

# Application of Micro-Electro-Mechanical Systems as Neural Interface

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**Abstract:** Micro-Electro-Mechanical Systems (MEMS) technology comprises of developing miniaturized mechanical and electro-mechanical elements such that the physical dimensions of these devices vary from micron to few millimeters in size. In various human disease disorders, the neural or body regulatory tissues are incapable of conveying commands directly to the target organ and unable to receive appropriate information from receptor mechanism to decide the future course of action. The MEMS based devices are playing important assistive role by becoming crucial interface in treating such disorders. These devices are increasingly being deployed inside the body at sub tissue levels to fulfill information receipt or command transmission gap, thereby enabling the governing tissue opportunity and environment to work effectively, leading to improvement in the neural signal recording and quality of life of the concerned individual. The aim of this paper is to review the present and future of MEMS based devices widely being employed as neural interface in penetrating probes, nerve regeneration, neuron culture and drug delivery devices depending on type of treatment provided to specific neural disorders. Further, they have been recently employed in developing advanced neuro-computer, nerve stimulators, wheel chair control based on head and hand movements and in medical robotics. Due to their stability, biocompatibility, usage and wider acceptability these MEMS based neural interface devices are providing future hope for their deployment in conquering various neurological disorders.

**Keywords:** MEMS, Neural interface, Penetrating probes, Regeneration devices, Cultured cells, Drug delivery.

## 1. INTRODUCTION

Micro-Electro-Mechanical Systems (MEMS) technology is defined as development of miniaturized mechanical and electro-mechanical elements by employing micro-fabrication techniques such that the physical dimensions of devices can vary from micron to several millimeters. The structure of such devices may range from simple to highly complex with electromechanical system having moving components [1]. MEMS usually consist of a central unit - the microprocessor that processes data and several other components that interact with the surroundings. The functional elements of MEMS are miniaturized structures – micro-sensors, micro-actuators, and microelectronics or microsystems which consist of both micro-sensors and micro-actuators. Among these most interesting elements are the micro-sensors that converts mechanical signal into an electrical signal (for e.g. inertial sensors, pressure sensors, magnetometers, chemical sensors, etc.) and micro-actuators that convert energy from one form to another (for e.g. microvalves, micropumps, microrelays and micromirrors)<sup>1</sup>.

Originally, these devices were used to build electrical and mechanical systems; however, with

advancement and development of modern micro-fabrication technologies, their application included different areas of biological, optical, magnetic and other systems. Most articles on MEMS related topics tend to cover large markets in automotive and consumer electronics but not for neurological applications; since the central nervous system (CNS) therapeutics are among the most difficult for pharmaceutical companies to develop partly due to the lack of detailed knowledge on the working of the healthy brain and nervous system, and how this changes with injury and disease [2, 3]. Further, the added difficulty is in getting drugs past the “blood-brain barrier” (BBB) which is a highly selective permeability barrier that separates the circulating blood from the brain’s extracellular fluid in the central nervous system, to enable site specific drug delivery. It is reported that 98% of the drugs for the brain are not able to cross the BBB which is responsible for the under development of CNS pharmaceuticals. With the advancement of MEMS and micro-fabrication technologies, neuroscience researchers are in their quest to understand the workings of the brain and the treatment of debilitating illnesses of the nervous system leading to motor disability. MEMS incorporated devices are already being deployed in medical industry to treat injuries and diseases of the nervous system, with several products already in human clinical trials<sup>2</sup>.

In this review paper, we focus and discuss the present state of art different neural interfaces

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employing MEMS technology that would vastly benefit the researchers, scientists, nanotechnologists, pharmacists and engineers working in these areas for developing robust devices to treat neurological disorders.

## 2. NEURAL INTERFACE

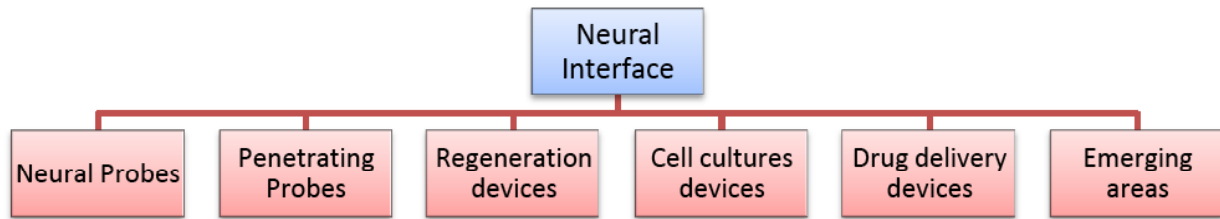
Neural interfaces (NI) are engineered devices operating at the intersection of the nervous system and an internal or external device, acting as artificial extensions to the body that restore or supplement function of the nervous system lost during disease or injury [4]. The need to develop NI devices arose due to the quest to understand the functioning of the nervous system and the activity of neurons. The ultimate goal of NI is to establish links for direct information exchange between the nervous system and the outside world either by stimulating or by recording from neural tissue that can serve as an aid to treat or assist people with disabilities arising due to defective neural function and neurological disorders. Cheung *et al* (2007) discussed NI, under the name implantable neural microsystem (NMS) that provides interface to the nervous system giving resolution to the physiological process with non-invasive methods. NMS connect neurons, electrically active cells of a nervous system and electronic circuit for the understanding of physiological process at cellular level and in neural prosthetic to help restoration of lost functions [5]. Few examples of commercially available NI are the cardiac pacemaker, deep brain stimulator and cochlear implants.

The electrical nature of MEMS devices makes them potentially useful for applications whereby neural stimulation, recording, or interfacing is desirable to treat neurological disorders. Stieglitz *et al* (2002) described the application of micromachining technologies to develop flexible micro-device that is light-weight, flexible and biocompatible for interfacing with the central or peripheral nervous system to treat neural disorders. They developed it using new assembling technology called micro-flex interconnection for connecting the flexible NI to the silicon microelectronics and developed flexible electrodes like sieve electrode for regeneration studies, cuff electrodes for interfacing with peripheral nervous system (PNS) and retina implant for ganglion cell stimulation [6]. Also, Amy *et al*. (2004) pointed out the biological integration of MEMS through the application of micro-fabrication technology and discussed innovative approaches for improving the physiological integration of MEMS systems within the human body. They concluded that MEMS technology serve as a novel tool for bringing significant

improvement in biological integration of a wide range of implantable devices [7]. Further, Judy (2000) discussed that micro-machining and MEMS are powerful tools for enabling the miniaturization of sensor and actuators by reducing the cost of MEMS particularly of those products which are used in high volumes for example micropumps, microactuators, microsensors, microneedles, microfilters, etc. Thus, due to various advantageous scaling properties and increasing acceptance, MEMS started to be employed in various fields with an increasing demand for sophisticated and robust implantable devices.

By the application of NI devices stable signal from the nervous system can be retrieved which can possibly make the control of prosthetic limbs or artificial organs much more efficient in performance and easy to use by the users. Rubehn *et al*. (2009) demonstrated 252 channel electrocardiograms (ECG) electrode array made of thin polyimide foil substrate which was designed to cover large part of hemisphere of macaque monkey cortex and allowed free movement of the animal between recording sessions. After four and half (4.5) months of implant fixation, the signals from the cortex were properly recorded without decline in signal quality. Their results allowed simultaneous recording over several brain areas and concluded that neuro-prosthetic device could be developed using ECoG electrode arrays as NI [8]. These demonstrations and devices can be used for better understanding and treatment of neural disorders. Thus, micro-fabricated NI promises to become a powerful tool for applications like the control of motor/sensory limb prostheses for amputees and the direct stimulation of spinal cord injuries along with understanding the physiological neural disease pathways as discussed by Lovell *et al* (2010). They discussed biological-machine systems integration (BMSI) with emphasis on neural interfacing from a medical point of view to replace or activate or record from the neural elements from the nervous systems. Further, they added that recent advances in BMSI are concentrated in the manipulation and locomotion domain to improve the quality of life of those suffering from organ loss [9].

According to Maluf *et al*. (1995), NI technologies generally fall into one of the three categories [10]. These are penetrating probes, regeneration devices, and cultured neuron devices [11], which are explained in the following sections. However, recent advancement in MEMS technology and their applications in varied fields allowed us to add two more categories – drug delivery and emerging areas (Figure 1).

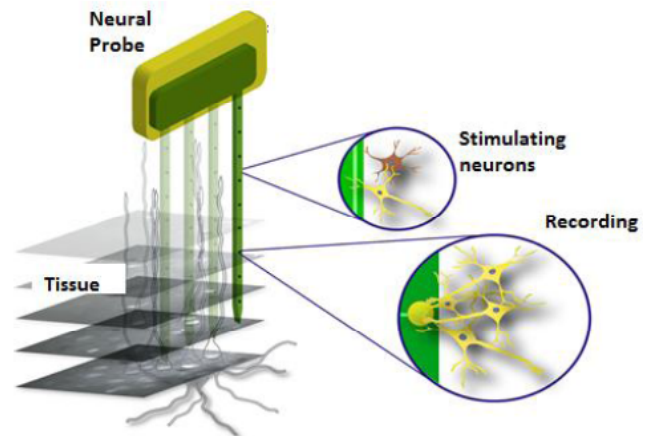


**Figure 1:** Broad classification of MEMS based Neural Interface.

### 3. NEURAL PROBES

The encyclopedia of nanotechnology defines MEMS neural probes (NP) [12] as “microscale implants for the brain or peripheral nervous system that use micro-electro-mechanical systems to assess function or stimulate activity in specific regions of the brain, ensembles of neurons, or neuronal fibers”. In short, neural probes are microstructures that form the connection between the biological neural tissues and the physical electronics. NP are currently finding applications in the treatment of neurological disorders like seizures, epilepsy, Alzheimer’s, dementia and also in paralyzed individuals, by assisting them to operate computer or robots through their neural activity. Additionally, NP had become important tools in recording neural activity by implanting the probe as close as possible to the target neuron for improving signal-to-noise ratio of recorded signal and target specific stimulation of cortical and sensory areas of the brain which lead to better understanding of behavior and functions of the nervous system. MEMS based NP are designed using micro-machining techniques consisting of single or multiple long protruding structures which vary in length from 200 $\mu\text{m}$  to 15mm and thickness from 10 $\mu\text{m}$  to 200 $\mu\text{m}$ . There are many emerging MEMS processes that can be used to fabricate NP with specific features such as ultra-long reinforced structures with integrated signal processing capability. In near future, the standardization of commercial MEMS processes could lead to the development of new neural probes that are cost-effective and mass-produced with ultra-long probe shafts and on-site/on-probe signal processing circuitry. This would enable to record extracellular potential from nearby neuron and allow the information encoded by the neuronal discharge to control external devices. The widespread use of silicon micromachining techniques to develop miniaturized neural probes and probe arrays has led to the establishment of the field of Neural MEMS [13, 14]. Moreover, silicon micro-machined probes capable of penetrating neural tissue for recording neural signals are helping in basic

neuroscience studies. Silicon micro-machined probes are being developed to interface with the CNS at cellular level due to its deep penetrating quality, thereby being widely employed for neuroscience studies. Kipke (2003) observed that all drugs are not able to enter the CNS, thus they developed a multifunctional implantable NP systems consisting of closely integrated chemical and electrical NI. These NP consist of silicon or polymer substrate having multiple metal sides for electrical recording and stimulation and has one or more channel for fluid delivery to the target area of the brain and spinal cord [15] (Figure 2).



**Figure 2:** MEMS based neural probe inserted in the tissue for stimulation and recording [66].

The use of silicon technology to create dense arrays of thin-film electrodes for single-unit recording in the nervous system resulted in sampling neural activity throughout a volume of tissue [16]. The resulting neural probes [17, 18] were the first examples of thin-film microelectrode arrays. Today, most approaches to penetrating probes for use in the CNS are based on silicon technology [19-21]. Further an improved multi-functional silicon NP that is capable of selectively delivering a chemical to a highly localized region of interest and recording neuron responses *in vivo* simultaneously is being used in drug delivery [22]. Kim *et al* (2013), presented the multi-functional silicon NP that consisted of a microfluidic channels for selective

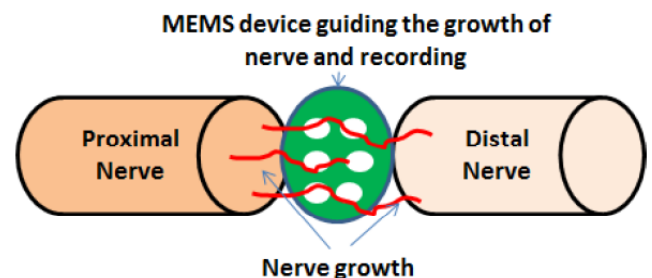
delivery of chemical and simultaneous monitoring of delivery process using multiple recording electrodes. They demonstrated neural spikes signals at the hippocampus of an anesthetized mouse that was successfully detected and recorded. Similarly, Son *et al* (2015) developed multifunctional MEMS neural probe for drug delivery and optical stimulation. They inserted their NP in the hippocampus of the rat and recorded signals that demonstrated successful *in vivo* experiments by optically and chemically activating neurons and recording neural spike signals from individual neurons. They concluded that multifunctional neural probe is an important tool in neuroscience having a wide range of applications including investigation of brain functions, discovery of new neural circuits for understanding mechanism of brain diseases [23]. Furthermore, the advancement in NP and their varied applications opened new windows for developing two-thirds (2/3) dimensional probes to understand the interplay of large cluster of neurons. Ruther *et al* (2010), discussed recent advances in NP and aimed at developing one dimensional, two dimensional, and three dimensional (3D) probes arrays combining both electric and chemical functionality for simultaneous recording and stimulation applications. The probes were assembled into 3D arrays with the use of dedicated platform on MEMS that comprised of highly localized drug delivery mechanism. They found that cortical microprobes reach the highest level of integration and performance, concluding that 3D electrodes can be used to understand the interplay of cluster of neurons [24].

Thus, optimizing such probe devices in the future will provide a wide range of uses in the neuroscience including monitoring the effects of drugs for treatment of physiological disorders and tracing neural activity coupled with stimulating specific brain areas to overcome neurological disorders.

#### 4. REGENERATION TYPE DEVICES

The term “regenerative type device” refers to a nerve interface device consisting of an array of electrodes called regenerative electrodes (RE) that guide the regeneration of transected peripheral nerve. In RE devices, an array of electrodes is incorporated within a nerve guidance channel in such a way that the axons from the transected nerve are constrained to regenerate through the channel within effective range of the electrodes. A regenerating nerve is allowed to regrow through a sieve-like silicon mesh on which an array of microelectrodes has been micro-fabricated

making it possible to record action potentials or stimulate axons (Figure 3). The regenerated tissue is then spatially fixed and “locked” with respect to the array of microelectrodes thus providing a stable and repeatable interface between the nerves and external control systems [25]. The principle underlying the RE is that peripheral nerve in mammals and humans has the ability to regenerate after being severed. Clements (2013) described RE design in which a polymer based thin film electrode array is integrated within a thin film sheet of aligned nano-fibers so that the axons regenerating from a transected peripheral nerve are topographically guided across the electrode recording site. They designed a scaffold-based RE that was used to shape the regenerative nerve structure around the integrated electrode array by guiding the growth of individual axons providing minimal obstruction to the cross-sectional area available to the regenerating nerve [26]. Further, Gregory *et al* (1994) reported a method for micro machined array of microelectrodes to provide parallel access to neural signals in peripheral and cranial nerves. They fabricated the microelectrode arrays on silicon substrates that were implanted surgically on the innervated nerves tissue, which held the device between axons and microelectrodes. Their goal was to provide an interface between amputee limb stumps and control robotic prosthesis, which will become helpful tools for neuroscience research and find clinically usefulness as NI [27] in near future.



**Figure 3:** Schematic representation of MEMS based regeneration device.

The peripheral nerve contains all the motor and sensory pathways associated with limb control and these pathways are known to retain significant functions even after injury or amputation [28]. Since peripheral nerves contain both motor and sensory fibers, it is able to deliver bidirectional communication in neuroprostheses by means of a single RE device. Nerve signals are recorded by the electrodes which are in proximity with the holes and an on-chip circuitry amplifies and preprocesses the recorded signals. The

amplified signals are then transferred to the unit which is controlling the prostheses. A variety of neuroprostheses exist having neural regeneration electrodes that are used to substitute or mimic sensory-motor functions particularly in hand prostheses and exoskeletons by replacing the lost human sensory-motor functions due to neural injuries or limb amputation [29, 30]. Dario *et al* (1998) developed a class of implantable regeneration type NI for mammalian peripheral nerve recording and stimulation using fabrication technology. They designed the NI for regenerating the sciatic nerve in a rabbit and demonstrated electrophysiological recovery in the regenerated nerve producing a visible leg/foot contraction upon stimulation. They concluded that such regeneration can be utilized in controlling the motor and sensory function of future prosthetic devices [31].

The theoretical concept of Llinás *et al* (1973) describing how silicon based microelectronic [32] peripheral nerve interface might someday be implemented for axonal growth and signal recording had seen the light of reality in 1974 when Mannard *et al* reported the first neural signal recording from a regeneration type array in animals [33]. These published works led to the development of regeneration type devices with the hope of using them to interface between an amputee's limb stump and an artificial prosthesis. Traditionally sieve-type RE was initially used consisting of a thin disk and perforated electrode. The thin disk was positioned near the path of axonal regeneration and perforated electrode acted as guidance channel through which regenerating axons could travel. The sieve-type RE was constructed using microelectronic technologies on silicon substrates having multiple holes that facilitated axonal regeneration and neural activity recording were reported in animals [34-37]. Many experiments demonstrated the potential of sieve electrode to stimulate and record neural activity, yet its clinical application were limited due to various drawbacks such as physical barrier posed by electrode array to growth of regenerating axons and electrodes geometry inducing signs of axonopathy<sup>29</sup>. Later polyimide-based electrodes were introduced that offered biocompatibility and stability for better nerve regeneration [38, 39] and selective stimulation and recording from group of regenerated fibres [40, 41]. Namsun *et al* (2014), reviewed penetrating neural microelectrodes that have been used traditionally and recent improved ones. They described that there are two types of electrode based on substrate - silicon and polymer-based material configuration. They found that silicon based

penetrating electrodes have minimal effect on implant tissue and are capable of maintaining the electrical performance of electrodes for a longer time but soft polymers are more favorable to neural tissues because they reduce the inflammatory response and tissue damage [42]. These types of microelectrodes are in high demand where spatial resolution and selectivity at cellular levels are required for recording and stimulation in the brain.

In the progress to improve the axonal regeneration several modified designs were proposed including non-obstructive regenerative electrodes and needle electrodes for bridging the sectioned nerve. More recently, alternative RE designs were explored for the development of regenerative scaffolds<sup>26</sup> and micro-channel electrodes [43]. Present research studies in animals demonstrate that these new approaches are achieving high selectivity in recording and stimulation of regenerated axons but clinical studies in humans are yet to be reported

## 5. CULTURED CELL DEVICES

Cell cultures are extremely useful in the understanding of cell dynamics and investigating their responses to various stimuli. It is well known fact that the neural cells interact in the form of action potentials with the recording or stimulating devices for example, the EEG recording is performed non-invasively through the skull, whereas the ECoG devices are directly implanted into the cortical areas for stimulation [44]. Neurons and neuron-like cells have been successfully cultured on silicon chips with micro-fabricated micro-electrodes<sup>34</sup> because micro-fabricated systems provide an excellent platform for the culture of cells which are extremely useful tool for the investigation of cellular responses [45]. MEMS provide excellent environment and great biocompatibility for cell adhesion and maintenance due to the several advantages such as cost-effectiveness, controllability, low volume, high resolution, lower risk of infection, sensitivity and interaction with materials. Ming *et al* (2009), in their review described the concepts of cultured cells interaction with biomaterials such as protein adsorption and cell adhesion. They discussed that in order to facilitate cell spreading, cell migration and cell differentiation, the adhesion between the cell and the substrate is an important factor and is performed by coating a layer of protein on the culture substrate. They further added that MEMS platforms has the ability to control the culture conditions such as the effects of

diffusion and delivery of soluble biochemical molecules, waste removal, nutrient depletion, mechanical forces, extracellular matrix remodeling and temperature. Thus, Peres *et al* (1999) reported the fabrication and electrical characterization of silicon microstructures containing gold microstructures and resistors for local heating and temperature monitoring in the neuronal culturing studies. They concluded that satisfactory neuro-electronics can be developed for controlling sensitivity, response time and power consumption of these devices which can be used in varied biomedical applications [46]. Further, Lin *et al* (2004) designed a MEMS micro-system to exert mechanical tension to modulate neural migration along radial glial between groups of neural stem cell to study the effect of tension on cerebral cortex neurogenesis. Their study showed that the embryonic brain tissue survives under tension and the cultured neurospheres supported neuronal migration which is a key process for the cerebral cortex development, thereby opening a new window towards understanding brain development [47].

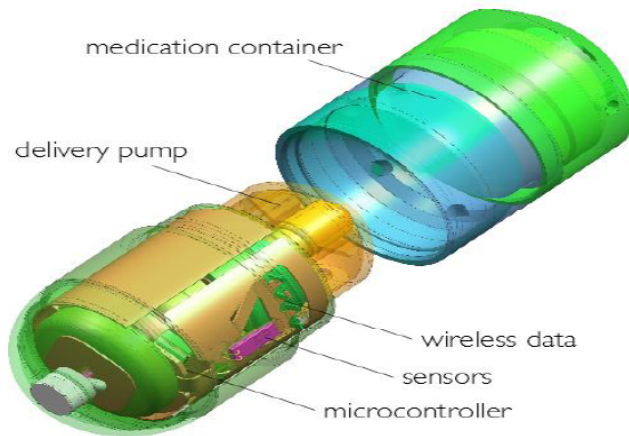
Though MEMS provide an excellent platform for the neuronal cell culture yet the geometrical structure of the micro-structures are often overlooked. The platform structure is of great importance because the nervous system in the living tissue is a network of many neurons arranged in a complex three-dimensional (3D) cyto-architecture but the existing neural cell platform employs 2-D culture systems [48]. Choi *et al* (2004) noted that 3D neural cultures, which are more anatomically similar to living tissue, may provide better physiologically relevant information and thus decided to work with neuron and glial 3D cultures to study cellular responses during traumatic neural injury as well interfacing with electrode and fluidic support, to provide unique monitoring and manipulation abilities. They developed 3D scaffold towers for cell culturing and successfully cultured hippocampal neurons of rat embryo.

Thus, for over a century now, numerous culture devices and methods have provided ideal microenvironments to glean insights into neuronal development with a unique advantage of growth of neurons, from the heterogeneous population. Neurochemical and cell signaling studies utilize neuronal growth measures *in vitro* to measure the duration of the polarization process, axonal elongation rates, and filopodial dynamics (space, time, and direction). New techniques that allow for additional measures of neuronal growth have the potential to aid

in cell signaling studies and investigations into the influence of neurotrophins, cytokines, and neurotoxins on neuronal biomechanics (e.g., stiffness and biomass accumulation)<sup>46</sup>.

## 6. DRUG DELIVERY

Development of drug delivery (DD) system (Figure 4) has been a hot research area in the pharmaceutical industry because of the problem posed by the blood brain barrier or BBB and the importance of controlling site specific delivery. It can be said that if the problem of molecular transport into the brain is resolved, the drug development in the treatment of CNS disorders will increase dramatically. MEMS DD devices are used in several biomedical applications because it can mimic the meta-stability of living organism and can accurately stimulate electrical impulse and deliver drug at the right place. Elman *et al* (2009), introduced first of its kind implantable DD system based on MEMS technology and named it IRD (implantable rapid drug delivery) device. The device consisted of miniature micro-pump for drug delivery having a capacity to release drugs at high rate and accuracy [49]. Thus, the application of MEMS technologies and micro-fabrication technique has significant implication in the DD devices for achieving targeted and controlled delivery. This technique can be employed during the controlled release of drugs especially hormones in a more effective and natural manner into the living system. Gurman *et al* (2014), in their review described various clinical applications of state-of-the-art controlled DD micro-devices in the treatment of cancer, endocrine and ocular disorder. They discussed clinical translation of DD micro-devices that promises a remarkable gain in clinical outcome and substantial social impact. They focused on various drug delivery devices from 1990 to 2014 like - cochlear implanted devices with pump for electronic control, neural probe, micro-needle transdermal patch and ocular device with electrolysis pump, implantable MEMS for DD, MEMS DD for emergency, microfluidic hydraulic MEMS based DD devices and microchip DD for osteoporosis. These devices offer a range of clinical applications in which tailored pharmacokinetics local release and high adherence are prerequisites. Use of these advanced drug delivery system promises improved treatment for variety of disorders [50]. One such advanced DD system is developed by Grayson *et al* (2004) called pulsatile drug delivery device using MEMS digital capability which helped in controlling amount of drug release compared to the traditional polymer based system [51].



**Figure 4:** MEMS based drug delivery system [67].

MEMS based DD devices are designed around an array of micro-reservoirs etched into silicon and each reservoir is covered with an individual gold membrane that can be filled with solid or liquid drug. The gold membranes are cathodes that can be individually addressed and electrochemically dissolved in chloride-containing solutions by the application of voltage. MEMS based implantable DD devices enable the user to program the desired DD profile based on the individualized medicine needs for the treatment of the patients. Thus, due to MEMS technology, the fabrication of miniature size and high performance medical devices has become practicable to congregate the critical medical requirements like controlled delivery with negligible side effects, improved bioavailability and therapeutic effectiveness [52]. In recent years, the most important advancement of MEMS and NEMS in biomedicine is microfluidic transdermal drug delivery (TDD) systems [53]. TDD systems deal with the movement of pharmaceutical compound through the skin to reach the systemic circulation for subsequent distribution in the human body [54]. TDD system consists of micro-pumps, micro-needles, reservoir, micro-flow sensor, blood pressure sensor, and required electronic circuit for necessary operations. Among them, micro-pumps and micro-needles are the most important components of microfluidic system particularly for drug delivery applications. Micro-pumps are used for delivery and treatment purposes. Micro-needles can be used as stand-alone devices and part of complicated microfluidic system in which micro-needles are integrated with other devices in the system. Micro-actuators are another important building block for many MEMS based devices, which generate forces or displacements to realize scanning, tuning, manipulating or delivering function [55]. Recent

advancements in micro-fluids have resulted in a variety of small-scale pumps and compressors. These devices have potential applications in drug delivery. Tetteh *et al* (2014), compared MEMS actuation mechanisms for micro-pumps in drug delivery systems and found that electrostatic actuation such as electromagnetic, piezoelectric, electro-thermal and electrostatic mechanism had been commonly adopted due to their advantages like low power consumption, quick response and simple structure [56]. Gensler *et al* (2012), successfully developed implantable DD system for controlling the dose, timing and target location using integrated electrolysis actuator for *in vivo* application of the device in mice [57].

## 7. EMERGING AREAS

Improvement in design technology and diversified applications of MEMS are allowing neuroscientists to explore varied areas and possibilities to show the emerging application of MEMS as neural interface. An interesting patented application is demonstrated by Hoppensteadt and Izhikevich (2001) showing that MEMS can be used to build a sophisticated information processing system by using the concept of MEMS and neuro-computing. They used MEMS oscillators to build an oscillatory neuro-computer having auto-corrective associated memory that stores and retrieves complex patterns [58]. Additionally, MEMS application as stimulators is another recent development. There are two types of stimulators namely - the transcutaneous vagus nerve stimulator (t-VNS) and the responsive neuro-stimulator system (RNS)[59]. In VNS the bipolar electrode pair is placed around the left vagus nerve in the neck to prevent seizures in epilepsy and is also effective in treating chronic or recurrent depression [60]. RNS is another interesting invention in this field, designed for the treatment of medically refractory partial epilepsy. RNS neuro-stimulator is a programmable device delivering electrical pulses, and cortical strip leads. It is claimed that it may "treat" epilepsy by detecting abnormal electrical activity in the brain and responding by delivering electrical stimulation to normalize brain activity before the patient experiences seizure symptoms. The neuro-stimulator is implanted in the cranium, and the electrodes are implanted near the seizure focus. A couple of studies using RNS on humans have been performed and the results are encouraging [61].

Further, Khorgade and Gaidhane (2011) described the application of MEMS in robotics for developing accelerometers, geophones, sensor digital compass,

oscillators, and microphones for creating self-balancing robots, tilt mode game controller, alarm system, and human motion monitoring devices [62]. The integration of MEMS technologies in exoskeletons with its advantageous features such as size, frequency response, range, reliability, wear ability and integral electronics is being presently employed in different robotic mechanisms for kinematics measurements [63].

Another application of MEMS based devices that is emerging is the development of intent controlled wheel chair for the disabled [64, 65]. Kaur and Vasisht (2013) developed an automated wheel chair based on head and hand movement of physically challenged person to facilitate their independent movement using MEMS accelerometer. They designed the wheel chair in such a way that it can move in any of the four directions, after the transmitter generates the intended head or hand movement.

## 8. CONCLUSION

It is known that MEMS based devices are synthetic or semi-synthetic devices, yet they are biocompatible, ultra-miniaturized with fairly good battery life and having connectors capable to provide long lasting interface with natural end-organs or nerves, however, still lot of work is required in developing newer avenues of biological control, standardizing equipment to reduce manufacturing costs, enhancing biocompatibility of materials used to prolong their implanted shelf life, and develop an inbuilt mechanism to collect energy from neighboring biological tissues or fluids [66], so that replacement of batteries are not required for a sustained life of the implanted MEMS device. Further, although MEMS devices are finding applications in different fields as neural interface however, it is worth mentioning that most of the experiments have been performed on animals till date. Thus, its usage in humans demands lots of clinical trials and medical approvals before it can actually be marketed or commercialized by the industry [67]. Additionally, the biocompatibility of materials for different application purposes is still being researched and understanding the perceived risk of infection, which exists in employing these devices in humans. However, they are still better than conventional needles and catheters which have much higher risks of infection, frequent visits to care provider, loss of productivity and low patient compliance when used on a mass scale. Hence, it is important that appropriate merger of different disciplines such as material science, nanotechnology, medical science, electronics and

biomedical engineering, etc. is achieved for the development of better devices that can treat the prevalent neural disorders in an effective manner.

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