Microsystems in Biomedical Engineering

by
Oddvar Søråsen
Department of Informatics, UiO
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Microsystems in Biomedical Engineering

- Material from course by FSRM
  - “Swiss Foundation for Research in Microtechnology”
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- Focus: Miniaturization of devices useful in biomedical engineering

- **Micromachining and MEMS technologies** are powerful tools!
Contents

- Definitions
- Technology and principles
- Applications
- Benefits
Terms

- **MEMS** (Microelectromechanical systems)
  - Miniaturization of electrical, mechanical, optical, fluidic, magnetic systems
- **Microtechnology** (e.g. MRL)
- **Microsystems** (Europe), MST
- **Micromachines** (Asia)
- “**Biomicrotechnology**”
  - Wide and highly dynamic field
  - Many different technologies
  - Typical: biomolecules/cells will be combined with technical structures
“Biomedical” applications

- Second largest application area for MEMS after automotive

- **Challenge:** identify niches with sufficient market potential to justify the long and expensive development process

- Forecast: MEMS-enabled chemical sensing and microfluidic systems will grow tremendously!
Technology

- **Microfabrication**: batch processing from IC -> expanded
  - Photolithography
  - **Bulk** micromachining
  - **Surface** micromachining (sacrificial + structural layers)

- **Silicon**, a central material:
  - + mechanical properties (stress – strain, “spenning – tøyning”),
  - + excellent piezoresistive material
  - - optical penetration
Bulk Silicon Micromachining

TRONIC’S

cnm + SensoNor
Surface Micromachining
Non-silicon microfabrication

- Metal (electroplating)
  - Used directly or as mould (plastic) (Ni, Cu, Au)
- Laser (cutting, removing glass, plastics, ceramics)
- Glass microstructures
- Plastic microstructures (laminate)
- Hybrid microstructures
Hewlett Packard Inkjet Nozzle Roadmap

- **ThinkJet 1985**: 12 orifices, 4 ml ink, 1.2 kHz, 96 dpi, 180 pl
- **DeskJet 1987**: 50 orifices, 17 ml ink, 5 kHz, 300 dpi, 85 pl
- **DeskJet 1200C 1993**: 104 orifices, 42 ml ink, 8 kHz, 300 dpi, 77 pl
- **DeskJet 850C (720C) CMY 1995 (1997)**: 3 x 64 orifices, 3 x 20 ml ink, 8 kHz (12kHz), 300 dpi, 30 pl (10pl)
- **DeskJet 850C Black 1995**: 300 orifices, 410 ml ink, 8 kHz, 600 dpi, 35 pl
- **DeskJet 2000C 1998**: 304 orifices, ~400 ml ink tanks, 12 kHz, 600 dpi, 8 pl
- **DeskJet 970C CMY 1999**: 408 orifices, 3 x 20 ml ink, 24kHz, 600 dpi, 5 pl
- **DesignJet 1000 Series 1999**: 512 orifices, ~700 ml ink tanks, 12 kHz / 600 dpi, 12 pl
MEMS structures and principles

- **Pressure** sensors
  - bending of beams, diaphragm
- **Inertial** sensors (accelerometers and gyros)
- Detection mechanisms:
  - **piezoresistive** elements, **capacitive** detection
- **Fluidic** systems
- Actuators (mirror deflection)
Piezoresistive pressure sensors

- Bondpad
- p-type diffused piezoresistor
- Metal conductors
- n-type epitaxial layer
- p-type substrate and frame
- Anodically bonded Pynax substrate
- Etched cavity
- Backside port
- Diaphragm boundary
- Piezoresistor
- Resistor contact
- Voltage taps
A Capacitive Accelerometer
Applications in Biomedical Engineering

- In **Vivo** systems (contact with patient bodies)
  - A. Electrical stimulation
  - B. Biosensors
  - C. MIS Minimally invasive surgery

- In **Vitro** systems (clinical settings)
  - Medical diagnostics
  - R&D in drug discovery and development
A. In Vivo: electrical stimulation

- **Neurostimulators** in the cardiovascular area
  - **Pacemaker**, defibrillator (flagships, most mature)
  - *All the main heart disorders are being treated with microelectronic implants!*
  - Future: Rate-responsive pacemaker (accelerometers, pressure/flow sensors)

- **Cochlear** implants (Otology)
  - Commercialized
  - Widespread use in children with profound deafness.
A. In Vivo: electrical stimulation, cont.

- Retinal implants (futuristic) (Ophthalmology)
  - Visual systems to the blind
  - Epiretinal implant device: Optobionics

- FES functional electrical stimulation
  - Bone growth stimulator
  - Bladder stimulators (small market yet)
  - Restoring movements to paraplegics (lammet fra livet og ned) and stroke victims (not in commercialization yet)
  - Dropped foot syndrome. Attaching electrodes to special nerve
Neurology and rehabilitation

- Limb function restoration
  - Sensors for **prosthetic devices**
  - Freehand system from NeuroControl Corp
    - approved FDA in 1997 for quadriplegics (can use their shoulder and upper arm, but not their hands)
    - Implanted in the chest - 8 electrodes
    - Can grip lightweight objects

- Telemetry
  - RF MEMS, inductive coupling
Neural-electronic interfaces

- Micromachined neural sensors and stimulators
  - control prosthetic limbs with signals from the brain or spinal column
  - MEMS:
    - many electrodes co-fabricated
    - tailor systems to the dimensions of individual cells

- Blocking brain signals that cause tremor (Parkinson)
  - Medtronic
Drug delivery

- **Aerosol**
  - Asthma, attack prevention
- Implantable **drug infusion pumps** (1980- to cancer pat.)
  - Small pump controlled by an electronic module
  - Biotelemetry unit, lithium battery
  - Refillable reservoir, catheter delivers drug where needed

**Advantages:** preprograming, versatile regulation, adapted to patient needs, patient compliance (tilpasning), lower risk of infection, delivery to targeted internal sites, reduced doses and side effects
Technology Analysis: Drug Delivery

STEAG microParts, Germany
Boehringer Ingelheim Pharma GmbH & Co. KG

Nebulisers for drug inhalers

Boehringer Ingelheim (D)
STEAG microParts (D)
Technology Analysis: Drug Delivery

Debiotech Chip
Technology Analysis: Drug Delivery

Debiotech Chip

Source: Debiotech
Patches, stents

- **Transdermal** patch systems
  - For *transcutaneous* delivery of drugs
  - (“passing, entering, or by penetration through the skin”)
  - Electrophoresis are used
  - At an advanced clinical trial stage

- **Stents!**
B. In Vivo: biosensors

- Sensors typically measure **physical** rather than **biochemical** parameters
- **Pressure sensors** inserted into a **catheter** and inserted into arteries (blood, bladder, cerebral spinal pressure)
  - **Blood pressure** sensors used during **surgery**
    - measuring intravascular **blood pressure**
  - **Brain pressure**
    - Highly invasive brain surgery
    - Patient still conscious
Implanted sensor: sown in place, light communication
Radi Catheter
Probe placement is facilitated by two depth markers located at 35 and 40 cm.
Technology Analysis: Monitoring & P.O.C
B. Biosensors, cont.

- Catheters (RADI) and endoscopes
- Ultrasound blood pressure
- Gastroenterology: **Swallowable camera**
  - Imaging Ltd, Israel
  - CMOS image sensors, ASIC, LED illumination, video telemetry, UHF radiotelemetry up to 5 hours (small intestine)
The Microprobe that can swim through the blood system

Introvascular ultrasound can build video images to detect signs of heart disease.

Graphic by John Smith
Technology Analysis: Catheters & Endoscopes

Given Imaging – Imaging System in a Pill

Pill - 11mm diameter 27mm long

Wireless link

Wired link

Source: Given Imaging Ltd
B. Biosensors, cont.

- Diabetes
  - Large activity
  - Commercial product:
    - GlucoWatch from Cygnus, CGMS sensor system
    - Spectroscopy used

- No in vivo sensors in common use for monitoring metabolics
  - due to sensor drift, perturbation of the surrounding tissue
The glucose-monitoring watch. Cross-section, top left. Comparison of prototype 1 COB and prototype 2 SMD board, top right. Prototype 1 final device, bottom left. Pre-series device, bottom right.
C. MIS Minimally Invasive Surgery

- “Keyhole surgery”
  - Micromanipulators
  - Miniaturized surgical microinstruments
- **Toolbox**:
  - Micropump, microvalves, microfilters, microneedles, microsyringes (sprøyter), incredibly sharp blades
- **Pressure** monitors are used
- **Catheters** with imaging capabilities, incl. ultrasonic probes
In Vitro devices: Biochips

- Miniaturize entire biomedical systems

- **Microfluidic** systems typically have
  - Smaller volume, reduction of system size
  - Precise control of sample volume
    - thermal, fluidic
  - Massively parallel tests
  - Possible reduction in system cost
In Vitro: Main technologies

- **Lab-on-chip** devices
  - Integrate different biochemical laboratory processes on a single chip

- **Microarrays**

- **Application** areas:
  - Monitoring: blood pressure, glucose, blood gas ++
  - Life science research and drug discovery
Biotechnology MEMS

“Lab-on-a-Chip”

Lab-on-a-chip concept for capillary electrophoresis

1. Sample input
2. Dilution buffer
3. Chemical reagent

Sample channel
Separation channel
Buffer waste
Sample waste

Sample Inlet
Manifold or Micro-Valve
Preconcentrators
Separators
Chemically-Selective Detectors
Pumps
Sample Preconditioning
Technology Analysis: Glass Microreactors

**Technical Data Sheet**

**mikroglas heat exchanger**

*mikroglas technik AG*’s product range for microreaction technology includes ready-to-connect modules such as static mixers, heat-exchangers or a combination of both. The *mikroglas* heat-exchanger has an especially higher efficiency compared to components made of other materials. The *mikroglas* heat-exchanger can also be made of ceramic, which further improves its heat-exchanging properties.

**Specifications**

- **FOTURAN glass or ceramic**
- **number of layers**: 7
- **layer thickness**: 0.2 mm to 1 mm
- **outer dimensions**: 150 mm x 170 mm x 25 mm
- **number of reaction channels**: 5
- **height**: 0.4 mm / 0.5 mm
- **width**: 1.0 mm
- **length**: 250 mm
- **heat-exchange area**: 1400 mm²
- **flow rate**: appr. 20 l/h
- **drop in pressure**: appr. 2.5 bar (water at 20 °C)
- **heat transfer coefficient**: appr. 5400 W/m²K
- **maximum viscosity**: appr. 12.5 Ns/m²
- **connection**: by ready-made Teflon tubes (1/4” UNF thread)
Lab-on-chip

- **Blood analysis** at the bedside ("point-of-care" testing)
  - Systems are microfluidic based
  - Tiny channels etched in the chip, glass, plastic
  - Transport of droplets of fluid by electrophoreses
  - Tiny pumps and valves in some cases
    - Most without moving parts
  - CD (centrifugal force), SAW

- Single use chip (HP and iSTAT), 2 min, 2-3 drops
iSTAT

- blood analysis
  - glucose, urea, pH, blood gases,
- portable POC device
- analyser + disposable cartridges
- microfluidic channels
- micro-fabricated thin-film electrodes
iSTAT Sensor Chips
Microarrays

- Integrate a high number of identical types of reactions on a single chip (two-dim)

- Discrete areas containing **biomolecules** that are capable of interacting specifically with a complementary molecule

- Can determine which component is present in a specimen

- Optical detection of pattern
Microsystems for genetic analysis

- Gene chips
  - DNA analysis
  - Calipher DNA analysis plate
  - Fragment of genome is identified on a chip surface
  - DNA amplification

- Protein chips
  - Different proteines or peptides are identified
Glass Microstructures Example

Caliper DNA Analysis Plate
Technology Analysis: Analysis Systems

Caliper DNA Chip
Drug discovery

- Microarrays, microfluidic systems
  - Drug development: “High Throughput Screening”
  - New drugs to the market faster
    - Microtitre plates
    - Microreactors
- “Pharmakogenomics”
  - Study the genes role in metabolizing drugs
  - Individual and different reactions on patients
  - Select the right type and dose for new drugs
Benefits of Biomicrotechnology devices

- In Vivo: **MEMS technology** is significant for the future development of medical implants and devices
  - More functionality
    - Combination of microstructures and bioactive molecules
  - Biocompatibility
    - Suitable packaging, biocompatible coatings
    - Silicon can be made **biocompatible** and even **biodegradable!!**
- Cost
  - Batch manufacturing
  - Disposable analyzers and sensors
Benefits

- In Vitro Devices
  - Biomolecular and biochemical analysis
    - Miniaturization
    - Parallelization
    - Acceleration
    - Speed up drug discovery
  - Powerful new diagnostic tools
    - Genetic analysis for the daily medical routine
    - Decentralized monitoring