



AMERICAN JOURNAL OF PHARMTECH RESEARCH

Journal home page: <http://www.ajptr.com/>

BioMEM's As Drug Delivery Systems- A Review

Ch. Sai Akshitha*, P. Tripura Sundari

*Department of Pharmaceutics, RBVRR College of pharmacy Affiliated to Osmania University,
Barkatpura, Hyderabad-500027, India.*

ABSTRACT

BioMEM's are the biologically oriented MicroElectro Mechanical systems which are currently giving good market in the medical field and also attracting many researches for its development. These devices are defined as "devices or systems, constructed using techniques inspired from micro scale and nanoscale fabrication that are mainly for processing, delivery, analysis of biological and chemical entities. These BioMEM's are having advantages over disadvantages. BioMEM's are capable of analyzing biochemical liquid sample like solution of metabolites, macromolecules, proteins, nucleic acid cells and viruses. And there is currently a large amount of BioMems work in the arena of drug delivery systems using micro fabrication technique. BioMems are under research in the field of drug delivery which helps in the future for the many dreadful diseases. This review mainly gives an information about the different applications of BioMEM's in the medical field.

Keywords: BioMEM's, Drug delivery System

*Corresponding Author Email: akshithacheruku22@gmail.com

Received 20 September 2019, Accepted 29 September 2019

Please cite this article as: Sai Ch *et al.*, BioMEM's As Drug Delivery Systems- A Review. American Journal of PharmTech Research 2019.

INTRODUCTION

BioMEM's are the micro-sized components having a sensor, transducer, actuator and electronic devices. In the case of pacemaker sensor that is present in the BioMEM's is used to sense (i.e. accelerometer). The patient's activity can be checked by the control circuitry present in BioMEM's and quickly stimulate one or more electrodes connected to the heart muscle¹. The stimulation of the electrode causes the heart beat faster and if there is any change in the patient's activity it will slow down the heart beat. BioMEM's pressure sensors are found in the blood pressure monitors, infusion pumps, catheters, and intracranial probes. Some of the BioMEM's used in the medical are unique in the sense that they incorporate biological molecules as an integral part of the device

BioMEMS is a subset of microelectromechanical systems (MEMS) and micro technology.

- BioMEM's used in medical field called BioMEMS. In general MEMS that are found in the smart phones are also found in the pacemakers. This microsystem technology provide a good market of about 6.6 billion dollars by 2018.
- There are two types of BioMEM's like biomedical mems and biotechnology mems. This biomedical MEMS deals within the body like biotelemetry, drug delivery, biosensors and other physical sensors where as biotechnology mems deals in-vitro like gene sequencing, pharmacogenomics, diagnostics².

Structure:

BioMEM's devices can have one dimension of submicron range of 100-200nm and the other dimensions of upto several millimeters. In case of the application they are good in the development of nanotechnology and the other end they plays an important role in the development of the larger devices in the medical field. These systems operate as either an open ended containing (sensor or actuator) system or a closed- loop system (auto regulation). There are also some implanted devices that are present in the current market such as fiber optic sensors that gives information via light from the different parts of the body to the central medical device and these BioMEM's can be used to operate in-vivo and in-vitro (inside or outside of the body) with an external power source³.

Fabrication of BioMEMS:

There are four processes for the fabrication of BioMEMS. The first photolithography or soft lithography which transfers a pattern a material. The second is thin film growth/ deposition in which film are grown and they are deposited on the substrate. Etching, the third kind of process, creates features by selectively removing materials (either thin films or substrate) in defined

patterns. The final kind of process is bonding where two substrates (often structured and with thin films) are bonded together.

Photolithography:

It normally contains a pattern drawn on a material

(called a mask) usually made of glass with the help of computer assisted design program. The material is a mask opaque on residue. The material is then spin rotated with photoresist, a photosensitive organic polymer. The photoresist polymer is made soluble by UV radiation. After the itching the photoresist is removed⁴. (Figure 1)

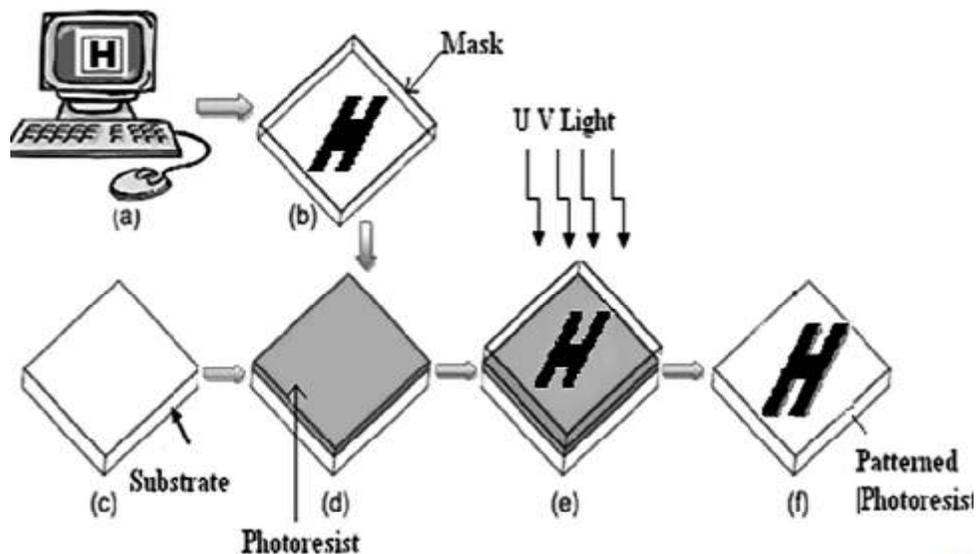


Figure 1: Configuration allocation with photolithography

Thin film growth:

Chemical vapour deposition is the method most commonly used for thin film growth. This method produces metal, ceramic and compound films through thermal oxidation. Physical vapor deposition is used to thin film growth layer by layer into substrate, it involves mechanical or thermodynamic means. Adsorption is a chemical deposition means especially meant for hydrophilic head groups.

Etching:

It has dry and wet etching both can lead to isotropic and anisotropic etching. Isotropic etching is etching in all directions equally where as anisotropic etching is direction specific. Wet etching is mostly used to produce microfluidic channels and microelectrodes. Dry etching generally uses gases like xenon difluoride.

Bonding:

Most processes, there will be bonding between two substrates to give a hermetic seal. Anodic bonding can be used to fuse silicon or glass plates. Thermal bonding can fuse glass or polymeric plates. Photo polymeric adhesives can bond any type of rigid substrates. (Figure 2).

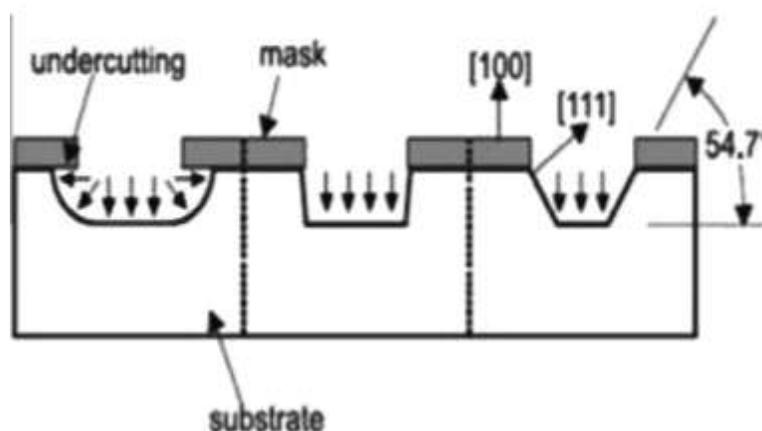


Figure 2: Overview of (left) isotropic and (right) anisotropic etching by (middle) dry etching or by (right) wet anisotropic etching.

Applications:

BioMEMS for Monitoring⁵ :

Following are BioMEM's used for continuous as well as specific monitoring applications.

- Blood glucose level for diabetics
- Antibody level monitoring in the patients with HIV.
- Blood cell concentrations for patients undergoing chemotherapy.
- Continuous monitoring of high-risk patients.

BioMEMS for Drug delivery

Development of drug delivery systems is another huge market. Several type of drug in-vivo drug delivery system are currently being tested and still working on high selectivity and specificity. Such components include liposomes vesicles to carry drug molecules towards the blood stream into a specific cancerous tissue where it attaches and release its drug and destroys cancerous tissue⁶. (Figure 3)

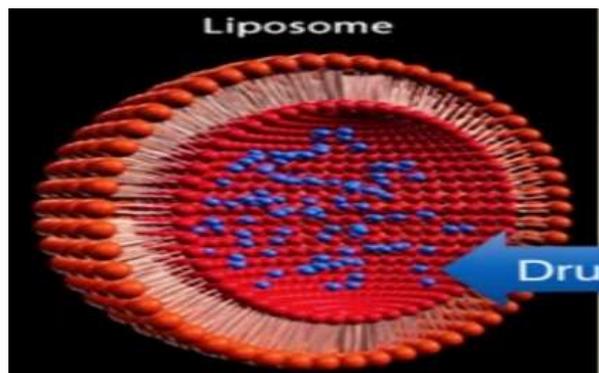


Figure 3: Liposome Vesicle (filled with the drug to be used for selective treatment)

BioMEMS enable the delivery of drugs, examples include the following:

- Antibiotic administration
- Intravenous nutritional supplementation
- Pain medication

BioMEMS as biosensors:

This image shows the microsized cantilevers to identify and engrab the molecules. The green particles on the surface of the cantilevers are antibodies. They identify a specific virus shown in figure as red dots such devices are BioMEM components. (Figure 4)

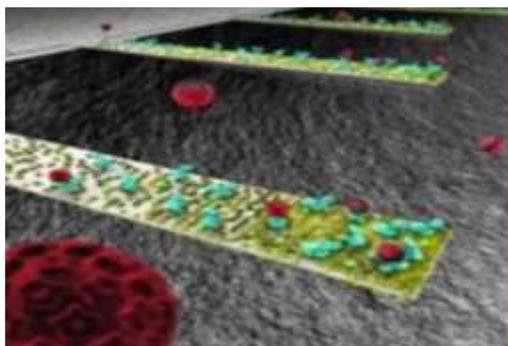


Figure 4: Biosensor

BioMEMS for Cell Culture

Grows cells in-vitro and in parallel.

- This array uses the micronized chambers and channels to create optimum environment for cell cultivation.
- This creates microenvironment for growing cells in parallel allowing for the analysis of multiple cell growth conditions.
- The environment in the cell growth are controlled by several other micro components within the system⁷. (Figure5).

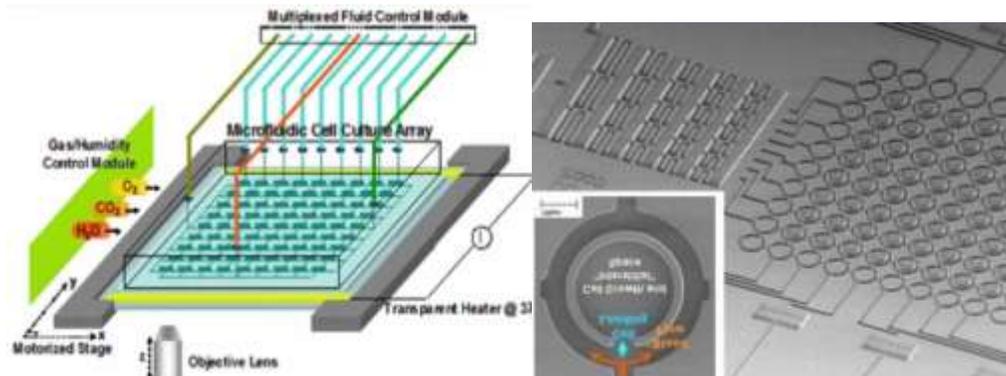


Figure 5: Cell culture Array

Cultivation of cells in vitro are also enabled by the applications of BioMEM's:

- Cell separation and counting
- Microenvironments for growing cells in vitro and analysis
- Magnetic microbeads used to levitate cells for 3-D cell culture.

BioMEM's sensor placement:

BioMEMS sensor placement on a patient depends on the device and its application and found in laboratories, doctor's offices and also found in on patient.

A sensor can be:

- Topical (applied to skin or placed in the mouth).
- Externally connected (In-vitro or external with in-vivo or internal device).
- Implanted (totally In-vivo).

Topical sensors: Applied to skin or placed in the mouth.

- Thermometer used for measuring the body temperature.
- Thick-film disposable thermistors and infrared ear thermometers have largely replaced the mercury thermometers.
- This thermometer is very non-impulsive and perfect for delicate situations because it goes virtually by the patient⁸. (Figure 6)



Figure 6: Infrared Ear thermometer

Externally connected BioMEMS:

Retinal prosthesis is an example of externally connected BioMEMS. It contains a micronized electrode array implanted on the retinal tissue on the back of the eye. The patient wears glasses contained a video camera, receiver and transmitter that process and send optical signals to the array stimulating the end of the electrode which in turn stimulates the cells below the retina. This stimulation travels from the optic nerve to the brain which interrupts the signal and provides the good visual. (Figure 7)

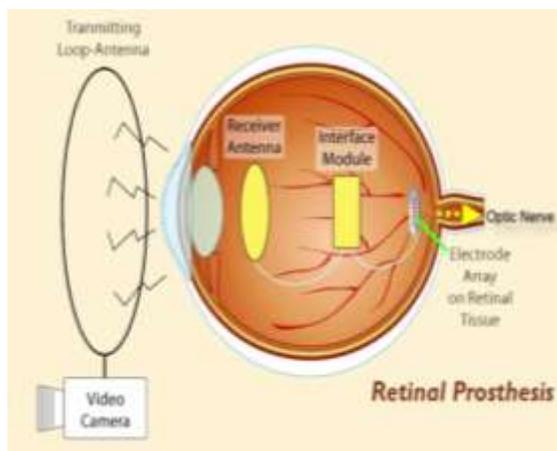


Figure 7: Retinal Prosthesis

Implantable or In-vivo BioMEMS:

- They have numerous possibilities but few of these devices were made into the market mainly due to biocompatibility issues⁹.
- Implantable BioMEM's have been in the market for years as defibrillator and pacemaker.
- Another in-vivo BioMEM's currently available in the market is this pill cam. It is having the size of about a tablet and contains a light source, battery, lens, antenna, transmitter.
- The patient swallows pill in the morning and goes about his daily routine. During the day it travels through the entire GI tract recording the images of the 2 frames/sec and having an eight hour battery life¹⁰.
- The images are transmitted from the pill to the receiver that patient wears on this belt. At the end of the day patient returns receivers to the clinic the images are then downloaded and analysed. (Figure 8)

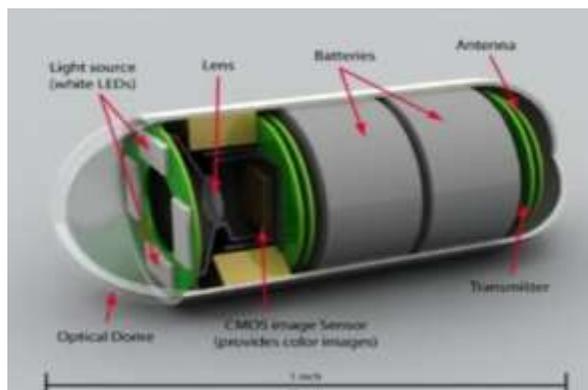


Figure 8: Pill cam (Capsule endoscopy)

Other implanted bioMEMS:

Neural probes: spinal cord stimulators to treat pain and pressure sensors for monitoring cardiovascular pressure, eye pressure, intracranial pressure. (Figure 9)

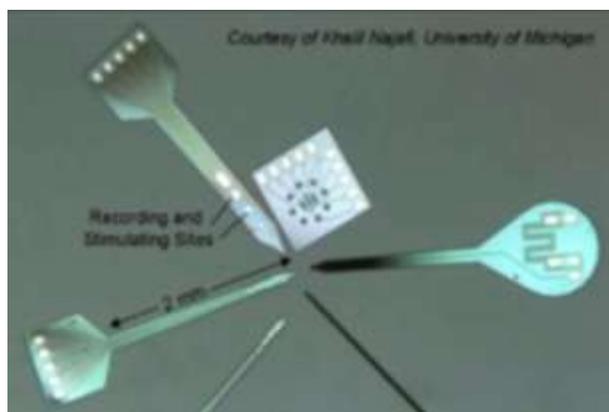


Figure 9: Neural probes (various probes for internal use)

Biological molecule sensors:

This is another category of bioMEMS using biological molecules as a component.

- In biology you have learned that some bio- molecules have the ability to detect and bind with other bio-molecules like antibody detecting and binding to a specific virus. This characteristic of biomolecule have a ability to develop a biosensor.
- An example of the biosensor is the home pregnancy test that employs certain antibodies with an attached test reporter group that detects the specific protein produced during the pregnancy.(Figure 10)

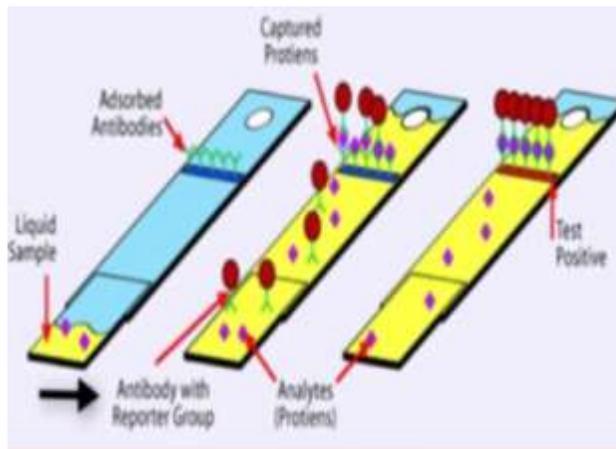


Figure 10: Home pregnancy Test

- Another example is the glucometer diagnostic biosensor which gives the blood glucose level for a diabetic with a single drop of blood.
- The pregnancy test and the glucometer are the types of microfluidic BioMEMS which are referred to as LOC (LAB ON CHIP).

LOC (LAB ON CHIP):

It is the test for one or more biomolecules with small sample of bioliquid. They can accurately test for many analytes with different bio-molecules from one small sample.

- This image shown here is such a device you can see the different channels through which sample flows. In each channel sample is tested for different analyte.
- The LOC is currently being used by astronauts for infections, allergy, deficiencies in the immune system.
- This LOC helps analyzing the tiny blood sample in about 2min. (Figure 11)

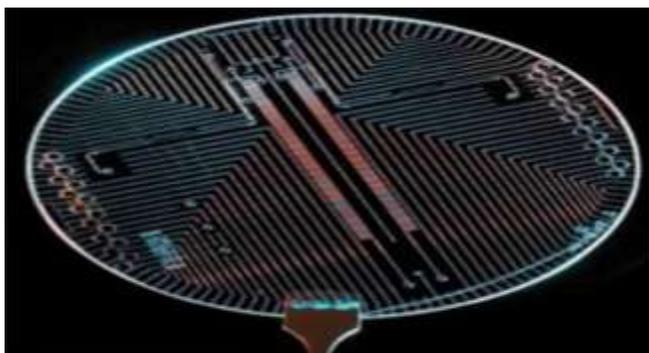


Figure 11: Lab-on-a- chip (LOC).

MEMS Glucose Sensors with Microtransducer :

In the below given figure is the insulin pump which contain a sensor, transmitter, cannula. whenever the body requires the insulin it detects and releases on the needed basis. (Figure 12)

Its components are

- (A) an external pump and computer
- (B) a soft cannula that delivers the insulin
- (C) an interstitial glucose sensor
- (D) a wireless radio device that communicates with the computer.

BioMEMS for Detection

BioMEM's can be used for detection, given as follows:

- It can be used as sensor for different chemical detection like toxins, ions, proteins.
- BioMEM's can be used for antibody detection and disease detection.
- These can also be used for the detection of bacteria, fungus and virus.
- BioMEM's can be used as examination devices (like endoscopes and catheters).

BioMEMS for Diagnostics

Examples of bioMEM's for diagnostics applications include the following:

- Disease identification (e.g., various cancers and autoimmune diseases)
- Protein isoform identification (used to assist in prescribing appropriate drugs for personalized medicine)

Antibody identification.

Internet of thing (IoT):

This connects the devices such as BioMEMS monitoring systems to a internet enabling the gathering and managing the information from those devices. This information inturn offers the opportunities for more and effective health benefits.

Ex: ECG Biosensors and pacemaker.

- ECG biosensor contains electrodes, electronic circuit and transmitter that monitor, measure and collect data regarding the patient's heart activity. The data is then transmitted wirelessly to the patient's smartphone or computer.
- Pacemaker are designed to send collected data wirelessly through the transmitter and the receiver device that is present next to the patient's bed. Every night when the patient sleeps the data is collected this collected data is send periodically to the doctor's computer without the patient's knowledge of any transmission. (Figure 13)

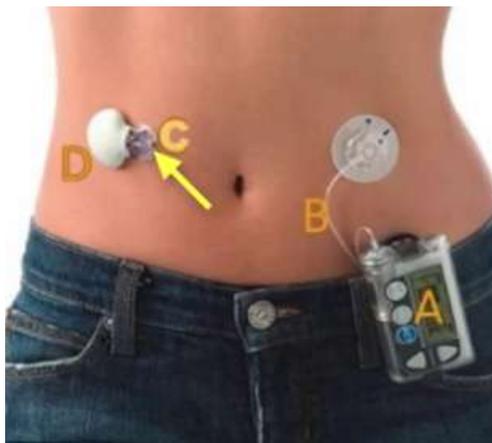


Figure 12: Therapeutics for Diabetics

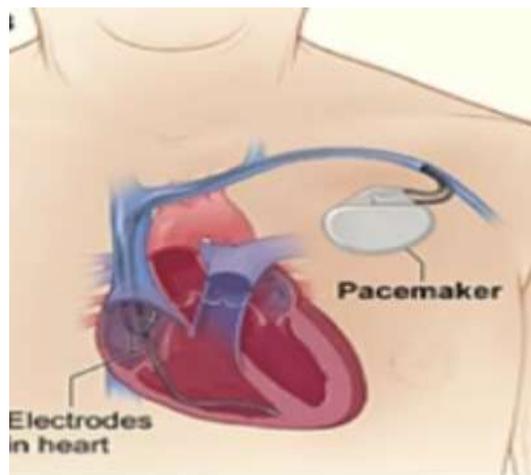


Figure 13: Pacemaker

CONCLUSION:

- With the grown market of 2.1 billion dollar it is safe to say that the BioMEM's devices are already impacting every aspect of our lives alternately. These systems promote to significantly improve the medical care in global scale.
- The applications of BioMEMS's are growing to the great extent in the recent years. MEMS technology has extended to wide area regarding the development of health care related products. This microfabricated systems has developed to great extent particularly in diagnostics and also in the field of drug delivery.

REFERENCES:

1. Goodsell, D. S. Wiley-Liss, Inc., Bio nanotechnology: Lessons from Nature. Hoboken, New Jersey 2004;1:498-503
2. Blawas, A.S., Reichert, W.M., Protein patterning. Biomaterials 1998;19:595– 609.

3. Blohm D.H., Guiseppi-elie A., New developments in microarray technology. *Curr. Opin. Biotechnol.* 2001;12: 41–47.
4. Esch, M.B., King, T.L., Shuler, M.L. The role of body-on-a-chip devices in drug and toxicity studies. *Annu. Rev. Biomed. Eng.*, 2001;13: 55-72.
5. Joel, V., Martha, L.G., Martin, A.S., Microfabrication in biology and medicine. *Annu. Rev. Biomed. Eng.* 2005;1: 401–425.
6. Choi, S., Park, J.K., Continuous hydrophoretic separation and sizing of microparticles using slanted obstacles in a micro channel. *Lab. Chip.* 2007;7:890–897.
7. Chun, M.S., Him, M.S., Choi, N.W., Fabrication and validation of a multi-channel type microfluidic chip for Electrokinetic streaming potential devices. *Lab. Chip.*1996; 6:302–309.
8. Davies, S.S., Biomedical applications of nanotechnology implications for drug targeting and gene therapy. *Trends Biotechnol.* 1997;15:217–224.
9. Yager, P. et al. “Microfluidic diagnostic technologies for global public health”. *NatureInsight* 2006;1:412-422.
10. Kretz, A. P. and D. Styblo. Toward Continuous Blood Glucose Monitoring. *MDDI.* 2003;2:123-132.

AJPTR is

- Peer-reviewed
- bimonthly
- Rapid publication

Submit your manuscript at: editor@ajptr.com

