Wearable Electronics 2 (2025) 18–22

Contents lists available at ScienceDirect

Wearable Electronics

journal homepage: www.keaipublishing.com/en/journals/wearable-electronics

Perspective

Wearable healthcare monitoring and therapeutic bioelectronics

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A R T I C L E I N F O

Keywords:
Wearable bioelectronics
Monitoring
Therapy
Closed-loop system
Personalized healthcare

A B S T R A C T

Bioelectronics is playing an increasingly vital role in continuous healthcare monitoring and precision therapy due to its flexibility, biocompatibility, patient-friendly design, and long-term stability. This perspective reviews the latest advancement of wearable bioelectronics, covering from multimodal monitoring for various health conditions to adjustable treatments for complex diseases. We then focus on the key challenges and opportunities for closed-loop monitoring-therapeutic wearable bioelectronics towards personalized healthcare and commercialization. By introducing artificial intelligence technology, optimizing integration functions and enhancing specific properties, wearable bioelectronics is expected to translate innovations from research to real-world biomedical applications.

Introduction

Wearable bioelectronics, with their exceptional mechanical flexibility, electrical functionalities, and biocompatibility, has attracted huge attentions in many domains such as health monitoring, human-machine interaction, and drug delivery applications, to meet the rising demands for digital medicine [1–3]. Different from the traditional bulky and rigid electronics with limited mobility and flexibility for practical applications, wearable bioelectronics shows great conformability and biocompatibility over human skin with customizable designs, enabling early diagnosis and precision treatment for various diseases, such as cardiovascular diseases and diabetes [4–6]. In detail, it could realize continuous monitoring of physiological information, including biophysical, biochemical, and electrophysiological signals, with high sensitivity, wide applicability, and real-time data analysis [7–11]. Meanwhile, traditional clinical treatments are often limited due to the inadequate drug tolerance (delay and non-continuity of medication) and adverse side effects (allergic reactions, inflammation, and immune system activation). In contrast, with the advanced performance and integrated functions, wearable bioelectronics is available for the precision treatment, including drug delivery, thermal therapy, electrical stimulation, and light therapy [12–15]. With the development of advanced materials, diagnostic technologies, bioelectronic interfaces, and structural designs, wearable bioelectronics shows promising potential to bridge the gap between monitoring and treatment.

In this perspective, we will provide a systematic discussion of recent advances in wearable bioelectronics towards personalized healthcare. We will first introduce the biomedical applications of monitoring various diseases such as respiratory disease, muscle injury, cardiovascular disease, mental health and systemic inflammation. Then, we will explore the therapeutic applications of wearable bioelectronics on multiple common health conditions, including hair loss, eye disease, chronic wounds, tumor, diabetes, and joint degenerative diseases. Lastly, by integrating wearable bioelectronics with multimodal monitoring and personalized therapy, we will emphasize the further development of closed-loop monitoring-therapeutic systems. To improve the sensitivity, selectivity, biocompatibility and commercialization of wearable bioelectronics, several strategies such as the involvement of artificial intelligence, implementation of personalized healthcare and adjustment of integration function will be further discussed.

Wearable monitoring bioelectronics

Wearable bioelectronics with ease of use, comfortability, compatibility and long-term stability, shows great potential in health monitoring and early detection of various diseases. This section provides a comprehensive overview on wearable bioelectronics for monitoring different health conditions and highlights the possibilities to advance personalized healthcare (Fig. 1).

Peer review under the responsibility of Editorial Board of Wearable Electronics

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https://doi.org/10.1016/j.wees.2024.12.004
Received 29 October 2024; Received in revised form 19 December 2024; Accepted 28 December 2024
Available online 22 January 2025
2950-2357/

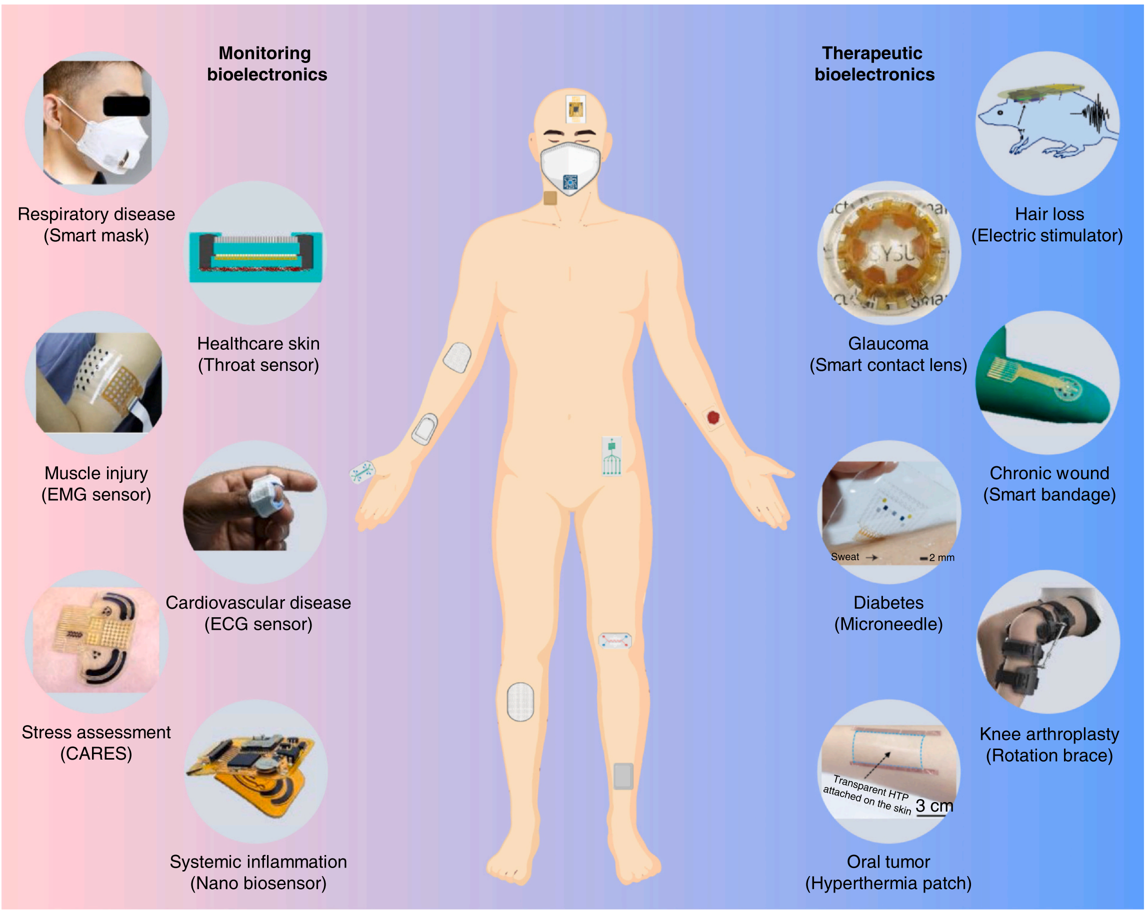

Fig. 1. Schematic diagram of wearable healthcare monitoring and therapeutics bioelectronics. Left section: typical wearable monitoring bioelectronics [16–21]; right section: representative examples of therapeutic bioelectronics [22–26,28].
This image has been adapted from the images provided by Biorender.com.

Biophysical and electrophysiological signals

With the advanced materials and versatile layouts, wearable bioelectronics serves as candidate to monitor and assess the activities of brain, heart, muscle, and nervous system, by measuring biophysical and electrophysiological information such as heart rate, temperature, electrocardiography (ECG), and electromyography (EMG). For instance, an integrated electronic skin can detect five physical or physiological activities related to human vocalization, including heartbeat, breathing, touch, and neck movement, enabling multimodal sensing capabilities [16]. It offers a promising solution to build integrated systems for telemedicine as we as human-machine interaction. For the electrophysiological signals, a wireless epidermal system integrates synchronous sensors for continuous ECG monitoring from the chest, alongside multispectral photoplethysmography of surrounding tissues, providing real-time cardiovascular disease surveillance [17]. The multimodal sensor system provides informative insights into the hemodynamic state for the management of cardiovascular disease. Different from ECG signals, a novel multi-channel patch is developed to capture surface EMG signals with high resolution and density for effectively monitoring muscle load and fatigue. This EMG patch could continuously track tendon displacement and ensure that the tendon stretch is within safe limits, significantly reducing the risk of muscle or tendon injury [18]. With the detection capability in electrophysiological signal recording, wearable bioelectronics provides essential technical support and platforms for disease diagnosis and treatment, daily rehabilitation training, and scientific exercise.

Biochemical signals

In addition to biophysical signals, to evaluate the health condition in a more comprehensive approach, it is essential to monitor biochemical information at the molecular levels. Biofluids, containing a broad spectrum of biomarkers, are impressive mediums for the detection of biochemical signals with the wearable bioelectronics. Recently, an innovative smart mask real-time monitoring system, focuses on the detection of exhaled breath condensate biomarkers for respiratory evaluation. This system combines serial cooling technology, automated microfluidic systems, highly selective electrochemical biosensing technology, and wireless data reading circuits to enable continuous multi-mode monitoring of the EBC, covering the analytical needs during daily activities [19]. Such prototype demonstrates its versatility, convenience and efficiency, serving as a powerful and effective tool for promoting clinical and medical research. A consolidated artificial-intelligence-reinforced electronic skin (CARES) was designed for the stress assessment by monitoring six key sweat biomarkers with three biophysical information including skin temperature, pulse waveform and galvanic skin response [20]. Additionally, a wireless wearable device could the inflammatory biomarker C-reactive protein (CRP) in sweat in situ, which incorporates iontophoretic technology for sweat induction, microfluidic module for sweat collection, and a graphene-based sensor array for sweat CRP evaluation [21]. The wearable bioelectronics with continuous monitoring of multimodal physiological information facilitates the development in medical healthcare.

Wearable therapeutic bioelectronics

The exploration of wearable bioelectronics could enhance the accuracy and efficiency in disease monitoring and offer convenience and opportunities for personal health management, making them an essential component of modern healthcare. Besides health monitoring, wearable bioelectronics can also serve as therapeutic methods in disease treatment, including physical therapies (electrical stimulation, thermal stimulation, light stimulation, and acoustic stimulation) and chemical therapy (drug delivery), thus allowing personalized treatment to significantly improve the quality of life and prognosis of patients.

Electrical stimulation

In terms of therapeutic applications for some diseases, wearable devices could employ electrical stimulation to treat or alleviate specific conditions. A stretchable wearable bioelectronic system was developed to promote tissue regeneration and accelerate wound healing through electrical stimulation, with high spatiotemporal resolution detection of biomarkers at the same time [22]. Another innovative therapeutic bioelectronic, a motion-activated electrical stimulation system, can enhance hair regeneration during activities. Such wearable configuration provides a practical approach for hair loss, which is beneficial to millions of people worldwide [23]. Wearable bioelectronics with electrical stimulation technology is highly controllable and easy to operate, serving as an efficient and personalized therapeutic platform.

Thermal stimulation

Besides electrical stimulation, wearable therapeutic bioelectronics could also perform thermal stimulation as a non-invasive intervention. A skin-tight thermal patch exhibits optical transparency, low electrical resistance, electrothermal conversion, and mechanical adaptability, enables effective promotion of subcutaneous tumor treatment progress and its impact on the skin [24]. With safety, non-invasive and mild thermal effect, this thermal patch can overcome the limitation of traditional cancer treatment, especially for patients experiencing recurrence after radiotherapy, chemotherapy or surgery, which allows for the palliative treatment to effectively reduce refractory pain caused by advanced tumors. As an impressive approach, it holds significant potential for treating other health conditions like osteoarthritis, cervical spondylosis, and chronic ocular surface inflammation.

Light stimulation

Wearable bioelectronics can be also incorporated with light therapeutic approach. A light-driven rhythmic photodynamic therapy device based on alternating current excitation is developed, which combines a flexible wearable sandwich device with an origami energy harvester. The system is designed to provide a self-driven, wearable treatment solution for long-term treatment of patients with chronic diseases, which paves a new direction of bio-photonic devices in the future [25].

Acoustic stimulation

Besides physical therapies mentioned above, acoustic stimulation is a promising technique to provide long-lasting on-demand treatment with wearable bioelectronics. For patients after total knee arthroplasty, a modularly wearable stent system was developed to facilitate self-rehabilitation evaluation, which can improve the quality of life for elder patients with the integration of cloud database and rehabilitation data [26]. The wearable stent system offers new possibilities for the development of remote intelligent healthcare technology.

Drug delivery

The integration of wearable bioelectronics and intelligent drug release technology is promising in personalized medicine. Incorporated with efficient wireless energy transmission circuit, a therapeutic contact lens was proposed to enable in situ measurement of intraocular pressure and activate on-demand anti-glaucoma drug delivery into the eye through iontophoretic process [27]. With minimally invasive design, intelligent wireless connectivity, and therapeutic functionality, this contact lens is feasible for efficient glaucoma treatment. For skin interface, a wearable sensor was developed for real-time monitoring and therapeutic feedback of diabetes through sweat, where the flexible materials enhance the effectiveness of biosensors and drug delivery systems with practical applications [28]. Bioelectronics that integrate wearable devices with drug delivery technology shows great potential in customized medical treatments and smart drug delivery systems, which promotes the continuous innovation and in-depth validation of clinical practice.

Through multiple strategies such as technology upgrading, cost reduction and function expansion, wearable monitoring bioelectronics have effectively addressed the challenges of continuous monitoring, data accuracy and wearing comfort. As for therapeutic applications, wearable bioelectronics is competent with data acquisition, system compatibility, and health resource allocation. The treatment methods, when combined with wearable bioelectronics, offer promising potentials in the medical industry. The adoption of these technological advances and solutions has significantly increased the popularity of wearable monitoring and treatment technology in clinical practice and daily health monitoring, and has provided strong support for precision medical diagnosis, early disease screening, treatment effect evaluation and efficient exercise training.

Perspective

This perspective introduces the recent advancements of wearable bioelectronics for continuous monitoring and precision treatment to some specific diseases, covering progress from wearable monitoring devices to therapeutic methods. Wearable sensors can continuously monitor human physiological signals noninvasively, owing to the properties including miniaturization, modularity, intelligence and high sensitivity. Additionally, wearable bioelectronics is promising for precise local electrical, thermal, optical and chemical stimulation in the treatment of diseases. The incorporation of monitoring and therapeutic capabilities enables the wearable closed-loop bioelectronics for automatic adjustments in drug delivery or physical stimulation in response to real-time variation of physiological parameters. As shown in Fig. 2, the closed-loop monitoring-therapeutic bioelectronics consists of three key components: (1) wearable biosensors for continuous monitoring of physiological signals, (2) data acquisition and analysis, and (3) treatment modules with well-designed therapeutic strategies.

In detail, when designing efficient closed-loop bioelectronics, several factors should be considered, such as system miniaturization, signal recording and decoding technology, and careful selection of materials, to ensure both functional efficiency and user comfort. Timing strategies for treatment require optimization to ensure the therapeutic effects, and reliable skin interface allows for stable and accurate signal acquisition and energy transfer during operation, to minimize the risk of secondary injury during removal. To further enhance the biomedical applications of wearable bioelectronics, it is essential to improve the sensitivity, selectivity and biocompatibility. Artificial intelligence can be involved to extract key features from collected information and provide personalized treatment, which is beneficial for commercialization with reliable manufacturing process and long-term clinical validation.

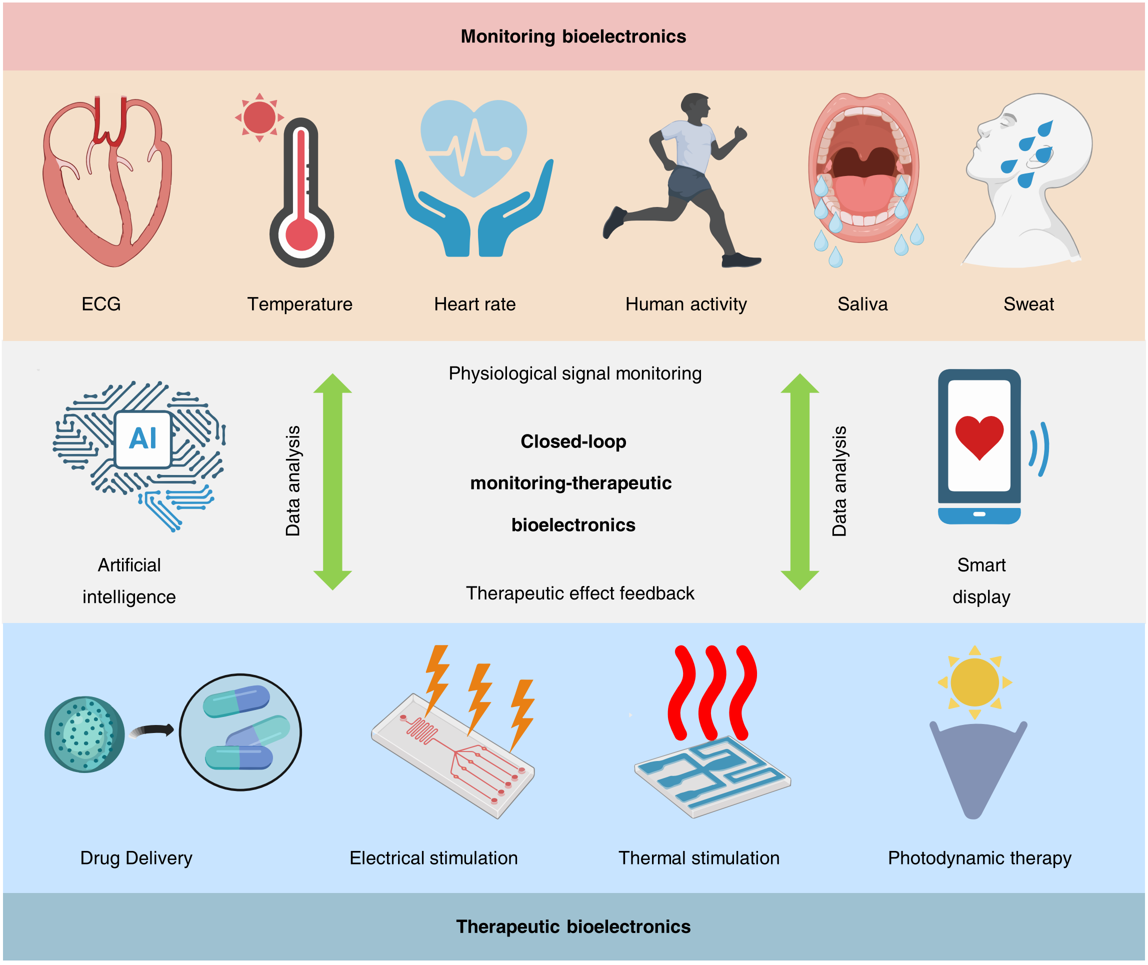

Fig. 2. The closed-loop monitoring and therapeutic bioelectronics with three core modules with the implementation of monitoring and therapeutic methods. This drawing is based on the images drawn by Biorender.com.

Sensitivity and selectivity

Multimodal sensing is increasingly preferred in real-time health monitoring, where sensitivity and selectivity are highly required to capture subtle fluctuations in the physiological signals, like vital signs and concentrations of key biomarkers. The accurate monitoring could facilitate the implementation of adjusted treatment and contribute to disease prevention and diagnosis. Several strategies can be employed, including the development of highly sensitive materials, the introduction of innovative sensing mechanisms, and the optimization of signal decoupling technologies, to enhance the detection capability of physiological information with higher accuracy. Meanwhile, wearable closed-loop bioelectronics can effectively differentiate the interferences among target biological signals and noise, which is competent in real-world scenarios. Particularly, for signal-triggered drug delivery, it is critical to precisely release drug to the specific area with localized therapeutic actions.

Biocompatibility

For wearable bioelectronics, it is essential to own properties such as flexibility, non-toxicity, and non-irritation, for safe and effective interaction with human skin. The progress of biocompatible materials offers a promising solution as they can minimize damage to the body during the working and removal process without invasive procedure and irritation. To further enhance the biocompatibility, innovative materials and structural designs are investigated to achieve multi-dimensional integration with optimal electrical, mechanical, and biological properties. Meanwhile, with the successful involvement of biocompatible materials, there is still a trade-off between mechanical robustness and electrical conductivity. The comprehensive understanding of the mechanism of material-biological interaction is also crucial to address potential negative effects on biological systems. With the improved biocompatibility, the developed bioelectronics could maintain long-term stability with intended functions and demonstrate reliability for monitoring and therapeutic applications.

Artificial intelligence

Data acquisition and processing are quite important in closed-loop bioelectronics, however, to build a robust infrastructure for data processing in bioelectronics, it is critical to develop reliable algorithms to separate target signals from background noise, enabling precise interpretation of physiological information. Although there is still difficult to recognize, classify and make decisions through complicated biological signals, recent advances in training methods, such as neural networks, could perform a comprehensive systematic analysis to provide informative insights into disease patterns to enhance the monitoring-therapeutic effectiveness of wearable bioelectronics. It is feasible to associate the connections between multimodal physiological information with health conditions, leading to the iterative optimization of predictive algorithms.

The incorporation of artificial intelligence with closed-loop bioelectronics shows great potential to improve the precision and effective of disease control by accelerating the decision-making process with more personalized and adaptive therapeutic interventions. With the self-calibration capability, it is possible to make decisions with complex physiological signals more efficiently. Moreover, it is crucial to create a comprehensive medical information platform with visualized data for patients to autonomously monitor health and disease progression. With the artificial intelligence algorithms, researchers and clinicians could understand the health conditions of patients and provide real time feedback accordingly to improve the patient outcomes and lower the burden of medical resources. This could improve the functionality and user-friendliness of closed-loop bioelectronics for personalized health management with preventative care.

Commercialization

Before the wearable bioelectronics advances to the development stage and large-scale commercial applications, careful assessment with relevant treatment procedures should be carried out in accordance with current medical paradigm, such as the FDA approval. In short, long-term and large-scale clinical studies should be conducted to comprehensively evaluate the efficacy, safety and stability of wearable bioelectronics in diverse physiological states. The development of cost-effective materials and manufacturing technologies are highly desired to support mass production with standard procedure. Additionally, it is crucial to optimize secure and convenient application strategies to ensure the accurate deployment and safe use of wearable bioelectronics.

Conclusion

In summary, driven by rapid advancements in materials science and an increasing demand for personalized healthcare, wearable bioelectronics is committed to developing closed-loop monitoring and therapeutic systems. To overcome the current challenges, cross-disciplinary collaborations among science, technology, and medicine are essential to facilitate research on multimodal sensing, drug design, and data processing, and to encourage the exploration on innovative materials and structural designs. Wearable monitoring-therapeutic bioelectronics demonstrates great potential in personalized healthcare over the traditional approaches, which is of vital importance to realize early detection, continuous monitoring and precision treatment of practical biomedical applications.

CRediT authorship contribution statement

Ya Zhang: Writing – original draft, Conceptualization. **Haotian Chen:** Writing – review & editing. **Yu Song:** Writing – original draft, Conceptualization.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

This work was supported by City University of Hong Kong (Grant No. 9382003) and the University Grants Committee's Teaching Start-up Grant (CityUHK Project No. 6000908).

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