Lecture 02: What is BioMEMS?

BioMEMS
- MEMS for chemical, biological, and medical applications
- Also called Lab-on-a-Chip (LOC), Micro Total Analysis Systems (μTAS)

Concept of μTAS
- Proposed by Andreas Manz in 1990 (A. Manz et al., Sensors and Actuators B1, 244-248)
- Use of integrated microfabricated devices for sample pretreatment, separation, and detection for chemical analysis
- Lab-on-a-Chip: To have a whole chemistry or biology lab on a single chip, from sample preparation to final analysis
- To have all the stages of chemical analysis such as sample preparation, chemical reactions, analyte separation, analyte purification, analyte detection, and data analysis performed on a single chip in an integrated and automated fashion
Several terms are used in the area of BioMEMS. However most of them are used without any specific definitions.

- BioMEMS
- LOC
- MicroTAS
- Microarrays
- Biomicrodevices
- Biochips
- Microfluidics

Biochips scan, process, and interpret biological data very rapidly.

- The technology is commonly known as Lab-on-a-chip or BioMEMS.
- Biochips apply microchip and microelectronics technology in the biotechnology and pharmaceutical industries.
- Biochips also bring together life sciences and information technology.
- These devices assist scientists to identify and compare selected sequences of amino acids and other complex molecules.
- The generic term biochip has other derivative terms such as protein chip, DNA chip, microarray, and gene chip.
- Biochips can be defined as 'microelectronic-inspired' devices that are used for delivery, processing, analysis, or detection of biological molecules and species' [Bashir, 2004]. These devices are used to detect cells, microorganisms, viruses, proteins, DNA and related nucleic acids, and small molecules of biochemical importance and interest.

LOC (or MicroTAS)

- Bio/Chemical/Medical Laboratory on a single chip
- POCT (point-of-care test)

Microarrays

- Tool for large-scale analysis of gene expression, enabling the activities of hundreds of thousands of genes to be monitored simultaneously. By comparing microarrays from different samples, scientists find clues about which genes are involved in certain processes, such as stages of development or response to disease.

Biomicrodevices

- Biomicrodevices are devices with feature sizes at the micrometer scale used for bio-, medical- or analytical applications (e.g., separation, bioreactions/synthesis, cell cultivation, bioanalytics). Biomicrodevices can use biological components to facilitate their function (e.g. antibodies for bioanalytics) or/and come in direct contact with biological components (e.g., biomicrodevices for cell separation). Biomicrodevices can be made from synthetic materials, natural materials and/or modified natural materials (e.g., silicon, polymers, metals, glass) and may contain biological components (e.g., immobilized DNA, proteins).

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Microfluidics

- One of core technologies for LOC/MicroTAS/Microarrays
- The science of building microminiaturized devices with chambers and channels for the containment and flow of fluids. With devices measured at the micrometer level and fluids measured in nanoliters and picoliters, microfluidics devices are widely used in ink jet printer heads and lab on a chip. The latter are used to analyze body fluids for medical purposes.
- Biochip is a generic term used to describe miniaturized devices based on a combination of microfabrication technology and life sciences. These devices are primarily based on microfluidics technology. The biochips employ miniaturization of biological separation and assay techniques to an extent that multiple and complex analyses can be accomplished on a "chip" small enough to fit the palm of the hand the so-called "lab on a chip" or micro total analysis systems (µTAS).
- Very tiny quantities (nanoliters) of sample and reagents are transported through micrometer-sized channels on the chip, where they undergo mixing, reaction etc. and are subject to analysis by techniques such as mass spectrometry, fluorescence detection, immunoassay, or virtually any conventional laboratory analysis technique.
- A typical biochip system consists of several microfluidic components, such as pumps, dispensers, microvalves, interconnects, multiplexers, etc.
[BioMEMS] Brief History

- 1980’s: Chemical sensors, micropump, microvalve
- 1990: Manz et al., µTAS concept
- 1991: Affymetrix was founded, DNA Microarray
- 1994: First µTAS Conference at the University of Twente, Netherlands
- 1995: Caliper and Cepheid were founded
- 1999: Caliper and Agilent Technology introduces first lab-on-a-chip commercial product
- 2001: Lab-on-a-Chip by Royal Society of Chemistry, First journal dedicated for BioMEMS
- 2002-2006: Manz et al, Review Paper Series for µTAS

[BioMEMS] Why Miniaturization?

- Limitation of Conventional Approach
  - Growing demand for fast, efficient, and accurate chemical analysis in areas such as drug discovery, biotechnology, medicine, and environmental monitoring
  - Need to move chemical analysis closer to the “User”, e.g., pregnancy test, blood glucose level test for diabetic patient, analysis of environmental sample
- Advantages
  - Better performance due to smaller sample size/small geometry
  - Low power consumption
  - Integration of various functionality
  - Reduction in sample/reagent consumption
  - Automation
  - Reproducibility at low cost using batch microfabrication → disposable
  - High throughput
  - Smaller is better (?)
  - time (↑), cost (↓), reliability (↑), accuracy (↑)

[BioMEMS] Our Dream

- A personal LOC device for DNA-based diagnostics
- A wireless communication network, and
- An intelligent system for patient data analysis and personalized therapy

[BioMEMS] Challenges

- From Concept to Commercialization
  - Still a relatively new technology
  - Each device/system is different → Hard to standardize the designs and processes (Different compared to IC industry)
  - Integrating different functionalities on a single chip has been more challenging than initially imagined
  - Interfacing chips to the macro world
  - Packaging of the system

- Fundamental Challenges
  - Molecular level interaction between samples and devices
  - Theory / tools /experience for macro devices/systems does not always apply to micro devices
**[BioMEMS] Biotechnology Industry**

- **NT + IT + BT**
  - Contents Discovery
  - Genomics
  - Proteomics
  - Chemogenomics
  - Information Processing, Bioinformatics
  - Hardware Platform
  - Micro Array
  - High Throughput System
  - Lab-on-a-Chip
  - DNA / Protein / Cell Chip
  - Clinic Diagnostic
  - Environment Sensor
  - Food Sensor
  - Bio-warfare
  - MEMS/Nano
  - Micro Fluidics
  - Optics
  - Microelectronics
  - System Integration

**[BioMEMS] Future Trends in NT + IT + BT**

- Time Line:
  - ~2000~
  - ~2010~
  - ~2020~
  - ~2030~
  - ~2040~

- **Nano In-Vivo Single Cell**
  - Macro In-Vitro Blood
  - LabAutomation
  - LOC
  - Implantable LOC

**[BioMEMS] Biochip Market**

- Annual rate of growth 38%: Market size 30B $ Estimated

**Assumptions**
- FDA approval
- Molecular diagnostics *1
- Replacement rate *2
- Chip cost
- Potential Needs

**Market for Research**
- For clinical study in drug screening or DNA Marker development

**Market for Diagnostics**
- Disease prediction and diagnostics

**Consumer & Vanity Market**
- Biosensors in Food, Environment market (Not required FDA approval)

**[BioMEMS] Example of BioMEMS Devices**

- Labchip for DNA and Protein Analysis
  - Caliper Life Sciences
  - Electrophoresis
  - Glass chip

**Example Devices**

- Labchip for DNA and Protein Analysis
- Caliper Life Sciences
- Electrophoresis
- Glass chip

**[BioMEMS] Future Trends in NT + IT + BT**

- In-Vitro: in an experimental situation outside the organism. Biological or chemical work done in the test tube (in vitro is Latin for “in glass”) rather than in living systems.
- In-Vivo: in a living cell or organism

**Example Devices**

- Immuno chip
- Microfluidics
- MEMS/Nano
- Microelectrode

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**[BioMEMS] Example of BioMEMS Devices**

- **Blood Analyzer**
  - i-STAT (→ now Abbot Point of Care)

**[BioMEMS] References**

- **Journals**
  - Lab Chip (Lab on a Chip)
  - Journal of Microelectromechanical Systems
  - Journal of Micromechanics and Microengineering
  - Sensors and Actuators A, B
  - Biomedical Microdevices
  - Analytical Chemistry

- **Conferences**
  - Micro Total Analysis Systems (MTAS)
  - IEEE MEMS
  - Transducers
  - Solid-state Sensors, Actuators and Microsystems Workshop

Useful Online Magazines / Newsletters (please subscribe all for free online newsletters if can)

- http://www.smalltimes.com
- http://www.mstnews.de/registration/registration.html
- http://www.yole.fr/pagesAn/Micronews/newslett.asp

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**LabCD**

- **Gamera BioScience (→ now Tecan)**
  - Centrifugal device on a compact disc-like
  - Optical detection using conventional CD player
  - Polycarbonate (PC)

**Biology**

- Centrifugal-driven Microfluidics
  - 10/08 M
  - Electrokinetic-driven Microfluidics
  - 10/14 W
  - Weekly Presentation 3

- Electrowetting-based Microfluidics
  - 10/16 W

- Pressure-driven Microfluidics
  - 10/02 M

- PMDS-Based Integrated Fluidic Circuits
  - 10/04 M

- Centrifugal-driven Microfluidics
  - 10/01 M

**Journals**

- Mid Term
  - 10/15 M

- Microvalve
  - 10/17 W

- Weekly Presentation 5
  - 10/19 W

- Micropump
  - 10/22 W

- Microfluidics Components
  - 10/24 W

- Weekly Presentation 6
  - 10/26 W

- Weekly Presentation 9
  - 10/29 M

- Pressure-driven Microfluidics
  - 10/04 M

- PDMS-Based Integrated Fluidic Circuits
  - 10/06 W

- Weekly Presentation 2
  - 10/08 M

**Useful Online Magazines / Newsletters**

- Mid Term
  - 11/02 F

- Weekly Presentation 7
  - 11/04 F

- Cells in Microfluidics 1
  - 11/05 M

- Weekly Presentation 8
  - 11/07 W

- Weekly Presentation 11
  - 11/09 W

- MicroPCR
  - 11/12 M

- Point-of-Care Test (POCT)
  - 11/14 W

- World-to-Chip Interfacing and Packaging
  - 11/16 W

- Weekly Presentation 6
  - 11/18 W

- Weekly Presentation 9
  - 11/20 W

- Weekly Presentation 11
  - 11/22 W

- Microfluidics Components
  - 11/24 W

- Weekly Presentation 5
  - 11/26 W

- Weekly Presentation 8
  - 11/28 W

- Presentation Workshop 1
  - 12/02 M

- Weekly Presentation 3
  - 12/04 M

- Weekly Presentation 5
  - 12/06 M

- Weekly Presentation 7
  - 12/08 M

- Weekly Presentation 9
  - 12/10 M

- Weekly Presentation 11
  - 12/12 M

- Weekly Presentation 1
  - 12/14 M

- Weekly Presentation 2
  - 12/16 M

- Weekly Presentation 4
  - 12/18 M

- Weekly Presentation 6
  - 12/20 M

- Weekly Presentation 8
  - 12/22 M

- Weekly Presentation 10
  - 12/24 M

- Weekly Presentation 12
  - 12/26 M

**Syllabus**

**EE 428/528 BioMEMS & Lab-on-a-chip**

**Week** | **Lecture** | **Date** | **Title**
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1 | [Syllabus] EE 528/428 BioMEMS & Lab-on-a-chip | 08/27 M | Syllabus / Introduction to MEMS
2 | 08/29 W | Introduction to BioMEMS
3 | 08/31 F | Introduction to NanoBiosensors
4 | 09/03 M | No Class. Labor Day Observed
5 | 09/05 W | MEMS Fabrication 1
6 | 09/07 F | BioMEMS Fabrication 2
7 | 09/09 M | Miniaturization in the Life Sciences 1
8 | 09/11 W | Miniaturization in the Life Sciences 2
9 | 09/12 F | No Class. Fall Recess & Thanksgiving
10 | 09/14 M | BioMEMS Fabrication 3
11 | 09/16 W | Lab Chip (Lab on a Chip)
12 | 09/17 W | Lab Chip (Lab on a Chip)
13 | 09/19 W | No Class. Fall Recess & Thanksgiving
14 | 09/20 M | Lab Chip (Lab on a Chip)
15 | 09/21 F | Lab Chip (Lab on a Chip)
16 | 09/22 W | Lab Chip (Lab on a Chip)
17 | 09/23 F | Lab Chip (Lab on a Chip)
18 | 09/24 M | Lab Chip (Lab on a Chip)
19 | 09/25 W | Lab Chip (Lab on a Chip)
20 | 09/26 F | Lab Chip (Lab on a Chip)
21 | 09/27 F | Lab Chip (Lab on a Chip)
22 | 10/01 M | Lab Chip (Lab on a Chip)
23 | 10/02 F | Lab Chip (Lab on a Chip)
24 | 10/03 W | Lab Chip (Lab on a Chip)
25 | 10/04 F | Lab Chip (Lab on a Chip)
26 | 10/05 F | Lab Chip (Lab on a Chip)
27 | 10/06 F | Lab Chip (Lab on a Chip)
28 | 10/07 F | Lab Chip (Lab on a Chip)
29 | 10/08 F | Lab Chip (Lab on a Chip)
30 | 10/09 F | Lab Chip (Lab on a Chip)
31 | 10/10 F | Lab Chip (Lab on a Chip)
32 | 10/11 F | Lab Chip (Lab on a Chip)
33 | 10/12 F | Lab Chip (Lab on a Chip)