Bio-Microelectromechanical Systems (Bio-MEMS)

GROUP 6

廖宇鴻 陳奕達 陳奐晴
OUTLINE - 1

• Introduction to Bio-MEMS
  • Traditional MEMS & Fabrication
  • Bio-MEMS feature
  • Materials
  • Manipulation
• Bio-MEMS in Biosensor and Diagnostics
• Bio-MEMS in Tissue Engineering and Medical implants
What is a MEMS?

- **Micro-**
  - Components 1~100 μm
- **Electro-**
- **Mechanical**
  - Sensor, Actuator (transducers)
- **System**
  - integrated different elements

Source: http://smartphoneworld.me/mobile-commerce-2-0-where-payments-location-and-advertising-converge/
Ex: MEMS Accelerometer

- Medical applications:
  - CPR compressions depth
  - Step counter
  - Physical training
- Wide Commercial Applications
  - Wii, Car, Smart Phone
- Inertial Measurement Unit
  - Integrated with Gyroscope, Magnetometers

3-Axis Integrated Accelerometer
Source: http://www.mems.ece.ufl.edu/bml/BML_Accelerometerproject.htm
MEMS Process

• Modified IC Fabrication Technology
  • **Deposition** (CVD, PVD...)
  • **Patterning** (Photolithography, e-Beam lithography ...)
  • **Etching** (Wet Etching, Dry Etching...)

• **Bulk/Surface** Micromachining

Source: CMOS-based chemical microsensors, Andreas Hierlemann and Henry Baltes
Bio-MEMS

• Advantages:
  • Sensitivity, Portability, Clinical Convenience

• Diagnostics & Drug delivery
  • Direct interaction with a biological environment

• Usually **Disposable, Large size**

• Conventional Silicon & Glass?
  • Bad Biocompatibility
  • Too expensive

Bio-MEMS Materials

- Polymers – Biocompatible, Cheaper, Stable
  - PDMS (elastomeric: can use soft lithography)
  - SU-8 (photoresist, high aspect ratio)
  - PMMA

SU-8 Photolithography Process
Source: Updates in Advanced Lithography ch5
By Athanasios Milionis, et. al

PDMS fabrication process
Substance (Cell, Protein, etc.) Manipulation

- **Electrokinetics**
  - Electrophoresis
  - Isoelectric focusing (IEF)
  - Dielectrophoresis (DEP)
    - no need to be charged, can work in DC or AC

- **Microfluidics**
OUTLINE - 2

• Introduction to Bio-MEMS

• **Bio-MEMS in Biosensor and Diagnostics**
  • Bio-MEMS as Miniaturized Biosensors
  • Glucose biosensor
  • Bio-MEMS for diagnostics
  • PCR Chip

• Bio-MEMS in Tissue Engineering and Medical implants
Bio-mems History

• In 1967, S. B. Carter reported the use of shadow-evaporated palladium islands for cell attachment.
• In 1985, Unipath Inc. commercialized ClearBlue, a pregnancy test still used today that can be considered the first microfluidic device containing paper and the first microfluidic product to market.
• In 1990, Andreas Manz and H. Michael Widmer from Ciba-Geigy, Switzerland first coined the term micro total analysis system (μTAS) in their seminal paper proposing the use of miniaturized total chemical analysis systems for chemical sensing.
• In 1991, the first oligonucleotide chip was developed.
• In 1993, George M. Whitesides introduced inexpensive PDMS-based microfabrication and this revolutionized the bio-MEMS field.
• In 1998, the first solid microneedles were developed for drug delivery.
• In 1998, the first continuous-flow polymerase chain reaction chip was developed.
• In 1999, the first demonstration of heterogeneous laminar flows for selective treatment of cells in microchannels.
Bio-MEMS as Miniaturized Biosensors

• Biosensors consist of:
  • Bioreceptor
    • antibody–antigen interactions
    • nucleic acid interactions
    • enzymatic interactions
    • cellular interactions
    • interactions using biomimetic materials
  • Transducer
    • mechanical detection
    • electrical detection
    • optical detection.
Kinds of Biosensors

• Micromechanical sensors

• Electrical and electrochemical sensors

• Optical sensors
Physical phenomenon detector → Detect physical change
Chemical phenomenon detector → Detect chemical change

Converter

Transfer Circuit
Voltage Output
Data saver and control interface

Amplifier
Glucose biosensor

• Made only of paper and a water-repellant polymer.
• Detect the levels of two key liver enzymes, AST (aspartate transaminase) and ALT (alanine transaminase).

Bio-MEMS for diagnostics

• Goals:
  • Make high-throughput genome analysis faster and cheaper.
  • Identify activated genes and their sequences.

• Methods:
  • genomic and proteomic microarray

• Application:
  • neonatal screening
  • identifying disease risk
  • predicting therapy efficacy
PCR (polymerase chain reaction) chips

- Amplification of DNA sequences
- Drawback:
  - Take hours to complete
  - Expensive reagent
- Rapid heat transfer and fast mixing
  - Larger surface-to-volume ratio
  - Short diffusion distances
- Portability for point-of-care application
A. Nasopharyngeal swab

B. PCR channel

C. Sample loaded with lysis buffer onto chip

Run chip

PCR heat zones

Answer read using capillary electrophoresis

Temperature (°C)

Concentration

Size
OUTLINE - 3

• Introduction to Bio-MEMS
• Bio-MEMS in Biosensor and Diagnostics

• **Bio-MEMS in Tissue Engineering and Medical implants**
  • Bio-MEMS in Tissue Engineering
  • Lung-on-a-Chip Device
  • Bio-MEMS in Medical Implants and Surgery
<table>
<thead>
<tr>
<th>Bio-MEMS in tissue engineering</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Conventional cell culture technology</strong></td>
</tr>
<tr>
<td>• unable to efficiently allow combinatorial testing of drug candidates, growth factors, neuropeptides, genes, and retroviruses in cell culture medium</td>
</tr>
<tr>
<td>• large number of cells and supplies</td>
</tr>
<tr>
<td>• bulky incubators</td>
</tr>
<tr>
<td>• human labour</td>
</tr>
<tr>
<td><strong>Microfluidic cell cultures</strong></td>
</tr>
<tr>
<td>• Automated</td>
</tr>
<tr>
<td>• lower overall cost</td>
</tr>
<tr>
<td>• higher throughput</td>
</tr>
<tr>
<td>• More quantitative descriptions of single-cell behaviour variability</td>
</tr>
</tbody>
</table>
Lung-on-a-Chip Device

- Simulates the contraction of the diaphragm, which triggers the intrapleural pressure to decrease, leading to an expansion of alveoli.
Bio-MEMS in Medical Implants and Surgery

- **Conventional Transdermal Delivery**
  - limited by the barrier properties of the outermost skin layer, the stratum corneum.

- **Microneedles**
  - deliver a broad range of different low molecular weight drugs, biotherapeutics and vaccines
  - In addition to applications in the skin, microneedles have also been adapted for delivery of bioactives into the eye and into cells.
Bio-MEMS in medical implants and surgery

- As a micron-scale device, a microneedle should be large enough to deliver almost any drug or small particulate formulation, but still be small enough to avoid pain, fear and the need for expert training to administer.

- A microneedle allows precise tissue localization of delivery, such as within the skin, the suprachoroidal space of the eye, and the cell nucleus.
Bio-MEMS in Medical Implants and Surgery

- force sensor array with several sensing points
- Each point (transducer) of the sensor array detects the force applied to the patient's tissue by the grasper.
- This force is translated to proportional pressures that are sent to a joystick in the surgeon’s hand. The surgeon "feels" the change in pressure and adjusts as needed.
Development of Bio-mems

- Precision, Accuracy
- Information digitalize
- Integration
- Efficiency
- Distance Monitor
- Reduce the Power Cost
Reference-1

- CMOS-based chemical microsensors, Andreas Hierlemann and Henry Baltes
- BioMEMS and Biomedical Nanotechnology Volume IV Biomolecular Sensing, Processing and Analysis, Edited by Rashid Bashir and Steve Wereley, Purdue University, West Lafayette, IN ---- CH4, 5, 13
Reference-2

• How to Sort Circulating Tumor Cells Part IV: Electrokinetic Separation
  https://pratted.wordpress.com/2012/11/26/how-to-sort-circulating-
  tumor-cells-part-iv-electrokinetic-separation/

• http://singularityhub.com/2010/06/28/3-ground-breaking-miniature-
  biosensors-that-could-change-world-medicine/

• https://en.wikipedia.org/wiki/Biosensor

• https://www.youtube.com/watch?v=-ew0bn8mGAA
Reference-3

• https://en.m.wikipedia.org/wiki/Lung_on_a_chip
• https://en.m.wikipedia.org/wiki/Bio-MEMS
• http://newsletter.sinica.edu.tw/file/file/77/7745.pdf