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Interventions of Bioelectronics and Biosensors on Oncology, Infectious and Neurological Diseases

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ABSTRACT

In the advancing world of health care, the integration and adaptation of biosensors and bioelectronics has made a profound impact. Various materials that make up functional biosensors and bioelectronics, such as 2D nanomaterials, Antibacterial Conductive Hydrogel (ACG) sensors, and man-made fibrous material will be discussed to evaluate and determine the effectiveness for applications. An additional factor that will be analyzed is the different methods that researchers have found in recent decades for innovative utilization of biosensors and bioelectronics. Some methods that will be discussed include the Layer By Layer (LBL) method, electrospinning, and microfluidic operations. The methods and materials will be analyzed in the context of various applications in the world of health care including cancer diagnostics, health monitoring, COVID-19 diagnostic testing, and tissue engineering. However, this publication will also investigate the ethical contradictions and issues that have surfaced as a result of testing their efficacy on certain experimental groups, including individuals diagnosed with cancer, infectious diseases, or neurological diseases.

Introduction

With the unparalleled innovation of bioelectronics, researchers have been analyzing the efficacy of bioelectronics as a notable form of technology in treating patients with neurodegenerative diseases, cancer, and infectious illnesses like COVID-19. Through formulating and manipulating new modes of bioelectrical properties and their synthetic forms, researchers have identified their efficacy in preventing the onset of cancer, as a non-invasive and accurate form of diagnostic tools. Additionally, bioelectronic devices have also served a promising role in enabling individuals to utilize monitoring devices that can help enhance mobility and detect physiological symptoms as well as movements. By introducing bioelectronic wearable devices, researchers successfully conveyed the depth of responsiveness, vibrations, flexibility in addition to elasticity. In the realm of infectious diseases, bioelectronics have also served a prominent role in diagnostic testing by amplifying and manipulating the nucleic acid to provide high efficiency, accuracy and affordability as COVID-19 diagnostic tools. In the scope of tissue regeneration for its biomedical engineering interventions, researchers have identified the form of manipulating the electrospinning properties to leverage and amplify electrical stimulation for biological tissues in treating neurodegenerative diseases. This publication will analyze various forms of bioelectronics, in addition to reviewing the ethical contradictions and limitations that have surfaced as a result of these technological advancements – as bioelectronics continue to revolutionize the field of biomedical engineering, by engineering better models, and ensuring these bioelectronic sensors adapt well with other medical devices, researchers can translate conventional bioelectronics to re-engineer better models, improve patient outcome, as well as the overall quality life of patients that are tested in their experimental groups.

Recent Advancements in Biosensors and Bioelectronics

In recent decades, the performance of biosensors and bioelectronics has been showcasing an upward trajectory due to the application of revolutionary concepts. One prominent factor to the advancement of biosensors is the increased integration of different nanomaterials. 2D nanomaterials are defined to be a single atomic plane, while 1D structures have dimensional limitations to 100 nm. (Chen et al., 2022) 1D nanomaterials such as nanotubes and nanowires have recently been discovered to be able to enhance biosensor responses through the modification of biological receptor molecules. On the other hand, there have been significant developments of 2D nanomaterial applications of biosensors as well as bioelectronics. The emergence of interest in 2D nanomaterials was prompted from the successful finding of graphene, by Geim and Novoselov in 2004. (Chen et al., 2022). Due to their immaculate findings, recent studies have recognized 2D nanomaterials to be desirable for biomedical applications because of properties such as an incomparably high surface-to-volume ratios and its ultrathin structures. The high surface-to-volume ratio not only promotes greater interactions of surface atoms, biomolecules, and cells within biosensors, but it also, as a result, enhances its sensitivity.

Another recent advancement in the field of biosensors, as a result of the use of nanoparticles, is the improvement of direct electron transfers (DET) (Murphy, 2006). This process, which is the transfer of electrons between the enzyme redox site and the electrode, was historically a difficult procedure because the redox site is often hidden within the enzyme. Recently, the application of 2D nanomaterials in biosensors have provided more surface area which is advantageous for direct electron transfers and general biomolecule immobilization.

Materials for Bioelectronic Applications: Components and Methods

Material science is the fundamental basis for exploring bioelectronic applications. For the specific case of the I2BL lab at the University of California, Los Angeles, the diagnostic tests are performed inside suspended chips on the circuit board. (Lin et al., 2022). The chip fabrication process includes layering 6 double sided tapes in between polyethylene terephthalate (PET) film. The shapes of the chips and PETs are both cut out by a laser printer from a computer aided design program called AutoCAD. In additional bioelectronics-based projects, computer aided design has rapidly gained popularity for material preparation.

As for the fabrication of nanomaterials, the Layer By Layer (LBL) method has proven to be effective when attempting to optimize accuracy. In the context of applications to bioelectronics, the LBL method implies a sequential deposition of various thin layers onto a prepared substrate or platform. The deposited layers all have individually unique functions and are made up of different materials, which allow the creation of functional nanostructures. Since this method works with thin layers in sequence, it offers precision and wide versatility during assembly (Iost et al., 2012).

Applications of Bioelectronics on Oncology and Cancer Diagnostics

One noteworthy application of bioelectronics is the promising prospect of how bioelectronics can be utilized to treat diseases such as cancer, as researchers leverage a paradigm shift for how bioelectronics medicine can be utilized by oncologists through manipulating their bioelectrical properties. Specifically, researchers established a new framework where instead of replacing enzymes, the products themselves could be replaced — Dr. L. Egyud synthesized carbonyls with masked carbonyl groups and released them to the National Screening Program, which uncovered some carcinostatic agents that lead to higher susceptibility of succumbing to cancer. When researchers synthesized the ethylamin derivative of methylglyoxal in its efficacy of preventing cancer, results were phenomenal in highlighting the efficacy behind manipulating the ethyl amine complex its radical form —further reiterating the prevalence of manipulating and transforming the bioelectronics form of carbonyls as a form of cancer diagnostics tools (Gyorgyi, 1973).

Furthermore, as researchers delve into novel forms of solution that could be non-invasive and serve as accurate diagnostic tools, researchers have analyzed saliva as a form of detecting cancer information. Specifically, capillary diffusion within the saliva enables biomarkers from serums to adhere to mediums, amidst its phospholipid bilayer (Haeckel and Hanecke, 1996) Thus, by reviewing these molecules at a macromolecule level, researchers can analyze salivary cancer biomarkers and relevant bioelectronics by assessing their varying forms of type, stage and sensitivity. (Mishra et al., 2016) From reviewing their properties and functions, prognostic biomarkers can be utilized to test for benign or malignant tumors, and diagnostic biomarkers can be utilized to assess the steady development of cancer. (Mishra et al., 2016)

Bioelectronics and its Interventions for Health Monitoring

Bioelectronics have advanced health monitoring processes through the emergence of wearable bioelectronic devices. Antibiotic Conductive Hydrogels (ACGs) are an arising and promising material that have opened up possibilities in linking bioelectronics and monitoring devices. ACG sensors are particularly suitable for integration because of their adjustable electrical properties, mechanical flexibility, and elasticity. (Wang et al., 2022) Most importantly, an ACGs' excellent responsiveness to stimuli is a valuable characteristic for further studies in motion detection and thus, health monitoring. (Wang et al., 2022) In recent years, these conductive hydrogels have been advanced to be sensitive to even external changes and factors such as temperature, force, and pressure.

Once integrated into wearable bioelectronic devices, the ACG sensors have the ability to capture motion signals such as, but not limited to, finger bending, elbow bending, or throat vibrating. With these motion signals, ACGs have proven to be able to monitor physiological signals or perform blood pulse detection. Similar to an ECG (electrocardiogram), the sensors will be able to capture the signals to monitor the body for health conditions. As evident in the figure below, the use of bioelectronic wearable devices helps demonstrate the various forms of motion detection. (Wang et al., 2022)

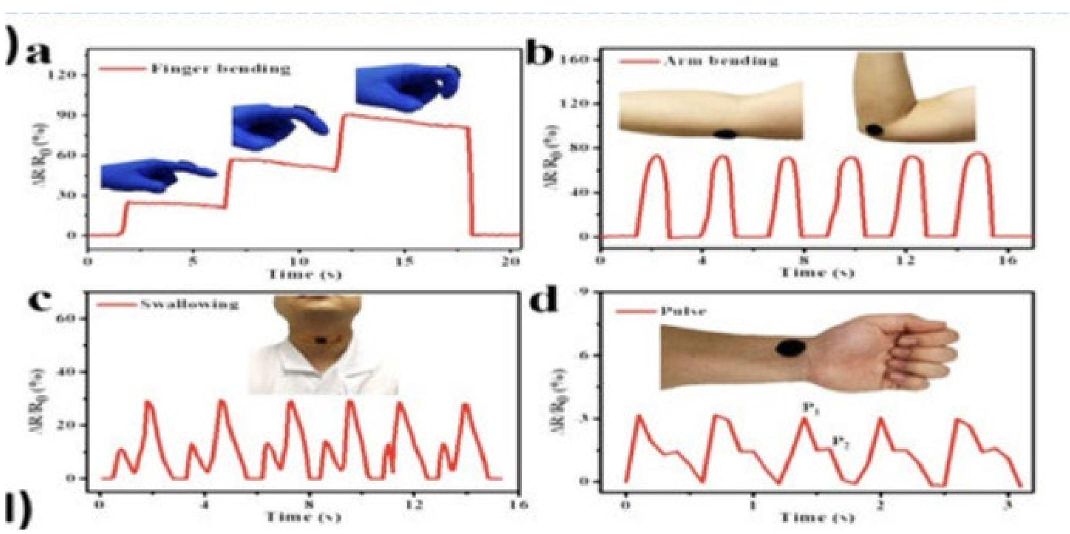

Figure 1. Graphical Illustration of Motion Detection Utilizing Bioelectronics

When it comes to health monitoring, ACGs and wearable bioelectronics will provide advantages that solve the issues of traditional biomedical devices. Traditional devices have limitations when it comes to complexity, affordability, accessibility, etc., which are all addressed by the emergence of this new technology. Ultimately, the incorporation of wearable bioelectronic technology will spark a revolutionary period of health monitoring.

Biosensors and Bioelectronics for COVID-19 Diagnostic Testing

The COVID-19 epidemic has reminded us of the importance of pandemic response and preparedness. Therefore, a significant application of biosensors and bioelectronics is in the development of efficient diagnostic testing. The Interconnected & Integrated Bioelectronics Lab (I2BL) at the University of California, Los Angeles facilitated the emergence of bioelectronics in the field of diagnostic testing in their recent project regarding COVID-19. I2BL used robotic agents (ferrobots) to create a microfluidic device that utilizes magnetism to carry out diagnostic testing. (Lin et al., 2022) Nucleic acid amplification tests are placed into a hand-held circuit-based platform where interactions with the test samples take place. The demonstrated integration of bioelectronics into diagnostic testing provides accuracy, affordability, and efficiency.

In other new studies, COVID-19 diagnostic testing has been advanced through paper-based electrochemical biosensors. Currently, the most well-known method of COVID-19 diagnosis is reverse transcription-polymerase chain reaction (RT-PCR)-based test. (Lin et al., 2022) However, the extensive list of limitations (affordability, availability, etc.) prevents it from being an effective method for mass testing. As a solution, scientists have employed the use of "lateral flow immunoassay platforms with optical detection (colorimetry/fluorescence) for targeting immunoglobulins" (Yakoh et. al., 2022) which is produced by SARS-CoV-2. These serological assays have been proven to be effective when it comes to detecting the antibodies, as it is use-friendly and rapid. In spite of these radical findings, the efficacy of using electrochemical sensors for antibody detection has not been proven to be successful by researchers; thus, instead, the electrochemical approach has been amplified for its interventions.

Bioelectronic Applications for Tissue Engineering and Tissue Regeneration

Natural fibrous structures in living systems are what researchers are trying to replicate when it comes to tissue engineering and regeneration. Notably, e-spin fins have been proven as one of the most novel forms of cutting-edge technology that can replace electrical models.

In recent studies, electrospinning has been realized as a useful tool for man-made fiber production. The products of electrospinning have mechanical properties and structures similar to that of tissues, which gives it the properties to stimulate natural tissues. This process of electrospinning has been able to fabricate materials used for the growing field of tissue engineering and bioelectronics. In recent studies, flexible bioelectronics have been found to provide health surveillance by electrical stimulation and compatibility with electrospun fibrous materials. Furthermore, e-spin technology, or in other words, bioelectronic applications are proven to take form as a flexible and biocompatible component that can seamlessly glide on biological tissues, to ensure they meet the standards of utmost comfort and reliable sensing. (Wan et al., 2022) Subsequently, these flexible bioelectronics have leveraged a high rate of biosensing, monitoring, therapy and intelligent form of healthcare that will continue to revolutionize themselves through novel forms of clinical findings and interventions. For instance, researchers currently are considering the prospect of integrating 3D printing with e-spin technology to ensure higher precision and temporal control – which can lead to successfully decreased testing time and cost for scaling these initiatives. (Wan et al., 2022)

In another research conducted on the use of bioelectronic applications in treating neurological disorders, research highlighted the prevalence and progression of utilizing thin-film flexible electrodes that can lead to neurostimulation in treating patients with neurodegenerative diseases. By integrating engineered electrodes with their surrounding host tissues, alternative design strategies that have been formulated from bioelectronic applications show a promising direction for researchers. (Nikkah et al., 2022)

Discussion, Limitations and Promising Future for Research

In spite of continuous adaptations and applications of bioelectronics on aiding individuals with various conditions, researchers have also pointed to the limitations and challenges of utilizing visual prostheses through bioelectrodes and devices as their applications on rehabilitation strategies and on peripheral nerve modulation have been diminished for their weak adaptations. (Palov et al., 2019) Specifically, the complex post-processing of electroencephalography data, noise correction and the optimization of toolboxes have been seen to have limited efficacy; thus, researchers must continue to analyze the progression of developing prevention and treatment strategies for neurodegenerative diseases by controlling as many extraneous factors as possible. (Palov et al., 2019) Arguably, other limitations have surfaced – specifically with the emergence of ethical contradictions and concerns surrounding lack of informed consent, contradictory research ethics, coupled by the protection and governance of intellectual property. When researchers conduct examinations and studies on the success of certain bioelectronics and tools, they must also consider factors like the need to protect the health of children, securing and protecting patient autonomy, as well as examining the potential positive or negative impact on quality of life. In the case of bioelectronic devices that are adapted to showcase brain-computer interface or regulation of brain matters, researchers have identified a concern if informed consent is not attained prior to the participants' exposure to these therapeutic interventions. (Packer et al., 2019)

Conclusion

In summary, bioelectronics presents a promising future for the interdisciplinary areas of neuroscience, electronics, materials science, molecular science and biomedical engineering. As continuous innovation in Artificial Intelligence, sensors, imaging and diagnostic tools amplify this industry, bioelectronic tools will not be eradicating or replacing traditional drugs — yet, through optimizing its various forms of devices, treatment plans and technology, researchers can continue to establish remarkable findings for patients that are diagnosed with cancer, infectious diseases or neurological diseases. However, while reviewing their effectiveness that adheres to industry regulations, researchers must also pay intricate attention to potential ethical dimensions and limitations to applying these research findings on rehabilitation, brain matter and on the microbiology of participants. In conclusion, these research findings show promising direction in delivering the utmost applications, technological interventions, diagnostics and testing tools that can alter the biological functionalities at a nanoscopic and macro-level, in addition to their usage on altering the brain components and matters for patients diagnosed with neurological diseases.

References

Chen, Fan, et al. "Structures, Properties, and Challenges of Emerging 2d Materials in Bioelectronics and Biosensors." *InfoMat*, vol. 4, no. 5, 2022, https://doi.org/10.1002/inf2.12299.

Iost, Rodrigo M., and Frank N. Crespilho. "Layer-by-Layer Self-Assembly and Electrochemistry: Applications in Biosensing and Bioelectronics." *Biosensors and Bioelectronics*, vol. 31, no. 1, 2012, pp. 1–10, https://doi.org/10.1016/j.bios.2011.10.040.

Lin, Haisong, et al. "Ferrobotic Swarms Enable Accessible and Adaptable Automated Viral Testing." *Nature*, vol. 611, no. 7936, 2022, pp. 570–577, https://doi.org/10.1038/s41586-022-05408-3.

Murali, Aparna, et al. "Emerging 2D Nanomaterials for Biomedical Applications." *Materials Today*, vol. 50, 2021, pp. 276–302, https://doi.org/10.1016/j.mattod.2021.04.020.

Murphy, Lindy. "Biosensors and Bioelectrochemistry." *Current Opinion in Chemical Biology*, vol. 10, no. 2, 2006, pp. 177–184, https://doi.org/10.1016/j.cbpa.2006.02.023.

Muñoz, Jose, et al. “Graphene-Based 3D-Printed Nanocomposite Bioelectronics for Monitoring Breast Cancer Cell Adhesion.” *Biosensors and Bioelectronics*, vol. 226, 2023, p. 115113, https://doi.org/10.1016/j.bios.2023.115113.

Shen, Hui-Min, et al. “Multi-Motion Robots Control Based on Bioelectric Signals from Single-Channel Dry Electrode.” *Proceedings of the Institution of Mechanical Engineers, Part H: Journal of Engineering in Medicine*, vol. 229, no. 2, 2015, pp. 124–136, https://doi.org/10.1177/0954411915570079.

Shi, Xiaofang, and Peiyi Wu. “A Smart Patch with On-demand Detachable Adhesion for Bioelectronics.” *Small*, vol. 17, no. 26, 2021, p. 2101220, https://doi.org/10.1002/smll.202101220.

Shi, Zhaoxia, et al. “Progress on the Application of Electrochemiluminescence Biosensor Based on Nanomaterials.” *Chinese Chemical Letters*, vol. 30, no. 9, 2019, pp. 1600–1606, https://doi.org/10.1016/j.cclet.2019.04.066.

Wan, Xingyi, et al. “Emerging Polymeric Electrospun Fibers: From Structural Diversity to Application in Flexible Bioelectronics and Tissue Engineering.” *Exploration*, vol. 2, no. 1, 2022, p. 20210029, https://doi.org/10.1002/exp.20210029.

Wang, Tengjiao, et al. “Motion Detecting, Temperature Alarming, and Wireless Wearable Bioelectronics Based on Intrinsically Antibacterial Conductive Hydrogels.” *ACS Applied Materials & Interfaces*, vol. 14, no. 12, 2022, pp. 14596–14606, https://doi.org/10.1021/acsami.2c00713.

Yakoh, Abdulhadee, et al. “Paper-Based Electrochemical Biosensor for Diagnosing COVID-19: Detection of SARS-COV-2 Antibodies and Antigen.” *Biosensors and Bioelectronics*, vol. 176, 2021, p. 112912, https://doi.org/10.1016/j.bios.2020.112912.

Zhang, Diming, and Qingjun Liu. “Biosensors and Bioelectronics on Smartphone for Portable Biochemical Detection.” *Biosensors and Bioelectronics*, vol. 75, 2016, pp. 273–284, https://doi.org/10.1016/j.bios.2015.08.037.