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Personalized Bioelectronics: Wearable and Implantable Interfaces for Closed-Loop Therapeutics

Aoife Murphy[1], Matthew O'Connor[2*]

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Abstract

This review aims to synthesize current evidence on wearable and implantable bioelectronic systems designed for closed-loop therapeutics, highlighting their architectures, interface designs, adaptive control mechanisms, and translational considerations. A qualitative literature review was conducted using 18 peer-reviewed studies selected from Scopus, PubMed, Web of Science, and IEEE Xplore, covering the period 2016–2025. Articles were included if they addressed wearable or implantable bioelectronics for adaptive therapeutic applications. Data were analyzed through thematic synthesis using Nvivo 14, with open, axial, and selective coding to identify main themes, subthemes, and key concepts. Theoretical saturation was reached at the 18th article, ensuring comprehensive coverage of technological, clinical, and ethical dimensions. Four major themes emerged: (1) smart bioelectronic architectures, including flexible, stretchable, and biocompatible materials integrated with miniaturized circuits and modular designs; (2) wearable and implantable interface engineering, featuring skin-integrated electronics, neural and muscular implants, biofluidic integration, and wireless communication networks; (3) closed-loop therapeutic mechanisms, encompassing biosignal acquisition, adaptive feedback algorithms, multimodal data fusion, and patient-specific actuation strategies; and (4) translational, ethical, and regulatory considerations, addressing clinical validation, data privacy, algorithmic transparency, accessibility, and sustainability. Collectively, these findings demonstrate that personalized bioelectronics enable real-time monitoring, autonomous adaptation, and individualized therapeutic interventions, representing a shift from conventional open-loop devices to intelligent, patient-centered healthcare systems. Personalized bioelectronics for closed-loop therapeutics represent a transformative frontier in healthcare, integrating advanced materials, adaptive control systems, and ethical governance to provide dynamic, patient-specific interventions. These systems have the potential to improve clinical outcomes, enhance patient quality of life, and support the development of sustainable, responsive healthcare ecosystems.

Keywords: personalized bioelectronics; wearable sensors; implantable devices; closed-loop therapeutics; adaptive control; patient-specific interventions; bioelectronic medicine.

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1. Department of Biomedical Engineering, Trinity College Dublin, Dublin, Ireland
2. Department of Environmental Engineering, University of Auckland, Auckland, New Zealand

*Correspondence: e-mail: matthew.oconnor@auckland.ac.nz

1. Introduction

Over the past decade, the convergence of bioengineering, materials science, and digital health has fostered a new era in personalized medicine—one that integrates electronic intelligence directly into the human body through wearable and implantable bioelectronic interfaces. These systems, designed for continuous monitoring and closed-loop therapeutic regulation, represent a paradigm shift from conventional reactive healthcare toward adaptive, data-driven interventions capable of real-time physiological feedback (Dagdeviren, Joe, Tuzman, Park, & Rogers, 2016). Personalized bioelectronics—comprising skin-mounted sensors, neural implants, and smart stimulatory devices—aim to achieve continuous communication between biological signals and electronic controllers, ultimately enabling individualized, self-regulating treatment pathways (Kim et al., 2020). This emerging discipline, often termed *bioelectronic medicine*, unites the precision of electrical engineering with the complexity of human physiology, offering unprecedented opportunities to diagnose, monitor, and modulate bodily functions in ways that traditional pharmacological or mechanical approaches cannot (Famm, Litt, Tracey, Boyden, & Slaoui, 2013).

The shift toward closed-loop therapeutic systems lies at the heart of this evolution. In contrast to open-loop medical devices that operate with preprogrammed responses, closed-loop systems actively sense physiological variables, process them through embedded algorithms, and deliver adaptive interventions (Zhu et al., 2023). For instance, implantable neuromodulators now adjust stimulation intensity based on real-time neural feedback, while wearable insulin delivery systems dynamically regulate glucose levels using continuous glucose monitoring (CGM) inputs (Elhady, 2021). Such precision aligns with the broader agenda of personalized medicine, in which therapeutic decisions are informed by real-time data rather than population-level averages. As machine learning and miniaturized electronics advance, the integration of personalized feedback loops within soft, biocompatible interfaces is enabling therapies that evolve with each patient's physiological state (Jeong et al., 2021).

Wearable bioelectronics have become instrumental in the democratization of health data. Flexible and stretchable materials—such as conductive hydrogels, graphene composites, and liquid metals—allow sensors to adhere conformally to the skin and capture electrophysiological, biochemical, or mechanical signals without discomfort or invasive procedures (Rogers, Someya, & Huang, 2019). These skin-integrated platforms can detect parameters such as heart rate, hydration, electrolyte balance, and muscle activation, transmitting them wirelessly to external devices or cloud databases for interpretation (Xu et al., 2022). By combining advanced material science with microelectronics, researchers have created epidermal systems that not only monitor but also stimulate tissues, offering therapeutic interventions for cardiac pacing, wound healing, and pain modulation (Huang et al., 2022). The flexibility of these systems has been further enhanced by the development of self-healing and biodegradable materials, which ensure durability under mechanical stress and environmental exposure (Zhao et al., 2023).

Parallel to these surface-level developments, implantable bioelectronics are revolutionizing the treatment of neurological, cardiovascular, and endocrine disorders. Devices such as deep brain stimulators, cochlear implants, and vagus nerve stimulators exemplify the clinical maturity of implantable technologies that modulate bioelectrical activity for therapeutic gain (Gater et al., 2021; Stieglitz & Navarro, 2020). Recent innovations have focused on improving long-term biocompatibility, miniaturization, and wireless control, allowing implants to operate autonomously for extended periods. For instance, wireless neural interfaces equipped with inductive charging and real-time telemetry now permit patients to receive uninterrupted care without the need for repeated surgical adjustments (Zhou et al., 2024). The emergence of soft, bioresorbable electronics further addresses challenges of chronic inflammation and foreign-body reactions, as devices dissolve harmlessly after completing their therapeutic function (Dagdeviren et al., 2019). These advances signify a growing convergence between *cyber-physical systems* and biological environments, where electronics become dynamic participants in the body's regulatory networks rather than passive instruments.

The principle of personalization extends beyond device design into the core logic of therapeutic decision-making. Traditional medical devices deliver uniform interventions, assuming homogeneity in physiological response; however, personalized bioelectronics introduce *adaptive control algorithms* that continuously learn from patient-specific data (Ghezzi et al., 2021). Artificial intelligence (AI) and machine learning models process multimodal biosignals—from electrocardiograms to neurotransmitter flux—to detect patterns, predict complications, and refine stimulation protocols in real time (Liu et al., 2022). These algorithms enable devices to adjust therapy intensity based on biomarkers of fatigue, stress, or inflammation, aligning intervention timing with the body's natural rhythms. As a result, closed-loop systems are beginning to resemble biological homeostasis, where feedback and adaptation sustain equilibrium. In diseases like epilepsy, Parkinson's, and diabetes, this adaptive architecture allows for continuous optimization of treatment efficacy while minimizing side effects and patient burden (Merrill, Bikson, Jefferys, & Krames, 2022).

A key enabling factor for such intelligent behavior lies in multimodal sensing and data fusion. Modern bioelectronic interfaces integrate multiple sensors—electrical, optical, chemical, and mechanical—into compact systems that can interpret complex physiological phenomena holistically (Li, Zhang, & Chen, 2020). For instance, the combination of neural recording electrodes and biochemical sensors provides a multi-layered perspective on the interplay between brain activity and metabolic processes. These data streams are processed through computational frameworks capable of handling temporal variability and cross-signal correlation. The inclusion of AI in this process enhances diagnostic precision and predictive accuracy, contributing to the realization of "smart therapeutics" capable of autonomous operation (Zhang et al., 2023). Nonetheless, this increasing computational complexity raises questions about algorithmic transparency and interpretability—ethical imperatives when such systems influence vital functions.

The clinical translation of these technologies presents both technical and ethical challenges. While experimental demonstrations have proven the feasibility of bioelectronic medicine in animal models and pilot human studies, large-scale clinical validation remains a significant hurdle. Long-term stability, device–tissue integration, and interpatient variability continue to limit widespread adoption (Stieglitz & Navarro, 2020). The regulatory environment for bioelectronic devices is also in flux, as agencies like the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) grapple with hybrid technologies that combine medical hardware, software algorithms, and biological interactions (Buch et al., 2020). Safety validation, algorithmic accountability, and cybersecurity are now viewed as integral components of device approval processes. To mitigate potential harms, frameworks for risk assessment, software verification, and ethical oversight are being developed to ensure that intelligent devices remain both effective and trustworthy (Topol, 2021; Yuste et al., 2022).

Beyond safety and performance, data privacy and ownership are becoming defining concerns for the future of personalized bioelectronics. Devices that continuously collect high-resolution physiological data inherently risk breaches of confidentiality, particularly when linked to cloud-based analytics platforms (Bonaci, Calo, & Chizeck, 2022). Emerging solutions include on-device encryption, blockchain-enabled audit trails, and differential privacy algorithms that anonymize data while maintaining analytical value (Hummel, Braun, & Danner, 2021). Ethical design also emphasizes *user agency*, ensuring that patients retain control over their treatment settings and data-sharing preferences (Yuste et al., 2022). These frameworks aim to balance technological autonomy with human autonomy—a principle central to the ethos of bioelectronic medicine.

The economic and social implications of personalized bioelectronics are equally significant. As production costs decline, scalability and accessibility will determine whether bioelectronic therapeutics can transcend specialized hospital settings to reach low-resource populations (Hummel et al., 2021). The promise of continuous monitoring and preventive care could alleviate healthcare burdens globally, especially in managing chronic diseases that strain medical infrastructures. However, equitable distribution demands that innovation be coupled with affordability and cultural adaptability. This necessitates interdisciplinary collaboration among engineers, clinicians, policymakers, and ethicists to design frameworks that support sustainable adoption (Gandhi et al., 2023). The integration of sustainability principles—such as eco-friendly materials, recyclable components, and low-energy operation—further aligns personalized bioelectronics with the global agenda for environmental responsibility (Wang et al., 2022).

In this context, personalized bioelectronics for closed-loop therapeutics represents a convergence of engineering precision and biological intelligence aimed at achieving real-time adaptability, reliability, and safety in healthcare. This review synthesizes qualitative findings from 18 recent studies to explore how personalized bioelectronic systems have evolved in architecture, interface design, control mechanisms, and ethical governance. Through thematic analysis, the review identifies four major domains: (1) smart bioelectronic architectures integrating flexible materials and autonomous power systems; (2) advanced wearable and implantable interfaces for robust human–machine integration; (3) adaptive closed-loop therapeutic mechanisms driven by biosignal feedback; and (4) translational, ethical, and regulatory considerations shaping global implementation. The goal is to provide an integrative perspective on how these dimensions collectively advance the vision of human-centered, self-optimizing healthcare ecosystems. As bioelectronics continues to dissolve the boundary between body and machine, it not only redefines therapeutic precision but also challenges humanity to reconsider the ethical, emotional, and philosophical contours of what it means to heal in an age of intelligent systems.

2. Methods and Materials

This review adopted a qualitative, exploratory design aimed at synthesizing recent scientific evidence on personalized bioelectronic systems, focusing on wearable and implantable interfaces utilized in closed-loop therapeutic applications. The design was structured around a narrative and thematic synthesis model to capture the complexity, multidimensionality, and emerging patterns within this interdisciplinary field that intersects materials science, biomedical engineering, and digital health technologies. As the study did not involve human participants or experimental trials, “participants” refer to the corpus of selected scholarly articles that constituted the unit of analysis. A total of 18 peer-reviewed articles were purposively selected based on their scientific relevance, publication quality, and direct contribution to themes such as adaptive biosignal monitoring, neural interfacing, and feedback-controlled therapeutic systems.

Data collection relied exclusively on an extensive literature review across leading databases, including Scopus, PubMed, Web of Science, and IEEE Xplore. Search strings combined relevant keywords and Boolean operators such as ("personalized bioelectronics" OR "bioelectronic medicine" OR "wearable interface" OR "implantable device" OR "closed-loop therapeutics") AND ("neural modulation" OR "biosignal feedback" OR "smart materials" OR "adaptive electronics"). The selection period covered studies published between 2016 and 2025 to ensure inclusion of state-of-the-art developments. Articles were included if they presented empirical findings, system-level frameworks, or design models directly related to closed-loop bioelectronic interfaces for personalized or precision therapeutics. Exclusion criteria removed purely theoretical modeling papers without physiological validation or review works that lacked methodological transparency.

All selected materials were imported into Nvivo 14 software for structured qualitative analysis and coding. Theoretical saturation was achieved after the 18th article, as no new conceptual categories or emergent mechanisms were observed beyond that point, indicating sufficient depth and diversity in the dataset.

Data analysis followed a qualitative thematic synthesis approach to identify, compare, and integrate recurring conceptual patterns across the selected literature. First, open coding was applied to textual data extracted from abstracts, methods, results, and discussion sections of each article to capture preliminary codes such as *bioelectronic feedback mechanisms*, *adaptive neural modulation*, *energy autonomy*, and *patient-specific calibration*. During axial coding, these open codes were organized into higher-order categories representing key analytical dimensions: device architecture, biosignal–electronics coupling, computational personalization, clinical translation, and ethical–regulatory considerations. Finally, selective coding integrated these categories into overarching themes that described the evolving landscape of personalized bioelectronics, focusing on the shift from static, one-size-fits-all systems toward dynamic, self-optimizing therapeutic interfaces. Coding consistency and thematic coherence were verified through repeated iteration within Nvivo to minimize researcher bias. The analytical process emphasized conceptual richness, theoretical depth, and interconnectivity between technological and clinical perspectives, thereby ensuring a comprehensive and credible synthesis of current scientific knowledge in this emerging domain.

3. Findings and Results

The foundation of personalized bioelectronics lies in the design and optimization of smart bioelectronic architectures, which integrate flexible materials, miniaturized circuits, and adaptive power systems to achieve seamless human–machine interfacing. Recent advances in stretchable and biocompatible materials—including conductive polymers, liquid metal interconnects, and hydrogel-based substrates—have enabled devices that conform intimately to biological tissues without impairing functionality or causing irritation (Kim et al., 2020; Huang et al., 2022). These material innovations are often combined with miniaturized circuit integration based on CMOS microchips and system-on-chip platforms, which support wireless communication and low-power operation for long-term monitoring (Jeong et al., 2021). The synergy between electronics and biology requires meticulous control of biocompatibility and longevity, achieved through self-healing composites, corrosion-resistant encapsulations, and biodegradable packaging that minimize inflammatory responses while maintaining electronic performance (Zhao et al., 2023). Multifunctional sensor design further extends these capabilities by embedding multi-analyte sensing elements—capable of simultaneously detecting biochemical, mechanical, and thermal signals—into hybrid structures for richer physiological data streams (Dagdeviren et al., 2019). The architecture of modern bioelectronic systems also reflects a modular design philosophy, enabling plug-and-play functionality, reconfigurable circuits, and hybrid mechanical–electronic integration that allows systems to be tailored for diverse therapeutic goals (Someya et al., 2020). Equally critical is the advancement of power management systems, incorporating micro-batteries, inductive wireless charging, and energy scavenging from biomechanical movement or thermoelectric gradients to ensure operational independence in implantable environments (Li et al., 2023). Altogether, these architectural innovations illustrate a decisive shift from rigid, externally powered devices toward soft, autonomous, and self-sustaining systems that adapt dynamically to human physiology and environmental conditions, laying the groundwork for a new era of precision bioelectronic medicine (Wang et al., 2022).

The second major theme centers on wearable and implantable interface engineering, which bridges material science, electronics, and biophysics to create robust human-integrated systems for continuous monitoring and intervention. Skin-integrated electronics represent a rapidly growing domain where ultrathin epidermal tattoos, textile-based electrodes, and stretchable conductive fibers enable long-term biosignal acquisition without discomfort or motion interference (Rogers et al., 2019). The expansion into neural and muscular implants—including microelectrode arrays, peripheral nerve interfaces, and optoelectronic stimulators—has revolutionized how clinicians and engineers approach conditions like Parkinson's disease, epilepsy, and chronic pain, offering adaptive neuromodulation at millisecond precision (Gater et al., 2021; Chen et al., 2022). Advances in biofluidic integration have also expanded diagnostic capabilities through sweat, saliva, and tear sensing systems that use microfluidic channels and enzymatic reactions to track biomarkers dynamically (Bandodkar & Wang, 2021). A critical enabling factor is wireless communication, where Bluetooth Low Energy, near-field communication, and inductive telemetry systems ensure secure real-time data transmission between body-worn sensors and cloud analytics platforms (Xu et al., 2022). The material–tissue interaction domain further refines interface reliability, focusing on optimizing mechanical impedance matching, enhancing bioadhesion, and employing bioinspired surface morphologies that promote long-term stability (Gonzalez et al., 2023). Meanwhile, implantable packaging technologies—such as hermetic encapsulation using ultrathin polymeric films—enhance durability under physiological conditions, while thermal and mechanical safety designs protect tissues from strain and overheating during extended operation (Zhou et al., 2024). Collectively, these advances have transformed bioelectronics into a symbiotic interface between humans and technology, capable of supporting long-duration therapeutic cycles and resilient to both biological and environmental challenges (Lee et al., 2021).

A defining hallmark of next-generation personalized bioelectronics is the development of closed-loop therapeutic mechanisms, in which sensing, computation, and actuation are integrated into an adaptive feedback system. The foundation of this paradigm lies in precise biosignal acquisition and processing, where electrophysiological, biochemical, and biomechanical data are captured through multi-modal sensors and refined via artifact suppression, adaptive filtering, and machine learning-based feature extraction (Xie et al., 2022). These signals drive feedback control algorithms that enable real-time modulation of physiological responses through proportional-integral-derivative control, reinforcement learning, or fuzzy logic systems that continually tune stimulation parameters to optimize therapeutic efficacy (Ghezzi et al., 2021). Various actuation and stimulation strategies—including electrical neuromodulation, optogenetics, ultrasound, and electrochemical drug release—serve as the physical means of implementing feedback, each chosen for its precision and reversibility (Famm et al., 2013; Zhang et al., 2023). Central to personalization is the incorporation of adaptive learning modules, which calibrate system parameters according to each patient's physiological response and evolving disease trajectory (Liu et al., 2022). Multimodal data fusion integrates diverse biosignals to provide comprehensive insights into patient state, enhancing both diagnosis and control precision through artificial intelligence models (Li et al., 2020). Finally, achieving full system autonomy and robustness—through self-calibration, noise reduction, and redundancy protocols—ensures that the closed-loop system remains reliable under variable conditions. Together, these advances mark the transition from reactive to self-regulating therapeutic platforms, capable of autonomously detecting dysfunctions, adapting interventions, and preventing disease exacerbation before symptoms emerge (Merrill et al., 2022).

The fourth thematic domain addresses the translational, ethical, and regulatory challenges that define the societal and clinical impact of personalized bioelectronics. Translating laboratory prototypes into real-world therapeutic devices requires rigorous clinical validation pathways, involving phased human trials, in vivo assessments, and cross-institutional verification to ensure reproducibility and safety (Stieglitz & Navarro, 2020). Concurrently, data privacy and security have emerged as central ethical concerns, as bioelectronic devices continuously collect sensitive physiological information. Encryption techniques, decentralized storage systems like blockchain, and anonymization frameworks are increasingly being employed to ensure data sovereignty and patient trust (Topol, 2021). Ethical design also extends to algorithmic transparency and user autonomy, ensuring that machine learning-based therapeutic decisions remain interpretable and that patients retain control over their treatment preferences (Yuste et al., 2022). Regulatory frameworks, including FDA, CE, and ISO standards, continue to evolve in response to the hybrid biological-digital nature of these technologies, demanding both medical device compliance and software safety certification (Buch et al., 2020). Another pressing issue is socioeconomic accessibility, as personalized bioelectronics risk exacerbating health inequities if affordability, scalability, and local infrastructure are not prioritized (Hummel et al., 2021). The field's success depends on interdisciplinary collaboration across engineers, clinicians, ethicists, and policymakers to establish standards that balance innovation with responsibility. Additionally, as environmental sustainability becomes a global concern, researchers are exploring eco-friendly materials and circular design principles to minimize electronic waste and energy consumption (Gandhi et al., 2023). Collectively, these considerations underscore that the future of personalized bioelectronics is not solely a technical endeavor but a socially and ethically integrated transformation of healthcare that merges human values with intelligent therapeutic systems (Bonaci et al., 2022).

4. Discussion and Conclusion

The findings of this review indicate that personalized bioelectronics, encompassing wearable and implantable interfaces for closed-loop therapeutics, have undergone substantial advances in recent years, enabling the development of adaptive, patient-specific, and highly integrated healthcare solutions. One of the major outcomes identified is the significant progress in bioelectronic architectures, particularly the integration of flexible, stretchable, and biocompatible materials with miniaturized electronic circuits. These architectures have facilitated seamless interfacing with human tissues, allowing devices to maintain functionality under dynamic physiological conditions while minimizing inflammatory responses and discomfort (Kim et al., 2020; Huang et al., 2022). The use of conductive polymers, liquid metal interconnects, hydrogels, and self-healing composites has enabled devices to achieve mechanical compliance with the skin or internal tissues, enhancing long-term reliability and patient comfort (Dagdeviren et al., 2016; Zhao et al., 2023). Modular design approaches have further allowed for customizable device configurations that can be tailored to individual patient needs, integrating multiple sensing and actuation modalities into a single coherent system (Someya et al., 2020). These findings align with prior studies that emphasize the critical role of material innovation in advancing wearable and implantable bioelectronics, highlighting that the mechanical and chemical properties of device substrates are crucial determinants of clinical efficacy and patient adherence (Rogers et al., 2019; Wang et al., 2022).

Another prominent result observed is the evolution of wearable and implantable interface engineering, which has expanded both the capabilities and accessibility of bioelectronic therapeutics. Skin-integrated electronics, such as epidermal tattoos and textile-based electrodes, have been successfully employed for non-invasive monitoring of physiological parameters including electrophysiological signals, hydration, and mechanical strain, demonstrating robust performance under continuous motion and long-term use (Rogers et al., 2019; Xu et al., 2022). Implantable interfaces, particularly neural and muscular implants, have shown remarkable efficacy in conditions such as Parkinson's disease, epilepsy, and chronic pain by providing targeted neuromodulation through microelectrode arrays, optoelectronic stimulation, and peripheral nerve interfaces (Gater et al., 2021; Chen et al., 2022). Biofluidic integration has further augmented device functionality, allowing real-time measurement of sweat, tear, and interstitial fluid analytes, which can be utilized to adjust therapeutic delivery in a closed-loop manner (Bandodkar & Wang, 2021). These findings are consistent with prior work indicating that hybridization of multiple sensor modalities, together with wireless communication technologies such as Bluetooth Low Energy and near-field communication, enables continuous, secure, and real-time data transmission that supports adaptive therapeutic interventions (Xu et al., 2022; Jeong et al., 2021). The convergence of these engineering innovations underscores that the evolution of interface design is a key enabler for personalized, responsive, and scalable bioelectronic solutions (Huang et al., 2022).

The review also highlights the functional advancements in closed-loop therapeutic mechanisms, which represent a central innovation of personalized bioelectronics. Devices are increasingly capable of acquiring multimodal biosignals, processing them using advanced algorithms, and delivering adaptive stimulation or drug release in response to detected physiological states (Famm et al., 2013; Ghezzi et al., 2021). Biosignal acquisition and processing have benefitted from enhanced filtering techniques, motion artifact suppression, and the application of machine learning to interpret complex physiological data streams in real time (Xie et al., 2022). Feedback control algorithms, including proportional-integral-derivative (PID), reinforcement learning, and fuzzy logic models, have demonstrated the capacity to autonomously modulate therapeutic interventions according to individual patient responses, achieving higher precision and minimizing adverse effects compared to conventional open-loop devices (Liu et al., 2022; Merrill et al., 2022). Actuation strategies such as electrical nerve stimulation, optogenetic activation, ultrasonic stimulation, and electrochemical drug release have been effectively combined with real-time sensing to create dynamic treatment platforms that adapt to changing physiological conditions (Zhang et al., 2023; Famm et al., 2013). These findings support previous studies that have emphasized the transformative potential of closed-loop bioelectronic systems in enabling self-regulating therapeutics that resemble biological homeostasis, particularly in the management of chronic neurological and metabolic disorders (Merrill et al., 2022; Li et al., 2020).

The analysis also indicates that the integration of adaptive personalization and multimodal data fusion enhances the precision of therapeutic delivery and monitoring. By incorporating individual-specific calibration and machine learning models that integrate data from electrical, mechanical, optical, and biochemical sensors, devices can continuously refine their interventions in response to evolving physiological conditions (Liu et al., 2022; Zhang et al., 2023). This multimodal approach not only improves diagnostic accuracy but also facilitates early detection of adverse events, such as seizure onset or arrhythmia, allowing preemptive interventions (Li et al., 2020). Prior research underscores that the use of AI-driven data fusion is critical for interpreting the complexity of human physiology, and for translating sensor outputs into actionable therapeutic commands (Ghezzi et al., 2021; Zhang et al., 2023). The development of autonomous calibration and redundancy mechanisms further ensures that these systems remain robust and reliable, even in the presence of sensor noise, variability in signal quality, or changes in environmental conditions (Merrill et al., 2022).

Translational, ethical, and regulatory considerations emerge as essential determinants for the implementation of personalized bioelectronics in clinical practice. Clinical validation, including phased human trials and multi-site verification, is necessary to ensure device safety, efficacy, and reproducibility across diverse patient populations (Stieglitz & Navarro, 2020).

Data privacy and cybersecurity represent critical challenges, as continuous physiological monitoring generates sensitive patient information that must be protected through encryption, anonymization, and secure data transfer protocols (Bonaci et al., 2022; Topol, 2021). Ethical design considerations emphasize patient autonomy, informed consent, and transparency in algorithmic decision-making, particularly as AI-driven devices gain greater influence over therapeutic interventions (Yuste et al., 2022). Regulatory frameworks are evolving to accommodate hybrid devices that combine hardware, software, and biological interactions, and compliance with standards such as FDA, CE, and ISO guidelines is essential for market authorization (Buch et al., 2020). Additionally, socioeconomic accessibility and environmental sustainability remain significant considerations, requiring devices to be cost-effective, scalable, and constructed from eco-friendly or recyclable materials to minimize healthcare disparities and ecological impact (Gandhi et al., 2023; Wang et al., 2022). These translational and ethical dimensions are consistent with prior literature highlighting that the successful deployment of personalized bioelectronics requires integration of engineering innovation with regulatory compliance and human-centered ethics (Hummel et al., 2021; Bonaci et al., 2022).

Despite these advancements, several limitations were identified in the reviewed studies. Most research remains in early preclinical or pilot human trial stages, limiting the generalizability of findings to broader populations and long-term clinical outcomes (Stieglitz & Navarro, 2020). Many devices have been tested under controlled laboratory conditions, which may not replicate real-world variability in patient activity, environmental exposure, or physiological stressors (Rogers et al., 2019). Additionally, while the integration of AI and multimodal sensing has improved adaptability, these systems introduce complexity that may hinder transparency, reproducibility, and interpretability of therapeutic decision-making (Liu et al., 2022; Yuste et al., 2022). Ethical concerns around data privacy and patient consent remain incompletely addressed in many studies, and standardized regulatory pathways for hybrid bioelectronic devices are still under development (Topol, 2021; Buch et al., 2020). The variability in materials, designs, and algorithms across studies also poses challenges for synthesizing best practices and establishing industry-wide benchmarks (Kim et al., 2020).

Future research should prioritize long-term, large-scale clinical studies to evaluate device efficacy, durability, and safety across diverse patient populations and physiological contexts (Stieglitz & Navarro, 2020). There is a need to develop standardized protocols for closed-loop bioelectronic system testing, including reproducible methods for evaluating responsiveness, adaptation, and system robustness (Zhu et al., 2023). Further exploration of AI-driven personalization algorithms should focus on interpretability, transparency, and integration with regulatory frameworks to ensure that patient outcomes remain accountable and reproducible (Ghezzi et al., 2021; Liu et al., 2022). Multidisciplinary research efforts are also warranted to address ethical, social, and environmental implications, ensuring that these advanced technologies are equitable, accessible, and environmentally sustainable (Hummel et al., 2021; Gandhi et al., 2023). Moreover, future studies should investigate strategies for combining wearable and implantable platforms into hybrid therapeutic systems capable of seamless, long-term, and self-optimizing interventions (Dagdeviren et al., 2016).

In practice, personalized bioelectronics have the potential to transform healthcare delivery by enabling proactive, adaptive, and precise therapeutic interventions. Clinicians can leverage these devices for real-time monitoring of chronic conditions, dynamic adjustment of treatments, and early detection of physiological anomalies, thereby reducing hospitalizations and improving patient quality of life (Famm et al., 2013; Merrill et al., 2022). Health systems may adopt hybrid wearable-implantable networks to facilitate remote monitoring, reduce the need for frequent in-person consultations, and optimize resource allocation in both urban and resource-limited settings (Xu et al., 2022). Additionally, developers and regulators can employ the findings of this review to inform design standards, ethical guidelines, and compliance pathways, fostering the safe and effective integration of adaptive bioelectronics into routine clinical practice (Buch et al., 2020; Yuste et al., 2022). By embedding continuous sensing, AI-driven adaptation, and closed-loop therapeutic control within human-compatible devices, personalized bioelectronics promise to create responsive, patient-centered healthcare ecosystems that extend well beyond traditional medical interventions.

Overall, this review underscores that personalized bioelectronics are not only technologically transformative but also clinically and ethically significant. By integrating advanced materials, adaptive control systems, multimodal sensing, and ethical considerations, these devices exemplify a new frontier in medicine—one in which therapy is dynamically tailored to the physiological and psychosocial needs of individual patients. The alignment of engineering innovation with human-centered healthcare principles ensures that closed-loop bioelectronic therapeutics have the potential to redefine patient outcomes, healthcare accessibility, and long-term wellness management. The evidence from the 18 reviewed studies collectively demonstrates that personalized bioelectronics is transitioning from proof-of-concept prototypes to increasingly viable clinical solutions, offering a framework for responsive, adaptive, and sustainable medical interventions in the twenty-first century (Kim et al., 2020; Dagdeviren et al., 2016; Stieglitz & Navarro, 2020).

Ethical Considerations

All procedures performed in this study were under the ethical standards.

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Conflict of Interest

The authors report no conflict of interest.

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