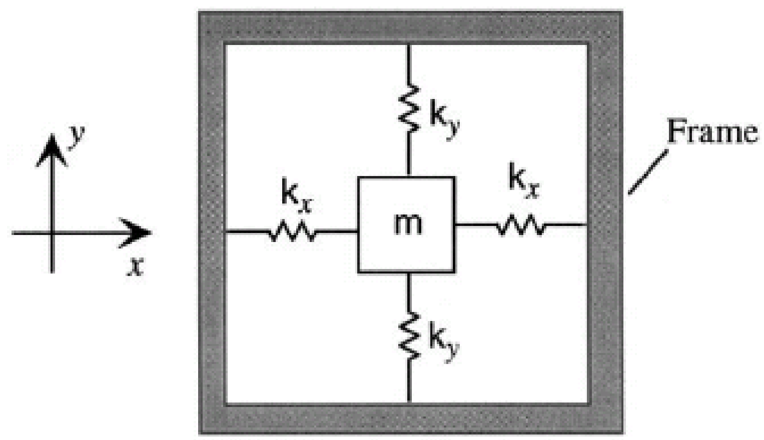
Microgyroscopes

- Operating principle: a mass in driven motion is used to sense the Coriolis force
- use vibrating proof-mass to sense rotation
- based on energy transfer between two vibration modes
- Ω_z induces a coupling between x,y modes

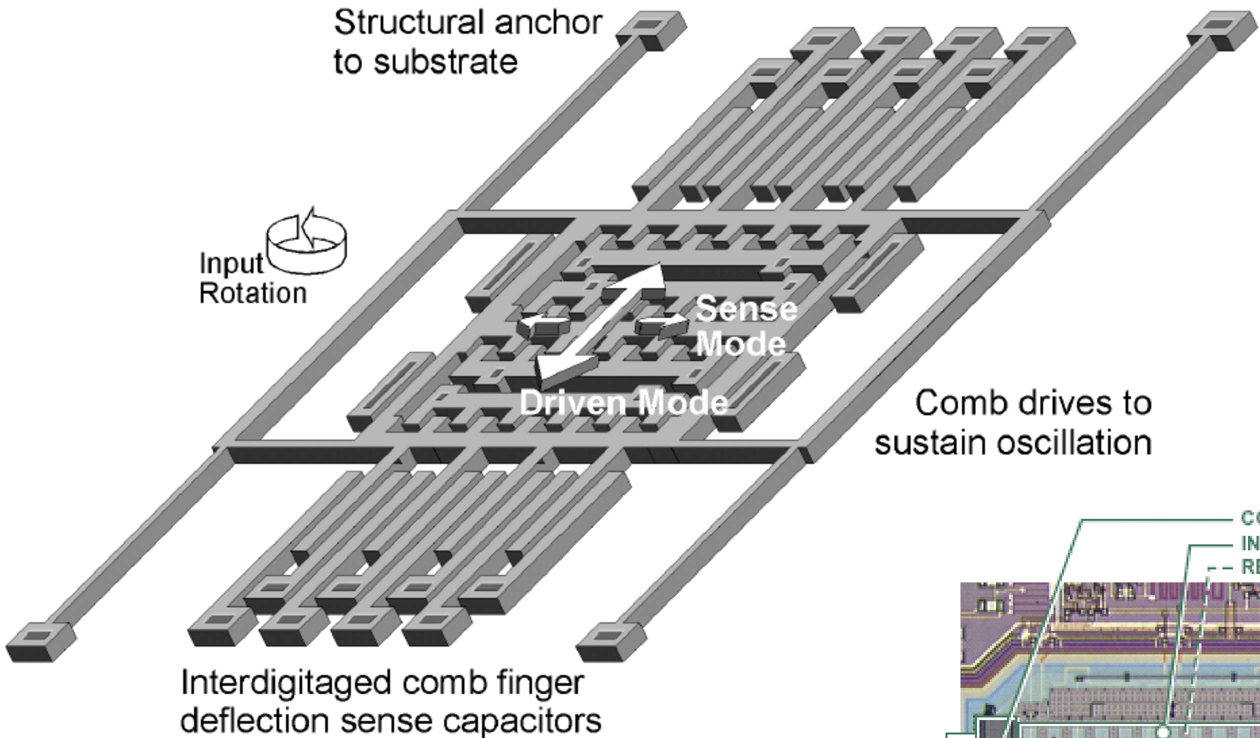


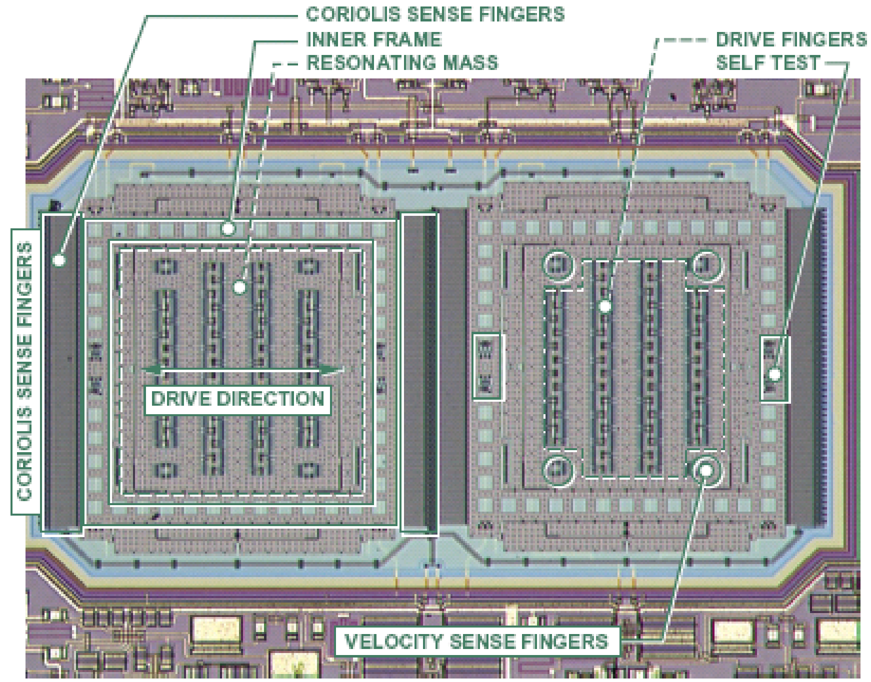


$$m\ddot{x} = F_{i,x} + 2m\Omega_z\dot{y} + m\Omega_z^2 x + m\dot{\Omega}_z y - k_{eq,x}x - b\dot{x}$$

$$m\ddot{y} = F_{i,y} - 2m\Omega_z\dot{x} + m\Omega_z^2 y - m\dot{\Omega}_z x - k_{eq,y}y - b\dot{y}$$

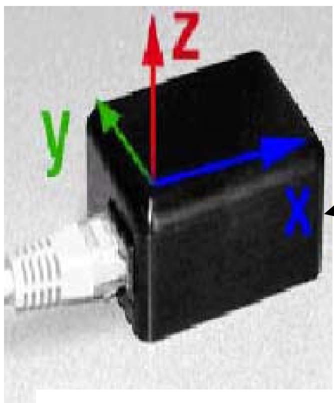
Resonant comb-drive gyroscope

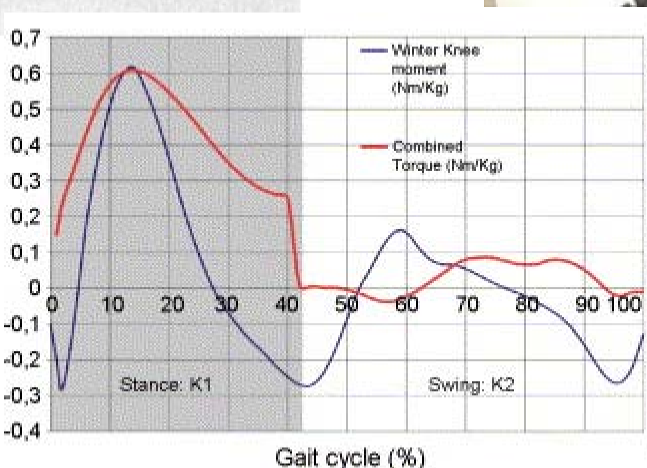


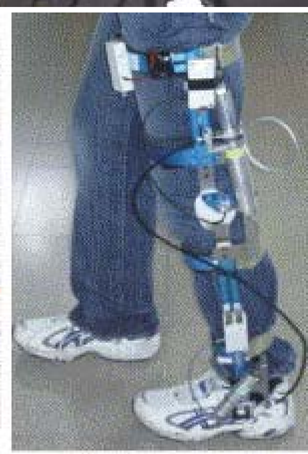


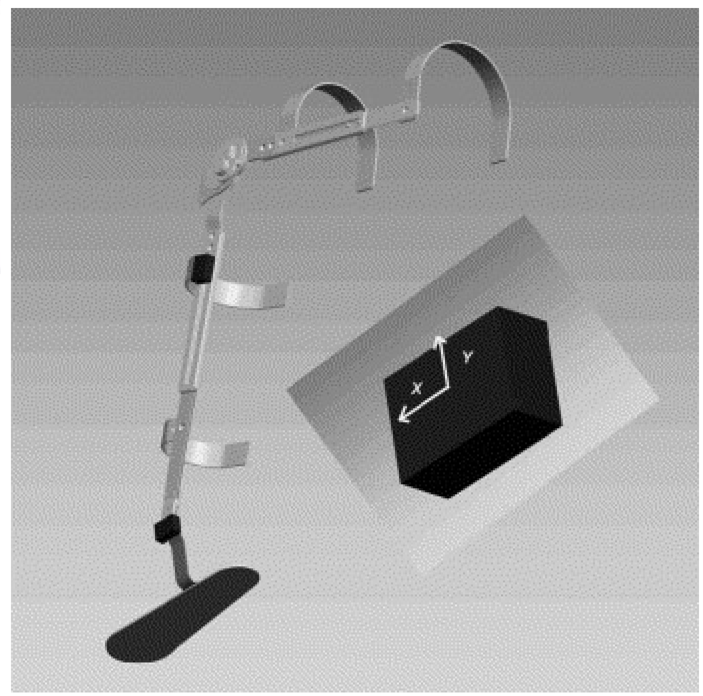
Applications

- IMU for wireless monitoring of patients with Parkinson’s disease
- IMU for the control of artificial limbs – coupling with neuronal control centers
- Implants for controlling the balance of older people







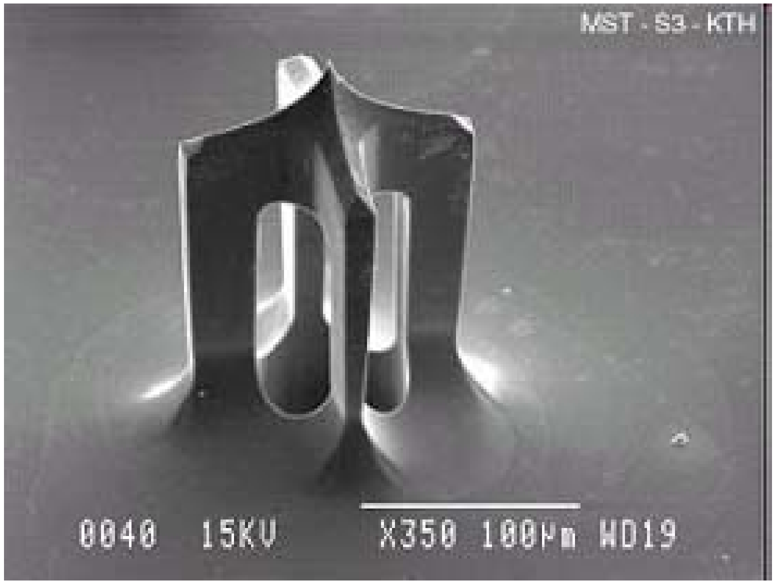


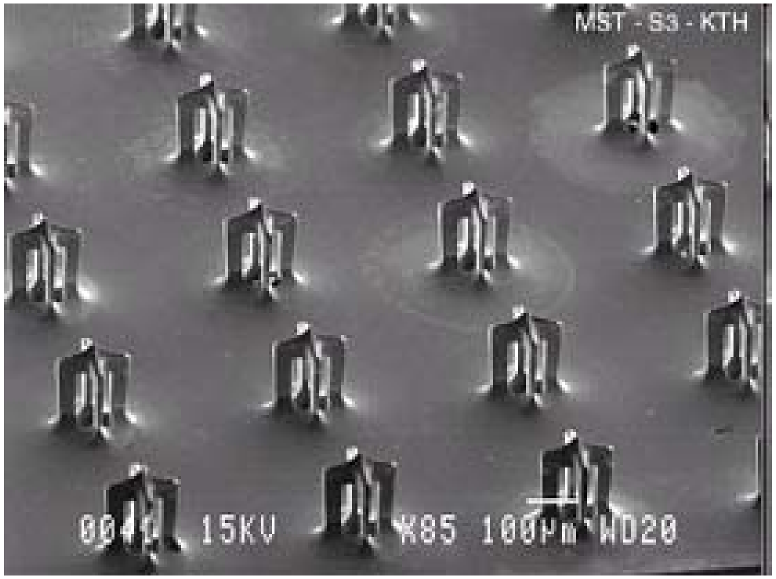
Portable/disposable drug-delivery

- Conventional drug delivery techniques: pills and injections -> often not suitable for new protein-based, DNA-based or other therapeutic compounds
- Alternative: using the skin as alternative route for administering systematically active drugs
- Advantages of **transdermal** (across skin) drug delivery: absence of degradation in the gastrointestinal tract and of first-pass effects in the liver (oral drug delivery) + elimination of pain and inconvenience of intravenous injections
- MEMS-based drug delivery:
  - regulation of drug doses to be adapted based on physical activity, food ingestion, circadian rhythms -> exm: insulin delivery
  - lower risk of infections
  - lower non-uniformity and better localization

Microneedles for hypodermal drug delivery

Low permeability of the human skin => the microneedles are long enough to penetrate beyond the stratum corneum layer (10-15um thick), but short enough to not reach the nerves in the deeper tissues

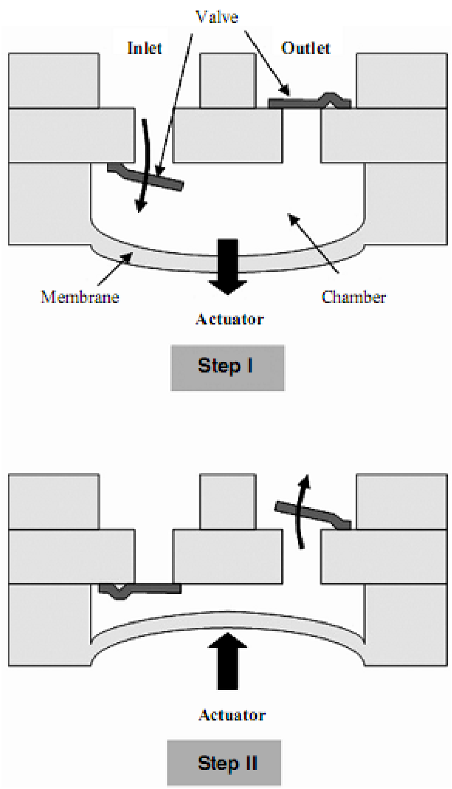


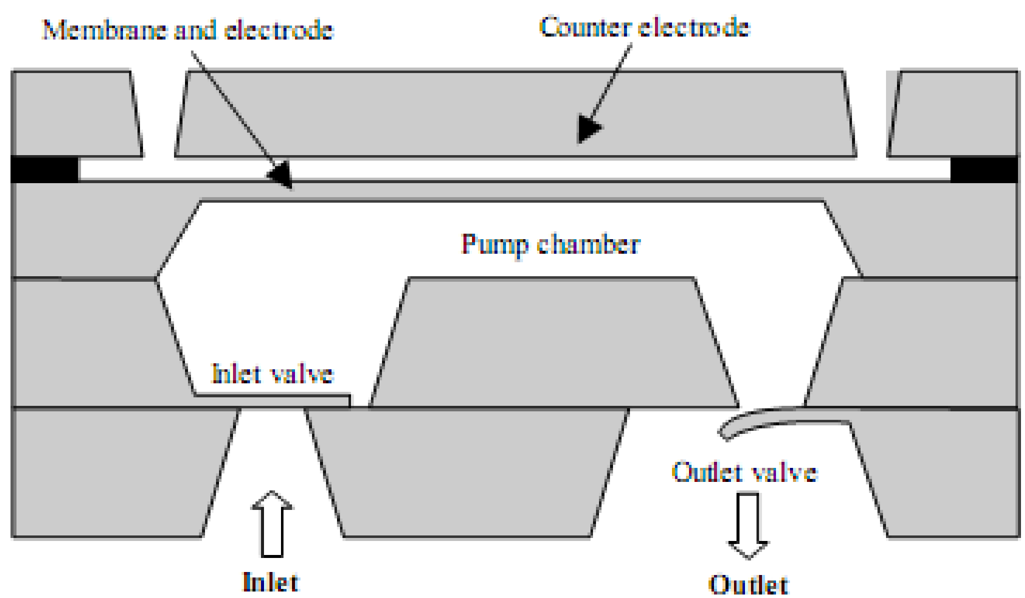


Microneedles from DEBIOTECH

MSTs for drug delivery

- Microneedles combined with microfluidic chips, sensors and electronics – closed loop systems to preset dose-time schemes -> drug delivery as needed
- Exm: insuline delivery system

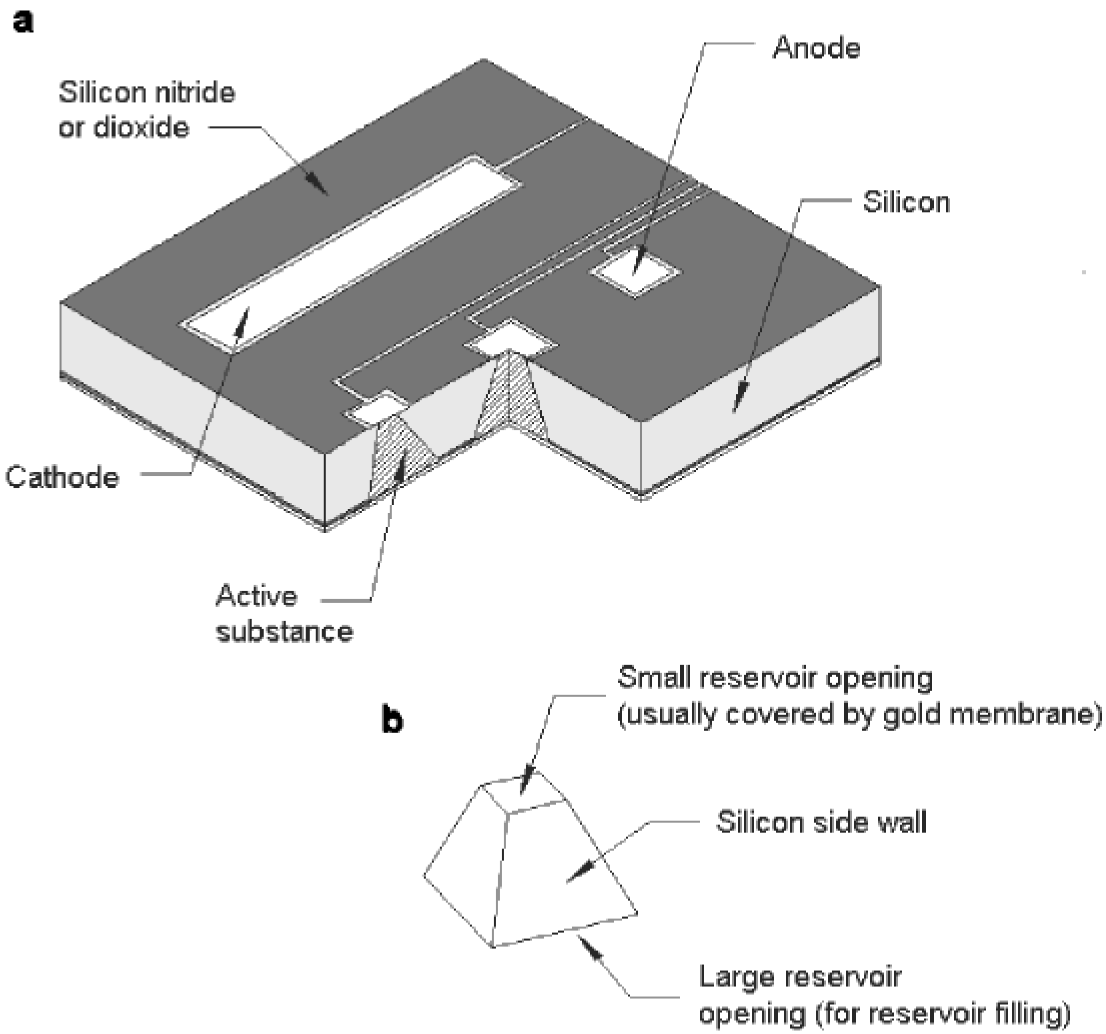




Therapeutic systems

- Pharmacological therapy challenge: maintenance of a steady therapeutic drug concentration level
- Conventional: oral, intravenous -> wide fluctuations in drug concentrations (low concentrations are ineffective, high levels may be toxic) + sustained subtherapeutic levels (exm: antibiotics) can result in development of resistant bacteria
- Eliminate fluctuations: drug delivered at a rate based on the pharmokinetics of the specific agent => needs ct monitoring of the drug level + target specific regions

Implantable delivery systems



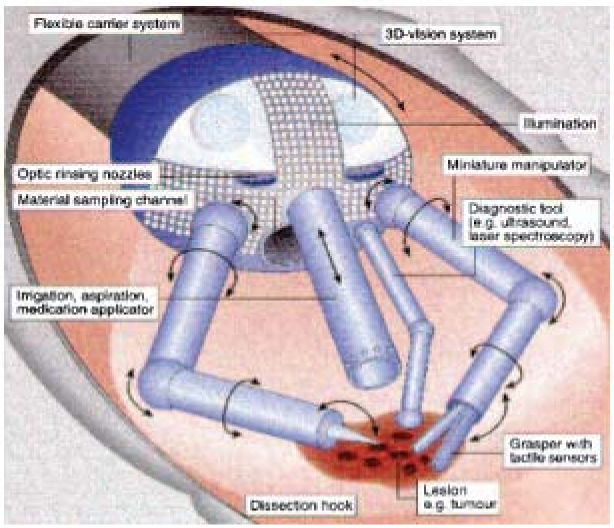
- suitable for chronic illness -> microsystems placed under the skin, refilled by injection, lower the infection risk
- drug delivery: micropumps based on piezoelectric, shape-memory alloy actuation, electrochemical dissolution

Surgical systems

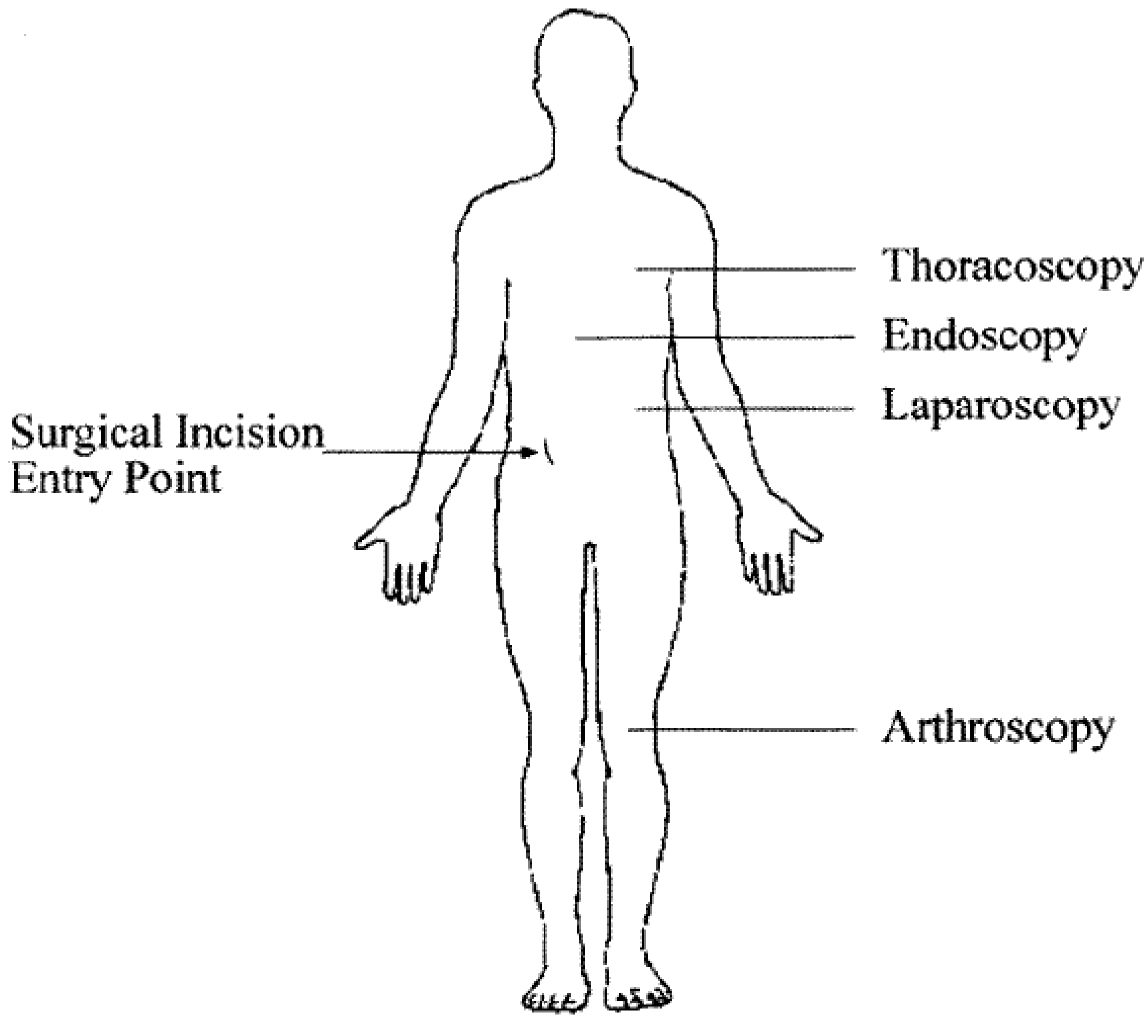
- Conventional surgery procedures: invasive + traumatic => high recovery costs, long time recovery needed, higher risks of post-operatory complications
- Minimally invasive surgery (MIS) tools: use small incisions or natural orifices to access the region of interest
  - microsurgical tools, catheters, endoscopes -> new procedures and approaches to surgery
  - extend the reach of surgery into previously inaccessible areas
- Areas of application of MIS: brain, heart and blood vessels (vascular), lungs (thorascopy), joints (arthroscopy), gallstones and kidneystones, esophagus and stomach (endoscopy), abdomen (laparoscopy)
- Most of the present gall bladder removals or other urinogenitary tract procedures are now MIS
- It has been suggested that 75% of thoracic and abdominal operations can be replaced by MI procedures

Minimally invasive surgery potential

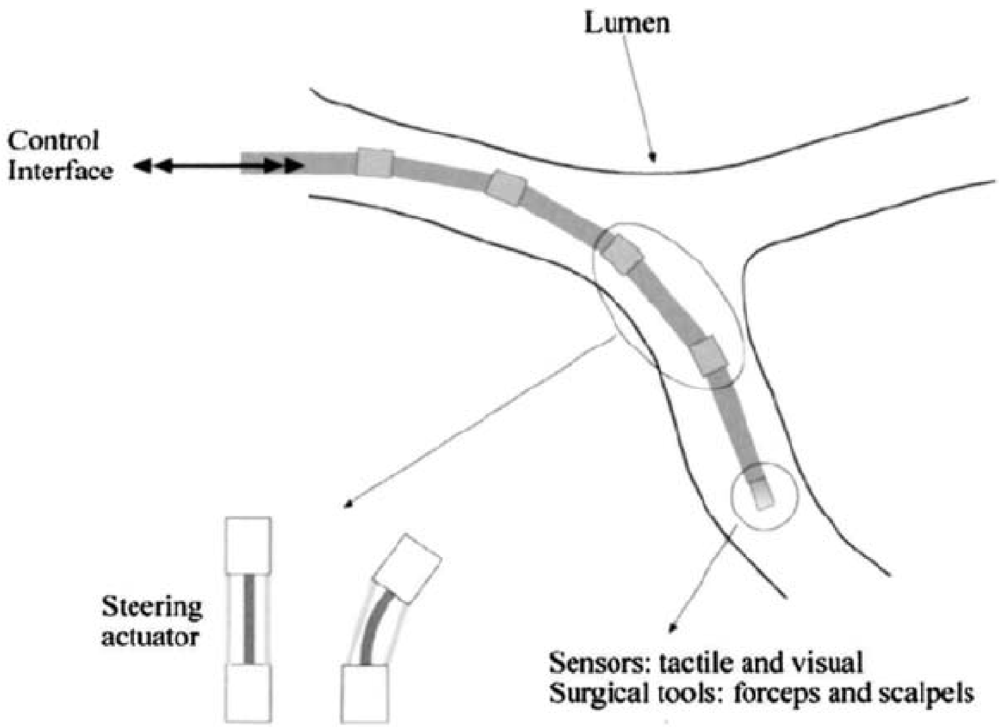
Microtools go beyond standard technologies: highly miniaturization for precise surgeries (ophthalmology, neurosurgery), sensor-enhanced surgical instruments



Early concept of a microrobotic multifunctional endoscopic device for the digestive track



Active medical tools

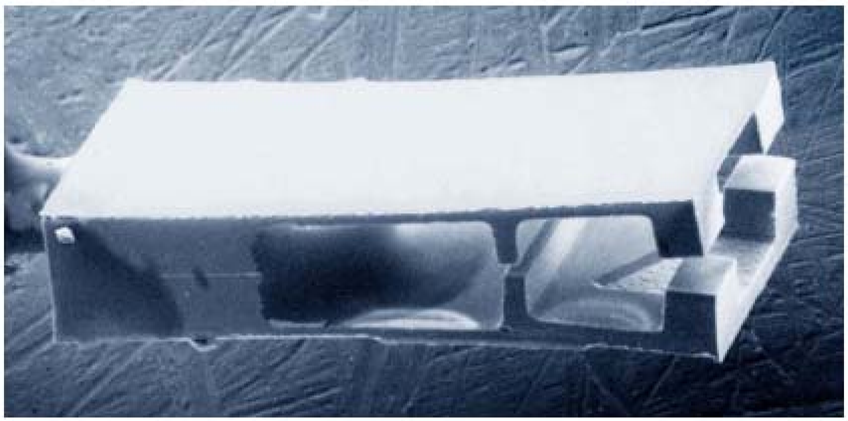


- active medical tools with intelligent control systems -> knee replacement surgery
- robotic systems -> remote telesurgery for dangerous or inaccessible locations

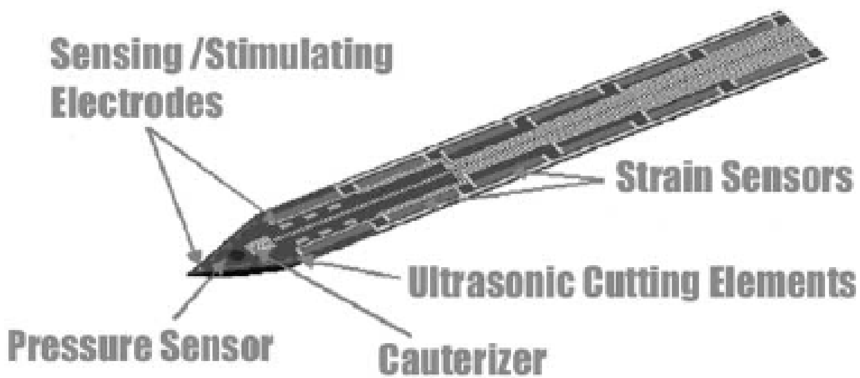
Challenges

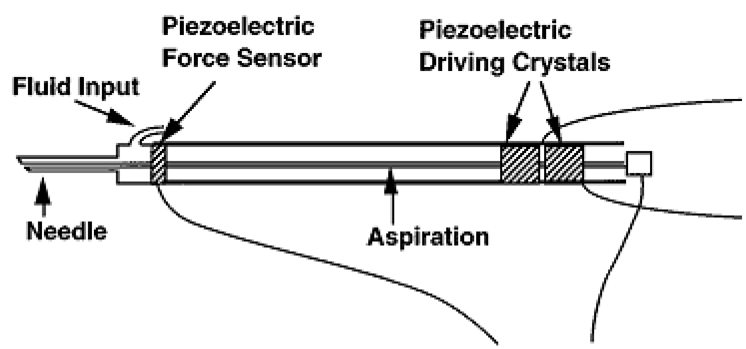
- MIS severely restricts the visual and tactile information available to surgeons -> tactile feedback is essential for identifying hidden tissue planes, accurate targeting of cancerous tissues and in delineating tissue boundaries
- Development of maneuverable systems that will not hamper the surgeon -> active catheter systems with integrated sensors and actuators
- Areas of microsystems applications: sensors (tactile/visual), motion control (active steering of catheters), surgical tools (forceps, grippers, scalpels)
  - Sensors: piezoelectric tactile sensors on catheter to aid in navigation through vessels (on pliant film), PVDF tactile sensor for endoscopic graspers, local blood pressure, flow velocity, oxygen saturation, microcamera systems
  - Motion control: manipulation and steering of passive catheters -> multilink active catheter using Si CMOS + shape-memory alloys actuators (6DOF/joint)

Microinstruments



- rotary cutting blades for atherectomy
- microforceps
- ultrasonic microscalpel tool with integrated piezoresistive sensors as force sensors

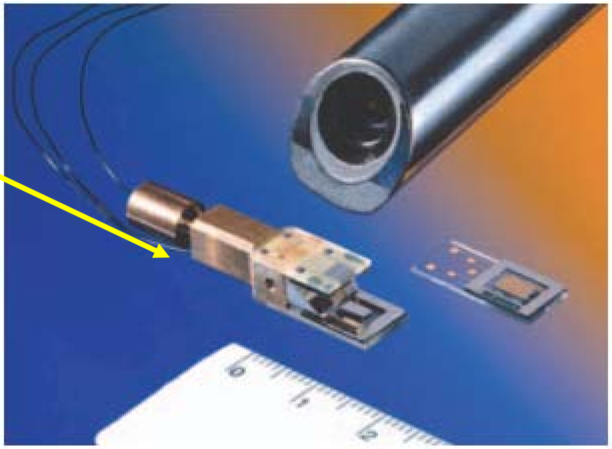




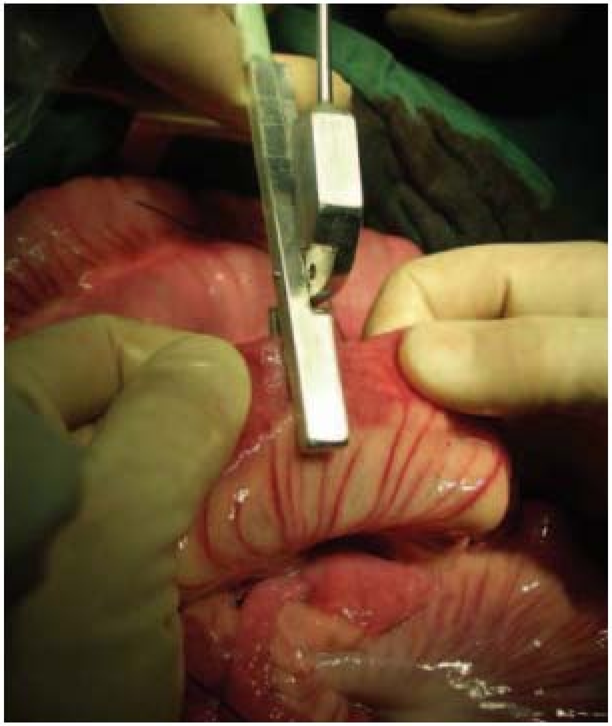
Enhanced sensing in MIS

- Exm: polymer sensor array attached to the tip of a laparoscopic instrument as disposable: conductive and resistive layers separated by a perforated membrane => pressure modifies the resistive coupling, indicating the force

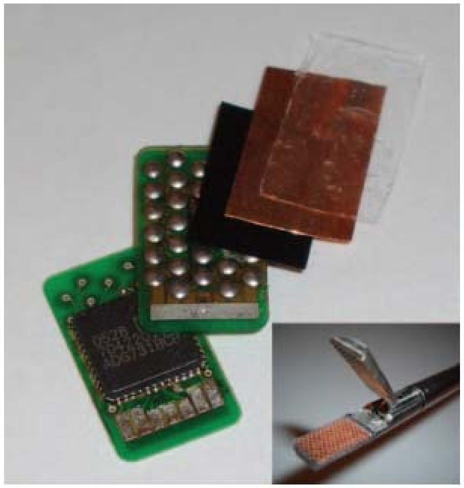
Bi-axial micro scanner with two silicon mirrors, compared to the size of a regular 10 mm laparoscope



Lymph node palpation



Polymer-based tactile laparoscopic instrument

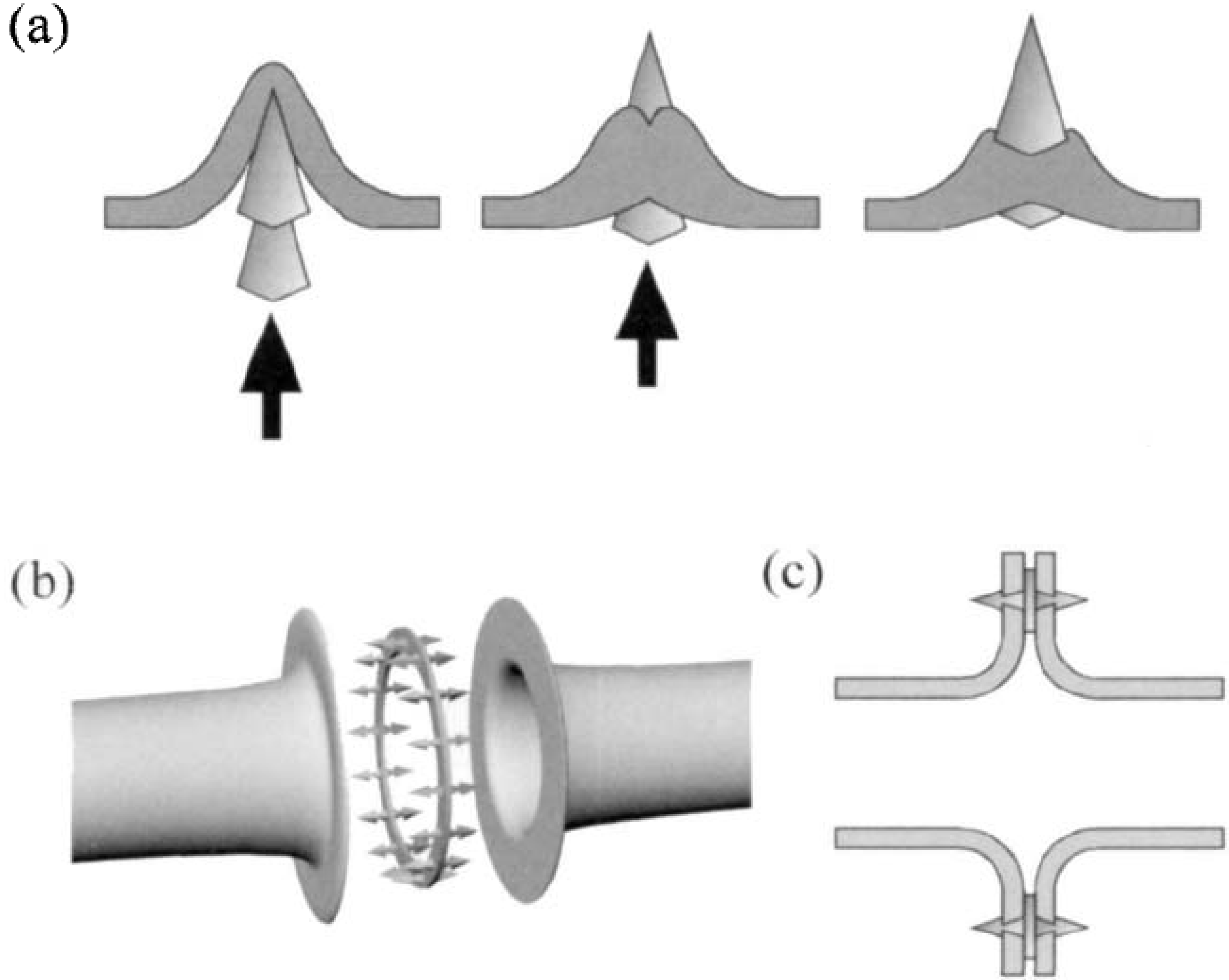


Tactile surgical instrument and force display

Tissue repair

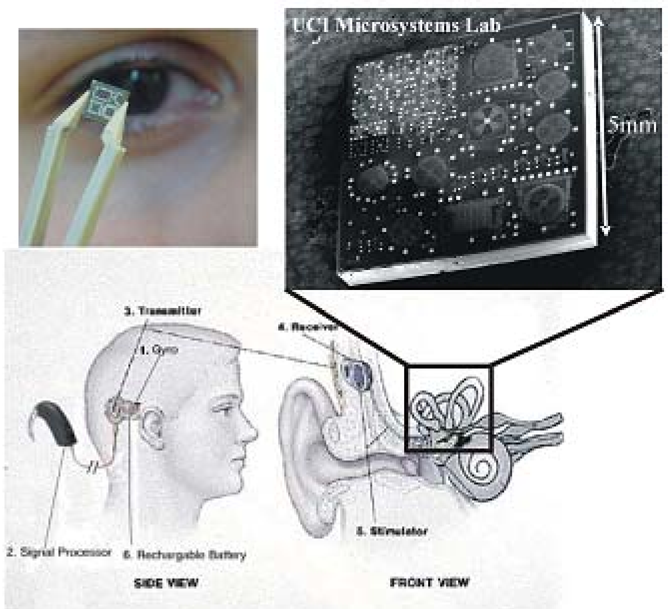
- Help seal surgical incisions (tissue staples), repair damaged tissues
- Conventional vascular anastomosis (joining the blood vessels) – difficult, time-consuming, significant damage to blood vessel walls
- Proposed anastomosis based on bulk micromachined structures (reentrant barb structures)

Suturing blood vessels



Implantable microsystems

- Telemetric implants – sensors of various types to measure specific health parameters (e.g. blood glucose, blood pressure or flow). Signals are then transmitted by telemetry to a read-out device outside the body (e.g. cardiac pacemakers or defibrillators)
- Advantage: improve patient monitoring and implant maintenance without the need to see the patient regularly

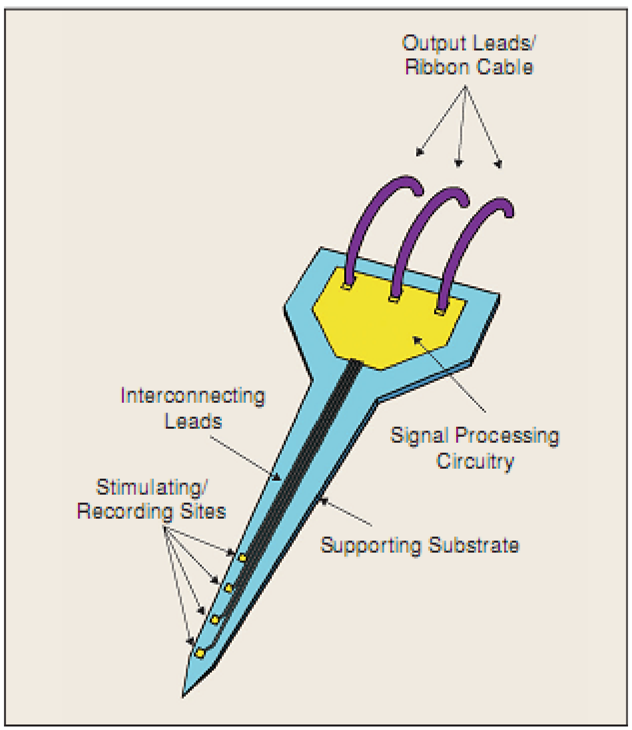


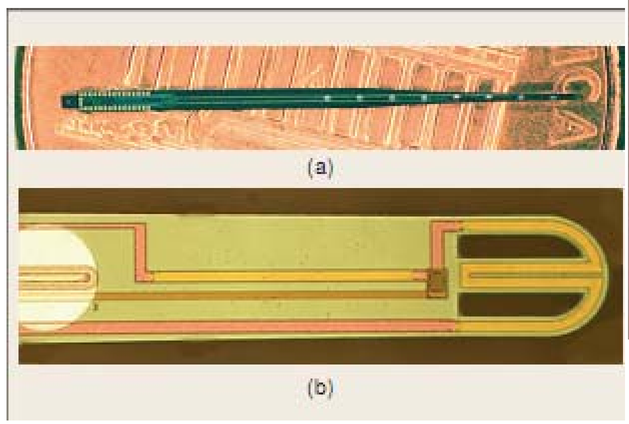
Implantable vestibular prosthesis

Implantable blood pressure monitoring

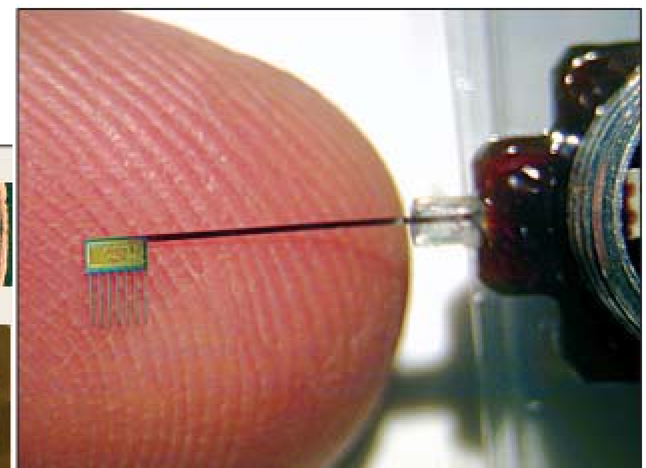
Si microsystems for neuroscience and neural prostheses

- Goal: interface with the central nervous system at the cellular level + bi-directional interaction
- Dense arrays of (thin-film) microelectrodes, coupled with electronic subsystems
- Large potential for therapeutics (deep brain stimulation) or neural interfaces to artificial organs





Multisite cochlear interface



64-site probe with Si ribbon cable