Biomedical applications of MEMS devices

Edmond Cretu
edmondc@ece.ubc.ca
K3063
“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=**
  - Micro-**electro**mechanical systems (USA)
  - Microsystem Technology (MST) (Europe)
  - Micromechatronics (Japan)

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)

- Light-modulating chip
- >100000 individually addressable micromirrors (10x10μm²)
- Binary tilting: ±7.5°
- 0.8μm CMOS SRAM on the substrate, beneath the layer of mirrors
Scaling modifies the design process

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

\[
F_{\text{surface tension}} \sim (\text{surface tension}) \cdot \text{perimeter} \sim S^1 \cdot S^1 = S^2
\]

\[
\frac{F_{\text{surface tension}}}{F_{\text{gravity}}} \sim \frac{S^2}{S^3} = S^{-1}
\]

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

• 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):

<table>
<thead>
<tr>
<th>Classes of MST applications</th>
<th>Relationship to human body</th>
<th>Current examples</th>
<th>Future application examples</th>
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</thead>
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<tr>
<td>Class 1 – extra-corporeal</td>
<td>Used outside of the human body</td>
<td>• Telemetric blood pressure measurement devices</td>
<td>• Wearable integrated physical activity and cardiovascular parameter monitoring</td>
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<td>• Wearable telemetric ECG foils</td>
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<td>• Point of care blood testing systems</td>
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<td>Class 2 – intra-corporeal</td>
<td>Used inside the human body, e.g. surgical instruments or interventional catheters</td>
<td>• Sensor-controlled ablation probes</td>
<td>• Tactile laparoscopic instruments for palpation</td>
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<td>• Cardiovascular sensor-controlled monitoring catheters</td>
<td>• Smart scalpels</td>
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<td>Class 3 – temporarily incorporated</td>
<td>Temporary incorporation, e.g. ingestion or injection or active placement with ancillary devices</td>
<td>• Capsule endoscopes</td>
<td>• Endoscopic microrobots and smart capsules</td>
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<td>• pH sensors temporarily fixed in the esophagus</td>
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<td>Class 4 – implantable</td>
<td>Long-term implants</td>
<td>• Cardiac rhythm management devices with telemetric signal transfer</td>
<td>• Smart orthopedic joint implants with sensors for functional monitoring</td>
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<td>• Intra-ocular lenses with pressure sensors (glaucoma monitoring)</td>
<td>• Retina implants</td>
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<td>• Endovascular stent grafts for aneurysm repair with pressure sensors (leakage monitoring)</td>
<td>• Implantable glucose sensors</td>
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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 $\Rightarrow$ acoustic array processing for better directivity and sensitivity
- The power of integration: acoustic system-on-chip
Accelerometers

- Operating principle: a movable micromass (ug) senses $a_{ext}$; readout electronics for sensing the induced stress or the displacement
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
- $\Omega_z$ induces a coupling between $x,y$ modes

$$a_{cor} = 2\Omega \times \vec{\Omega}$$

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

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

Structural anchor to substrate

Input Rotation

Sense Mode

Driven Mode

Comb drives to sustain oscillation

Interdigitated comb finger deflection sense capacitors
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.
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

Polymer-based tactile laparoscopic instrument

Lymph node palpation

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

(a)

(b)

(c)
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
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