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Review on Application of Bio-MEMS

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Abstract: MEMS or Micro-Electro-Mechanical Systems are a combination of Electrical and Mechanical components inside mill to micro-scale chips. The components are generally integrated on a single chip by several microfabrication techniques. BIOMEMS is a subset of MEMS. It deals with MEMS used in the biological field. Bio-MEMS uses micro-sensors, transducers, actuators, and micromachines. It generally applies to biological systems and particularly human health. From any disease diagnosis to drug delivery, it's only MEMS which made it easy for us to handle.

Keywords: BIOMEMS, Microfabrication, Micromachining

I. INTRODUCTION

Bio-MEMS or Biomedical Micro Electro Mechanical System is a field that can be considered as the subset of MEMS. The application of MEMS devices has brought a renaissance in the field of Medical Diagnosis and Treatment. Researches on BIOMEMS started back in 1967 but the growth was slow. However, during the early '90s, the discovery of drugs revolutionized this field. The reasons for this revolution were due to the much-awaited miniaturization of the devices using MEMS technology along with reduced cost and higher reliability of the devices. MEMS sensors like pressure sensors, critical sensors used during surgery, long term sensors for prosthetic devices are some of the most common and basic applications of MEMS in the medical field. The application of BIOMEMS is growing exponentially, it is the branch with high potential for further advancements.

II. MEMS TECHNOLOGY

MEMS technology that is used today is a result of a series of developments in the structure of devices in micro or nano dimensions. Silicon is used as the basic material in device's fabrication due to its special property, that it can form complex micro 3D structures like channels or

pyramids. Micromachining process on silicon and other substrates with some other processes result in such 'micro-scale' fabrications.
Fabrication takes place through a series of processes:

a) Patterning technique
b) Material removal process
c) Material deposition process

The first step to fabricate a MEMS device involves applying a photo resistive layer on the Silicon wafer and then mask it to get a pattern. The mask should be of the same shape and size as the pattern to be extracted. Then, after the pattern is drawn using UV rays, the pattern is now masked to eliminate the unwanted part above the wafer either by dry or wet etching.
Now in this review, we will discuss the fields where entry of BIO-MEMS results in a massive advancement. The following are the fields mentioned above-

A)Detection using sensors

Detection is mainly done by different kinds of sensors which are vastly downsized (in micro range) with the help of

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MEMS. Each micro ranged sensors have a bio-receptor that detects certain parameters and a transducer that converts that information into a signal that can be provided to electronic systems.Depending on where the sensor is placed it is classified as topical(e.g- thermometer) or externally connected(e.g- cochlear implant) or implanted(pacemaker).Furthermore, sensors can be differentiated based on the mode of detection like micromechanical sensors Which uses micro ranged cantilevers that can detect any change in the environment like change in pressure, stress, mass or forces, electrochemical which can be amperometric(detects a change in current e.g- detection of ureal cholesterol) or potentiometric(senses change in potential difference e.g- ISFETS) or conductometric (measures by a change in impedance), optical sensors which function by sensing fluorescence or chemiluminescence or surface Plasmon resonance.

B) Tissue Engineering & Cell Culture

The main goal of tissue engineering is to replace or improve biological tissues. Cell culture works on testing different genes and drugs. Micro-fluidics brought huge changes in cell culture. Micro-fluidic types of equipment eliminated the use of large-scale machines like incubators and also making it more economical and informative. However extra care should be taken in flow control. Stem cell engineering is also improved by BIOMEMS. The main area of interest of stem cell engineering is retrieving and differentiation of stem cells to use them in cell therapy. BIOMEMS helped to control different parameters for growth control like the cell to cell interaction, fluid shear stress, etc. Microarrays are used for studying stem cells. BIOMEMS devices impacted the process of embryoid body formation and curing infertility. MEMS devices like micro-wells micro-fluidic devices are used to control the embryoid cell architecture which leads to cell differentiation and cell renewal. Micropumps, microvalves optimized sperm selection.

C)Diagnostics

Diagnosis is mainly the process of determining disorders or diseases. BIOMEMS brought micro ranged devices which made point of care possible. Point of care is the process of diagnosis of the patient beside his or her bed improving the health care. Microfluidic systems take body fluids and perform cell sorting, lysis, amplification, analyte detection and show the results. One easy example is the home pregnancy test kit. Micro-array is another piece of equipment for the detection or identification of certain parameters. DNA-microarray and protein-microarrays are used to gain information on DNA and proteins. However, retrieving rare DNA structures or proteins or cells amplifying them is an important process. Micro ranged PCR chips does the job by conducting polymerized chain reactions.

D)Drug discovery & delivery

Determination of suitable drugs for a particular disorder or disease is done using microarrays. In the next step, drugs are delivered to that particular location of the body where the drug is required. It is done using micro-needles and micro reservoirs. Microneedles are of the size of less than 300um and they penetrate the skin without hurting. They come in different shapes like a candle, spikes, pyramidal, etc. Micro- reservoirs contain the drug and using the micro-pumps drug is sent to the required location. More research is being carried out to improve the efficiency of this process. Drug delivery can be triggered or time-release or sensor-based. Efficient equipment for diabetes patients is already available in the market. It consists of biosensors that detect the glucose level of blood and if required sends insulin using micro-pumps and micro-needles.

E) Medical implants

Several implantable microelectrodes are developed to collaborate with the nervous system and determine different diseases and disorders. Michigan and Utah electrodes are a prime example of this.

F) Surgical Applications

1. *Minimally Invasive Surgery:* This is a technique that allows the surgical tools to reach down to the size scale of individual cells and provide access for manipulation in previously inaccessible areas of the body. The main advantages of this technique include lesser trauma, reduced post-operative pain, and quicker recovery time.

2. *Microtools and tactile sensing:* Conventional surgical tools have limited capability when it comes to manipulation of small structures such as nerves and vessels of small diameters. To achieve higher spatial resolution, researchers have developed tools such as micro-grippers, micro-tweezers, micro-forceps, and micro- scissors with the aid of microfabrication techniques [44, 45]. In MIS procedures, a major problem faced by surgeons is the lack of sense of

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touch. To overcome this limitation microfabricated devices capable of restoring and enhancing tactile sensation are being looked into [47, 48].

3. *MEMS Cutting tools:* Research has been looking into the development of such nano-knives which are made sharper by etching silicon precisely along its crystal planes [46]. A surgical device called a data knife was developed by Verimetra. Inc (Pittsburg, PA, U.S.A.) consists of a scalpel outfitted with different strain sensors along the edges of the blade to sense the amount of force being applied. A vibratory mechanism produced by piezoelectric actuation is used in this device for cutting through tissues. Other sensing mechanisms included in this device are pressure sensors, temperature sensors as well as impedance sensors for measuring tissue impedance [49].

4. *Endoscopy:* The technique to view the inside of the gastrointestinal tract has now been reduced to capsular endoscopy through the advancement of MEMS [50]. These wireless capsules consist of components like image sensors, LED illumination devices, telemetry units for signal transmission, and control electronics, all reduced to miniature sizes by microfabrication techniques. The first capsule-type endoscope, M2A was developed and commercialized in 2001[51].

Several physiological parameters like body temperature, blood pressure oxygen concentration, pulse rate, respiratory rate, etc are vital in any kind of disease. MEMS-based micro-pressure sensors are used to design devices that can track blood pressure, intraocular pressure, respiratory rate, heart rate, etc. I (Intra Ocular pressure sensors) amused for detecting Glaucoma. Modern wheelchairs, hearing aid transducers are designed using MEMS. Smartwatches, wearable devices that track pulse rate use MEMS sensors embedded with an electronic system.

G) Prosthesis

Neural prostheses are a set of devices that utilize electrical stimulation to reactivate the function of the damaged or disabled nervous system. Electrical stimulation is used to generate action potentials in specific areas of the nervous system for restoring functions. To restore neural functions, locating the exact point of trouble, and then minutely performing the task with minimum damage to the surrounding tissues was most important. Thus, every focus was put to miniaturize the neural probes. Several types of research made the miniaturization of neural probes integrated with circuitry for amplification, multiplexing, spike detection, and wireless transmission of power and bidirectional data feasible. These extraordinary developments are presently facilitating prosthetic devices for many debilitating neurological disorders [52]. Microfabrication comes as a boon to get the above task done. It offers the advantage of producing a highly dense neural probe array on a single platform that is capable of fitting in within the tissue. If a nerve malfunctions, all we need to do is to locate the point of malfunction and replace that portion with artificially made neuro-probes [53]. This process of neural treatment is done by using Regenerative Electrodes. This remarkable concept was first introduced by Marks in 1969[54] and demonstrated by Mannard and coworkers in 1974[55]. They successfully recorded neural signals from regenerated nerves in amphibians using mechanically drilled holes. This technique was later developed and further miniaturized through micromachining techniques. Prostheses improved even further. Through detailed observation of the fundamental function of the Retina, it brought a means by which a blind can get back his/her sight. Out of the several diseases that result in blindness, certain diseases are limited mainly to the outer retina due to loss or malfunction of photoreceptor cells. In the wake of a retinal prosthesis, such disorders got the potential to be treated to a satisfactory percentage. MEMS technology provides ways for developing these delicately minute prosthetic devices such as ‘artificial silicon retina’ for improving the eyesight of the visually impaired. These implants stimulate the optical nerve cells mimicking the photoreceptor cells thereby producing visual sensations in the brain[56]. To summarise, the main function of the retinal prosthesis is to detect light reflected from any surface and transform them into artificial stimulus such as electrical signals which could be sensed by the human brain.

H) Microfluidics

We have already used MEMS in surgery, prosthesis, drug delivery, and in various other fields. There we used artificial devices to work as natural ones. However, there is a problem with those which went un-noticed. The problem, that the devices used to seem foreign bodies to the WBC, and thus by the protective measurement of our body, it will clot our blood and hence we fail to achieve our objective. At this juncture, comes the idea of producing an artificial environment to resist clotting. Microfluidics, come in as a boon to help us create this environment. Manually, it is impossible to create this environment as the fluids to be used here have Reynolds’s Number less than 100 as it has to be used in extremely low quantity, and thus we need micropumps and microvalves to induce the fluids required. Micropumps and Microvalves are produced using MEMS technology to induce the fluids required [57] only to fool WBC so that it does not consider those devices as foreign bodies. These devices provide transport of small, accurately measured liquid quantities. One of the earliest developed micropumps for biomedical application was an insulin delivery system developed by Smit et al[58].

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The devices used as a substitute for our natural organs are also produced by MEMS technology. Now comes the field of tissue where MEMS came as a blessing. The artificial environment produced by the microfluidics, make cells and tissues respond. Those fluids activate the cells hence the tissues thus maintain the stability of the body. MEMS also brought a massive change in the bio-field of Vitro Fertilization. Now embryos can be produced by artificial means using MEMS technology. Mouse embryos are produced by MEMS-based microfluidic elastomeric channels [59-62].

III.CONCLUSION

Journey with MEMS started in 1990 with the discovery of the first microfluidic device for pregnancy tests has now changed the medical world. We can now do everything from detection to cure with MEMS devices. It took three decades to upgrade from a system where people used to admit and they had to wait for some days for the report to come to a system where we can check about our health condition in few hours. Bio-MEMS came as a boon to the Medical field by minimizing the size of the devices as well as enhancing the accuracy of the report. New researches are going on to make those commercial laboratory products even small so that people can use it as a domestic product. If we can succeed it will bring a drastic change in the field of Pathology. To conclude, we say that only MEMS made it possible for us to jump so high, and with further researches, it will continue to overcome the technical shortcomings in times to come. The version of this template is V2.

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