CHAPTER 1

INTRODUCTION TO MEMS IN BIOLOGY AND HEALTHCARE

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1.1 INTRODUCTION

Microelectromechanical systems, commonly abbreviated as MEMS, have introduced a class of miniaturized devices and systems with high sensitivity and rapid and accurate delivery of functions. In general, these devices are realized with broadly two sets of unique micromachining processes, that is, surface micromachining and bulk micromachining (Basu *et al.*, 2019a, 2020a). A typical MEMS system includes mechanical movable components interfaced with electrical circuitry that can interface with signals going in and out of the device (Nayak *et al.*, 2013; and Basu *et al.*, 2019b). Biomicroelectromechanical systems (BioMEMS) and miniaturized biomedical devices produced through micromachining techniques have revolutionized the healthcare and medicine sectors through a variety of smart sensors (Basu *et al.*, 2019c) and implantable devices (Bhattacharya *et al.*, 2007a, 2008a), and also hybrid and integrated sensors-on-microchips (Basu *et al.*, 2016, 2019d). The main deliverable of these devices enables these systems to have a smarter, faster, and efficient way to solve existing problems in drug delivery applications (Li *et al.*, 2004), sample culture and characterization, better management of implants (Meng, 2020), etc. Additionally, the ability for batch fabrication among these classes of micro-devices allows a continuous and rapid supply of huge quantities of these devices to the healthcare system at a significantly low cost (Basu *et al.*, 2020b). In the 21st century, it has been predicted that MEMS will find a big footprint in the biomedical industry in comparison to other sectors (Manoharan and Bhattacharya, 2019; and Mohd Ghazali *et al.*, 2020).

Physical MEMS, i.e., MEMS devices that would be used for the measurement of physical parameters, such as acceleration, velocity, and temperature, started being integrated into the biomedical domain as early as the 1980s (Barkam *et al.*, 2013; and Cobo *et al.*, 2015). This is when micromachined pressure and inertial sensors were commercially developed and integrated into direct biological applications (Sezen *et al.*, 2005; and Basu *et al.*, 2019e). Only later on, as this integration happened successfully and

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the need for small-scale devices was fueled by the requirements of the Human Genome Project, was the field named as the more specialized biological MEMS (BioMEMS). One such MEMS (Basu *et al.*, 2016) device was a reusable pressure sensor that was used to measure blood pressure within patients.

Since then, MEMS pressure sensors in combination with micro-antenna, and other application-specific integrated circuits (ASICs), have been used in a variety of areas of direct biological consequence. Examples are contact lenses (Huang *et al.*, 2013) for continuous monitoring of intraocular pressure (IOP) among glaucoma patients, sensors for monitoring of aneurysms (Allen, 2005), and chemical and biological sensors (Shantanu *et al.*, 2010). Modern defibrillators and pacemakers include micromachined accelerometers (Chinitz *et al.*, 2018) to keep track of the heartbeat and rhythm, so as to provide necessary protection against cardiac arrest or heart attack. Recently, hearing aids integrated with MEMS microphones (Mallik *et al.*, 2019) have shown performance in a small object that is similar to that by conventional, bulky hearing aids. Bioinspired microphones (Ishfaque *et al.*, 2019), on the other hand, have shown great promise toward improving directionality, and have recently been commercialized to improve audio performance within consumer devices (Ni *et al.*, 2009; and Puleo *et al.*, 2007).

At the heart of all these devices exists a MEMS actuator or sensing element that normally converts the stimuli to be sensed to a measurable signal through a transduction step (Kusano *et al.*, 2017). The actuation among MEMS devices integrated in biomedical devices includes various interconversion approaches that are executed through piezoelectric (Avram *et al.*, 2019), electromagnetic (Yunas *et al.*, 2020), thermo-responsive (Khoshnoud and De Silva, 2012), thermo-pneumatic, and pneumatic (Yahiaoui *et al.*, 2012) means. Molecular recognition or biomolecular detection via mass sensing (Adreeja *et al.*, 2017; Basu *et al.*, 2019f; and Basu and Saha, 2020) has been a widely adopted method of sensitive detection. MEMS resonators with a specific frequency reference, commonly called the resonant frequency, can be loaded with biomolecules. The resultant shift in the resonant frequency indicates that binding of the biomolecule has occurred. The surface of such MEMS resonators is frequently coated with materials that adhere specifically to certain specific biomolecules (Basu *et al.*, 2019g; and Bhattacharya *et al.*, 2019), which improves the selectivity to biomolecules by promoting strong binding to specific targets (Gupta *et al.*, 2020).

Microfluidics or “a lab-on-chip” is a class of MEMS devices that enable point-of-care (POC) diagnosis and so provide a portable solution to analyze body fluids in a very cost-effective way (Sezen *et al.*, 2005; Manoharan and Bhattacharya, 2019; and Mohd Ghazali *et al.*, 2020). A microfluidic MEMS system may include micro-channels, micro-valves, micropumps (Kant *et al.*, 2017a), micro-mixers, micro-filters (Caton and White, 2001), micro-sensors, and micro-reservoirs (Kant *et al.*, 2013), which are commonly fabricated on a hard substrate such as glass and silicon, sometimes in combination with soft polymeric materials. Surface acoustic wave (SAW) resonators (Kamal *et al.*, 2020), as well as flexural plates with piezoelectric transduction (Ghosh *et al.*, 2011; and Basu *et al.*, 2019h), have been demonstrated to provide frequency-selective mixing and pumping of the fluids being measured (Kotzar *et al.*, 2002). Implantable biomedical devices have been proposed as an effective solution to deliver medicines in a controlled manner to a particular portion of the human body. Such devices normally contain micro-valves (Singh *et al.*, 2015), micro-reservoirs (Kant *et al.*, 2013, 2017b), and micro-actuators (Ardila Rodríguez *et al.*, 2009). The micro-reservoirs store the medicine involved in a liquid form. The micro-actuator controls the out-flow of the liquid-phase medicine, with the micro-valves being in sync with the micro-actuators (Bhattacharya *et al.*, 2008b). When it comes to implantable solutions, there has been a demand for biocompatible and chemically inert materials. At the same time, the materials need to be processed with conventional MEMS fabrication platforms and the cost of processing must be low. Silicon is on the expensive end of the materials spectrum, due to its cleanroom-oriented fabrication; this makes biocompatible and nonbiodegradable polymers as alternatives to conventional silicon, as they are easy to process. Such polymer-based BioMEMS devices are particularly useful for implantable solutions and disposable cartridge-type devices where low cost is very important (Singh *et al.*, 2015; and Sundriyal and Bhattacharya, 2018).

Owing to micromachining processes, micro-needles of various sizes and tip shapes have gained significant popularity in drug delivery, biosignal recording and tracking, blood extraction, cancer therapy, and many other applications (Bhatt *et al.*, 2016). Micro-needles attached to microfluidic platforms allow easy sample extraction and analysis in a sequence of well-controlled steps (Zhang *et al.*, 2009). Micro-needles equipped with micro-actuators can be injected into a human body to provide necessary pre-surgical information (Bhattacharya *et al.*, 2008c; and Courtenay *et al.*, 2020). Ultrasound imaging in conjunction with beam forming can be used to construct three-dimensional images from the part of the body under investigation (Wang *et al.*, 2020). With the advent of MEMS technology, and thereby microsurgical tools, minimally invasive surgery (MIS) has shown great promise over conventional open surgery procedures due to quick recovery, cost minimization, and reduced injury to neighboring tissues. Such microsurgical tools are constructed of mechanical components such as micro-tweezers (Shi *et al.*, 1995), micro-motors (Balachandar *et al.*, 2016), and clamps (Park *et al.*, 2014), and are commonly attached to handheld devices with precise control. MIS has already expanded into angioplasty, catheterization, endoscopy, laparoscopy, neurosurgery, etc. (Bhattacharya *et al.* 2007b, 2010). Angioplasty is a medical procedure to insert a stent inside a cardiac blood vessel via a catheter. The stent is then expanded in the next stage of the process to maintain stable blood flow, thereby reducing the probability of heart attack due to narrowing of cardiac blood vessels. Such stents are currently fabricated with conventional micromachining processes (Bhattacharya *et al.*, 2006, 2008a; and Korampally *et al.*, 2006).

With the advent of wearable devices, MEMS technology has played a key part in limiting the overall size of devices within a small form factor with low power consumption. As the name suggests, “wearables” are continuously worn by the user and the user’s activities are tracked and displayed on the device with a sensor network. The most commonly used sensors among wearables include pressure sensors, magnetic field sensors, accelerometers, temperature sensors, and humidity sensors. Despite the device actively working inside the physical environment, the sensor network within the device provides efficient and accurate data of the human activities through machine learning (ML)

(Liu *et al.*, 2008; and Barazani *et al.*, 2020) and artificial intelligence (AI) algorithms, which bind the sensor network together with an ASIC. Smart watches are one the most popular examples of wearable devices (Chauhan and Bhattacharya, 2017).

This book has been written to provide a perspective of the topic of MEMS as applied to biology and healthcare. It is divided into 11 chapters in three distinct sections. These three sections cover the topics "Biological MEMS: recent perspectives," "Microfluidic MEMS for sensing," and "Wearable MEMS devices and sensors." Each section then discusses three or four topics, providing knowledge to enlighten graduate students, postdoctoral researchers, and research professionals engaged in advanced MEMS-related research. This book is expected to serve as a handy reference on biosensors and the biomedical micro-device community that employs MEMS processes. The book may serve as a reference book for those following undergraduate and postgraduate programs covering MEMS and very large-scale integration (VLSI) courses as electives, irrespective of the majors they are pursing.

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