J. Inst. Eng. India Ser. B (December 2023) 104(6):1377–1388
https://doi.org/10.1007/s40031-023-00924-w

REVIEW PAPER

Recent Advances in Bio-MEMS and Future Possibilities: An Overview

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Received: 7 October 2021 / Accepted: 16 September 2023 / Published online: 4 October 2023

Abstract Microelectromechanical systems (MEMS) are a technology that allows engineers to create small, integrated devices with electrical and mechanical components to perform tasks carried out by macroscopic systems. MEMS devices are interfaces of the digital world (computer) and the analog world (our surroundings) with the capability of sensing and controlling. System-integrated chip technology is used to make these devices. The main advantages of MEMS are lightweight, ease of fabrication, reduced size, low-power operation, and the possibility of electrical and electronic device interaction. These MEMS devices find applications in biomedical fields such as detection, analysis, diagnosis, therapeutics, drug delivery, cell culture, microsurgery, and genome synthesis. This review paper discusses recent MEMS research, emphasising biomedical applications and advances. This paper includes functional components, technologies involved in manufacturing, and current trends in Bio-MEMS devices. This study discusses the Bio-MEMS device's accuracy, design problems, prospective applications, and new possibilities.

Keywords Bio-MEMS · Micro-fabrication · Three-dimensional printing · Cantilever beams · Biochip · Laboratory-on-chip devices

Introduction

The population boom in the previous few decades has fuelled the rapid rise of microelectromechanical system (MEMS) technologies in biomedical field applications. MEMS are integrated devices with both electrical and mechanical components to perform various tasks carried out by macroscopic systems [1–4]. The need to replace the time-consuming and inaccurate old laboratory-based diagnosis technique with a rapid diagnostic solution with high accuracy arose because of the expanding population. Bergveld conceived the idea of a microscale system for chemical analysis [5]. Researchers have used MEMS fabrication technology to construct enhanced medical infrastructure. Bio-MEMS technology is quickly evolving, with biosensors, pacemakers, and micro-dosing drug delivery applications.

Bio-MEMS technology has been evolving since the early 1990s and is continually improving. MEMS technology begins in the USA. MEMS are also known as Microsystems Technology in Europe and Micromachines in Japan [1]. Researches on MEMS have shown a tremendous contribution to novel technologies providing new approaches in treating many challenging problems such as touch [6, 7], pressure [8–12], temperature [13–15], distance [16], humidity [17–20], image [21], sensors, microphones [22–25], gyroscopes [26–29], accelerometers [30–33], and magnetometers [34–36]. Globally, MEMS are capturing a big scale market of $25 billion by 2023 as per references [37, 38]. It comprises micro-fabrication techniques, microfluidics, sensors, actuators, drug delivery systems, implantable micro-devices, micro-total-analysis systems (μTAS), electronically integrated circuit, micro-reservoir, micro-pump, cantilever, rotor, channel, valves, and laboratory-on-a-chip devices [39]. Surface and bulk micromachines are the two main components of MEMS construction. This paper presents an

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overview concerning the introduction to Bio-MEMS, their design, applications, and challenges.

Transducers are MEMS devices that transform signals from one form to another. MEMS devices sense the information or data and send it to the controller unit for processing based on the control algorithm. The actuating units operate accordingly to provide output [40, 41]. The MEMS devices have the benefits of being lightweight, ease of fabrication, reduced size, low-power operation, and possible electrical and electronic device interaction. However, MEMS devices are small, delicate, prone to particle contamination, and the moving parts can become out of calibration [42].

In the biomedical field, MEMS devices find applications in drug delivery and synthesis, laboratory-on-chips [43] or biochips [44, 45], microsurgery, diagnostics, micro-therapy, micro-total analysis systems (μTAS) [46], artificial organs, genome sequencing and synthesis, cell manipulation, and characterisation [47, 48]. MEMS devices used in biomedical applications are bio-microelectromechanical systems (Bio-MEMS).

Bio-MEMS is a system or device fabricated with technologies motivated by the insinuation of micro/nanoscale fabrication used for processing, manipulating, delivering, and analysing the manufacturing of chemicals and biological entities. Bio-MEMS combines various parts of technology injected into a biological system, which may evaluate and stimulate by multiple physical, chemical, or electrical means. Bio-MEMS incorporates many scientific disciplines, such as material science, physics, chemistry, biotechnology, mechanical, electronics, and electrical engineering [49]. Therefore, to fabricate a Bio-MEMS device, all these disciplines' collaborative effort is necessary.

This review paper presents the present status of research in Bio-MEMS and their applications to provide insight for detailed studies that rely heavily on such biological measures. This paper comprises four sections. Section 2 covers design, techniques, and goals. Section 3 discusses various applications, and Sect. 4 has a detailed discussion of recent trends in the field of Bio-MEMS.

Design, Techniques and Goals

Materials for Fabrication

Semiconductors are used to design and fabricate Bio-MEMS devices based on the integrated circuit. Due to the increase in functionality and complexity, various materials are utilised to manufacture the devices. Different materials are used for insulation, adhesive purposes. As a semiconductor, other than silicon, various polymers, metals with nanocomposite, inorganic materials, and ceramics are found suitable based on application and requirement. Silicon dioxide and silicon nitride are used for insulation purposes. Silicon is used due to the advantages of conductivity, resilience, robustness, performance reliability, easy processing, and low cost of fabrication due to the abundant availability of the resources [50].

Due to multifold functionality, new materials have been added to fabricate Bio-MEMS devices, such as germanium-based materials, inorganic materials, ceramics, polymers, and metal nanocomposite materials. These materials have added advantages of flexibility, easy processing, chemical and biological properties, insulation, biocompatibility, and low cost [51]. Desired electrical, magnetic, and mechanical properties [52–54] can be attained by mixing the adaptive proportion of polymers with filler material.

Recently, glass and inorganic materials have been widely used because of their benefits with modern fabrication technologies [55–57]. For example, glass has exceptional characteristics in terms of hardness that suppresses channel deformation, chemical and biological inertness, and better optical transparency. However, it has the drawback of high cost and takes a lot of time because of complex processing. Piezoelectric (inorganic) materials have better output with less cost and easy processing [58–60].

Functional Components of Bio-MEMS

Careful monitoring and necessary procedures are taken during the analysis, research, and production of Bio-MEMS. A single component in Bio-MEMS is critical to obtaining a suitable analysis result. The following sections go over some of the fundamentals of MEMS.

Biosensors

Biosensors combine a physical or chemical transducer (with biologically sensitive parts) to detect chemicals in a particular external environment selectively and quantitatively. They can detect cells, proteins, DNA (presence of the molecule itself, or, more precisely, some specific sequence via binding of a single-strand molecule to its complementary one in the biological system) and tiny compounds if appropriately synthesised. Depending on the measured quantity (physical or chemical), target destination (specific tissue/bulk body water), and our demands on them, biosensors employ a range of detecting procedures [61–63]. The most widely used techniques include mechanical cantilever sensors work by bending the cantilever (mechanical deformation can be translated to an electrical signal via a piezo-resistor), or mechanical vibrations (mass sensing mode). The type of material to use is determined by the substances or quantities to be evaluated. Silicon cantilever sensors are commonly used to detect DNA, proteins, and cancer indicators, among other things (prostate-specific antigen) [64, 65].

For easy detection in various conditions, electrochemical approaches use well-known electrical variables (conductance, electric current, and voltage). Amperometric biosensors for redox processes (glucose detection to monitor hydrogen peroxide generation or oxygen consumption), gas and lactate detection, and metabolic blood parameter evaluation. Potentiometric biosensors monitor potential (voltage) variations between electrodes. The base component is a field-effect transistor (ion-sensitive field-effect transistor ISFET) constructed from silicon nanowires and carbon nanotubes, allowing the fabrication of numerous sensors at nanoscale dimensions (high surface area to volume ratio).

Conductometric biosensors measure conductance variations in response to changes in the ionic environment between electrodes, signalling a bio-molecular reaction involving DNA, proteins, antigen/antibody reactions, or cellular metabolic excretion [66, 67].

Actuators

Although "actuators" refers typically to device components that are responsible for performing a specific function, we use it in this context to refer to entire devices (or their modules) that are purposely and deliberately affecting the biological system or its physiology (e.g. drug delivery systems). Actuation systems either chemically or electrically stimulate the biological organism [68, 69]. These devices often use "micropumps" as the driving components for delivering medications or other therapeutic substances into the desired location within the human body. Depending on the pumping function's mechanism, they can be classified as mechanical (electrostatic, thermo-pneumatic) or non-mechanical (magneto-hydro-dynamic, electroosmotic, chemically based) [70–72]. Table 1 lists the many types of micropumps, along with their names, advantages, and disadvantages.

Energy Harvesters

Embedded power generators can provide necessary power by harvesting energy from the body's essential functions if the battery power source is insufficient (temperature gradients within the body for thermoelectric generators). A piezoelectric nanowire-based generator may transform the biomechanical energy of muscular contraction into electricity, allowing low-frequency energy scavenging from regular and irregular motions caused by living biological systems. For small gadgets, it provides very little energy [73–75].

Electrodes

The MEMS terminals have outstanding signal-gathering capabilities, and determining the cathode material is critical. For the examination, electrode material qualities such as high conductance, high impedance, low opposition, and good biocompatibility are required. Cathodes are divided into two portions. The partner comes first, followed by the reference section. When the signal is obtained from the reference and counter terminals, the voltage difference between

Table 1 Various types of actuators with advantages and shortcomings

S. No	Type of micropumps	Name of actuator	Advantages	Shortcomings
1	Mechanical	Electrostatic	It can blend a variety of doses up and deliver the final product into micro-channels	High applied voltages and structure intricacy
2	Mechanical	Piezoelectric	It requires a high voltage induction up to a certain level and is operated at a relatively high frequency	The electric signal is an electrical charge rather current or voltage
3	Mechanical	Thermo-pneumatic	Produces large pressure and displacement in the membrane	Complicated structure, slow response, low efficiency. Not applicable in high-frequency operations
4	Mechanical	Shape-memory alloy (SMA)	After the heating/cooling cycle capable of restoring its original shape right	High-power consumption
5	Non-mechanical	Osmotic-type	No requirement for external power (mechanical or electrical)	The semi-permeable diaphragm might depart from the substrate after a certain period Low flow rate and low response with long time delay
6	Non-mechanical	Capillary-type	The controlled quantity of fluid can be released with variation in outlet fluidic resistance	Reported maximum flow rate is very low, as required in biochips
7	Non-mechanical	Bubble-type	More than two types of doses can be blended at the time of expansion or collapsing cycles	The heating process is a significant drawback as it is not preferred. So the application is limited

these two anodes can be evaluated using differentiating circuits and how it confirms the signal varieties [76].

Flexible MEMS microelectrodes provide more significant advantages than rigid microelectrodes, such as low volume and molecular weight, low cost of production, and ability to conform to brain tissues. A microelectrode for the neural interface can record neural signals and stimulate the nervous system. It connects the tissues to the implanted devices as a tissue-machine interface. In Reference [77], the advantages of flexible MEMS microelectrodes over stiff microelectrodes and their fabrication methodologies are discussed. The main issues with microelectrodes have also been explored, including tissue injury, immunological reactions, and mechanical damage.

Accelerometers

MEMS-based accelerometers are both cost-effective and portable, allowing for various applications in wearable devices such as health monitoring and aviation. A voltage frequency converter has been embedded in a wireless accelerometer with MEMS to measure low amplitude vibrations and low frequency to compute mechanical seismic response. The natural frequency of a peak in the 13.10 Hz to 17.90 Hz range is estimated using these computed vibrations, which are classed by low amplitude (Figs. 1, 2 and 3).

Using accelerometers to determine development information would improve the precision of human data sources and aid in recovery, allowing unwell persons to regain muscle firmness and improve their walking capacity. The design of MEMS accelerometers considers the suitable streamlining of parameters such as operating recurrence, transmission capacity, damping proportion, power applied, and the MEMS structure's confirmation weight [78–80].

Hydrophone

MEMS hydrophone depends on a fish sidelong line designed by a short cycle to accomplish adaptability. The MEMS hydrophone provides the vector guidance of the submerged sign and, for the most part, a low-recurrence signal [81, 82].

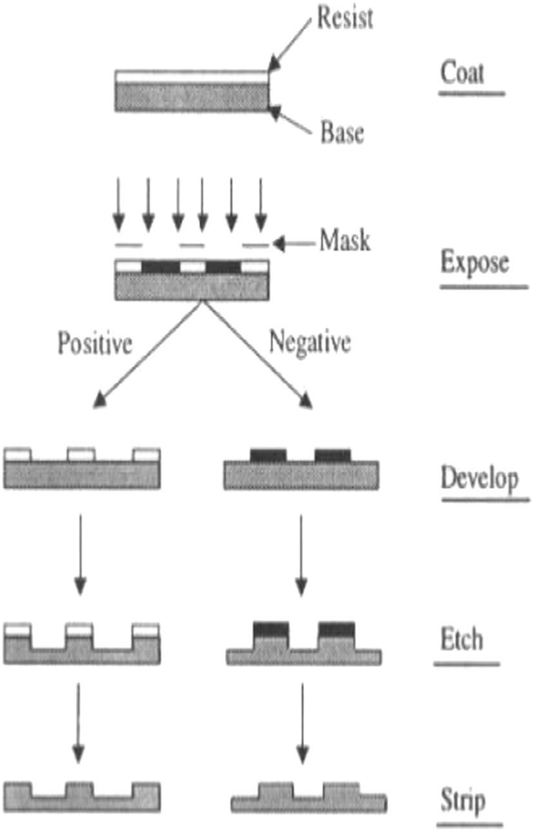
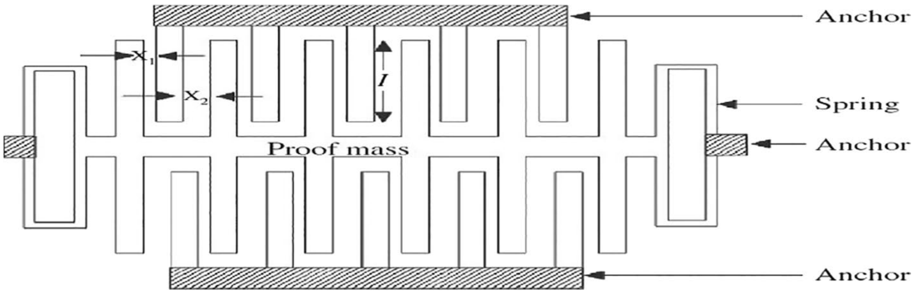


Fig. 2 Description of the basic lithography technique

Cantilever Beams

A cantilever is a rigid structure with a fixed and free end. They have various applications as sensors and are used in testing multiple diseases with the help of sensing layers. The simulation occurred by the deposition of antigens on the beams can be seen in Intellisuite software, and this helps in the analytical study of the change in frequency response appearing with a change in different parameters like length or width of the cantilever beams [83–85].

Fig. 1 Prototype of capacitive accelerometer [78]



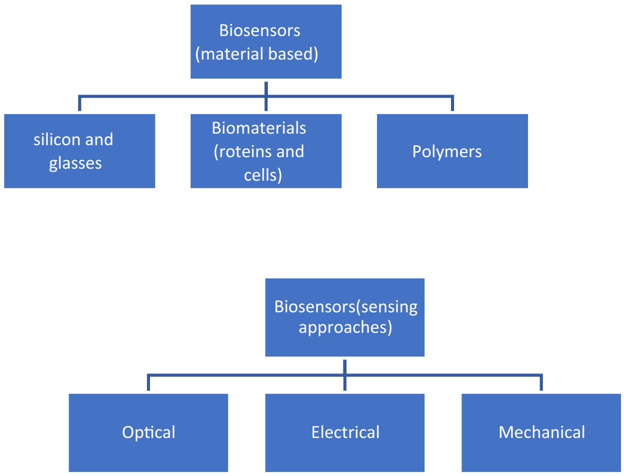


Fig. 3 Classification of biosensors [97]

Micropumps

In [86], a thorough analysis of the micropumps was provided. Micropumps are the devices used to deliver drugs into the body of patients as therapeutic. The major design and fabrication concerns are high resolution, reliability, biocompatibility, high volumetric flow rate, and power consumption. Technically, these devices may be non-mechanical or mechanical type. Magnetohydrodynamic, electrohydrodynamic, electroosmotic, chemical, osmotic-type, capillary-type, electrowetting (EW), bubble-type non-mechanical micropumps have been investigated in Bio-MEMS [86]. New opportunities for fluid machinery are made possible by the developing MEMS technology on a highly specific length scale. Mechanical pumps bridge the floor range gap between nanomechanical pumps and classical microscale pumps, which ranges between the several micro-litre to several ml per minute. The macron size in this range has a surface-to-volume ratio that is significantly greater than that in microscale, which results in high-viscus forces and restricts down scaling of well-known mechanical pump principles [87–89].

Technologies Fabrication Technologies

The micromachining techniques incorporated in integrated circuit domains, such as surface micromachining and bulk micromachining, are used to fabricate MEMS devices. Other methods include oxidation, sputtering, thin film deposition, photolithography, chemical vapour deposition (CVD), ion implantation, and laser micromachining.

Surface Micromachining

Surface micromachining is a fabrication technique that involves the deposition and patterning of a mechanically supporting layer called the sacrificial layer on a substrate and does not involve the bulk of substrates. The thin films, structural layers are subsequently deposited on the sacrificial layer using photolithography [90–93]. On completion of the fabrication process, the sacrificial layer is removed so that it does not damage the structural layer and micromechanical devices are released from the substrates. These layers are etched using either wet etch (acid) or dry etch (ionised gas). In general, silicon oxide is used as a sacrificial layer, and polysilicon is used as a substrate layer. Surface micromachining is different from bulk micromachining, which uses a silicon wafer that is selectively etched and the microstructures produced are much smaller than the structures built by bulk micromachining. There are many combinations of structural and sacrificial layers, and depending on the process, the combination of layers is made accordingly. The basic function of surface micromachining is as follows: (1) substrate-silicon wafer, (2) deposition of the sacrificial layer (silicon oxide), (3) deposition of cantilever layer, (4) active region patterning, (5) etching of sacrificial layer [94].

Bulk Micromachining

Bulk micromachining involves selective etching of the substrate's inside to fabricate microstructures. Bulk micromachining is one of the ancient techniques for fabricating MEMS devices [95, 96]. It can fabricate devices with integrated electronics. Devices such as pressure sensors and microphones are fabricated using bulk micromachining since it is a commercially viable technique. It can produce structures like cantilevers, membranes, etc. The etching process in bulk micromachining can be done using wet/dry etching or other physical methods. Anisotropic etch is the most commonly used to etch silicon. The silicon wafers are used as a substrate for bulk micromachining. The disadvantage of bulk micromachining is the control of etch depth, and though it is an inexpensive and old technique, in the case where electronics are not associated with devices. This technique is not cost-effective. The typical description of the bulk micromachining fabrication process is as follows: (1) polishing silicon wafers, (2) deposition of cantilever layer, (3) active region patterning, (4) masking of the top oxide layer, (5) removal and patterning of bottom oxide, (6) removal of silicon from the bottom by wet/dry etching, (7) removal of oxide to release cantilever [97].

Laser Machining of Material

Laser designing on polymeric materials is viewed as a green and quick assembling measure with low material choice boundaries and high movability. Moving photon vitality of the laser light to polymer is testing, in any case, as it is straightforward to a wide scope of frequencies, which requires the age of high pinnacle forces to trigger a nonlinear retention impact. Carbon dioxide (CO_2) lasers are among the most oftentimes utilised lasers for modern applications over significant stretches since their hardware is generally straightforward and requires low capital venture. Laser micromachining is a cycle of removal, which is utilised to eliminate the undesirable aspect of the material dependent on the ideal plan. The removal cycle relies upon the materials and the removal boundaries. The laser micromachining does not need the cover to move the example to a more extensive scope of the materials, and it additionally gives the high goal of the pictures [98].

Lithography

Lithography in MEMS fabrication is the shifting of a pattern to a photosensitive material by exposure to light or any other radiation source. Lithography is a major process for the fabrication of MEMS devices. With the development of this technology, stereo-lithography and soft lithography have been developed for the fabrication of polymeric devices.

Stereo-lithography is one of the versatile and powerful methods of fabrication technologies. This involves computer-aided design (CAD) for the fabrication of parts. This CAD file narrates the geometry and size of the parts to be built, and the parts to be built can be worked out using 3D drawing computer software, mathematical equation, or derived from imaging technologies like magnetic resonance imaging (MRI). This decreases the time from days to hours of fabrication. The feasibility of utilising the data from scans makes these fabrication technologies to be widely used in biomedical applications [99]. The resins used for stereolithography are commercially limited, and this is considered a major disadvantage of this technique.

The soft lithography technique was primarily utilised for the fabrication of microfluidics devices. It is a valuable method of moulding the elastomeric substrate, such as polydimethylsiloxane (PDMS), onto the master mould. The process requires a master mould, liquid pre-polymer PDMS, curing agent to be poured over the master mould, and heating. The master mould is fabricated using a basic lithography technique. The pre-polymer takes the shape of the master mould and generates negative relief of the master mould on heating. Soft lithography is a cost-effective, easy, and inexpensive method with a replication accuracy of 10 µm [97].

The electron beam lithography (EBL) machines used now can write on areas up to mm^2, making it one of the critical tools in micropatterning over a variety of materials. E-beam resists at lower temperatures, including a conductive Cr coating and through careful calibration in voltage and exposure dose results in the successful EBL on Parylene C substrates. This helps in withstanding the strain usually occurring at higher temperatures. A micro-pattern with an order of magnitude greater than that of normal MEMS was achieved with high resolution. This combination of EBL and CVD Parylene C promotes the flexibility of Bio-MEMS with submicron features.

Layer-by-Layer (LBL) Coating

The principle behind LBL coating is the periodic immersion of the substrate in polyelectrolyte solutions of opposite charge, which leads to the multiple-layer formation on the surface. The electrostatic interaction between the layers causes the adhesion of the layers. In addition to it, the thickness of these layers can be adjusted within a wide range (a few nanometres–several micrometres). Triply periodic minimal surfaces (TPMS) along with LBL coating exhibit multiple bio functionalities, and they also have zero mean surface curvature, which increases bone tissue regeneration performance [100].

Additive Manufacturing or 3D Printing

Though 3D printing technologies do not provide sufficient design for MEMS devices, and most of the materials are not suitable for biological applications, there are a few areas in which 3D printing helps to fabricate new structures for new applications. Additive manufacturing techniques are used for the creation of a porous structure which will improve the regenerative capacity of bone substitutes as well as in better osseointegration of bone implants in multiple in vivo experiments. Additively manufactured meta-biomaterials, due to their highly adjustable surface area, allow drug delivery agents and reduce bacterial devastation on implant regeneration [100] with topology optimisation creation of optimised geometry based on the defined goals and constraints.

Applications

Biomedical and human-centred applications for MEMS-based sensor technologies are numerous. A biosensor is a device that records data from biological events. The thermometer and stethoscope are two simple, relatively ancient biosensors. There are now a plethora of sensors available for pregnancy testing, cholesterol monitoring, DNA analysis, food allergy detection, and a variety of other uses. Sensors are mostly utilised for crucial surgery, long-term sensors, and at-home laboratory-quality diagnosis.

Expanded MEMS technologies, as well as low-cost and low-power rated microcontrollers and related telemetry modules, have been key factors in the development of biological sensors in health care [101]. Biosensors are made using various materials and sensing techniques. Below is a list of several sensors and their applications.

Auscultation is the first and most crucial stage in clinical diagnosis. The sound from an electronic stethoscope should go through three layers of medium: two layers of the diaphragm and the internal cavity. As a result, sensitivity and precision are compromised. As a result, the piezoresistive concept was used to create an electronic heart sound sensor with a real-time waveform display and a good signal-to-noise ratio. It is made from silicon wafers and SOI wafers (silicon on insulators). The oscilloscope displays the electrical signal changed from the heart sound vibration, proving the accuracy of the diagnosis. In [102], an electronic heart sound sensor has been proposed.

By applying 28KDa antigen to the left beam and 57KDa antigen to the right beam on sensing layer Si, a MEMS sensor with two cantilever beams was used to detect chronic renal disease and blue baby disease at the same time. Intellisuite software can simulate the deflection of a beam owing to an increase in mass. The deflection and frequency response were calculated at various lengths, widths, and thicknesses. The coated layers for sensing over the cantilever's surface can detect multiple diseases at once [83].

Artificial Organ on a Chip

Organ on chip is a 3D microfluidic cell culture chip that restores all of an organ's activities and functions. Many attempts have been made to create an artificial organ in vitro that mimics the traits and properties of our body's organs. Cell–cell contact, cell–matrix interaction, blood flow, and 3D geometrics are some of these properties. Organs such as the lungs, gastrointestinal tract, and arterial networks have been reconstructed as organs-on-a-chip. This idea can be utilised to effectively find and produce drugs, and it is a significant advance in biomedical engineering.

Micro-Biochips

Micro-biochips are miniature versions of biomechanics that allow for the response and detection of various biomolecules. This aids in the detection of numerous diseases, harmful components, and other issues. The design of biochips is determined by the intended usage. For example, a microchip with a piezoelectric pump and valve fixed to the supply channel for controlled flow rate and conveyance is utilised for reagent supply and mixing (shown in Fig. 4), whereas for performing photolithographic manufacture of Ah-immunoassay biochips was used, and microbeads coated with Avidin [103] were used for the entire assay process, followed by micro-fluorometry for detection.

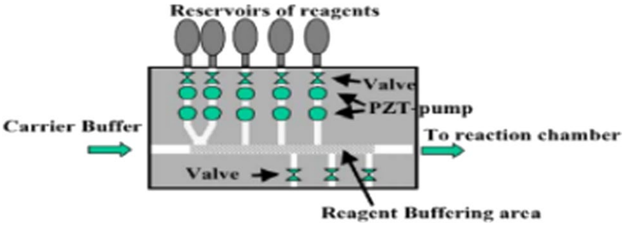


Fig. 4 Schematic configuration of the 5-channel sample and reagents supply micro-biochip unit [103]

Laboratory-on-a-Chip

Laboratory-on-a-chip, as well as "micro-total-analysis-system"—μTAS, commonly refers to a rather complex device, integrating all the basic components (ports, sensors/detectors, integrated circuits) into fully functional units, offering at least some level of biological system's parameters evaluation. From the specific biological condition, through data acquisition, up to overall assessment (and potentially taking relevant action), usually leads a pretty long journey: obtaining appropriate sample properly, preparing it for further processing (i.e. via electrophoresis), detecting particular substances (cells, proteins, DNA), evaluating the overall biological condition and desirably utilising acquired information (storing it into embedded memory module, transmitting to physician's computer, or taking desirable action subsequently—i.e. releasing the optimal amount of drug for treating life-threatening situation. Whereas typical μTAS systems usually provide valuable diagnostic information, adding selected "actuator" modules, which affect the biological system based on information obtained from the μTAS module, allows the creation of complex devices suitable for quickly diagnosing certain health conditions and consequently treating those conditions efficiently on a long-termly sustainable basis.

Discussion and Recent Trends

Machines have become an increasingly important element of life as contemporary society has progressed. MEMS/Bio-MEMS technologies have advanced tremendously over the last three decades. MEMS fabrication technology is constantly improving. This has reduced the amount of time spent developing items and has accelerated their development. MEMS has developed unique solutions and techniques due to significant application drivers such as healthcare and environmental sensing. Biosensors in smartphones have also been created recently as an everyday health monitoring activity [101]. Bio-MEMS' interdisciplinary character, which draws on expertise from various sectors, has resulted in several advancements and research findings. For example, a thorough understanding of DNA hybridisation has led to the development of cancer detection sensors.

Wireless devices employing MEMS technologies have been used to monitor intraocular pressure (IOP) on a regular basis. Glaucoma is one of the leading causes of blindness, impacting millions of individuals around the world. Cardio MEMs, which have been approved by the FDA, are also used to monitor pressure in heart failure patients.

Paracetamol, glucose, lactate, and other biomarkers are successfully monitored using the i-IronIC subcutaneous device. The use of neuro-stimulators to give chronic pain management is another area of intense research. The FDA-approved Stim Wave Freedom-4SCS system is an example of a neuro-stimulators for back and lower limb pain treatment. Although concentrating on a single component is beneficial, it would be preferable if the micro-instrument could measure many factors, as a situation can be influenced by more than one parameter. Electrical stimulation will provide a more suited treatment with fewer adverse effects after examining the electrical networks of the human body.

Making wearable accelerometers with MEMS that are specifically designed for detecting neurological diseases like Parkinson's disease can significantly assist people in impoverished and developing nations in getting an estimation and testing device. MEMS accelerometers based on the capacitive rule are the best choice for the plan since the gadget requires high affectability at a low-recurrence extent, starting from DC. Sensor check is in working explicit ranges to estimate side effects. Material, mathematical, and fundamental aspects of the sensor must be improved, so that it can act to the expected extent and details.

Even though ICP plays an essential role in the body in detecting unusual changes, it has not yet resulted in the discovery of any ordered illness. However, this type of monitoring can easily spot early signs of neurological disease. Later on, the single-module sensor will be stretched out for bio-implantation with remote information transmission in long-haul recording, as it has been shown to be effective in the detection of parallelism. For evaluating the pH of the arrangement, place an $Ag/AgIO_3$ reference cathode next to the Sb_2O_3 working terminal. Poisonous elements, such as cadmium or mercury, are used to make the terminals [104].

Microfluidics and Bio-MEMS based on the tunnelling effect may detect cells and structures. The size of Bio-MEMS is determined by the cell size to be noticed. Bio-MEMS membrane deformation provides crucial information about the cell under research, allowing its potential usage in blood tests to be investigated [105]. The manufactured microfluidic chip was used to examine the detection of specific toxicity using intact immobilised bio-luminescent bacteria recombinant Escherichia coli (*E. coli*) strain GC2. The research proves that Bio-MEMS may be used to determine toxicity in sediment, water, and soil samples. [106]. To stimulate bone tissue regeneration and to prevent implant-associated infections [100] created, AM permeable meta-biomaterials with multi-practical layer-by-layer coatings through upgraded osteogenic separation of MSCs. This biomaterial displayed a solid antibacterial reaction with up to eight significant degrees decrease in the quantity of both planktonic and follower microscopic organisms and no biofilm arrangement. Furthermore, in osteogenic movement, the gatherings containing BMP-2 displayed a multi-crease increment in mineralisation and altogether improved ALP action.

The laser ablation techniques can be applied to fabricate Bio-MEMS components such as reservoirs and complex connecting channels on the polymer, which can be used in DNA sequencing and enzyme assays [98]. Laboratory-on-chip tests manufactured with saps polymerization by SLA (stereo-lithography) and PMMA (polymethylmethacrylate) are created with various surface medicines and mechanical control of the saps. In this paper, the manufacturing cycle of laboratory-on-chip dependent on the SLA-added substances strategy is explored specifically. The SLA cycle is utilised to consolidate the substrate layers made of polymerized saps developed layer by layer and the PMMA straightforward spread. In contrast with the conventional cycle, the two materials are not coupled by utilising glue (requiring extra material, straightforwardness issues, and devoted advance of manufacture) by using the polymerizations of similar gums as cement media. At that point, the stripping test technique is utilised to approve the grips quality of the joint with various treatments of surface and mechanical control of the tar. At last, the mathematical model of attachments is adjusted with test boundaries got from the stripping test ready to help the counts of union cut-off in various calculations [107].

There have been numerous advancements in mobile healthcare applications. The recent COVID-19 failure has intensified interest in developing sensor technologies for rapid virus diagnosis and monitoring. Microfluidic chips have recently gained popularity in the biomedical field, allowing the incorporation of multiple medical tests on a single chip. Government investments are also being made in the fabrication of microfluidic chips. Scientists are also developing sensors for detecting cancer in the blood. The increased demand for next-generation sequencing will increase the demand for microfluidic chips. Everyday, new Bio-MEMS strategies and innovations emerge to make the impossible possible.

Conclusions

In-depth information about Bio-MEMS devices and their potential applications was provided in this research. Biocompatible materials have been employed as Bio-MEMS membranes to improve devices' interface with the biological environment. The application affects how Bio-MEMS are designed. On silicon substrates, we produced coating patterns with the requisite characteristics and functions using conventional photolithography and plasma polymerization methods. It has been researched to use Bio-MEMS with multiple cantilever beams to simultaneously detect a variety of human disorders. Because they deliver better, quicker, and more precise results than conventional medical techniques like PCR and ELISA, Bio-MEMS are more promising than those techniques. Both chronic renal disease and blue baby disease have been successfully identified. pH sensors provide advantages including suitable mass production and streamlined processing.

The new research area based on the integration of pH sensors with microfluidics with reference electrodes improves the output performance. Fabric-based Bio-MEMS are widely used in biomedical applications, such as proprioceptive sensing systems for therapy assessment, pelvic tilt measurements, and stamping methods. A more efficient and cost-effective process for sensor fabrication is proposed. However, repeatability and sensor durability must be considered.

It is now possible to improve resolution and temperature accuracy to 0.01 per cent full scale with a thermal sensitivity of 1 mK using Raman spectroscopy. ICPF (Ionic conducting polymer film) and bimetallic micropumps have more advantages, particularly for implant-oriented biological applications, and can be improved further. The scaling down of size has improved compatibility and efficiency. The multifunctional ability of these Bio-MEMS is bringing their applications to a higher level and a larger community, making it one of the most dependable and promising technologies of the future.

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