**Southwest Center for Microsystems Education (SCME)**
**University of New Mexico**

# Diagnostic BioMEMS Overview Learning Module

This learning module contains three (3) units:
Primary Knowledge (PK) – reading material
Activity: Diagnostic BioMEMS Research
Final Assessment

*BioMEMS (biomedical MicroElectroMechanical Systems)*

*Diagnostic bioMEMS have been increasing in number every year. This learning module provides an introduction to some of the diagnostics tools currently in use and possibilities for future bioMEMS. A research activity provides the opportunity for you to do your own research of a specific diagnostic MEMS that is of interest to you.*

Target audiences: High School, Community College, University

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Website: www.scme-nm.org

# Diagnostic BioMEMS Overview
## Primary Knowledge (PK)
## Participant Guide

**Description and Estimated Time to Complete**

BioMEMS (biomedical MicroElectroMechanical Systems)

Diagnostic bioMEMS have been increasing in number every year. This learning module provides an introduction to some of the diagnostics tools currently in use and possibilities for future bioMEMS. A research activity provides the opportunity for you to do your own research of a specific diagnostic MEMS that is of interest to you. In this unit you explore areas in diagnostic medicine that are currently impacted or will be impacted by the introduction of bioMEMS. You study the advantages and disadvantages of adapting existing and developing new diagnostic laboratory tests for MEMS technology.

Estimated Time to Complete

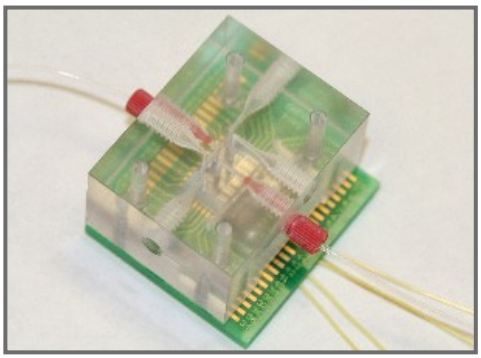
Allow at least 20 minutes to review this unit.

**Introduction**

Medical diagnostic techniques have become increasingly sophisticated. Wouldn't it be nice to have a medical device that could identify clues within our bodies to tell us what our ailments might be? If you have ever watched Star Trek, you can imagine what such a device would be like – a handheld optical or x-ray scanner used externally to "see" what is happening inside. The possibility of such a device is becoming closer to reality and already exists in certain forms.

One such device is a miniaturized, portable version of a blood-analysis machine used by astronauts in the International Space Station. On such long missions, astronauts need the ability to analyze blood samples in real-time to diagnose infection, allergies, anemia or deficiencies in the immune system. This device, a type of lab-on-a-chip (LOC), is about the size of a cell phone or TV remote. The LOC in used today, called the portable clinical blood analyzer (PCBA), requires a tiny drop of blood (as small as a 65 microliter sample) and provides results in 120 seconds. The blood analysis includes glucose level, pH, potassium, sodium and more.[1]

The image right shows one of the original LOC prototype tested on 2006. The current LOC, the PCBA, is a hand-held device with the LOC, a display screen, on board microprocessor and storage for up to 50 test records. The unit "measures 3.5 cm x 6.5 cm x 18 cm and weights 0.54 kg".[1]



*Lab-on-a-chip – Blood Analysis [Photo courtesy of Y. Tai, California Institute of Technology]*

There are several other bioMEMS devices that perform "science fiction" like diagnostics awaiting medical approval. However, to diagnose particular diseases or conditions, specific biological markers (e.g., antibodies, proteins, genes) need to be identified. Scientists are still in the process of deciphering the biomarker landscape associated with specific disease states.

There are many reasons why the scientific, health, and defense communities are excited about diagnostic bioMEMS technology. BioMEMS tests are cost effective, easier to administer, and can possibly be used for *in vitro (external)* or *in vivo (internal)* monitoring. *In vitro* and/or *in vivo* monitoring means that people who are susceptible to a heart attack or who have had a heart attack can be monitored 24/7 for both the physical and chemical signs that indicate that an attack is preeminent. The graphic illustrates an ECG patch (electrocardiogram) that a patient wears for continuous monitoring of his heart rhythms.

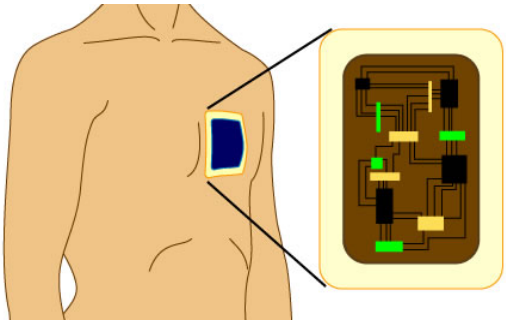



*Illustration of a MEMS electrocardiogram (ECG) patch monitor. Such a device is being developed by Belgium's IMEC for monitoring a patient's arrhythmias all day and night.*

The less obvious advantages and disadvantages are the physics of microfluidic technology. Medical diagnostics can require the handling of liquid samples. This requires bioMEMS devices to be able to move microliter amounts of liquid samples such as blood and urine. Such a requirement challenges microfluidic technology.

The areas of diagnostic medicine that also being imparted are clinical chemistry, patient examinations and monitoring, and medical imaging. BioMEMS in these areas are having a positive impact, particularly in underdeveloped countries that presently do not have the expensive diagnostic medical technology of developed countries. The versatility and portability of bioMEMS allow for the presence of medical devices in places where none have gone before.

This unit discusses the advantages and disadvantages of adapting existing diagnostic laboratory tests and materials to MEMS, the areas in medicine that are being impacted and how, and examples that are being tested.

**Objectives**

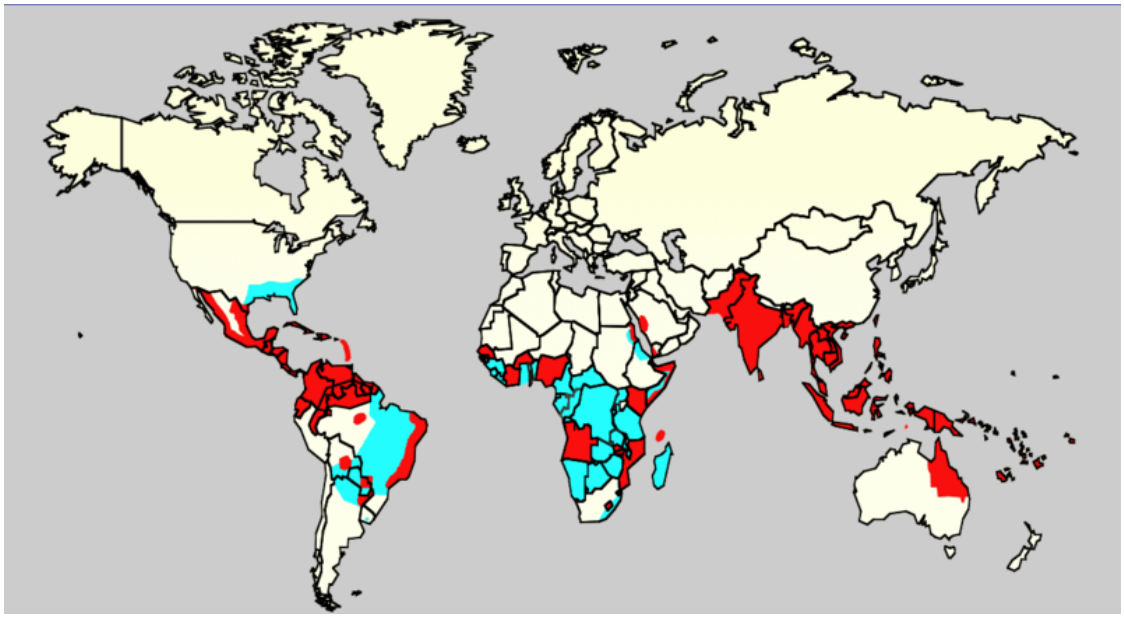
- Discuss examples of at least two diagnostic bioMEMS medical devices currently in use.
- Describe three main areas in medical diagnostics that have been impacted by bioMEMS technology.

**Key Terms** *(These terms are defined in the glossary at the end of this unit.)*

Assay
Biochips
Biomarkers
Capillary Force
Clinical chemistry
In vitro
In vivo
Lab-on-the-chip (LOC
Medical imaging
Microfluidic
Micro-total-analysis systems (μTAS)
Molecular Diagnostics
Multiplexing
Patient examination
Patient monitoring
Pharmacogenetics
Point-of-care
Quantum Dots
Quantum Effect
Receptor
Serum

**Diagnosing Dengue Fever**

An example of a bioMEMS that is currently being tested is a microchip assay that detects Dengue Fever, an acute illness that causes fever, rash, headaches, and muscle and joint pains. Dengue Fever is caused by one of four viruses that are transmitted by mosquitoes.[2] Presently; fifty to 100 million people worldwide are affected each year by Dengue Fever. The map shows active (cyan) and recent (red) cases as of 2006. [3]



Distribution of Dengue Fever in the world as of 2006.
*[Map produced by and courtesy of the Agricultural Research Service of the US Department of Agriculture]*

*Updates of Dengue cases*

*August 2017 – "144,052 suspected cases have been reported to the Epidemiology Unit" in Sri Lanka alone.*[14]

*World Health Organization (WHO) data:*

*2015: over 3.5 million reported cases in the Americas, SE Asia, and Western Pacific with 2.35 million of those cases being in the America alone.*
*2016: 2.38 million reported cases in the Americas with Brazil alone reporting about 1.5 million (3 times higher than 2014).*
*2017 (as of epidemiological week 11): 50,172 cases reported by the Region of Americas (a reduction compared to previous years)*
*"An estimated 500,000 people with severe dengue require hospitalization each year, and about 2.5% of those affected die."*[16]

There are several problems associated with the diagnosis and treatment of Dengue Fever.

- Early diagnosis is very difficult.
- Once diagnosed, there are no good drugs for treatment, especially if the disease has progressed.
- The mortality rate is high.
- If someone is immune to one type (virus) of Dengue Fever, he/she is not immune to the other three types of Dengue Fever.
- Programs to eradicate the mosquito responsible for transmitting the virus have not been effective (e.g., Governments spray the outside areas but the mosquito is found inside buildings).

In theory, as with many diseases, early diagnosis and treatment would decrease the mortality rate.

In 2006 scientists developed a test that identifies the four dengue viruses. Artificial receptors for a viral protein that is on the outside of the virus were made by polymerizing monomers into polymers on a microchip. These polymers were then cross-linked in the presence of that viral protein, thus forming a "plastic-type impression" of one of the virus binding sites. The microchip has been tested with serum samples from Dengue patients. The tests were positive for 18 of 21 patients with the disease, and 0 out of 16 for individuals without the disease. This diagnostic microchip is still in the process of being tested as part of the approval process.[4] You can review this process more in depth at this link: http://bit.ly/2vdQ9PD

In 2014 the results of a study were published that showed positive results of using a colorimetric ELISA (Enzyme-Linked Immunosorbent Assay) for a point-of-care (POC) dengue detection system on a LOC compact disc. This ELISA was found to have "clinical sensitivity of 95.2% and specificity of 100%". The POC has an integrated platform that allows minimal input from the user while being able to display results via a smartphone application, making the results easy to read and interpret. It's "portable, low cost, and can easily be manufactured" making it ideal for POC diagnosis.[15]

**Advantages and Disadvantages of Diagnostic bioMEMS**

Diagnostic bioMEMS have several advantages over macro-sized devices, but also a few disadvantages. Following are advantages of bioMEMS devices in diagnostic testing:

1. Due to smaller volumes, reaction concentrations and temperatures are quickly achieved, resulting in a faster test result.
2. Tests are more sensitive and specific since the detector is the size of the target species.
3. Test volumes are smaller so cost of reagents is decreased and the environmental impact is smaller (less waste).
4. Microdevices are amenable to point-of-care, either in vitro or in vivo.
5. MEMS technology allows for miniaturization and portability.
6. BioMEMS are a safer platform for chemical, radioactive, or biological studies because of large integration of functionality and low stored fluid volumes.
7. BioMEMS are amenable to multiplexing and massive parallelization due to compactness.
8. Depending on chip design, there is the possibility of lower fabrication costs, allowing for cost-effective disposable chips, fabricated in mass production.

Following are disadvantages of bioMEMS devices in diagnostic testing:

1. MEMS technology for biomedical applications is considered a novel technology and has not developed to the point of current diagnostics technologies, especially when human interface or device implantation is required.
2. Detection principles may not scale down well, leading to low signal to noise ratios.
3. Physical and chemical effects, like quantum or capillary forces, can create problems at the molecular level as a result of the small size becoming a dominant force.

Let's take a look at more bioMEMS diagnostic tools.

**Clinical Chemistry**

Clinical chemistry and molecular diagnostics are the largest users of first generation bioMEMS devices, particularly high-throughput microfluidic devices. The basis for this is point-of-care (POC) or in the office testing by microfluidic-based micro-total-analysis systems (μTAS) and Lab-on-a-chip (LOC) devices. Even though μTAS and LOC terminology is used interchangeably there are differences.

- μTAS are usually hybrids of many biochips, integrated electronics, and external supports for chemical analysis that perform all or part of a chemical analysis.
- A LOC device refers more specifically to a microfluidic chip or other device that performs a well-defined task or a series of tasks on a single chip.

The photo *(right)* shows a "lab on a chip" that was designed to sequence large genomes quickly and cost-effectively. Researchers predicted that this work ultimately could provide important medical benefits, allowing preventative and therapeutic care tailored to each patient's genome.[5]

In general, biochips include LOC devices and microarray devices. Microarray devices are mainly being used commercially for drug discovery and development.

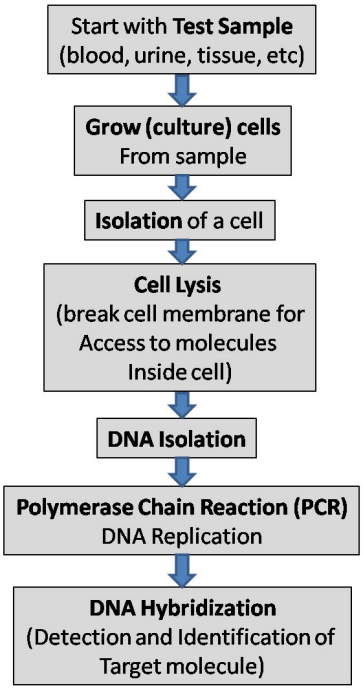
*Lab-on-a-Chip (LOC)*
*Printed with permission. From*
*Blazej,R.G.,Kumaresan,P. and Mathies, R.A.*
*PNAS 103,7240-7245 (2006).*

## µTAS Diagnostic Testing

The panel of reactions shown in the flowchart is a basic design for a µTAS device that could be used to detect genetic diseases, pathogens in the blood such as the HIV virus, or genetically determine what drugs a person should take for cancer treatment (i.e., pharmacogenetics).

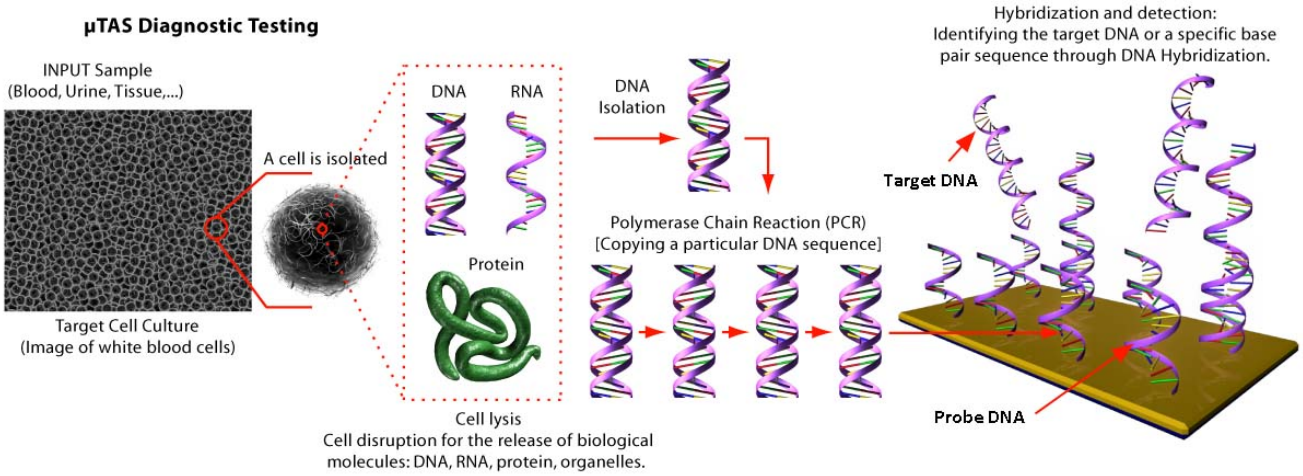
How would the test work? Let's take for example a woman who has developed blood clots after taking estrogen for two months for menopausal symptoms. It is suspected that she has a genetic defect known as Factor V Leiden. This defect increases a person's tendency to develop blood clots and is the most common hereditary blood coagulation disorder in the United States. It is present in 2-7% of the Caucasian population and 1.25% of the African American population. This genetic defect is caused by a single base change in the DNA making the coagulation Factor V more resistant to activated protein C. This increases the predisposition to blood clot formation.[6]

*(Refer to the SCME Learning Modules on DNA and DNA to Protein)*



For the μTAS test, a blood sample drawn from the woman could be injected right into the device. The following is an example of a diagnostic flow for the μTAS test. *(Refer to diagram below)*

1. The white blood cells are targeted and isolated.
2. Individual cells are lysed (broken up).
3. The DNA inside the cell is isolated.
4. The Polymerase Chain Reaction (PCR) reagents specific for this defect are added.
5. If the defect is present, the DNA containing this defect is amplified.
6. Specific labeled probes for that DNA are added.
7. If the DNA is present, they bind (hybridize) to the DNA probes.
8. If the probes bind, their label is detected.




**Polymerase Chain Reaction Lab-on-a-chip (PCR LOC)**

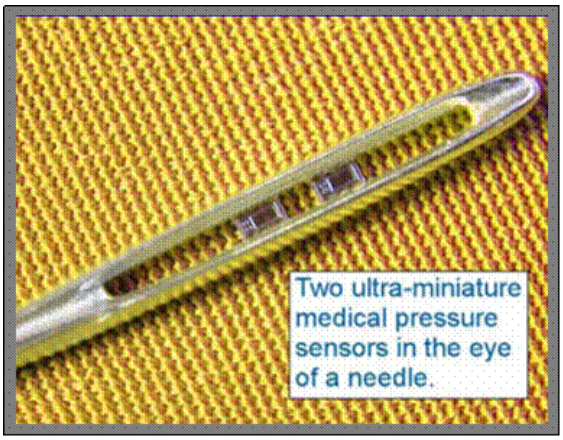
A LOC performs the Polymerase Chain Reaction (the amplification of DNA) step in the μTAS diagnostic. All of the steps described before and after PCR are normally done by the lab technician; however, MEMS technology has now enabled the development of cell culture devices as well as biochips for DNA hybridization. The highly complex systems found in present day clinical labs, including molecular diagnostics, are excellent candidates for μTAS devices.

*(For more information on DNA and clinical laboratory tests, please review the SCME DNA Overview and Clinical Laboratory and BioMEMS Learning Modules, respectively.)*

**Patient Examinations and Monitoring**

Several bioMEMS have been developed and proven to be effective for the following sensing and/or measurement applications:

- Pressure in arteries
- Spinal fluid
- Brain cavity
- Body temperature
- Force generated by muscles
- Skin tension
- DNA factors and biomarkers (i.e. if and when validated)
- Glucose
- Ions
- Gases (i.e. oxygen and carbon dioxide)

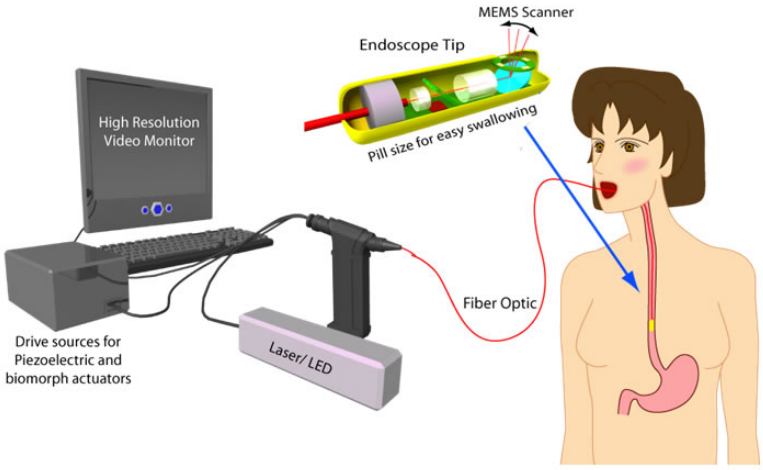



**Integrated Sensing Systems Sensors**

*[Image courtesy of ISSYS]*

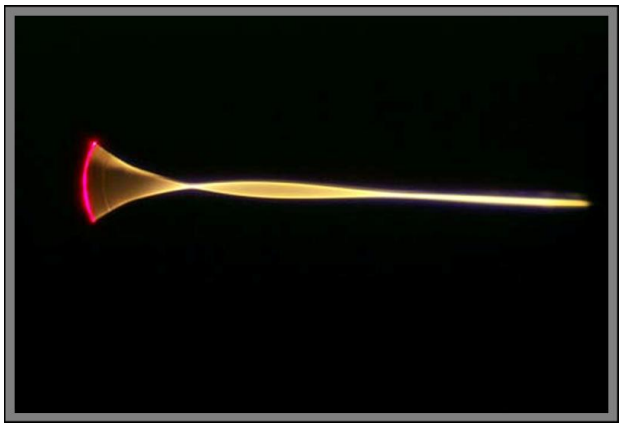
Shown in the figure are 2 early prototype Integrated Sensing Systems, Inc.'s (ISSYS) implantable sensors. These sensors are wireless, self-powered, and small enough for two of them to fit inside the eye of a needle. In 2005 animal studies showed that these sensors could measure cardiac output and intracranial pressure, indicating the ability to detect and monitor congestive heart failure and diseased heart valve function. Since these studies, ISSYS was awarded a patent in 2010 for "implantable sensors for non-invasive monitoring of biological pressures for the effective measurement of chronic diseases" and then in 2013, another patent for "wireless, batteryless, implantable hemodynamic sensors that are anchored within the heart" to measure cardio parameters such as pressure and provide disease management for patient with cardiovascular disease.[7] In 2014 CardioMEMS was given FDA approval for an implantable wireless device that measures pulmonary artery pressure. With such approval, such devices may well be on their way to becoming common standard diagnostic tools for cardiac patients.

**Medical Imaging - Single Fibered Endoscope System**




MEMS technology in the area of medical imaging includes the use of the new nanodyes, such as quantum dots. It also includes optical measurement devices such as a micro-optical scanner. A diagram illustrating such a scanner is shown in the figure. Notice that the endoscopy imaging device is a small pill-sized device connected to a fiber optic cable. For patients undergoing an endoscopy, this little pill is much easier to swallow! This device contains a micro-optical scanner.

The micro-optical scanner is a MEMS device that includes optics and electronics. The MEMS is placed inside the 1 mm diameter tip of a flexible endoscope. The fiber scanner is driven in one dimension with a piezoelectric actuator, producing a line scan. The microscope image of the micro-optical fiber scanner and its one-dimensional scan is shown below. The diameter of the fiber tip, where red laser light is exiting, is approx. 10 microns.



By knowing and controlling the fiber position and acquiring backscattered intensity with a photodetector, an image is acquired. The result of this research will allow doctors to see within body cavities never before accessible (such as sinus cavities), and be able to leave this less-invasive scope within the body for long-term dynamic monitoring of chronic diseases (such as chronic sinusitis).[8]

Micro-optical fiber scanning system. *"Fiber is vibrating at 40.4 KHz with an angular displacement of 80 degrees. Single mode fiber with a cladding diameter of 125 micron was used.*[8]

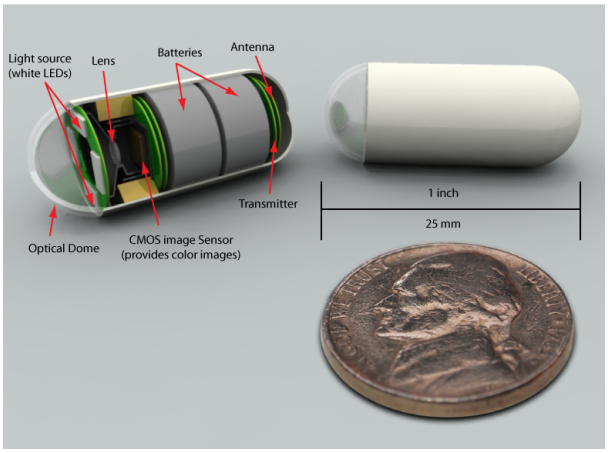
*[Image Courtesy of Eric Seibel and Mark Fauver]*

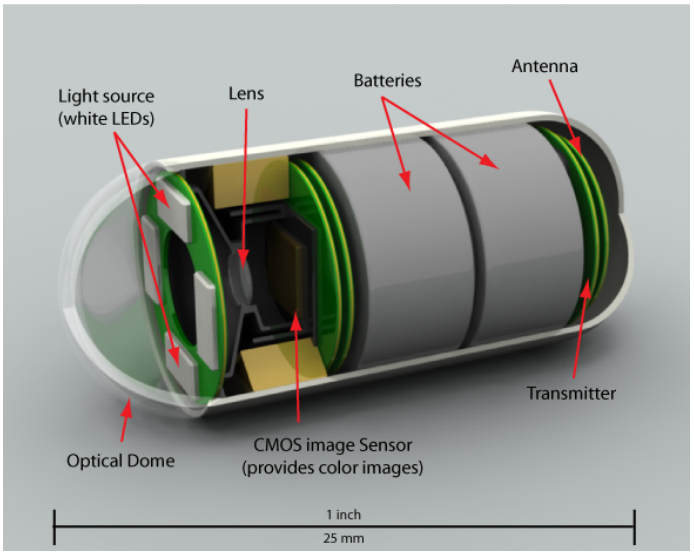
*Sample Micro-Optical Scanner Image*

A sample image formed with the macro-sized version of the fiber optic scanner is seen to the right. A single micromachined optical fiber, optimized for its dynamic properties to maximize scan frequency, tip displacement, and field of view is responsible for this picture. The letters in this image are 2.5 mm high and the field of view is 5.9 mm x 4.4 mm. *[Image courtesy of Eric Seibel, PhD]*[9]

**Pill Cam for Endoscopies/Colonoscopies**

Today this technology has continued to advance to the benefit of the patient. When the physician needs to see inside the stomach and particularly the small intestine, the "pill" is no longer attached to the fiber optic cable. The patient swallows the pill, and after the pill has traveled through the entire digestive system, recording and transmitting video, it is naturally discharged and flushed. As illustrated below, the length of the "pill" or pill cam is about the diameter of a nickel. The pill cam's diameter is a little larger than a calcium tablet.




Inside the pill cam is a light source, imaging processor, and lens that produce high definition images. The images are tranmitted via the transmitter/antenna to a receiver on the patient's belt. The pill cam contains a small battery that supplies power to the internal components.

The process of using the pill cam involves a brief visit in the early morning to the doctor's office. The patient swallows the pill and then is given a receiver that is about the size of a cell phone. The patient attaches the receiver to a belt or piece of clothing and goes home. At the end of the day, the patient returns the receiver to the doctor's office. The video is downloaded into a program that scans the video for any anomalies. Those sections of the video are marked for the physician to view and determine if there is a potential problem. This project is a great example of being able to go where no one has gone before.

## Summary

Based on the ability to detect and quantify changes in cells and tissues as a result of disease, the main areas in medical diagnostics which have been impacted by bioMEMS technology are

- clinical chemistry,
- molecular diagnostics,
- patient examination and monitoring, and
- medical imaging

Several biomedical principles used for diagnostic purposes have enabled the development of bioMEMS diagnostic devices. For example, each of the following produces a biological molecule (biomarker) or physical change that can be detected:

- Pathogenic agents such as bacteria and viruses produce detectable chemicals.
- Certain medical conditions produce specific antibodies or proteins (e.g., Pregnancy produces a protein that can be detected in the urine).
- DNA replication produces mRNA and proteins.
- Cancer, infections and injuries can create physical changes in cells or tissues that can be seen and measured.

As new diagnostic bioMEMS are being realized, current developments are already in use. Below are a few examples:

- A PCR, which has been adapted to bioMEMS technology, is being used to detect the genetic defect, Factor V Leiden.
- The viruses that cause Dengue Fever or HIV can be detected using either a μTAS or LOC.
- Cancerous cells or tissues in the colon can be visualized (i.e., endoscopy) using a micro-optical scanner.
- Cells and tissues infected with viruses and bacteria, such as in the sinuses, can be visually identified using the same micro-optical scanner.
- A pressure sensor can measure a change in blood flow through a diseased heart valve as well as intracranial pressure in hydrocephalus patients.

## Food For Thought

1. What are the advantages and disadvantages of developing diagnostic bioMEMS?

2. Why is the development and implementation of diagnostic bioMEMS important to developing countries?

3. What are some areas of diagnostic medicine that could benefit from diagnostic MEMS?

## References


[1] "Portable Clinical Blood Analyzer – i-STAT (PCBA)" ISS Science for Everyone. NASA. International Space Station. July 19 2017. https://go.nasa.gov/2vw1Ood

[2] Dengue Fever. MedicineNet.com. http://www.medicinenet.com/dengue_fever/article.htm

[3] Map of the Distribution of Dengue Fever in the world as of 2006. Map produced by and courtesy of the Agricultural Research Service of the US Department of Agriculture (Public domain), Source: Slide #8 of a presentation by Gary G. Clark, PhD. Entitled "Dengue: An emerging arbovira"

[4] " Artificial Receptors in Serologic Tests for the Early Diagnosis of Dengue Virus Infection". Dar-Fu Tai. Clinical Chemistry 52: 1486-1491, 2006. http://www.clinchem.org/cgi/content/full/52/8/1486

[5] "The beauty of the pursuit of knowledge as seen in this "lab on a chip"." UC Berkeley News. January 2, 2007. http://berkeley.edu/news/media/releases/2007/01/02_nanoimage.shtml

[6] "Detection of factor V Leiden from a drop of blood by PCR-SSCP." Corral, J., Iniesta, J.A., Gonzalez-Conejero, R., Vicente. V, Thrombosis and Haemostasis 76, 735-737, 1996.

[7] "First in-human implantation of an ISSYS wireless implantable hemodynamic monitor". MEDTECH. I-Micronews. Yole Developpement. June 6 2014. http://bit.ly/2wFvRyF

[8] Single fiber flexible endoscope: general design for small size resolution, and wide field of view. Seibel, E. J., Smithwick, Q.Y.J. Brown, C.M. and Reinhall, P.G. (2001) Proceedings of the SPIE, Biomonitoring and Endoscopy Technologies, 4158 29-39.

[9] (Figure 4B). Lasers in Surgery and Medicine 30:177-183(2002). Seibel & Smithwick.

[10] "Microfabrication." Arizona State University. (Microfabrication and soft-lithography capabilities used in thin and thick film biosensors and micro total analysis systems ( μTAS). 2004.

[11] Artificial Receptors in Serologic Tests for the Early Diagnosis of Dengue Virus Infection by Tai, Dar-Fu, Chug-Yin Lin, Tzong-Zeng Wu, Jyh-Hsiung, and Pei-Yun Shu Clinical Chemistry 52: 1486-1491, 2006.

[12] Microfluidic diagnostic technologies for global public health by Yager, Paul, Thayne Edwards, Elain Fu, Kristen Helton, Kjell Nelson, Milton R. Tam, and Bernhard H Wiegl Nature 442 412-418 (27 July 2006).

[13] Continuous Subcontaneous Glucose Monitoring in Children with Type 1 Diabetes by Chase, Peter H MD, Laura M. Kim BS. Susie L Owen RN, Todd A MacKenzie PhD, Georgeanna J. Klingensmith MD, Robert Murtfeldt, and Satish K. garg MD Pediatrics vol. 107 No.2 Feb 2001 pp. 222-226.

[14] "Dengue Update". Epidemiology Unit. Ministry of Health. Sri Lanka. http://bit.ly/2qE2Hf6

[15] "A Colorimetric Enzyme-Linked Immunosorbent Assay (ELISA) Detection Platform for a Point-of-Care Dengue Detection System on a Lab-on-Compact-Disc.". Aung Thiha. Fatimah Ibrahim. Faculty of Engineering. University of Malaya. Sensors 2015, 15, 11431-11441.

[16] "Dengue and severe dengue". Fact Sheet. World Health Organization. April 2017.

[17] "Implantable wireless Pressure Sensors for Treatment of Congestive Heart Failure." Sensors & Transducers e-Digest. Vol 61, Issue 11, November 2005: Product News. http://www.sensorsportal.com/HTML/DIGEST/november_05/Pressure_sensor.htm

[18] Titan WIHM. Titan Wireless Implantble Hemodynamic Monitor. ISS Integrated Sensing Systems. MEMS Implantable Device. http://mems-iss.com/titan-wihm/

**Related SCME Learning Modules**

- Chemical Sensor Arrays (CSA)
- DNA Overview
- DNA to Protein
- Clinical Laboratory Techniques and bioMEMS

**Glossary of Key Terms**

Biochips: Micro-electronic devices that detect, analyze, process, and deliver materials.

Biomarkers: Chemical indicators of a biological state. Changes in the biomarker landscape, both identity and amount, should correlate with a risk or progression of a disease, or with the susceptibility of the disease to a given treatment.

BioMEMS' effect on patient examination: Can be done in the doctor's office or over the Internet utilizing point-of-care devices (in vitro or in vivo) while communicating with a healthcare worker.

BioMEMS effect on patient monitoring: Can be done in a hospital or outside of a hospital with point-of-care devices (in vitro or in vivo) that continually provide information concerning the state of the patient.

Capillary force: Where the intermolecular forces between a solid and a liquid are greater than the intermolecular forces between liquid molecules. This results in a concave meniscus where the liquid is in contact with the solid. It is also responsible for the drawing up of a liquid in a narrow tube.

Clinical chemistry: The area of pathology generally associated with the testing of bodily fluids.

In vitro: Outside of the body.

In vivo: Inside of the body.

Lab-on-the-chip (LOC): Subsets of μTAS. LOC refers more specifically to a microfluidic chip or other device that performs a well-defined analytical task.

Medical imaging: The techniques and processes used to create images of the human body for clinical purposes.

Microfluidic: The movement of very small volumes (micro to picoliter range).

Micro-total-analysis systems (μTAS): Miniaturized devices that perform all or part of a biochemical analysis. They may be hybrids of multiple chips, integrated electronics, and external supports.

Multiplexing: Testing more than one sample at a time or testing more than one parameter at a time.

Pharmacogenetics: The convergence of pharmacology and genetics dealing with a genetically determined response to drugs.

Point-of-care: When the patient is diagnosed, where the patient is located, which is not necessarily in the doctor's office or hospital.

Quantum Dots (QDs): Spherical/cubical nanocrystals which emit a spectrum of colors when illuminated with ultraviolet light. They possess quantum characteristics, optically and electronically. They are1000x brighter than conventional dyes and do not bleach out like conventional dyes presently being used in basic research and medicine. They are nontoxic and can be covalently linked to biological molecules without affecting the activity of the molecules. They are useful in biological imaging in medical diagnostics and drug discovery.

Quantum Effect: At a 100 nanometers and below, atoms and molecules no longer obey the laws of classical physics and instead exhibit what is known as the "quantum effect" (e.g. gravity has a negligible effect at this scale compared to the normally weak van der Waals forces, which become a dominant force at this small level.)

Receptor: A molecule that receives and responds to a neurotransmitter, hormone, antibody, or other substance.

Serum: The straw-colored, blood plasma from which clotting factors have been removed.

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