International Journal of
INTELLIGENT SYSTEMS AND APPLICATIONS IN ENGINEERING
ISSN:2147-6799 www.ijisae.org Original Research Paper

Implantable Bio-Electronic Devices for Health Monitoring

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Submitted: 05/09/2024 **Revised:** 17/10/2024 **Accepted:** 27/10/2024

Abstract: Innovative approaches to clinical diagnosis and therapy are becoming more possible because to the proliferation of bioelectronic implants. Alongside the incorporation of electrical interaction, the incorporation of fluidic technology into such implants permits the creation of additional complementary pathways for sensing and intervention. In point of fact, the electrical and fluidic technologies have the potential to collaborate in a bioelectronics implant in order to achieve the creation of a comprehensive therapeutic platform. The most prominent uses of fluidic-enabled bioelectronic implants are presented in this viewpoint piece, along with the techniques of operation and material options that are explored. In addition to this, a prospective that looks ahead is provided on new prospects, as well as crucial materials and technical problems.

***Keywords**: Innovative, diagnosis, incorporation, comprehensive.*

Introduction

New opportunities in the field of medicine have been made available as a result of the confluence of biology and electronics. The use of bioelectronics enables direct engagement with intricate biological systems, which in turn enables a deeper comprehension of the functioning of these systems via the use of a variety of sensing modalities in conjunction with targeted treatment. In particular, implantable bioelectronics have emerged as an essential component of contemporary medical practice. Devices such as pacemakers, spinal cord stimulators, and cochlear implants are responsible for enhancing the quality of life for thousands of patients each year. 1/ 2

The effect and applications of this rapidly expanding area of medicine are expected to be expanded thanks to the many bioelectronic technologies that are now under development. Recent advances include peripheral nerve interfaces for immune system regulation, thin-film flexible electrocorticography devices for neural recording and stimulation, wireless and bioabsorbable pacemakers for cardiac monitoring, and periphery nerve interfaces for cardiac monitoring. 7,8, In a similar vein, conducting polymers, such as PEDOT:PSS, are increasingly being employed in place of traditional metal electrodes in order to form an electrical contact with surrounding tissue that has a low impedance and a high capacitance. ages 9–12 In addition, a growing body of information has brought to light the significance of mechanical qualities and device shape in terms of moderating the reaction of foreign bodies to implants of this kind. a 13 As a result, bioelectronic implants are increasingly made of materials that are soft and flexible in order to better match the mechanical qualities of the tissue that surrounds them.

In addition, the use of thinner materials makes it possible to carry out conformal covering of the intricate surfaces that are characteristic of the majority of the body's components, such as the brain, the skin, or the heart. 5, 14, and 15 The incorporation of fluidics into implants is becoming more possible as a result of material improvements in bioelectronics, which are allowing for extensions of functionality. The interactions that are based on fluids with the body have been an essential component of medical treatment for a very long time. Fluids from the body are collected on a regular basis for the purpose of diagnosis and the monitoring of important biomarkers, while the therapy is provided via the use of fluidic medication infusion.

Considering that fluids are the driving force behind many therapeutic treatments, including fluidic systems that are comparable to those used in bioelectronic devices might provide novel avenues of interaction with tissues and metabolic processes. For instance, this may include the use of bioelectronic contact with the body at the cellular level, such as the administration of tumor-

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suppressing molecules16 during chemotherapy, or it could involve the use of macro-scale interaction to govern organ function, such as the mechanical help of the heart. a 17

There is also the possibility that fluidic components might alter form in response to both internal and external forces, which opens up possibilities for sensing as well as shape-actuation, which can be used to, for instance, decrease surgical footprints.

In this viewpoint, we give a forward-looking view on the potential and problems that are present in the field of bioelectronic implants with integrated fluidic components. We also provide a short summary of the current state of the art in this area.

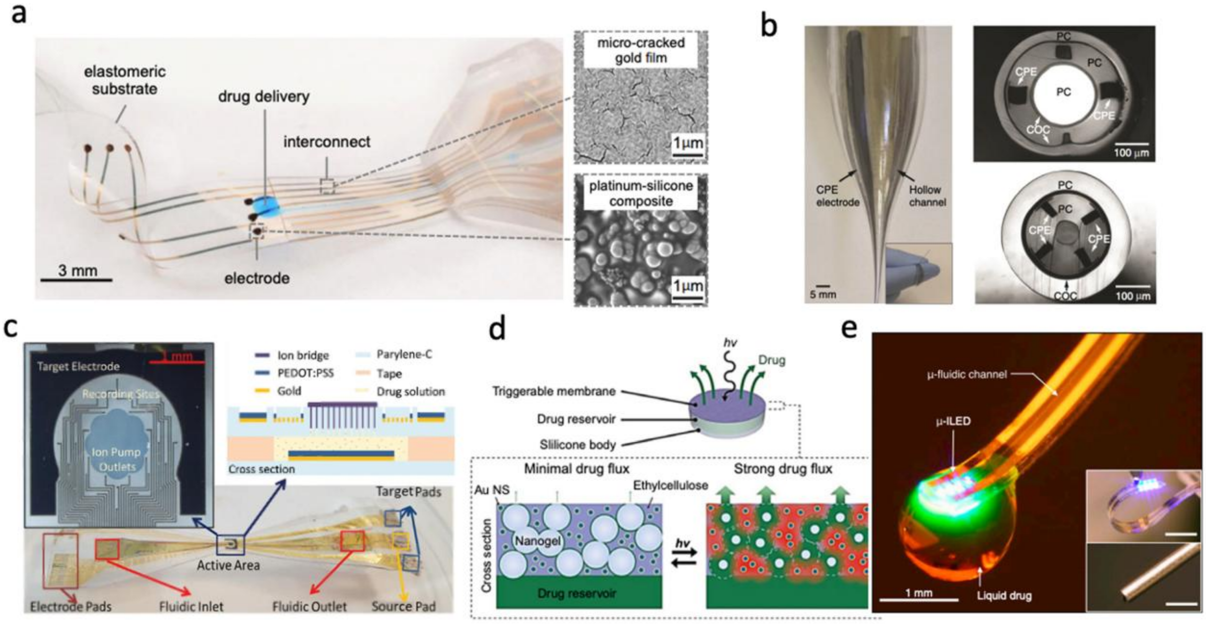


Fig. 1 Different drug delivery devices

Control systems

Hardware and software are the components that make up control systems. These control systems include the algorithms that cause the release of medications. Earlier research in this field focused mostly on open-loop systems, which are characterized by the fact that medication release is manually initiated upon the activation of certain circumstances. The activation of a micropump or a power supply or electric field are examples of interventions that match this description. Another crucial factor to take into account is the media via which this intervention will be delivered. Wireless control, for instance, could be more advantageous in research projects that include animals that are free to move about, but cable connections might not have a major impact on research projects that involve animals that are tied. Nevertheless, wireless systems such as radio frequency (RF) may be cumbersome and costly, whilst choices based on infrared (IR) may be restricted due to line-of-sight limits. The creation of miniaturized, Bluetooth low energy devices that are readily integrated with manufactured devices has been made possible by recent technology advancements. These devices allow for the control of medicine delivery from mobile devices. 53rd The creation of closed-loop systems, which are systems that do not need the involvement of humans, has also occurred as a result of further advancements achieved. The numbers 22,54,55 These devices have the ability to recognize when certain circumstances are fulfilled and may then initiate the administration of drugs on their own. To monitor the circumstances of the surrounding environment, however, a sensing component is necessary. Changes in the surrounding environment are what set off the release and distribution of the drug mechanism. As an example, when a certain threshold is surpassed. In addition to monitoring for changes in pH, temperature, and pressure, the sensors may also check for levels of chemical activity. Electrophysiology signals may be monitored and recorded by implants that have this capacity. Additionally, customized algorithms can be used to initiate the administration of medications in the event that the signals depart from the "normal" range or surpass a predetermined threshold.

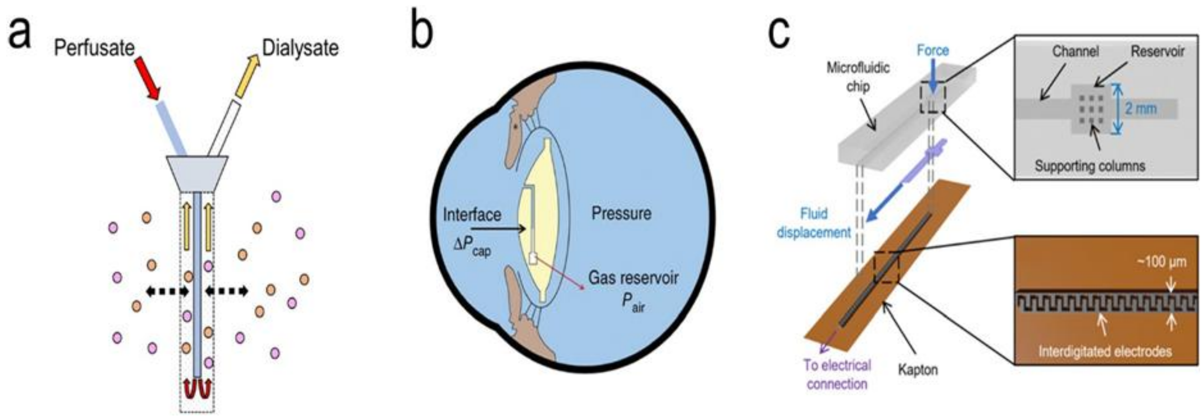
One such device, which is based on PDMS and was introduced by Salam et al.12, is capable of detecting and controlling seizures in real time intracerebrally. They made the discovery that the pattern of seizure onset is heterogeneous and suggested a personalized approach to the threshold adjustment of closed-loop systems for seizure applications. Machine learning and neural networks are increasingly being used to determine what constitutes "normal" or "abnormal" behavior in order to resolve individual variances. These systems will adapt to each unique patient. The integrated custom microprocessor is responsible for transmitting the control signal that is to be triggered. In its most basic form, this may also be accomplished via the use of platforms like as Arduino and Raspberry Pi. On the other hand, in applications that are more complicated, a foundry is used to develop and build Application-Specific Integrated Circuits (ASICs) that are personalized to the application. 56 and 57

Sensing

Across a broad range of industries, including healthcare, fluidic-enabled bioelectronic sensors have found widespread use. (58,59) Continuous health monitoring, illness diagnosis, and sports science are all areas that make substantial use of wearables that are based on microfluidic technology. ages 60–63 In a wearable or in vitro capacity, it is possible to detect a wide variety of analytes; nonetheless, glucose is the most often investigated therapeutically relevant biomarker for the development of new sensing techniques. 64 and 66 In addition to the detection of biomarkers, there is a significant amount of use of microfluidic devices for the purpose of pressure sensing. 67–70 years Despite the fact that implantable devices are not as widespread as wearables, there are specific applications that may benefit from their passive, long-term, and high-resolution capabilities.

Microdialysis

Microdialysis, for instance, is a sampling technique that has gained widespread acceptance in the field of neurology. It is used for the purpose of continuously measuring the concentrations of analytes in extracellular fluid. (71–73) An example of a micro-dialysis probe may be shown in Figure 2(a), which depicts a semipermeable membrane that is connected to intake and output tubing components. Throughout the process, an aqueous solution, known as perfusate, is continually infused into the intake. When this occurs, small solutes are able to pass through the semipermeable



Using microfluidics for bioelectronic sensing, as shown in Figure 2 The microdialysis probe is shown here with the intake (perfusate) and outflow (dialysate) tubes in visible position. During the process of constantly perfusing the input with an aqueous solution, tiny solutes are allowed to pass through the semipermeable membrane via the process of diffusion. At this point, the analyte of interest may be detected at the outflow at regular intervals. b) An embedded intraocular pressure (IOP) sensor that can detect pressure in order to keep track of individuals who have glaucoma symptoms. Until equilibrium is attained with the gas contained inside the reservoir, intraocular fluid is allowed to enter the sensing channel (shown by the circular black line). Once equilibrium is achieved, the gas–liquid interface may be photographed by a camera or a smartphone that has been particularly designed for the purpose. (This article was used with the permission of Springer Nature 1976 Copyright

2014) For the purpose of force measurements, a microfluidic sensor has been inserted inside the complete hip replacement implant. Fluid is pushed along a microfluidic channel that is integrated with electrodes that give a capacitance readout when a force is applied to the channel. This is a reproduction with permission. 77% The Authors retain all rights to their work until 2021.

Pressure

It is also possible to monitor pressure in a variety of tissues using fluidic implants that have been created. (78–80) There has been a report of a microfluidic-based sensor that allows for intraocular pressure (IOP) measurements to be taken in real time using a bespoke optical system carried out by a smartphone camera. Is 76 In-clinic measures of intraocular pressure (IOP) are often done since they are essential for the diagnosis and treatment of glaucoma. The intraocular pressure (IOP) is very variable, with a typical range of 10 to 21 mm Hg. However, a snapshot might be deceiving due to the fact that IOP is frequently changeable. 81% The sensing mechanism, which is seen in Figure 2(b), is both simple and efficient. Capillary forces and intraocular pressure (IOP) are responsible for driving liquid into an airtight microfluidic channel, which in turn compresses the gas within the reservoir until the gas pressure is level with the liquid pressure. Any increase in the intraocular pressure (IOP) will result in the interface moving closer to the gas reservoir, whilst any decrease in the IOP will result in the interface moving closer to the channel opening. For the purpose of determining the location of the aqueous-air interface, the device that is used to do the pressure readout is a smartphone camera that is fitted with an optical adapter and includes image processing software. PDMS is used in the fabrication of the IOP sensor chip, which is then coated with parylene-c to minimize air leakage. The chip is manufactured using conventional lithography.

Using a single-use sensor called VERASENSE, it has already been shown that the percentage of effective ligament balance in total knee replacement surgery increases from fifty percent to ninety-two to one hundred percent. 82 When balance is accomplished, there is a 3.2 percent reduction in the number of complications. It is a significant unmet need that this capacity be available in complete hip replacement. A bioelectronic pressure sensor that is enabled by microfluidics has been created in order to measure force feedback inside the hip joint, with the goal of reducing the likelihood of implant failure occurred. 77% The fluid reservoir seen in Figure 2(c) undergoes deformation and displacement along the channel when a force is applied to it. This causes the fluid to move down the channel. An increase in capacitance occurs as a result of the interaction between the displaced fluid and the integrated electrodes. Immediately when the force is released, the fluid is brought back to the reservoir. A soft elastomeric microfluidic chip layer has been included into the sensor, along with a Kapton substrate that has integrated electrodes that have been printed using an aerosol jet. The whole hip replacement is equipped with sensors in six different places, making it a potent research instrument that can be used to assist with implant placing and can also be used to a variety of orthopaedic surgeries.

Shape actuation

The use of soft materials in the production of actuators, which results in the creation of a moving system that can be controlled, is a rapidly expanding topic in the subject of soft robotics. Innovative implanted bioelectronic prostheses have the potential to include fluidic-based soft robotic implants, which is an interesting prospect. It is possible to employ soft fluidic systems to drive shape actuation of bioelectronic implants. This may be done in order to lessen the invasiveness of the implant during the implantation process and to provide mechanical stimulation to the body once the implant has been placed. In addition to the fact that there is a growing interest in converting these actuation methods for implanted prosthesis, there is also a growing interest in the use of fluidic-based technology for the further development of robotic surgical equipment to assist in minimally invasive surgery. In an ideal scenario, prostheses that are used to assist or replace organ function would mirror the normal internal structure and material qualities of the organ in order to limit the impact of the natural immune response. Therefore, the actuation and shape-changing methods that are used by soft-robotic technologies have the potential to be a helpful tool that can be translated for the construction of implanted prosthesis.

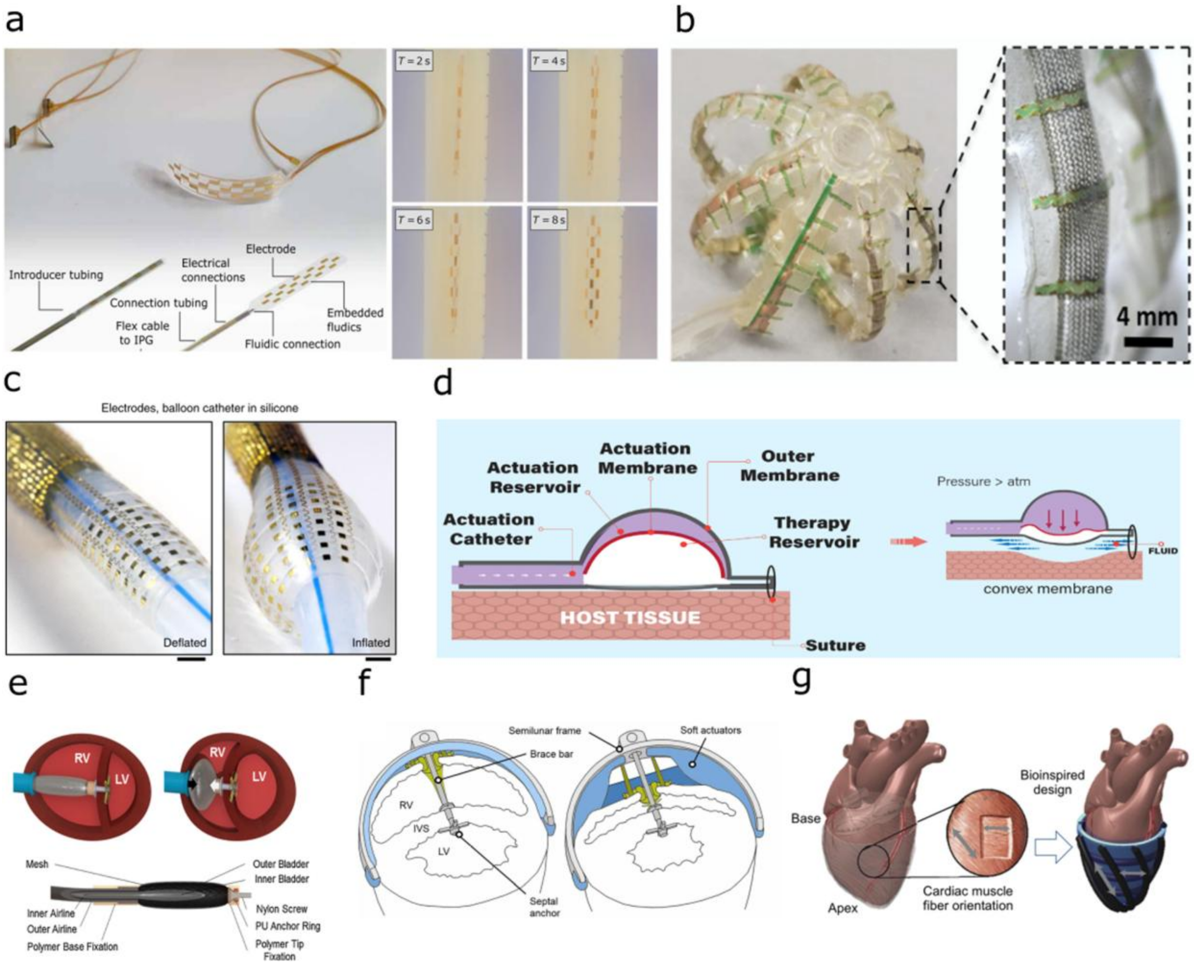


Fig. 3 Implants with fluidic shape actuation

Conclusion

It is important that promising technologies be linked with development paths for (clinical) translation as fluidic-enabled bioelectronics continue to demonstrate their maturation.

The technologies that are being addressed in this article have, up until this point, mostly been evaluated in pre-clinical models that are located in very early stages. These models include acute and short-term studies conducted on rodents, big animals, and human cadavers. Further validation in relevant models will be required before the product may be used in clinical settings. This validation will often include a demonstration of the product's long-term safety and effectiveness in vivo. The use of sophisticated ex vivo84 and in vitro models for accelerated aging101 has the potential to expedite the discovery of failure mechanisms and other technical hurdles prior to the conduct of such in vivo research.

There is a high probability that more biocompatibility testing will be necessary, especially for implants that combine new materials. Finally, fluidic-enabled bioelectronic implants may find use as pre-clinical research tools, which might eventually lead to the discovery of novel medicines while also derisking later clinical translation of related technologies. This provides a stepping stone to the clinic, which is the ultimate goal.

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