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Distinct advantages and novel applications of BioMEMS

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ABSTRACT

With the great progress of production processÿMEMS have applied to a lot of areas in recent yearsÿand today they have become “fundamental devices”ÿwhich are comparable with the IC. In this paperÿwe first discuss the main distinct advantages of MEMS as well as the important differences between MEMS and ICÿthen some latest research progresses on biomedical, environmental and microfluidics applications of MEMS are reviewed. Finally, possible future developments of BioMEMS are prospected.

KEYWORDS

MEMS;
BioMEMS;
IC;
Sensor;
Biomedical;
Environmental;
Microfluidics;
Application.

INTRODUCTION

The acronym MEMS stands for **M**icro **E**lectro **M**echanical **S**ystems with the focal point being the second “M” (mechanical) and thence ultimately the concluding “S”. MEMS are integrated micro-scale systems combining electricalÿoptical or other (magnetic, mechanical, thermal, fluidic, etc.) elements typically fabricated using conventional semiconductor batch processing techniques, namely, MEMS are macro-engineering at microscale, they have two main features: (1) design structures/devices/systems at micro/nano scale, (2) typical microsystems involve multiple physical domains. These systems are designed to interact with the external environment either in a sensing or actuation mode to generate state information or control it at a different scale[1,2]. MEMS are the exotic cousins of semiconductors and integrated circuits (ICs), originally based on silicon wafer fabrication techniques, but adding the dimensions of space, flexion and continuously variable output similar to analog devices. BioMEMS are MEMS that have biological and/or biomedical functions or applications.

Some of the key advantages of MEMS[3,4] are,

- The ability to miniaturize physical interactions to nearly the same degree as IC’s.
- The related ability to reduce the sample-size of measurands.
- The ability to integrate sensing, analysis and re sponse in a miniature package.

MEMS is not a single product or marketÿbut an engineering tool-kit applied to a wide array of markets. Simpler, but by no means trivial, sensing devices (pressure, inertial, thermal,etc.) are finding more diverse applications and finally emerging into consumer markets, such as accelerometer and gyroscopic MEMS devices for the iPhone, Wii and Playstation game controllers. Within these MEMS, we typically see integration, on a single silicon substrate of not just electronic devices as on the chips, but also mechanical elementsÿsensors and actuators. In addition to the commonly present materials in silicon ICs, other materials such as ceramics and most recently carbon nanotube, CNT, arrays are also being incorporated into MEMS. The resulting microsystems have shown, for a variety of applicationsÿunprecedented levels of miniaturization (reliability) and new capabilities[5,11].

MEMS VERSUS IC

MEMS are a class of physically small systems that combine electronic functions with optical, mechanical, thermal and others. MEMS encompass the process-based technologies used to fabricate tiny integrated devices. MEMS are a logical extension of microelectronics and IC technology. As an extension of IC technology, the production of MEMS devices benefits from years of IC manufacturing experience. For instance, technologies such as microlithography, chemical etching, vapor deposition, and electroplating can be used to create the microstructures of MEMS. The products range in size from a few micrometers to millimeters. These devices/systems have the ability to sense the environment, process and analyze information, and respond with a variety of mechanical and electrical actuators on the micro scale, and generate effects on the macro scale.

As a manufacturing technology, MEMS has several distinct advantages[3,4]:

- MEMS technology has the characteristics of interdisciplinary. Its diversity of applications has led to an unparalleled range of devices and synergies across previously unrelated fields, for instance, biomedicine and microelectronics, semiconductor physics and microoptics.
- By MEMS technology and batch fabrication techniques, one can produce components and devices with higher performance and reliability, such products have obvious advantages with small size, light weight and low cost.
- MEMS technology provides the basis for the fabrication of products that cannot be manufactured by other methods. Hence, MEMS have become a universally applicable technology such as IC microchip.

However, three points makes it very different[3,4]:

- MEMS products are usually application specific, resulting in a wide range of very different products.
- The number of MEMS products will be always less than that for semiconductor IC's. A good example is the inkjet printer. The four inkjet nozzles are operated using printed circuit boards with tens of other silicon devices.
- Unlike IC manufacturing, there is no "unit cell" (like the transistor) in MEMS technology. This leads to a more diverse technology base with more development and engineering work. Hence, it is more expensive and more difficult to maintain MEMS technology.

Some important differences between MEMS and IC are summarized in TABLE 1. There is also lack of a stable front-end technology (no Complementary Metal-Oxide Semiconductor) (CMOS) equivalent) in MEMS. Moreover, there is a multidimensional interaction space in MEMS, for instance, there is not only electrical connections but also optical connections. MEMS are a very complicated multidisciplinary field, in which physics, chemistry, materials science, mechanics and engineering play an important role. In addition, the end-product functionality of MEMS is often tightly related to the process used to make it. This can be vividly expressed as "one product, one process". At this point the MEMS are completely different with the IC industry where so many products share a common process.

TABLE 1 : Important differences between MEMS and IC

	MEMS	IC
Unit Cell	No unit cell	Transistor
Front-end Technology	No single stable technology	CMOS
Interaction Space	Multidimensional	Electrical
Basic Disciplines	Multidisciplinary	Physics and engineering
Process or Fabrication Technology	One product, one process	Many products share a common process

Therefore, the current research is evolving toward a "MEMS unit" that is not a single "unit cell" (e.g. transistor in IC), but small, specifically designed, components libraries that could be refined over time to become "standard building blocks" for each MEMS device domain.

MEMS technology is a enchanting and far-reaching area. It has played and will continue to play a very vital role in both science and human society. Especially, it has translated physical properties and material characteristics into structures and devices that can have a large positive impact on people's everyday life.

SOME RECENT APPLICATIONS OF BioMEMS

Until recently, sensors are a major application for MEMS devices. Today, BioMEMS have become the largest and most diverse applications of MEMS devices. Applications for BioMEMS devices exist in clinical medicine, environmental, biological and chemical analysis. Applications from one area often overlap with other areas. Applications can be broadly placed into the following categories[12-16] :

- clinical diagnostics and therapeutics,
- environmental applications,
- food safety, and
- bioprocessing.

MEMS technology is an engineering solution for biomedical problems. From component aspect, BioMEMS is the research of microfabricated devices for biomedical applications. BioMEMS usually contains sensors, actuators, mechanical structures and electronics. Such systems are being developed as diagnostic and analytical devices at diagnostic and analytical devices. BioMEMS is expected to revolutionize the field of medicine. Clinical applications of BioMEMS include both diagnostic (utilizing MEMS sensors and transducers) and therapeutic (such as drug delivery actuators) applications.

In medical field MEMS have the following applications[12]:

- Precise dispensers for small amounts of liquids found in needleless injectors and drug delivery systems.
- Sub-dermal glucose for monitoring monitor glucose levels and delivery of the insulin.
- DNA microarrays for testing of genetic diseases and other biological markers.
- Medical diagnostics for blood analysis, cells counts and urinalysis.
- Polymerase chain reaction(PCR) for DNA replication.

In particular, pressure sensors in biomedical field have the following applications:

- Blood pressure sensors.
- Intracranial pressure sensors.
- Pressure sensors in endoscopes.
- Sensors for infusion pumps.

Main differences between MEMS and BioMEMS are summarized in TABLE 2. BioMEMS are being researched for possible applications in a variety of areas, but have already led to multiple applications in the following areas[13-15]:

TABLE 2 : Comparing MEMS with BioMEMS

MEMS	BioMEMS
Silicon based Material	Biocompatible Material
Electrical & Mechanical interface, integration	Biomolecular & physical parameter (electrical,mechanical,optical) transducer integration
Moving part in micromachining system——active component	Motion medium in passive substrate——microfluidic driving force

- Detection.
- Analysis.
- Diagnosis.
- Therapeutics.
- Drug delivery.
- Cell culture.

BioMEMS encompasses all interfaces and intersections of the life sciences and clinical disciplines with microsystems and nanotechnology. Main related areas are the following[16]:

- Micro and nanotechnology for drug delivery.
- Tissue engineering, harvesting, manipulation.
- Microfluidics and miniaturized total analysis systems.
- Nano-scale imaging, and integrated systems.
- Biomolecular amplification.
- Sequencing of nucleic acids.
- Molecular assembly.
- Proteomics.
- Biosensors.

In the remaining part of this section, we focus on some new applications of BioMEMS in three fields.

BIOMEDICAL APPLICATIONS OF BioMEMS

BioMEMS sensor placement depends on the device and its application. A sensor can be[12,16]

- topical (applied to skin or placed in the mouth)
- externally connected (*in vitro* or external with *in vivo* or internal device)
- implanted devices (totally *in vivo*)

Topical sensors

They are applied to skin or placed in the mouth. One familiar device is the thermometer used for measuring body temperature. Thick-film disposable thermistors and infrared ear thermometers have largely replaced the mercury thermometer.

Externally connected sensors

They contain both an *in vivo* part and an external part. An example of such a device is the cochlear implant. These devices contain a microphone, a speech processor, a transmitter and receiver/stimulator, and an electrode array. The implant does not restore normal hearing, but it does give a deaf person a useful representation of his environment and helps him understand speech. Another example is the glucometer. These devices have an implanted glucose sensor that communicates with external components, such as a computer and micropump.

Implanted devices

This area of BioMEMS has numerous possibilities, but few of these devices have made it to market. Implantable BioMEMS that have been on the market for years are defibrillators and pacemakers. Other emerging applications for implantable devices include neural implants and spinal cord stimulators to treat intractable pain and spasticity. The implantable microelectrodes for neural applications are based on thin-film polymer foils with embedded microelectrodes for both recording and stimulation. Implantable pressure sensors are being tested that can be used in cardiovascular monitoring, glaucoma monitoring, and monitoring of intracranial pressure.

ENVIRONMENTAL APPLICATIONS OF BioMEMS

They are a growing part of the BioMEMS field. For example, a gene from a firefly is added to mammalian cells so that the cells glow when exposed to the toxin dioxin. As the amount of dioxin increases, the cells glow more brightly. This assay provides a quick and simple test for dioxin. The figure shows how the firefly luciferase reporter gene luminesces to test for the presence of dioxin in environmental samples. Another application uses cultured mammalian cells to predict lethal toxicity of chemicals in humans. The initial application used a micropipette tip to hold the cells. This assay can be adapted to a MEMS device[17].

Both environmental scientists and homeland security personnel are interested in the rapid detection and identification of bacteria and pathogens. Researchers have developed microsystems which concentrate components specific to certain pathogens, then release these to a micro gas chromatography unit so that the components can be separated. The separate components are passed to a surface acoustic wave sensor array (SAW) for component identification. A working example of such a system was developed by Sandia National Labs. This device will provide portable, rapid detection and early warning of the presence of pathogens in air or water.

MICROFLUIDICS AND BioMEMS APPLICATIONS

Another MEMS platform used in diagnostic BioMEMS makes use of microfluidic components. Integrated fluidic microchips allow separations, chemical reactions, and calibration-free analytical measurements to be directly performed in very small quantities of complex samples such as whole blood and contaminated environmental samples. This technology lends itself to applications such as clinical diagnostics (including tumor marker screening) and environmental sensing in remote locations. Lab-on-a-Chip (LOC) systems enable sample handling, mixing, dilution, electrophoresis and chromatographic separation, staining and detection on single, micro-integrated systems[18].

BioLOC is developing a lab on a disk to perform ELISAs (Enzyme-linked Immunosorbent Assays) on a polymeric compact disk. ELISAs use antibodies as biosensors. They have been widely used for detection and quantification of biological agents (mainly proteins and polypeptides). An ELISA's high selectivity and sensitivity draw great interests in clinical, food safety, and environmental applications.

FUTURE DEVELOPMENTS OF BioMEMS

MEMS products have successfully made the complete transition into the consumer space. Today, literally billions of MEMS devices are manufactured every year for a wide variety of consumer applications, and MEMS developers have begun to turn their attention more and more to BioMEMS. Today, there are precious few successful BioMEMS devices on the market.

In the area of implantable devices, CardioMEMS has an implantable pressure sensor for monitoring aneurysms. Cochlear implants are routine, allowing deaf people to hear. In the area of microfluidics, companies such as Caliper and Cepheid manufacture chips and plastic fluidic components for biochemical analysis and diagnostics. However, there are many much more important and much more impactful devices on the horizon, such as retinal implants, health monitoring systems, protein detection arrays, and continuous, implantable chemical sensing. Over the next 10 years, this next generation of BioMEMS innovations will transform medicine as we currently practice it and understand it[12-17].

In addition, national security is of increased importance related to the growing fear from terrorist attacks and outbreaks of infectious human or animal diseases. This drives a need for small multi parameter instruments to test water, air, blood and so on for microbiological threats[19].

On the other hand, there is a tendency to develop more flexible and cheaper production technologies. It is expected that this tendency will be driven by the production research into typical low cost, large surface area devices (for instance, solar cell, displays, wearable electronics) and disposable diagnostics devices.

Finally, a huge number of products will originate from the large amount of nanotechnology research investments, in many cases MEMS will act as an interface between the nano and human size world[7,9,11,14].

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