Journal of Semiconductors
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Citation: B Q Yang, Z Zhang, and T Lei, Living electronics meets semiconducting hydrogels[J]. *J. Semicond.*, 2026, In Press .
View online: http://www.jos.ac.cn/article/shaid/fb5786a80fad6881589fa8724d6d9897a5f4aee1c95ef90b0fcb8c2e3a84731f

RESEARCH HIGHLIGHTS

Journal of Semiconductors, 2026, 47:
DOI: 10.1088/1674-4926/26020009
CSTR: 32376.14.1674-4926.26020009

JOS

Living electronics meets semiconducting hydrogels

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Citation: B Q Yang, Z Zhang, and T Lei, Living electronics meets semiconducting hydrogels[J]. *J. Semicond.*, 2026, accepted, https://doi.org/10.1088/1674-4926/26020009

Living electronics is an emerging discipline that integrates living materials with electronics, aiming to bridge the long-standing gap between electronic devices and dynamic biological systems. Unlike conventional bioelectronics, which largely rely on passive integration at biological-electronic interfaces, living electronics involves living units as integral components that perform core functions such as sensing, computing, or therapy, while establishing dynamic electrical interactions with the abiotic components. In these systems, engineered bacteria or functional cells serve as the active units, while the electronic counterparts transduce biological outputs, such as fluorescence or extracellular electron transfer (EET), into electrical signals, enabling intelligent bio-hybrid systems. Enabled by advances in synthetic biology, living electronics exhibit rich programmability and selectivity, ranging from genetically edited bacteria for the detection of diverse substances to cells capable of synthesizing and secreting therapeutic agents on demand[1]. Furthermore, living electronics intrinsically favor dynamic, adaptive, and self-healing behaviors[2], as living components can continuously regenerate, remodel, and respond to environmental cues. These characteristics open new opportunities for bio-integrated therapy and intelligent sensing.

However, realizing such deep integration places stringent and often conflicting demands on material properties. Electronic materials must simultaneously satisfy requirements in electronic performance, mechanical compliance, morphological compatibility, and long-term biocompatibility, while operating reliably in aqueous and biological environments. Meeting these requirements with traditional electronic materials has proven challenging. In this context, semiconducting hydrogels have recently emerged as a promising platform. By combining ionic-electronic mixed conductivity, rich circuit functionality, tissue-like softness, and a three-dimensional (3D) porous architecture[3], semiconducting hydrogels offer a unique opportunity to meet the stringent requirements and provide a new direction for living electronics.

Ideally, a fully realized living electronic device should seamlessly integrate sensing, signal processing, and therapeutic functions within a single system. However, owing to current technical limitations, most state-of-the-art biohybrid devices still focus on isolated functionalities. Therefore, based on the functional role of the living components, current developments in living electronics can be broadly categorized into two directions based on their functions. The first, biointerface-centered living electronics, focuses on integrating engineered cells or bacteria with electronic devices to provide therapeutic or regenerative capabilities. Early examples include tissue-engineered neural interfaces by loading neural cells onto electrode surfaces[4–7] (Fig. 2(a)). However, most of these studies lacked *in vivo* validation or faced challenges related to long-term inflammation[5]. Beyond neural repair, engineered cells or bacteria can also serve as "living pharmacies" for disease treatment[8] (Fig. 2(b)). Shi *et al.* reported an active biointegrated living electronics (ABLE) platform that integrates bioelectronics with a bacteria-laden hydrogel to enable simultaneous physiological sensing and therapeutic intervention for inflammatory skin diseases[9]. In these systems, electronics largely act as passive readout or stimulation modules, limiting signal transduction to 2D surface, without volumetric sensing, intrinsic amplification, or distributed computation.

The second, biologically actuated electronics, aims to improve or expand device functionality by using cells or bacteria as active components for sensing or computing[10–12]. Engineered bacteria can be programmed to respond to specific chemical, thermal, or pH stimuli by expressing fluorescent proteins or performing EET[13]. These biological responses are then transduced into electrical signals via nearby electronics. For example, an ingestible bacterial electronic system was developed to accurately diagnose gastrointestinal bleeding in swine using heme-responsive engineered probiotic *E. coli*.[10] (Fig. 2(c)). Engineered cells have also been utilized to build genetic circuits and neuromorphic devices[14, 15]. Gao *et al.* demonstrated that the electroactive bacterial strain *Shewanella oneidensis*, when interfaced with an organic electrochemical transistor (OECT), could modulate channel conductance via genetically regulated EET. This enables programmable logic operations and the realization of a biohybrid synaptic device[15] (Fig. 2(d)). Although microorganisms actively modulate electronic outputs, the electronic functionality remains largely confined to discrete interfaces, with signal processing and complex circuit functions reliant on external circuits rather than occurring *in situ*.

To date, living electronics have limited integration between biological activity and electronic performance. This limitation arises largely from the interfacing materials in conventional designs. Current interfacing materials used in living electronics either lack electrical properties (e.g., gelatin[9] or fibrin[7] hydrogels) or are too rigid to match the modulus of living cells (parylene encapsulation[14] or 2D PEDOT:PSS film[15]). Consequently, these systems fail to simultaneously provide *in situ* signal amplification and favorable microenviron-

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Received 5 FEBRUARY 2026; Revised 1 APRIL 2026.

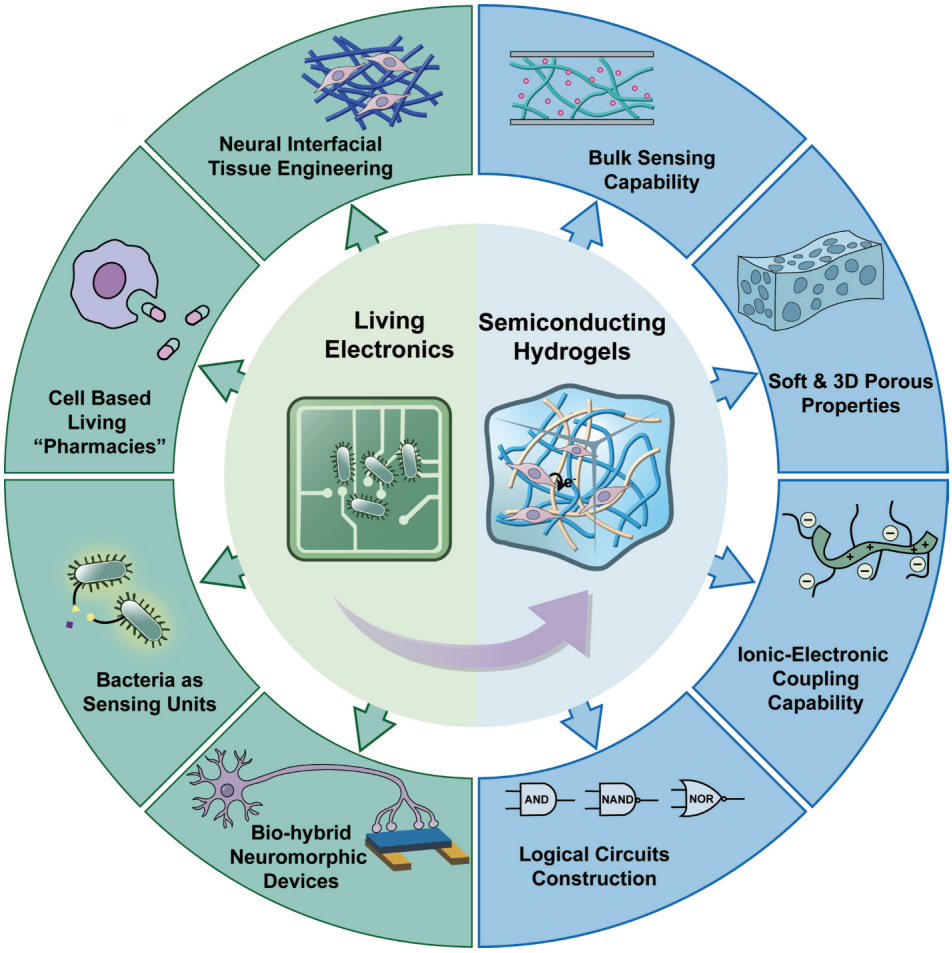

Fig. 1. (Color online) Overview of living electronics and semiconducting hydrogels: applications and future prospects. This schematic illustrates semiconducting hydrogels could serve as an ideal platform for living electronics, enabled by their bulk sensing capability, mechanical softness, intrinsic porosity, efficient ion-electron coupling and logical operation ability.

ments for cell adhesion and growth. Furthermore, restricting cell-device interactions to 2D planar surfaces limits the volumetric coupling of biological signals. Breaking this limitation is a critical bottleneck for the field. The next generation of living electronics is therefore envisioned as systems in which cells and electronic components interact directly, transducing signals *in situ* and mutually enhancing each other through mechanical, optical, or electrical modalities, while combining rich electronic properties, tissue-like softness, and dynamic adaptability.

Semiconducting hydrogels have emerged as a promising solution to meet these requirements, offering distinct advantages combining tissue-like softness, rich circuit functionality, bulk sensing, and high biocompatibility. In 2024, our group reported the first semiconducting hydrogel, P(PyV)-H, by electrostatically crosslinking a water-soluble semiconducting polymer with its counterion disodium 1,3-benzenedisulfonate (DBS^{2-})[16] (Fig. 2(e)). The n-type semiconducting hydrogel exhibits both high biocompatibility with excellent semiconducting properties, enabling the fabrication of complex circuits such as complementary inverters for effective signal amplification (Fig. 2(f)). In addition, this non-organic solvent processing strategy has recently been proven significantly important in constructing cell-based living electronic systems. Subsequently, research on semiconducting hydrogels has attracted widespread interest. Wang *et al.* reported a p-type semiconducting hydrogel by a solvent-exchange strategy using semiconducting polymer p(g2T-T) and polyacrylic acid hydrogel[17]. This semiconducting hydrogel presented a low modulus under 100 kPa, matching that of skin and muscle. They also demonstrated that the hydrogel's 3D porous architecture enables efficient diffusion of analyte molecules (such as glucose) throughout the hydrophilic network, which allows for highly efficient coupling between analyte molecules and enzymes immobilized within the bulk semiconducting hydrogel (Fig. 2(g)). This volumetric interaction enhances biochemical reactions and induces a higher density of charge carriers within the polymer backbone compared to traditional 2D planar interfaces, thereby greatly enhancing the sensitivity of the OECT device. The bulk sensing effect has been previously demonstrated using hydrogel-encapsulated bacteria, which achieve a signal-to-noise ratio (SNR) over 30 times higher than the non-hydrogel electrode[19]. Recently, Zhang *et al.* systematically investigated how the dimensional increase of semiconducting hydrogels improved the electrical properties of OECTs, in contrast to conventional thin-film transistors, whose performance declines as the thickness increases[18] (Fig. 2(h)). They displayed regulated cell growth within PEDOT hydrogel, illustrating the feasibility of cell culture and organoids formation. A hydrogel electrolyte was also utilized to replace conventional liquid electrolytes, which may serve as an encapsula-

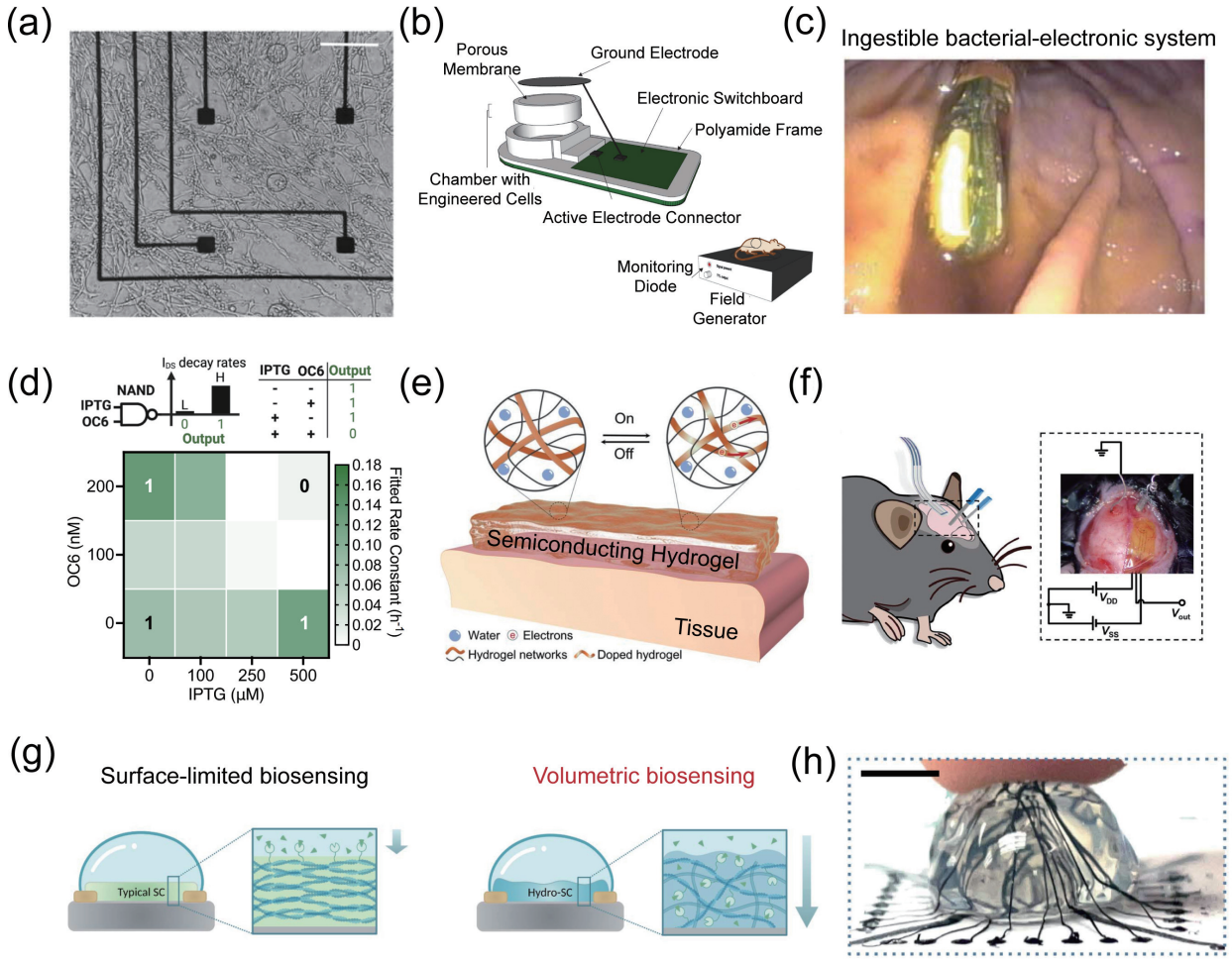

Fig. 2. (Color online) (a) Induced pluripotent stem cell (iPSC)–derived myocytes on flexible electrode arrays[7]. Reproduced with permission from Ref.[7]; Copyright (2023) the author(s) under the terms of the Creative Commons CC BY license. (b) Three-dimensional model of a bioelectronic implant integrated with engineered electrosensitive human β cells for diabetes management[8]. Reproduced with permission from Ref.[8]; Copyright (2020) The American Association for the Advancement of Science. (c) An ingestible bacterial-electronic system for gastrointestinal health monitoring[10]. Reproduced with permission from Ref.[10]; Copyright (2018) The American Association for the Advancement of Science. (d) Genetic logic gate based on bio-hybrid OECT[15]. Reproduced with permission from Ref.[15]; Copyright (2024) the author(s) under the terms of the Creative Commons CC BY license. (e) Illustration of the working mechanism of an n-type semiconducting hydrogel[16]. Reproduced with permission from Ref.[16]; Copyright (2024) The American Association for the Advancement of Science. (f) Mouse electrocorticography (ECoG) recording with a complementary inverter based on n-type semiconducting hydrogel[16]. Reproduced with permission from Ref.[16]; Copyright (2024) The American Association for the Advancement of Science. (g) Comparison of the surface sensing in conventional biosensors *vs.* the bulk sensing effect of semiconducting hydrogels[17]. Reproduced with permission from Ref.[17]; Copyright (2024) The American Association for the Advancement of Science. (h) Photograph of a PEDOT-based 3D hydrogel OECT[18]. Reproduced with permission from Ref.[18]; Copyright (2025) The American Association for the Advancement of Science.

tion layer of living electronics, preventing the escape of cells or bacteria.

Currently, research on semiconducting hydrogels remains largely within the scope of conventional bioelectronics. However, we believe that the key advantages of semiconducting hydrogels endow them with great potential in constructing living electronics. First, their three-dimensional porous networks enable volumetric sensing and abundant cell-semiconductor interactions, considerably improving sensors' sensitivity and SNR. Second, their hydrophilic nature and ionic-electronic coupling allow them to retain more powerful electrical functionality in aqueous and biological environments. Third, the inherent softness and porosity address the longstanding mismatch between rigid electronics and living systems while facilitating nutrient transport for embedded cells or microbes. Finally, semiconducting hydrogels can be utilized to build logical circuits, enabling the realization of genetically programmed logic gates and biohybrid neuromorphic devices. Integration with living systems may further endow semiconducting hydrogels with additional properties such as self-healing and improved interfacial adhesion.

While semiconducting hydrogels hold great promise for constructing living electronics, several key challenges remain to be addressed. First, most semiconducting polymers are intrinsically hydrophobic and insoluble in aqueous environments, which hinders their direct integration with living systems. Developing water-soluble semiconducting polymers, such as P(PyV) demonstrated in our previous work, represents a promising strategy, but achieving high electrical performance while maintaining biocompatibility remains nontrivial. Further molecular and structural design strategies are therefore required to meet the demands of living electronics. Sec-

ond, fabrication and patterning processes may introduce mechanical, thermal, or chemical effects that can compromise the viability and functionality of embedded living components. Maintaining high cellular activity and viability throughout device fabrication and operation, therefore, remains a significant challenge, particularly in high-resolution or multi-step processing techniques. Third, the physical dimensions of bacteria are typically around 1~5 μm, which can disrupt the microscale morphology of semiconducting polymer networks and impede charge transport pathways, leading to a decrease in electrical properties. This imposes higher requirements on the design of future materials and devices.

Beyond these considerations, several additional challenges also merit attention. For example, long-term stability at the bioelectronic interface remains limited due to material degradation, biofouling, and the dynamic nature of biological environments. In addition, scalable manufacturing and the reproducibility of such hybrid living systems are still largely unexplored.

This work summarized the current design principles and application scenarios of living electronics. We pointed out the limitations of existing approaches, where 2D interfaces hamper effective electrical transduction between cells and electronics, preventing true integration between living tissues and electronic functionality. Semiconducting hydrogels provide a solution that combines bulk interaction features, ionic-electronic coupling characteristics, excellent biocompatibility, and logical operation capability. Studies have confirmed the feasibility of cells growing within semiconducting hydrogels and the enhancement of electrical signals through their bulk sensing effect. Looking forward, semiconducting hydrogel-based living electronics present significant opportunities by combining "native" electronic functions with biological functions, including *in situ* signal capture, processing, amplification, distributed computation, and responding. We believe the development of semiconducting living materials and related bioelectronics could open up the door for long-term biosensing in complex environments and biofluids, closed-loop treatment of diseases, and biomimetic neuromorphic devices, as well as organoid chips and drug development. Further research may focus on integrating multicellular systems, enhancing long-term stability, and scaling up biohybrid circuits to fully realize the potential of next-generation living electronics.

Acknowledgements

This work is supported by National Natural Science Foundation of China (T2521001), and Beijing Natural Science Foundation (2262050).

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