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Review

Beyond 25 years of biomedical innovation in nano-bioelectronics

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THE BIGGER PICTURE Nano-bioelectronics represent a synergistic integration of nanotechnological precision with the multifaceted nature of biological systems. Since its emergence, the discipline has witnessed evolution propelled by a suite of technological breakthroughs including biochemical sensing, intracellular recording, neuromodulation, and brain-machine interfaces. This review highlights the contribution of nano-bioelectronic materials and devices in advancing biomedical interventions in the past decades, and it looks forward to their potential for environmental surveillance, improving agricultural productivity, optimizing energy utilization, and even enhancing artistic endeavors. Research in nano-bioelectronics encompasses a wide range of scales. On the molecular scale, it has been studied intensively in cellular operations and intercellular dialogue, facilitating deciphering of biochemical, biomechanical, and bioelectrical languages. On the societal scale, its deployment in environmental observation, and agricultural practices herald innovative strategies for ecosystem management. Anticipated future directions would concentrate on the refinement of devices capable of integrating with biological matrices. Furthermore, advancements in scalable manufacturing processes are deemed critical for expanding accessibility and application.

SUMMARY

Nano-bioelectronics, which blend the precision of nanotechnology with the complexity of biological systems, are evolving with innovations such as silicon nanowires, carbon nanotubes, and graphene. These elements serve applications from biochemical sensing to brain-machine interfacing. This review examines nano-bioelectronics' role in advancing biomedical interventions and discusses their potential in environmental monitoring, agricultural productivity, energy efficiency, and creative fields. The field is transitioning from molecular to ecosystem-level applications, with research exploring complex cellular mechanisms and communication. This fosters understanding of biological interactions at various levels, such as suggesting transformative approaches for ecosystem management and food security. Future research is expected to focus on refining nano-bioelectronic devices for integration with biological systems and on scalable manufacturing to broaden their reach and functionality.

INTRODUCTION

The essence of biological complexity spans across the nanoscale dimensions, particularly from 1 to 100 nm, the regime in which life's critical structures and processes find their footing. For example, DNA strands, which are about 2 nm wide, and proteins, with their 5–50 nm dimensions, function optimally at this scale where their sizes are intricately linked to their roles and interactions within the cell. The nanoscale is crucial to the functioning of cellular organelles, including mitochondria, the endoplasmic reticulum, and the Golgi apparatus, all of which are pivotal for energy production and biomolecule synthesis. The cytoskeleton, with its network of microtubules, intermediate filaments, and actin filaments, operates at this scale, maintaining cellular integrity and facilitating intracellular transport and communication. Understanding these interactions is vital for the development of biosensors, drug delivery systems, and therapeutic strategies.

The fusion of nanomaterials, electronics, and biology gave rise to the field of nano-bioelectronics[1] in recent decades (Figure 1). This interdisciplinary field has benefited from technological leaps such as the atomic force microscope, tools that have allowed

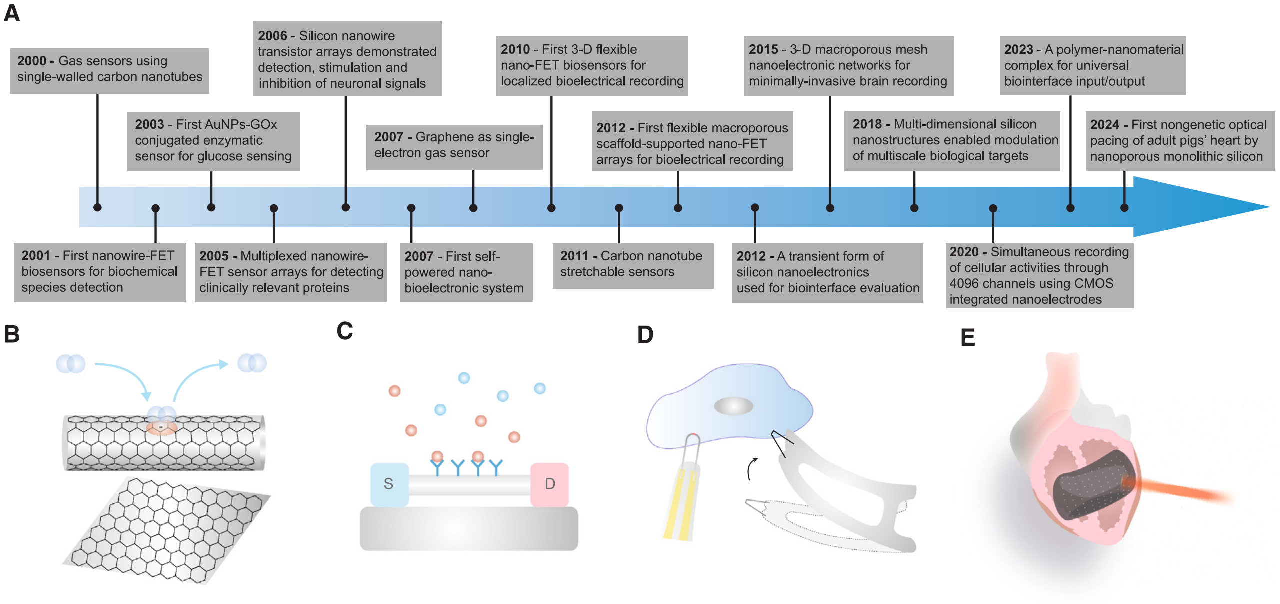


Figure 1. Advancements in nano-bioelectronics for biological applications

(A) Milestones of nano-bioelectronics over the past two decades.[2,3–6,7,8,9,10–18]

(B) Carbon nanotubes and graphene have been demonstrated for gas sensing based on adsorption and desorption. Molecular gasses act as electron donors or acceptors that affect local density of states and the resistance of the nanoelectronics device.[3,4,6]

(C) Nanowire-based FET devices have been used for specific detection of biomolecules. The recognition of biomolecules through the receptors cause a change in the local charge states, affecting the channel transconductance.[10,11]

(D) U-shaped and kinked 3D nanowire FETs have been leveraged for intracellular electrophysiology studies. This provided higher electrophysiological signal fidelities compared with the extracellular microelectrode arrays.[13,19]

(E) Monolithic thin-film photoelectrochemical devices have showcased leadless modulation of biological tissues. The monolithic film has achieved random-access and photostimulation of cells, *ex vivo* and *in vivo* rodent tissues as well as *in vivo* pig heart models.[16,18,20]

us to see and manipulate the biomolecular world. These advancements, coupled with bioinformatic insights, such as those from multi-omics and synthetic biology, have paved the way for nano-bioelectronics that interfaces with biological systems at the molecular level. While nano-bioelectronics has its roots embedded in improving healthcare and medical technologies, its future applications are broad and transdisciplinary, with possibilities and opportunities for technological advancements and societal benefits across a wide range of disciplines.

At the heart of nano-bioelectronics[1] lies an array of nanostructured components (Figure 1) for biological sensing and modulation,[21,22] including semiconductor nanowires,[2,23] carbon nanotubes,[3–5] graphene nanomembranes,[6] supramolecular or polymeric networks, and metallic nanostructures.[1,7,8,24] Nanostructured field-effect transistors (FETs), in particular, stand as a cornerstone device configuration. The design and synthesis of these materials directly impact the deployment of these components in applications such as intracellular recording and tissue engineering. Addressing issues such as Debye screening,[24] which occurs in environments of high ionic strength, is crucial for enhancing the sensitivity of FETs. Progress in surface modification techniques,[25,26] including those employing aptamers,[27–30] has led to improvements in specificity and sensitivity. The ephemeral nature of silicon and reactive metal species in aqueous environments has pivoted their application toward transient bioelectronics,[9,31–34] whereas carbon-, carbide-, and noble metal-based materials are being used for their durability in long-term applications.[1]

The integration of nano-bioelectronics within the domain of brain-computer interface (BCI) technologies[35–37] is a subject of debate. The progression toward more advanced, miniaturized, and lightweight devices, akin to those pioneered by Neuralink, signifies recent progress in the field. Nanoscale engineering may refine BCIs to a degree where they can spatiotemporally decode and modulate neural pathways with high accuracy, opening possibilities for treating neurological conditions and augmenting cognitive abilities. This review first discusses the typical research and applications of nano-bioelectronics, deliberately reducing emphasis on BCIs due to the extensive literature coverage, and explores emerging non-biomedical applications. We also address the challenges and forthcoming opportunities in our conclusions.

DECADES OF BIOMEDICAL INNOVATION

The advent of nano-bioelectronics marks a convergence of nanotechnology and biological research, catalyzing an era of innovation that transcends traditional boundaries of science and engineering at the macroscopic length scales (Figure 1). This interdisciplinary field harnesses the capabilities of nanoscale materials to interface with biological systems in new ways to unravel biological mysteries and engineer solutions to pressing medical challenges. The foundational goal of nano-bioelectronics is not only to enhance our understanding of life at the molecular level but also to pioneer advanced diagnostic and therapeutic devices that could revolutionize personalized medicine and beyond. As we check the nuances of biosensing and modulation, and their implications for the future of healthcare and biological research, it is essential to recognize the transformative potential nano-bioelectronics holds.

Biosensing

In the initial stages of nano-bioelectronics research, the focus was predominantly on the sensing of biomolecules and bio-particles, specifically targeting the detection and quantification of biological entities such as DNA, proteins, and viruses.[24,11,38] This direction was driven by the goal of analyzing biological molecules at the nanoscale, utilizing the distinct properties of nanomaterials combined with the precision offered by electronic systems. This resulted in highly sensitive detection of biomolecules with detection limit as low as nano- to sub-picomolar range.[10,11] A portion of this research also delved into exploring the dynamics and kinetics of biomolecular interactions at the single-molecule level.[38] The capability to monitor individual molecules in their interactions with surrounding environments or other molecules is crucial, providing insights into biological mechanisms that are often not discernible in bulk analysis. These insights include elucidating the molecular recognition processes and the conformational changes, and the impact of environmental factors on these molecular dynamics. One notable example is the use of nanowire-based nano-bioelectronics for the electrical characterization of single molecules translocating through nanopores (Figures 2A–2C).[39] These nanopores are typically created using nanolithography techniques, enabling the sequential passage of individual molecules. The monitoring of these translocation events involves measuring alterations in electrical properties, such as ionic current or resistance, as each molecule traverses the pore.

The detection of analytes using FETs equipped with ligand-specific receptors is typically hindered by the Debye length limitation, which involves shielding by the electrical double layer. A study by Nakatsuka et al. achieved the detection of small molecules under high-ionic-strength conditions typical of physiological environments by integrating printed ultrathin metal-oxide FET arrays with deoxyribonucleotide aptamers.[27] These aptamers, selected for their adaptive binding to targets, undergo target-induced conformational changes (Figure 2D). The alterations in the negatively charged aptamer phosphodiester backbones near the semiconductor channels modulate conductance in physiological buffers, facilitating sensitive detection. The method enabled the sensing of both charged and electroneutral targets, including serotonin (Figure 2E), dopamine, glucose, and sphingosine-1-phosphate, through aptameric stem-loop receptors specifically isolated for this purpose.

Since 2016, the field of nano-bioelectronics has made advancements in interfacing with cellular systems such as neural and cardiac tissues.[12,13,15,19,35–37,39–47] Early efforts utilized planar FET arrays and single FET devices for extracellular neural and cardiac interfaces. Later, the development of freestanding FET probes,[13,19,41,42,45] such as those from kinked Si nanowires (Figure 3A) and nanostructured conductors (Figures 3B and 3C)[48–51] capable of intracellular access and recording, revolutionized electrophysiological recording since the development of the patch-clamp technique. Nanopillars, with their high aspect ratio and customizable surface properties, offer a robust platform for stable intracellular access. The vertical orientation and sharp tips of nanopillars allow for penetration of cell membranes with minimal invasiveness, enhancing the recording stability.[48,50] Nano-mushrooms, characterized by their cap-and-stem structure, mimic the natural extracellular matrix, promoting cell adhesion and growth. The larger surface area of the "cap" allows for increased interaction with the cell membrane, potentially reducing the mechanical mismatch and facilitating a more stable intracellular connection.[52,53] In addition, surface chemistry modifications, such as the incorporation of cell adhesion molecules or conductive polymers, can improve electrical coupling and reduce the impedance at the interface, further enhancing signal quality and stability.[54,55] For example, Zhao et al. explored curved inorganic nanostructures[19] for neural recording and developed a nanowire-based field-effect transistor (NWFET) with a three-dimensional (3D) U-shaped configuration (Figures 3D–3F) using a fabrication process involving a sacrificial nickel layer. Their design, enhanced with a phospholipid bilayer coating for membrane fusion, allows the NWFET to penetrate cell membranes and access the cytosol for localized recording. The 3D curved NWFET offers several advantages, including intracellular neural recordings and the potential for multiplexed recording from single cells or networks. Its U-shaped design facilitates smooth cell entry and is consistent with the understanding of membrane tension and cortical cytoskeleton dynamics.[56,57]

In biointerfaces beyond the single-cell level, engineered tissues[14,58,59] and organoids[60,61] have been studied, particularly for modeling neural and cardiac development and diseases. However, a critical need exists for advanced methodologies that enable long-term, minimally invasive electrical activity recording in these systems. Current technologies such as patch-clamp, penetrating microelectrodes, planar electrode arrays, and substrate-attached flexible electrodes are inadequate for chronic recording in suspended organoids while preserving the organoids' structural integrity. Addressing this challenge, a new flexible electronics technology, inspired by kirigami art and named kirigami electronics (KiriE),[62] has been developed by Yang et al. (Figures 4A–4C). Their device transitions from a 2D layout to a 3D one, with a dynamic and morphing structure with patterns resembling spirals or honeycombs. This integration occurs without altering the organoids' morphology, cytoarchitecture, or cell composition (Figure 4A). In addition, KiriE is compatible with optogenetic and pharmacological interventions, proving its efficacy in simulating genetic disease phenotypes and in observing corticostriatal connectivity within assembloids following optogenetic stimulation (Figures 4B and 4C). In another study, ultrasoft electronic nanomeshes[59] (Figure 4D) were designed to monitor the field potentials of cardiomyocytes derived from human induced pluripotent stem cells cultured on hydrogels. These nanomeshes permit dynamic movement of the cardiomyocytes without disruption (Figures 4D and 4E). Due to their softness, the nanomesh-equipped cardiomyocytes demonstrate natural contraction and relaxation motions. Finally, the development of an innovative *in situ* electro-sequencing

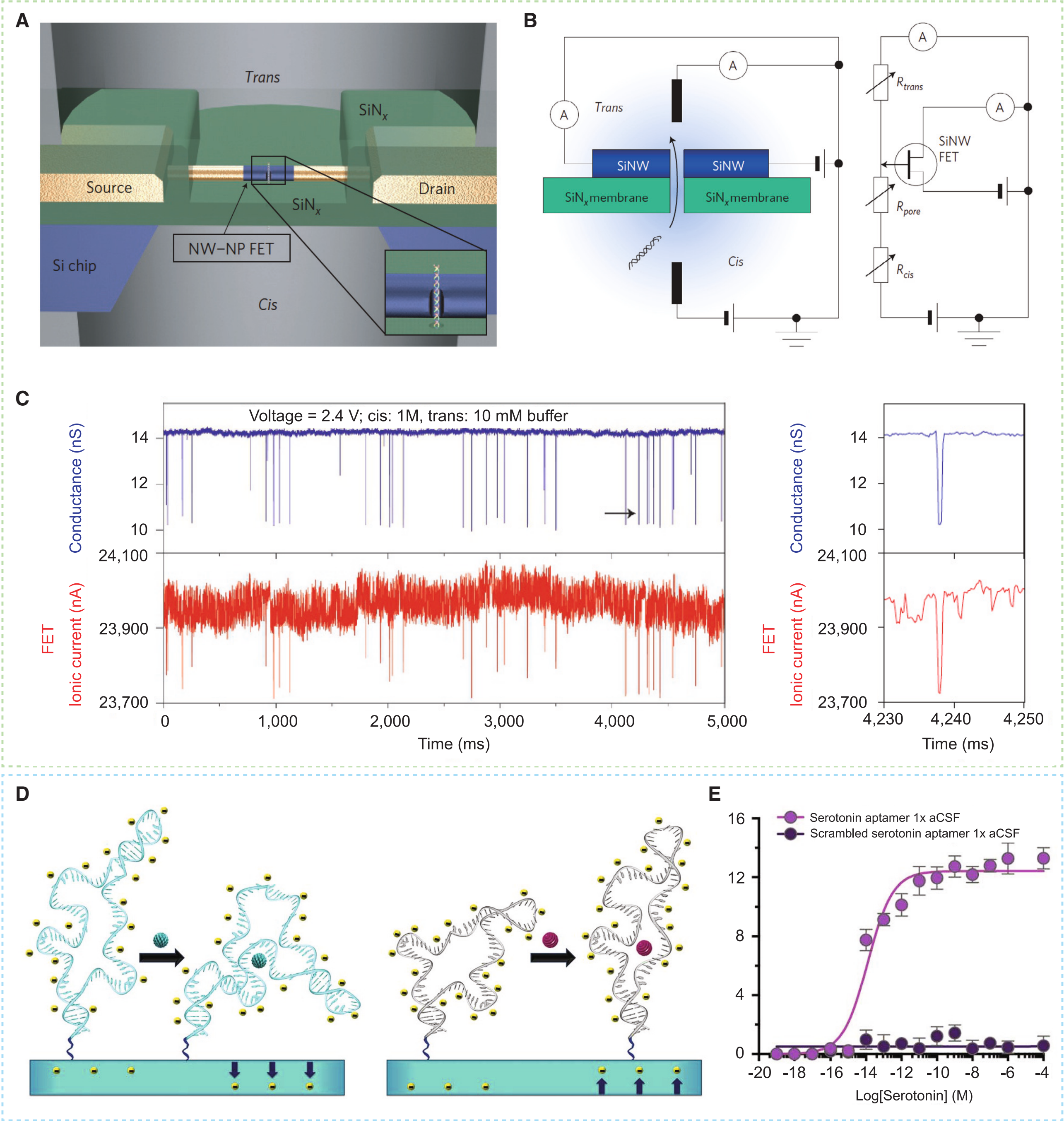


Figure 2. Notable examples of biomolecular sensing via nanoscale FETs

(A–C) Detection of DNA through local electrical potential by nanowire-nanopore sensors.[39] (A) Illustration of experimental setup for nanowire-nanopore (NW-NP) measurements, with an inset providing a detailed view of the nanopore region. (B) Nanowire-nanopore sensing mechanism: on the left, a schematic of the sensing circuit is shown, while on the right, an equivalent circuit diagram is illustrated. The silicon nanowire (SiNW) is highlighted as a critical component. (C) The single-channel nanowire-nanopore FET detects DNA translocation, with simultaneous recording of ionic current and FET conductance signals at a bias voltage of 2.4 V. The right panels provide detailed views of individual ionic current and FET conductance events, as indicated by black arrows in the ionic current traces on the left.

(D and E) Overcoming Debye length limitations in small-molecule sensing with aptamer-field-effect transistors.[27] (D) The hypothesized mechanism of target-induced reorientation of stem-loop aptamers in proximity to semiconductor channels, affecting the electrostatic environment within or near the Debye length. On the left, aptamers are shown reorienting closer to the FET channels, leading to electrostatic depletion of the channels (e.g., for dopamine, glucose), whereas on the right, aptamer stem-loops reorient away from the channels, enhancing transconductance (e.g., for serotonin, sphingosine-1-phosphate [S1P]). (E) Response of serotonin aptamer-FETs to serotonin concentrations in artificial cerebrospinal fluid (aCSF), displaying concentration-dependent responses, in contrast to negligible responses observed with scrambled serotonin sequences. Error bars are ± SEM with *N* = 6.

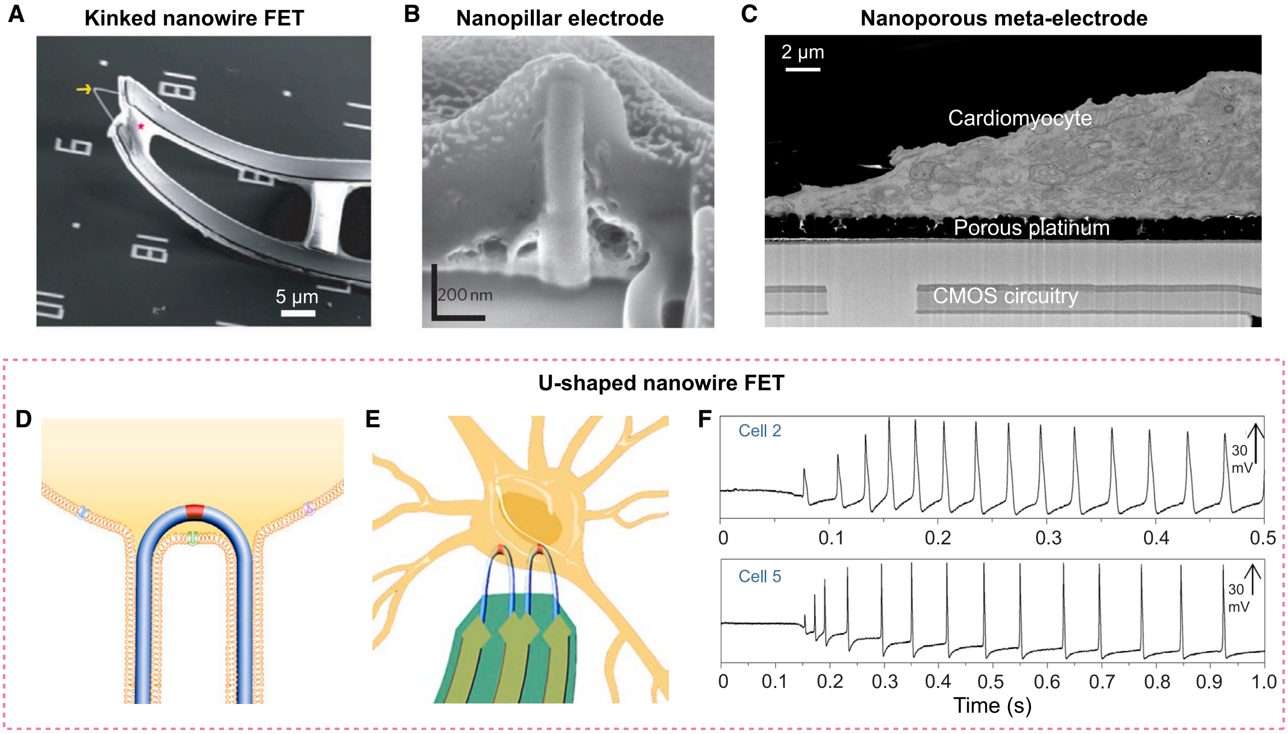


Figure 3. Application of nano-bioelectronic devices in intracellular electrophysiology

(A) Utilization of kinked nanowire FET for intracellular recording.[13] Scanning electron microscope (SEM) depiction showcases the initial state of the device, with the nanoscale FET and the polymer SU-8 highlighted by a yellow arrow and a pink star, respectively.

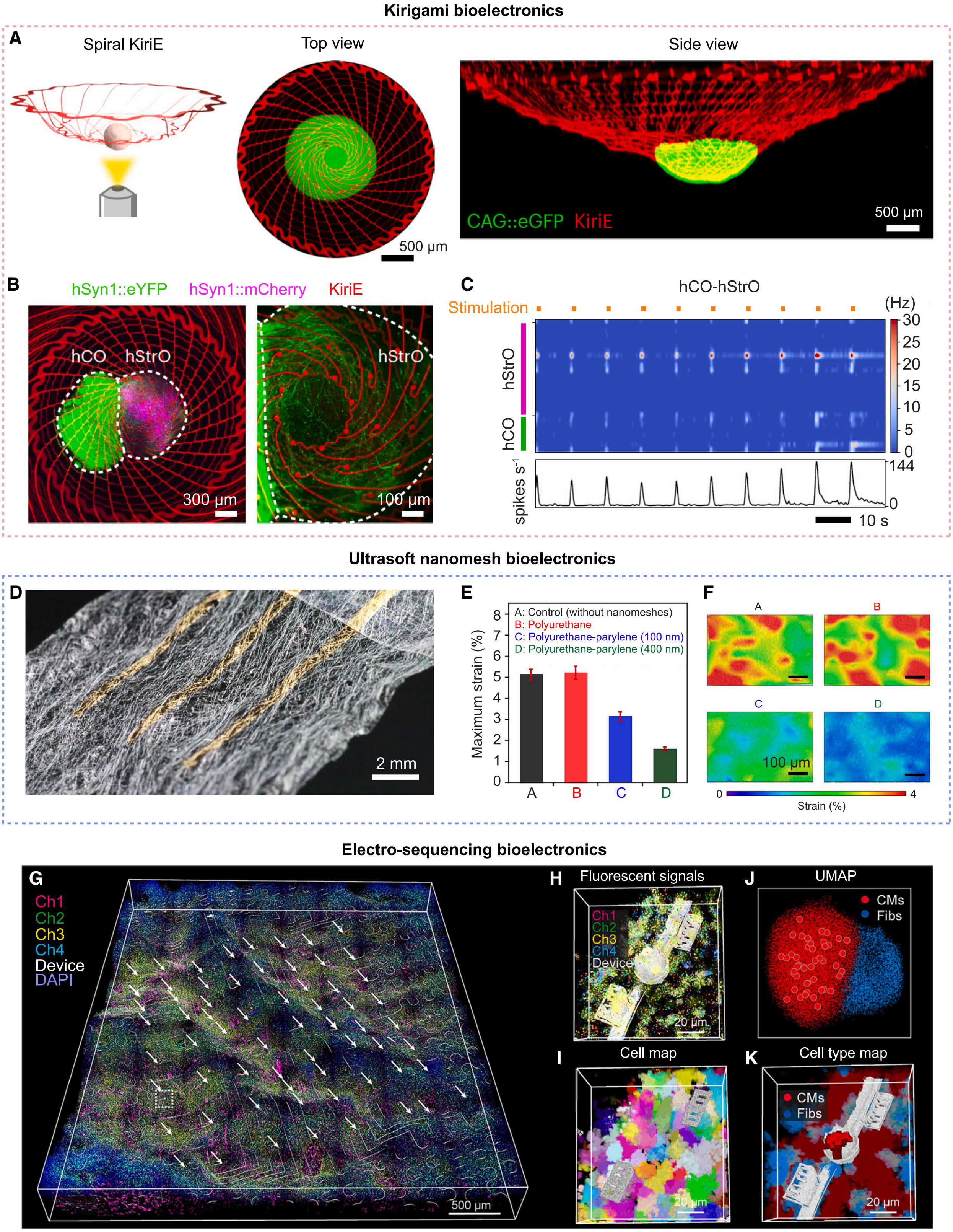
(B) Nanopillar-electroporation-based intracellular capture of action potentials.[48] Focused ion beam milling reveals the cellular-nanopillar electrode junction, demonstrating complete cellular encapsulation of the nanopillar electrode.

(C) Plasmonic meta-electrodes for intracellular network-level recordings via high-density complementary metal-oxide semiconductor (CMOS) multi-electrode arrays.[51] Cross-sectional SEM images exhibit HL-1 cells cultured and immobilized on CMOS-MEA meta-electrodes, with a porous platinum layer atop the CMOS metallic connectivity.

(D–F) Introduction of the ultrasmall U-NWFET probe for electrophysiological research.[19] (D) Diagrammatic representation of intracellular recording utilizing a U-NWFET probe. The integration of a short-channel U-NWFET with the cellular membrane is achieved through internalization and formation of a high-resistance seal, facilitating recordings of amplitude. The sensitive p-type Si NWFET region and the metallic NiSi section on the U-shaped nanowire are denoted in red and blue-grey, respectively, with the nanowire surface modified by phospholipids. (E) Conceptual illustration of concurrent multisite intracellular recordings from a singular neuron using paired U-NWFETs on one probe arm. (F) Sequential intracellular recording of action potentials from distinct neurons utilizing a singular U-NWFET probe without necessitating re-modification. The sequential order of cell measurement is indicated by cell numbering.

(electro-seq)[58] by Li et al., merges flexible bioelectronics with RNA sequencing to capture millisecond-scale electrical activity and single-cell gene expression within intact biological networks, such as cardiac and neural tissues. Applied to human-induced pluripotent stem cell-derived cardiomyocyte patches, *in situ* electro-seq facilitates multimodal analysis, delineating cell states and developmental trajectories through combined assessments of electrophysiology and gene expression at the cellular level. This technique, enhanced by machine-learning analysis, elucidates gene-to-electrophysiology relationships throughout cardiomyocyte development and enables the reconstruction of gene expression evolution from stable electrical measurements, offering potential for creating spatiotemporal maps in electrogenic tissues to uncover mechanisms of electrophysiological functionality and disorder.

In recent years, applications of nano-bioelectronics *in vivo* from the nervous or cardiac systems have been extensive.[15,17,35–37,43,63,64] The development of these devices is primarily driven by the need to conform to the complex topography of biological tissues or to establish interfaces with single-cell resolution, thereby providing high-fidelity and high-density recordings of electrical activity with minimal tissue damage or foreign body response. While the focus in this aspect has been on the sensing components, progress has been made in the interconnect or substrate elements.[17,64,65] For example, Le Floch et al. have developed a novel 3D implantable electronic platform[64] for neural recording, where their platform utilizes perfluorinated dielectric elastomers (Figure 5A) and soft multilayer electrodes (Figure 5B) to achieve spatiotemporally scalable single-cell neural electrophysiology. The elastomers demonstrate stable dielectric performance for over a year in physiological solutions and are softer than traditional plastic dielectrics. The 3D integrated multilayer soft electrode array maintains flexibility at the tissue level, thereby reducing chronic immune responses in mouse neural tissues. In another example, Jiang et al. developed an interface[17] for creating stretchable hybrid devices suitable for



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implantable and on-skin monitoring of physiological signals. Their research addressed the need for interconnects that can withstand stress and prevent debonding failure between these modules. The interface uses a combination of interpenetrating polymer and metal nanostructures (Figure 5C), allowing modules to be connected simply by pressing them together, without the need for adhesives. As a demonstration, Jiang et al. used this interface to assemble stretchable devices for *in vivo* neuromodulation and on-skin electromyography (Figure 5D). In another example, Lu et al. reports the creation of a thin, elastic, conductive nanocomposite achieved by cryogenically transferring laser-induced graphene (LIG) onto a hydrogel film.[65] This cryogenic process improves the bonding between the nanoporous graphene and the crystallized water within the hydrogel (Figure 5E). This bonding technique utilizes the hydrogel to dissipate energy and provide an out-of-plane electrical path (Figure 5F). As a result, cracks in the LIG can be continuously deflected, leading to over 5-fold increase in its intrinsic stretchability. The authors have applied this innovative approach to develop multifunctional wearable sensors for on-skin monitoring (Figure 5G) and cardiac patches for *in vivo* detection.

Modulation or programming

Recent progress in biomodulation research[16,20,23,66–76] highlights the potential of nano-bioelectronics in treating neurological and cardiovascular diseases. This includes the development of organic electronic devices capable of delivering neurotransmitters with high precision to specific neural targets,[71] and the use of vagus nerve stimulation as an effective means to modulate immune functions, offering therapeutic benefits in autoimmune diabetes by modifying immune system behaviors.[68] Furthermore, multifunctional neural interfaces that incorporate light sources, electrodes, thermal sensors, and microfluidic channels have been designed to facilitate research into brain-viscera interoceptive signaling.[77] These interfaces have proven effective for applications as varied as modulating the mesolimbic reward pathway in the mouse brain to controlling intestinal sensory cells that influence feeding behaviors through wireless technologies. In pediatric medicine, the advent of morphing electronics[70] that adapt alongside tissue growth is anticipated to decrease the need for repeat surgical procedures. The advancement in bioresorbable bioelectronics leverages degradable polymer substrates,[78] including poly(lactic-co-glycolic acid), polycaprolactone, and poly(lactic acid), alongside metal components such as magnesium-, zinc-, and iron-based alloys for electrodes and interconnects,[79] as well as semiconductors such as silicon.[9] These materials generally exhibit minimal inflammatory responses, facilitating their use in various biomedical applications.[80]

Imaging techniques have been employed to track the degradation process and ensure that materials do not migrate before they are absorbed or excreted.[81] It is also essential to evaluate the metabolism and excretion pathways of both the materials and their degradation byproducts, ensuring that they do not pose systemic risks.[82] This innovative approach to imaging reduces the need for surgical interventions to remove the devices post-treatment, enhancing patient recovery and comfort. Ultrasound-activated power sources can be used for temporary operation followed by rapid bioresorption, offering the possibility to manage peripheral neuropathy without necessitating surgical removal.[69] For example, iron sulfide nanoclusters have been shown to enable precise and localized generation of nitric oxide (Figure 6A), a key lipophilic messenger in the brain, thus facilitating the targeted modulation and investigation of nitric oxide-induced neural signaling events (Figure 6B).[83] Some of these advancements, initially more applicable to larger systems, are paving the way for their integration into nano-bioelectronics, promising to enhance therapeutic strategies across various medical fields.

Biological modulation has also been achieved through the development of freestanding nanostructure configurations, which focus on modulating bioelectrical activities without directly integrating with the electronic elements. This research leverages a broad spectrum of materials[84] such as nanostructured silicon,[16,20,23,72,75] mechanoluminescent nanoparticles,[85–87] quantum dots,[88] macromolecular nanotransducers,[89] and organic thin-film photovoltaics[90,91] for cellular and tissue modulation. A standout advancement in this area is the development of porosity-based silicon heterojunction (Figure 6C),[20] elevating

Figure 4. Nano-bioelectronic innovations for electrical interfacing with engineered tissues and organoids

(A–C) The KiriE platform[62] facilitates prolonged integration with organoids without disrupting the development of human cortical organoids (hCOs). (A) Displays both top (middle) and side (right) perspectives of CAGeGFP-labeled hCOs situated on the spiral KiriE device (left), captured through live-cell confocal microscopy. The medium's level was reduced to enhance the visibility of KiriE's structural changes. (B) Live-cell confocal fluorescence imagery of a corticostriatal assembloid (outlined with dashed lines), where the left image illustrates the proximity of both hCOs and hStrOs to the electrodes at KiriE's core. The right image provides a closer look at the hStrO, with the green channel vividly depicting the eYFP+ projections from hCO into hStrO. Scale bars, 300 μm (left) and 100 μm (right). (C) Heatmap demonstrates the neural activity's firing rate within a corticostriatal assembloid on day 167 of differentiation (with $n = 20$ channels in hStrO and $n = 7$ in hCO), revealing increased activity in both hCO and hStrO following optogenetic excitation of ChrimsonR-expressing hCO, with orange lines marking the durations of 590 nm light pulses.

(D–F) A nanomesh device[59] is shown to dynamically track the pulsations of cardiomyocytes derived from human induced pluripotent stem cells (hiPSCs) without imposing mechanical restrictions. (D) An optical snapshot of the manufactured nanomesh device. (E) Movements of cardiomyocyte sheets attached to the nanosubstrate, reporting the maximum strain observed in nanomesh-affixed cardiomyocyte sheets (N = 5). (F) Localized contractions within cardiomyocyte sheets denoted by the colored region. The parylene's thickness is noted in parentheses, where nanosubstrates devoid of parylene demonstrated synchronized deformation patterns concurrent with the cardiomyocytes' rhythmic contractions.

(G–K) Multifaceted profiling of molecular and functional cellular states via *in situ* electro-sequencing.[58] (G) 3D reconstructed fluorescence image of the ongoing *in situ* electro-sequencing process within a hiPSC-CMpatch electronics hybrid, with white arrows pointing to electrode locations. (H) A magnified view of the fluorescence signals highlighting the electrode-embedded area within the white dashed square from (G). (I) A 3D cell segmentation map with cells color-coded differently. (J) A UMAP visualization identifying major cell types among the sequenced cells, categorized through Leiden clustering, with electrically recorded cells accentuated. (K) A 3D map of cell types, each labeled according to its cell type using the color scheme from (J), with the electrically recorded cells distinctly marked in deep red.

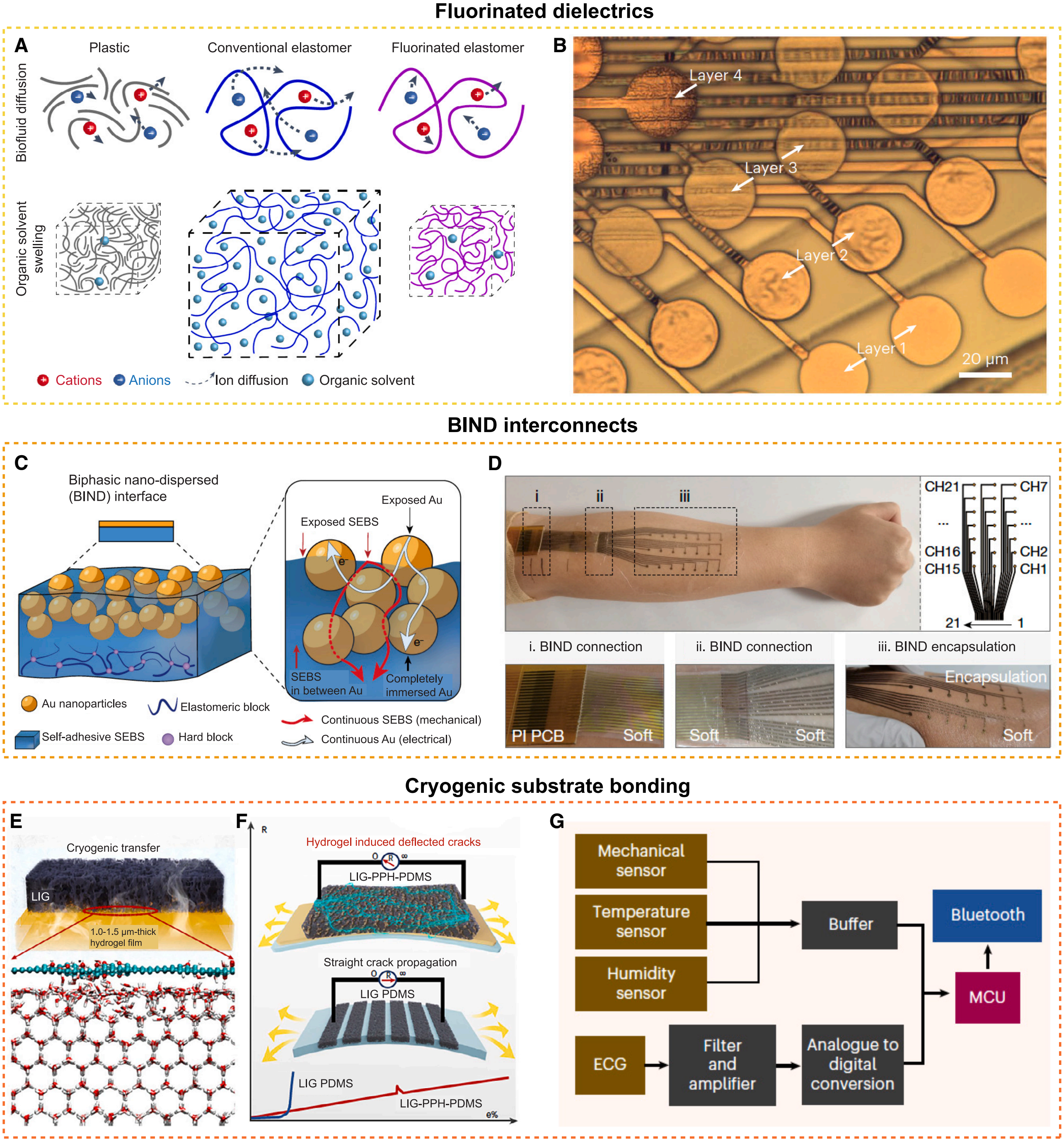

Figure 5. Recent advances in interconnect and substrate development for *in vivo* nano-bioelectronics enhancement

(A and B) Utilization of fluorinated elastomers as durable, pliable dielectrics.[64] (A) Diagrams depicting ion diffusion and solvent swelling impacts on traditional plastic, a standard elastomer, and a fluorinated elastomer. (B) Bright-field microscopy image illustrating the multilayered construction of a neural probe.

(C and D) Development of a universal interface for modular assembly of stretchable electronics.[17] (C) Depiction of a BIND interface, with a detailed view (right) revealing the SEBS and Au layers, while the interlocking nanostructure ensures cohesive mechanical and electrical connectivity. (D) Image of an EMG electrode array positioned on a human arm (upper left) alongside the 21-channel electrode design (upper right). Enlarged sections illustrate the various BIND connection types: flex-soft, soft-soft, and soft-encapsulation.

(E–G) Innovation of stretchable graphene-hydrogel interfaces for wearable and implantable bioelectronics.[65] (E) Schematics for transferring laser-induced graphene (LIG) onto ultrafine PPH films (with thicknesses of approximately 1.0–1.5 μm) employing a cryogenic transfer technique, supported by molecular

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photostimulation to new translational applications.[18] These membranes utilize a non-genetic modulation approach (Figure 6D), suitable for larger animal models, and offer spatial and temporal resolution for non-invasive biological manipulation.[18]

Furthermore, the evolution of colloidal self-assembly in material synthesis has extended into nano-bioelectronics, with supramolecular science techniques creating novel biointerfaces. A notable invention are carbon-based monolithic membranes. These membranes are constructed through micelle-enabled self-assembly (Figure 6E), featuring hierarchical porosity, interdigitated microelectrodes, and micro-supercapacitor behaviors.[47] This device can modulate cardiomyocyte contraction rates and retina (Figure 6F) electrophysiological responses with capacitive charge injection, showcasing the potential of self-assembled membranes in bioelectrical modulation. In parallel, protein engineering[92–94] has introduced novel nanostructures, such as filaments and lattices, using repeat protein oligomers. These structures, which offer control over molecular arrangement, may have applications in nano-bioelectronics if their conductive properties can be enhanced to parallel those of naturally occurring conductive protein nanowires in bacteria.[95]

Researchers have also explored the use of biological modulation for enabling biological programming akin to synthetic and systems biology.[22] A bioelectronic communication network exemplifies this by employing redox mechanisms for signal transmission between a bioelectronic interface and a microbial community.[96] This network, integrating microbial species with electronic systems, dynamically regulates and monitors biological activity through a live bioelectronic transducer mechanism. The bacteria, upon receiving redox molecule signals from electrodes, activate genes to produce therapeutic peptides, while a co-culture provides electronic feedback. This system illustrates the feasibility of controlled bioelectronic communication and the execution of pre-programmed biological functions.

PERSPECTIVE ON EMERGING NON-BIOMEDICAL AREAS

The applicability of nano-bioelectronics stretches beyond the biomedical sphere and has transformative potential in non-biomedical sectors such as environmental monitoring, agriculture, energy, and even computational systems. While these applications are in their nascent stages, they inherit a promise from the successes in bulk bioelectronics. This foundational success lays the groundwork for innovative solutions that could revolutionize how we interact with and manage our environment, produce and consume energy, cultivate our food, and process our information. The potential for nano-bioelectronics to contribute to sustainable agriculture, environmental preservation, efficient energy utilization, and advanced computing systems exemplifies its role as a pivotal technology for the future. However, the leap from laboratory breakthroughs to real-world applications involves many challenges, including scalability, integration, and regulatory compliance. Nevertheless, the trajectory of nano-bioelectronics research indicates a promising avenue for interdisciplinary innovation, where the confluence of nanotechnology and bioelectronic principles could address some of the most pressing challenges of our time.

Environmental and physiological monitoring

Nano-bioelectronic sensors can detect trace levels of environmental pollutants and toxins. For example, gold nanoparticle-decorated electrodes have been leveraged for the electrochemical detection of heavy metal ions such as Cd^{2+}, Pb^{2+}, Cu^{2+}, and Hg^{2+}.[97–99] These sensors harness the sensitivity and selectivity afforded by nanotechnology to deliver real-time assessments of water or air quality, thus enabling proactive environmental management. We also envisage a portable and wireless detection of environmental toxins by optoelectronics, where the photoelectrochemical responses are modulated by the presence of the species of interest.

Wearable nano-bioelectronic sensors can provide constant physiological monitoring, which is essential for detecting health deviations from established healthy baselines. Present-day wearable technologies, including smartwatches, electronic tattoos, straps, and especially sensor-equipped face masks (Figure 7A),[100,101,102] demonstrate potential for broad-spectrum chemical and biological detection. This enables the identification of various pathogens and the monitoring of environmental toxins.

The integration of advanced transducers—optical, electrochemical, and chemiresistive—with microfluidic technology and CRISPR/lateral-flow assays is poised to transform personal protective equipment. This integration promises to enable the detection of airborne contaminants and dangerous substances in real time, thereby enhancing public health and safety in the face of pollution and potential biohazards.

Agriculture and food industry

Nano-enabled devices can help achieve sustainable agriculture via the Internet of Plants (IoP), utilizing nano-sensors for precise, real-time data on soil and atmospheric conditions to improve crop yields and resilience.[107,108] These include the use of cost-effective atmospheric nano-sensors repurposed from consumer electronics and advanced gas nano-sensors to collect critical nanoscale environmental data for crop management. Nano-bioelectronic sensors, resembling health monitoring smartwatches, can monitor crop vitality at the molecular level, enabling preemptive stress management. The sustainable energy-powered, autonomous, wireless nano-sensor networks promise scalable, minimally invasive IoP networks. Interdisciplinary efforts are crucial for integrating these nano-sensor networks with growth models, enhancing data-driven, eco-friendly agricultural practices.

Sensors such as single-walled carbon nanotubes (SWCNTs) and graphitic electrodes implanted on plants can be used for

dynamics simulations for surface binding energy estimations. (F) Illustrative depiction of the differences in crack propagation in LIG with and without the PPH interlayer, accompanied by conceptual graphs showing the resistance changes (R) relative to tensile strain (ε%) in both conductive nanocomposites, where LM stands for liquid metal. (G) Application of a thin, stretchable, and multifunctional LIG-based sensor system for dermal monitoring, complete with a schematic of the flexible printed circuit board equipped with wireless capabilities and a microcontroller unit (MCU).

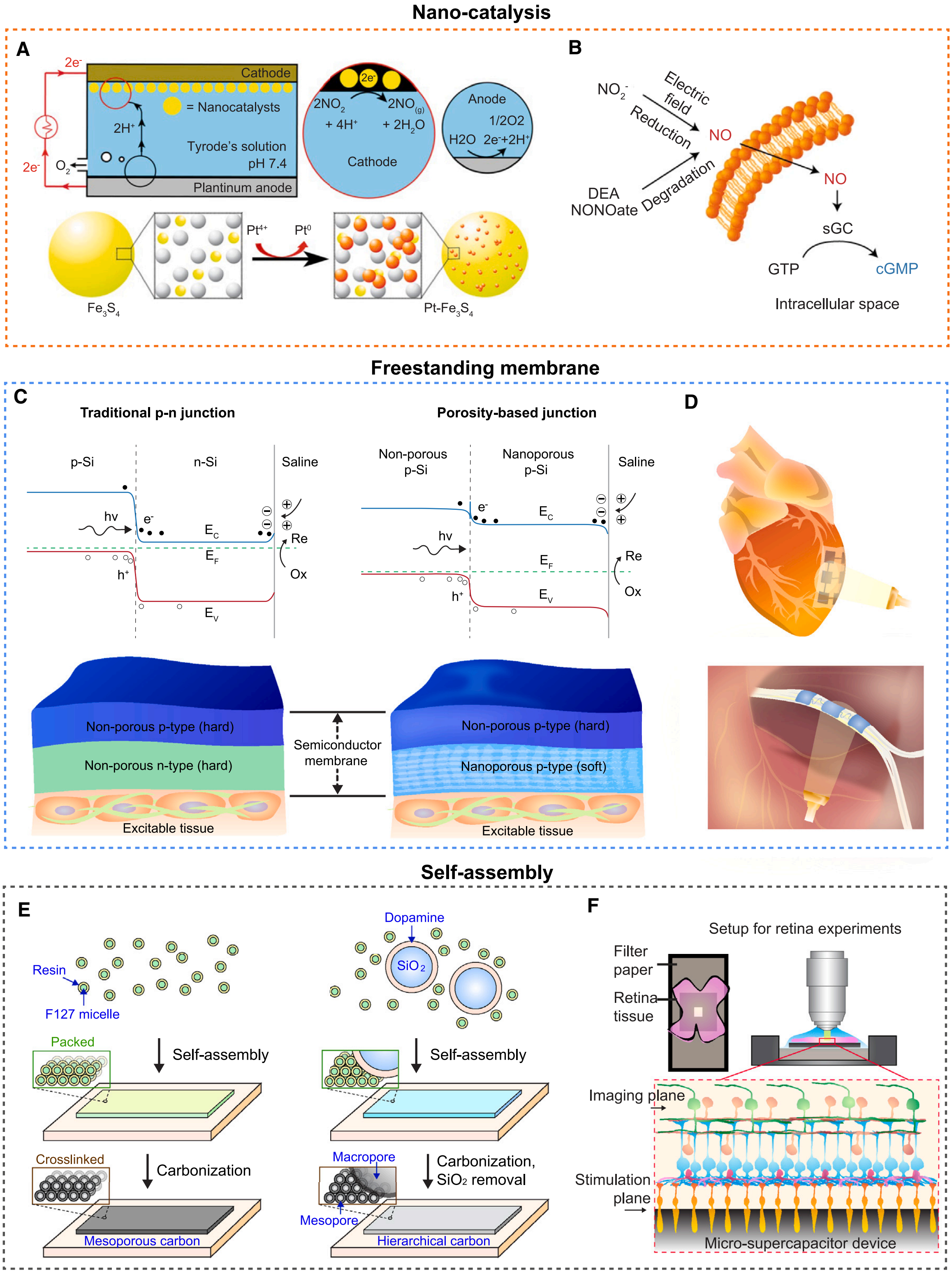

Figure 6. Advancements in nano-bioelectronic modulation techniques

(A and B) *In situ* electrochemical synthesis of nitric oxide for neuronal modulation.[83] (A) The electrochemical reduction of nitrite (NO_2^-) to nitric oxide (NO) is catalyzed by Fe_3S_4- and Pt-decorated Fe_3S_4 nanocatalysts. The upper panel illustrates the NO delivery system based on electrochemistry. The lower panel

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real-time monitoring of plant health and environmental conditions. These sensors, acting as a second skin, wirelessly report on volatile organic compounds (VOCs) such as ethylene, crucial for fruit ripening monitoring, with sensitivity down to 5 ppm (Figure 7B).[103] High-resolution graphene and SWCNT-based conductive inks can also enable real-time plant humidity and water status monitoring, critical for drought stress management. Future developments continue to focus on improving sensor sensitivity and selectivity, even under variable environmental conditions, targeting VOC detection in the ppb range.

The integration of these nanobiotechnology-based sensors with agricultural systems can help monitor crop health conditions through optical and wireless communication with agricultural equipment.[109] However, challenges in applicability, accuracy, and durability must be addressed for nanobiotechnology-based sensors, requiring designs for multiplexing various chemical signals and environmental parameters with a stable and long lifespan in relation to the growing season. Integration with machine sensory, learning, and actuation systems will further optimize crop conditions, allowing for precise therapeutics delivery and autonomous agricultural operations.

In the food industry, nano-bioelectronics can be used for monitoring food quality[110–112] and for ensuring food supply chain integrity. For example, nano-bioelectronic sensors and radiofrequency identification systems offer benefits for detecting food spoilage and enhancing food safety, outperforming traditional methods with their ability to identify a range of substances, including bacteria and spoilage-related chemicals, through the conversion of chemical signals into electrical signals for digital monitoring and food quality assessment.

Energy utilization

In energy production, nano-bioelectronics has emerged as a critical field for the innovation of bio-batteries and biofuel cells. Utilizing microbial bioelectric mechanisms, researchers have converted metabolic processes into electrical energy, with implications for enhancing the output and scalability of energy systems, and particularly for self-powered personal devices that derive power from endogenous biological processes.[113] For example, Yu et al. have developed a perspiration-driven, battery-free electronic skin capable of sophisticated metabolic analysis.[114] This device, embedded with an array of sensors and powered by lactate biofuel cells, boasts an architecture of nanostructured elements that yield a power density of 3.5 mW/cm^2 from sweat. The system's durability is demonstrated by its stable 60-h operational window, during which it continuously monitors metabolic biomarkers, temperature, and interfaces with prosthetics via Bluetooth—a testament to the potential of nano-bioelectronics in medical and robotics applications.

Focused efforts to optimize the anode function in microbial fuel cells (MFCs) have led to increases in bacterial load and conductivity, thanks to the application of nanotechnology. A notable contribution from Cao et al. detailed an approach using reduced graphene oxide-silver nanoparticle (rGO/Ag) scaffolds within Shewanella MFCs, which facilitate the release of Ag$^+$ ions and foster the formation of conductive biofilms (Figure 7C).[104] This synergy of materials and biology has markedly increased the electron transfer rates, enhancing MFC efficacy beyond the limitations of conventional models.

Triboelectric nanogenerators represent a cutting-edge advancement in biomechanical energy-harvesting technologies, offering a viable energy solution for leadless pacemakers. These nanogenerators have been effectively designed in various structures and with multiple materials to transform biomechanical energy directly into electrical energy.[115–117] Complementing these innovations, Liu et al. have introduced a self-powered intracardiac pacemaker (SICP) that employs triboelectric nanogenerator technology to capture the biomechanical energy of cardiac movements.[118] Designed for intravenous implantation into the ventricular chamber, the SICP successfully achieves energy harvesting with power management. Empirical validation in porcine models has showcased the device's capability to treat arrhythmia while also hinting at its longevity, demonstrating the feasibility of triboelectric nanogenerators in clinical settings.

Furthermore, Sim et al. have explored the utility of silver nanowire-enhanced silicone transducers for *in vivo* energy harvesting.[119] These mechanoelectrical devices, when tested within the cardiac environment of swine, have shown promising electrical outputs, signaling a new chapter for autonomous power supply in implantable medical devices, and addressing a historical obstacle in device longevity and patient autonomy.

Computation and data storage

DNA-based nanotechnologies

DNA's base-pairing rules enable the design of precise nanostructures and patterns. This programmability allows for the creation of complex, custom-shaped nanoscale architectures that are challenging to achieve with traditional manufacturing processes. The convergence of DNA nanotechnology with nanobioelectronics is propelling a transformative shift, enabling intricate biological and electronic interactions. DNA nanostructures exhibit exceptional stability,[120,121] suitable for intracellular

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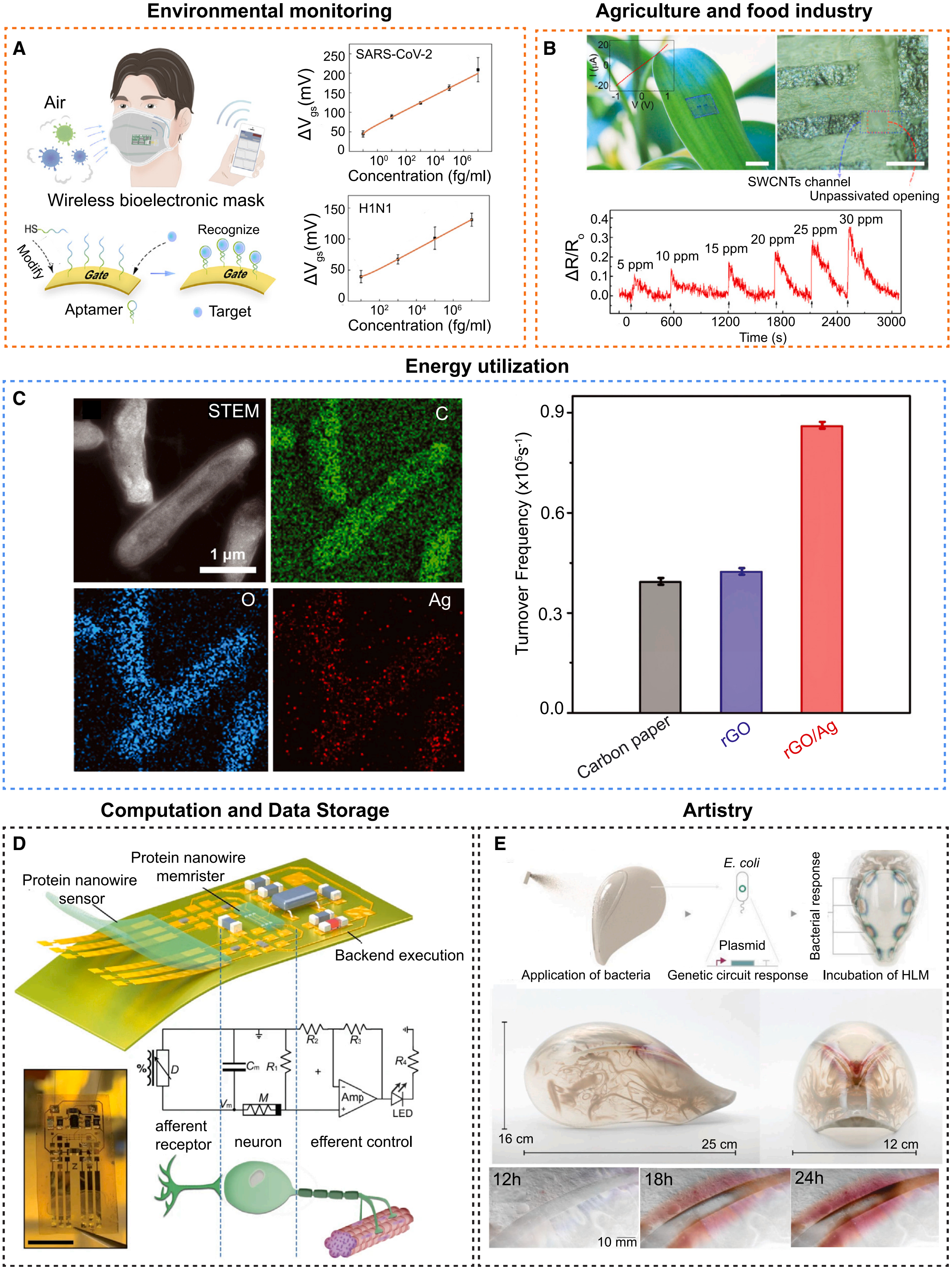
depicts the galvanic replacement process used to enhance Fe_3S_4 nanocatalysts with Pt nanoparticles. The atoms of Fe, S, and Pt are represented in yellow, white, and red, respectively. (B) This panel illustrates the NO-sGC-cGMP signaling cascade within intact cerebellar neurons, highlighting the role of guanosine 5′-triphosphate (GTP).

(C and D) Nanoporous/non-porous silicon heterojunctions for enhanced photoelectrochemical activity and biointerface applications.[20] (C) Diodes, essential components of solar and photoelectrochemical cells, exploit the intrinsic electrical field of a p-n junction to separate photogenerated electron-hole pairs. In photocathodic processes, electrons can migrate to the surface of n-type silicon to partake in reduction reactions. Variations in porosity within p-type silicon can lead to diode-like band alignments conducive to robust photoelectrochemical performance without doping alteration. (D) Flexible, thin silicon membranes with nanoporous/non-porous structures enable the stimulation of rat hearts *ex vivo* and sciatic nerves *in vivo* with low-energy light pulses.

(E and F) Micelle-assisted self-assembly of carbon membranes for bioelectronic interfaces.[47] (E) The process of fabricating hierarchical porous carbon involves: (1) synthesizing mesoporous carbon, followed by (2) generating hierarchical carbon with both mesopores and macropores. (F) A schematic detailing the experimental arrangement for retinal stimulation is presented.



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applications such as organelle targeting and drug delivery, circumventing the use of traditional transfection methods. These advancements bolster the therapeutic potential within nanobioelectronics.

DNA-based bioelectric sensors have extended the frontier of intracellular exploration, notably with the RatiNa probe and DNA nanodevices such as pHlicKer and Voltair, which measure intracellular sodium, pH, and potassium levels, and membrane potentials in organelles.[122,123] Such precision in targeting specific organelles enhances our understanding of cellular physiology.

DNA data storage is advancing through refined coding and algorithms,[124,125] leveraging DNA's stability[121] and charge transport capabilities[126] for computational applications. While conventional bottom-up assembly methods face challenges in ensuring the accuracy and repeatability, DNA's inherent specificity and programmability provide a high degree of control, enabling the consistent assembly of components at the nanoscale. The scalability of DNA-templated electronics could be enhanced by leveraging biological replication mechanisms, potentially reducing costs and facilitating integration with existing semiconductor processes. The creation of electronic devices using DNA templates[127] can achieve higher functional complexity and adaptability. The use of dynamic DNA modification technologies[125] and CRISPR-responsive materials[128] may lead to new applications in bioelectronics and biosensors.[129]

These developments lead to a new era where DNA-based sensors integrated with nano-bioelectronics may revolutionize bioelectrical mapping and stimulation, potentially leading to bioelectrical computing systems that exploit cellular signaling, opening avenues for data storage and processing rooted in bioelectric states.

Neural network-inspired circuits

The nano-bioelectronics offers opportunities toward neuromorphic systems that emulate brain-like computation, integrating advanced nanomaterials and neuroscience-driven computing for enhanced energy efficiency. Key to this evolution is unraveling the physics[130] of neuromorphic computing, advocating for a radical transformation of electronics and promoting small-scale systems for experimental insights. Nanomaterials such as quantum dots, nanowires, nanotubes, graphene, and transition metal dichalcogenide nanostructures are critical in these systems for their synaptic properties,[131] but their scalability remains a challenge.

Organic electronics[132] are advancing neuromorphic computing with resistance-switching mechanisms, although miniaturization to nano-scales and energy management pose obstacles. Nonetheless, their tunability and biocompatibility hold promise for organic neuromorphic systems. The fusion of neuromorphic circuits with robotics[133] suggests potential for efficiency in dynamic settings, indicating a future convergence of cellular biology and engineering.

Photovoltaic detectors employing 2D semiconducting metal sulfides[134] are innovating vision systems, leveraging characteristics suitable for photonics-integrated neuromorphic computing. Spintronic devices[135] are being explored to replicate neural networks through magnetic textures, aiming at compact, energy-efficient systems. In addition, sustainable neuromorphic interfaces are being developed using protein nanowire memristors[105] for bio-signal processing and energy harvesting, relevant for wearable tech and IoT (Figure 7D).

Quantum materials, such as topological insulators, graphene and gallium,[136] offer pathways beyond binary logic by enabling quantum computing elements that operate based on the principles of superposition and entanglement.[137] These materials can process information in ways that traditional binary systems cannot, potentially leading to dramatic increases in computational power and efficiency.[138]

Phase change materials (PCMs) such as $Ge_2Sb_2Te_5$ and $Ge_2Sb_2Se_1Te_4$ are used in creating neuromorphic circuits that mimic the plasticity of synapses in the brain. By exploiting the electrical resistance and optical property changes in these materials, circuits can simulate synaptic weight adjustments, a fundamental aspect of learning and memory in neural networks.[139] This approach allows for the implementation of analog computing principles, offering a more nuanced and dynamic method of information processing compared with binary logic.

Incorporating materials into neural network-inspired circuits challenges the traditional binary logic paradigm and opens new avenues for computing that are closer to the way our brains operate. Spanning nanomaterials, robotics, organic electronics, photovoltaics, spintronics, PCMs, and sustainable interfaces, this domain is poised to revolutionize computation and harness the brain's power for a wide range of applications.

Artistry

Nano-bioelectronics may transform interactive art and fashion wearables into dynamic expressions of human creativity and functionality. This interdisciplinary field generates powerful sensors and devices that are revolutionizing user engagement in art installations and fashion.

Interactive art now utilizes nano-bioelectronic sensors for immersive, participatory displays that evolve with viewer

Figure 7. Perspective on emerging non-biomedical areas

(A) Aptamer-functionalized ion-gated transistor device on bioelectronic mask enablesquantification of SARS-Cov-2 and H1N1 virus based on gate voltage response (ΔV_{gs}).[100]

(B) Single-walled carbon nanotube (SWCNT)-graphite device is transferred onto a surface of a live leaf, enabling real-time sensing of dimethyl methylphosphonate gas at a ppm level.[103]

(C) STEM-EDX mapping of *Shewanella oneidensis* on reduced graphene oxide/silver (rGO/Ag) electrode reveals bacteria decorated with Ag-nanoparticle. *Shewanella*-Ag hybridization enhance turnover frequency of a microbial fuel cell.[104]

(D) Wearable neuromorphic device featuring sensory and memristor component utilizing microbially produced protein nanowires.[105]

(E) Hybrid living material (HLM) in the shape of A mask is fabricated a by 3D inkject printing technique with the addition of genetically engineered *E. coli*. Over 24 h incubation, chromogenic response of *E. coli* to chemical signals yields gradient coloring of the HLM mask.[106] The death mask (Vespers III) is created with artistic query: "What remains once life has been lived? Can the death mask drive the formation of new life?" (https://oxman.com/projects/vespers-iii).

interactions, such as responsive floors in installations that create visual and auditory feedback from visitors' movements. In fashion, smart wearables embedded with these sensors offer not only style but practical utilities, such as health-monitoring clothing[140] that tracks vitals and conveys data to smartphones for improved lifestyle and health awareness.

Advancements in interactive fabrics[141–144] are driving the creation of textiles that change in response to the environment or user inputs, such as scarves that shift color with temperature, highlighting adaptability and personal expression. In addition, nano-bioelectronics supports sustainable fashion through durable nanomaterials and real-time adaptive garments for better environmental responsiveness.

Finally, living nano-bioelectronic art may redefine the artistic landscape through the integration of living materials,[145–147] 3D printing,[148–151] and bioelectronic sensing. This interdisciplinary approach merges nanotechnology, bioelectronics, and artistic creativity[106] to craft dynamic pieces that evolve and interact with viewers, echoing environmental conscientiousness through the use of sustainable materials (Figure 7E). These artworks incorporate living cells and microorganisms[145–147] with synthetic structures to create responsive, interactive canvases that react to human presence and emotional states, challenging perceptions of life and interconnectivity. The digital-to-physical creation process utilizes 3D printing for intricate designs that may grow and adapt, reflecting the viewer's biological and emotional signals. This new art form may not only be participatory and customizable but also a reflection on the integration of sustainability in art, pushing boundaries in how art is experienced and conceptualized. Challenges remain in ensuring the safety, biocompatibility, durability, and power efficiency of these technologies,[141,142] with research ongoing to develop materials that can change color, transparency, or form in response to stimuli.

SUMMARY AND OUTLOOK

The nano-bioelectronics domain heralds an innovative era, fundamentally revolutionizing methodologies in healthcare, and holds potential for impacts on environmental and food monitoring, agriculture, energy utilization, computation, and artistic expression. This revolution is predicated on the exploitation of nanoscale material properties and their integration with biological systems, leading to the creation of devices and platforms characterized by unparalleled sensitivity, specificity, and functionality. Such advancements include the sophisticated engineering of biosensors for real-time, *in vivo* biological process monitoring and the conception of circuits inspired by neural networks, mimicking the computational efficiency of the human brain, thereby promising a profound transformation of our societal infrastructure.

Nonetheless, the advancement trajectory of nano-bioelectronics encounters challenges. A paramount hurdle is achieving the integration of nano-bioelectronic devices with biological systems, a milestone for erasing the boundaries between biological and electronic domains. This objective necessitates the innovation of novel materials and device architectures that are capable of molecular- and organelle-level biological recognition, all the while mitigating adverse immune reactions. Another pivotal challenge lies in scaling nanofabrication techniques to fulfill the requirements of broad application scopes, which demands enhancements in manufacturing processes to ensure cost-efficiency and environmental sustainability.

Furthermore, the deployment of nano-bioelectronics, especially within biomedicine and personal monitoring domains, introduces complex ethical considerations and privacy issues. The establishment of stringent ethical frameworks and transparent, consent-based data management protocols is imperative for upholding public trust and promoting ethical development practices within the nano-bioelectronics field.

Confronting these challenges necessitates a collaborative, interdisciplinary strategy, integrating insights from materials science, engineering, biology, ethics, and policy analysis. Ongoing advancements in materials science and nanofabrication, coupled with comprehensive biocompatibility assessments and ethical governance, are essential for cultivating the subsequent generations of nano-bioelectronic devices. Embracing these challenges as avenues for innovation and progress, the nano-bioelectronics field is poised to extend its influence, presenting solutions to some of the most urgent challenges confronting humanity in contemporary and future contexts.

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AUTHOR CONTRIBUTIONS

P.L., S.K., and B.T. conceived the idea and wrote the manuscript.

DECLARATION OF INTERESTS

The authors declare no competing interests.

REFERENCES

1. Zhang, A., and Lieber, C.M. (2016). Nano-Bioelectronics. Chem. Rev. *116*, 215–257. https://doi.org/10.1021/acs.chemrev.5b00608.
2. Tian, B., Zheng, X., Kempa, T.J., Fang, Y., Yu, N., Yu, G., Huang, J., and Lieber, C.M. (2007). Coaxial silicon nanowires as solar cells and nanoelectronic power sources. Nature *449*, 885–889. https://doi.org/10.1038/nature06181.
3. Kong, J., Franklin, N.R., Zhou, C., Chapline, M., Peng, S., Cho, K., and Dai, H. (2000). Nanotube Molecular Wires as Chemical Sensors. Science *287*, 622–625. https://doi.org/10.1126/science.287.5453.622.
4. Collins, P.G., Bradley, K., Ishigami, M., and Zettl, A. (2000). Extreme Oxygen Sensitivity of Electronic Properties of Carbon Nanotubes. Science *287*, 1801–1804. https://doi.org/10.1126/science.287.5459.1801.
5. Lipomi, D.J., Vosgueritchian, M., Tee, B.C.K., Hellstrom, S.L., Lee, J.A., Fox, C.H., and Bao, Z. (2011). Skin-like pressure and strain sensors based on transparent elastic films of carbon nanotubes. Nat. Nanotechnol. *6*, 788–792. https://doi.org/10.1038/nnano.2011.184.
6. Schedin, F., Geim, A.K., Morozov, S.V., Hill, E.W., Blake, P., Katsnelson, M.I., and Novoselov, K.S. (2007). Detection of individual gas molecules adsorbed on graphene. Nat. Mater. *6*, 652–655. https://doi.org/10.1038/nmat1967.

7. Xiao, Y., Patolsky, F., Katz, E., Hainfeld, J.F., and Willner, I. (2003). "Plugging into Enzymes": Nanowiring of Redox Enzymes by a Gold Nanoparticle. Science *299*, 1877–1881. https://doi.org/10.1126/science.1080664.
8. Abbott, J., Ye, T., Krenek, K., Gertner, R.S., Ban, S., Kim, Y., Qin, L., Wu, W., Park, H., and Ham, D. (2020). A nanoelectrode array for obtaining intracellular recordings from thousands of connected neurons. Nat. Biomed. Eng. *4*, 232–241. https://doi.org/10.1038/s41551-019-0455-7.
9. Hwang, S.W., Tao, H., Kim, D.H., Cheng, H., Song, J.K., Rill, E., Brenckle, M.A., Panilaitis, B., Won, S.M., Kim, Y.S., et al. (2012). A Physically Transient Form of Silicon Electronics. Science *337*, 1640–1644. https://doi.org/10.1126/science.1226325.
10. Cui, Y., Wei, Q., Park, H., and Lieber, C.M. (2001). Nanowire Nanosensors for Highly Sensitive and Selective Detection of Biological and Chemical Species. Science *293*, 1289–1292. https://doi.org/10.1126/science.1062711.
11. Zheng, G., Patolsky, F., Cui, Y., Wang, W.U., and Lieber, C.M. (2005). Multiplexed electrical detection of cancer markers with nanowire sensor arrays. Nat. Biotechnol. *23*, 1294–1301. https://doi.org/10.1038/nbt1138.
12. Patolsky, F., Timko, B.P., Yu, G., Fang, Y., Greytak, A.B., Zheng, G., and Lieber, C.M. (2006). Detection, stimulation, and inhibition of neuronal signals with high-density nanowire transistor arrays. Science *313*, 1100–1104. https://doi.org/10.1126/science.1128640.
13. Tian, B., Cohen-Karni, T., Qing, Q., Duan, X., Xie, P., and Lieber, C.M. (2010). Three-Dimensional, Flexible Nanoscale Field-Effect Transistors as Localized Bioprobes. Science *329*, 830–834. https://doi.org/10.1126/science.1192033.
14. Tian, B., Liu, J., Dvir, T., Jin, L., Tsui, J.H., Qing, Q., Suo, Z., Langer, R., Kohane, D.S., and Lieber, C.M. (2012). Macroporous nanowire nanoelectronic scaffolds for synthetic tissues. Nat. Mater. *11*, 986–994. https://doi.org/10.1038/nmat3404.
15. Xie, C., Liu, J., Fu, T.M., Dai, X., Zhou, W., and Lieber, C.M. (2015). Three-dimensional macroporous nanoelectronic networks as minimally invasive brain probes. Nat. Mater. *14*, 1286–1292. https://doi.org/10.1038/nmat4427.
16. Jiang, Y., Li, X., Liu, B., Yi, J., Fang, Y., Shi, F., Gao, X., Sudzilovsky, E., Parameswaran, R., Koehler, K., et al. (2018). Rational design of silicon structures for optically controlled multiscale biointerfaces. Nat. Biomed. Eng. *2*, 508–521. https://doi.org/10.1038/s41551-018-0230-1.
17. Jiang, Y., Ji, S., Sun, J., Huang, J., Li, Y., Zou, G., Salim, T., Wang, C., Li, W., Jin, H., et al. (2023). A universal interface for plug-and-play assembly of stretchable devices. Nature *614*, 456–462. https://doi.org/10.1038/s41586-022-05579-z.
18. Li, P., Zhang, J., Hayashi, H., Yue, J., Li, W., Yang, C., Sun, C., Shi, J., Huberman-Shlaes, J., Hibino, N., and Tian, B. (2024). Monolithic silicon for high spatiotemporal translational photostimulation. Nature *626*, 990–998. https://doi.org/10.1038/s41586-024-07016-9.
19. Zhao, Y., You, S.S., Zhang, A., Lee, J.H., Huang, J., and Lieber, C.M. (2019). Scalable ultrasmall three-dimensional nanowire transistor probes for intracellular recording. Nat. Nanotechnol. *14*, 783–790. https://doi.org/10.1038/s41565-019-0478-y.
20. Prominski, A., Shi, J., Li, P., Yue, J., Lin, Y., Park, J., Tian, B., and Rotenberg, M.Y. (2022). Porosity-based heterojunctions enable leadless optoelectronic modulation of tissues. Nat. Mater. *21*, 647–655. https://doi.org/10.1038/s41563-022-01249-7.
21. Prominski, A., Li, P., Miao, B.A., and Tian, B. (2021). Nanoenabled Bioelectrical Modulation. Acc. Mater. Res. *2*, 895–906. https://doi.org/10.1021/accountsmr.1c00132.
22. Li, P., Kim, S., and Tian, B. (2022). Nanoenabled Trainable Systems: From Biointerfaces to Biomimetics. ACS Nano *16*, 19651–19664. https://doi.org/10.1021/acsnano.2c08042.
23. Parameswaran, R., Carvalho-de-Souza, J.L., Jiang, Y., Burke, M.J., Zimmerman, J.F., Koehler, K., Phillips, A.W., Yi, J., Adams, E.J., Bezanilla, F., and Tian, B. (2018). Photoelectrochemical modulation of neuronal activity with free-standing coaxial silicon nanowires. Nat. Nanotechnol. *13*, 260–266. https://doi.org/10.1038/s41565-017-0041-7.
24. Tian, B., and Lieber, C.M. (2019). Nanowired Bioelectric Interfaces. Chem. Rev. *119*, 9136–9152. https://doi.org/10.1021/acs.chemrev.8b00795.
25. Yang, X., Qi, Y., Wang, C., Zwang, T.J., Rommelfanger, N.J., Hong, G., and Lieber, C.M. (2023). Laminin-coated electronic scaffolds with vascular topography for tracking and promoting the migration of brain cells after injury. Nat. Biomed. Eng. *7*, 1282–1292. https://doi.org/10.1038/s41551-023-01101-6.
26. Zhang, A., Zwang, T.J., and Lieber, C.M. (2023). Biochemically functionalized probes for cell-type-specific targeting and recording in the brain. Sci. Adv. *9*, eadk1050. https://doi.org/10.1126/sciadv.adk1050.
27. Nakatsuka, N., Yang, K.A., Abendroth, J.M., Cheung, K.M., Xu, X., Yang, H., Zhao, C., Zhu, B., Rim, Y.S., Yang, Y., et al. (2018). Aptamer-field-effect transistors overcome Debye length limitations for small-molecule sensing. Science *362*, 319–324. https://doi.org/10.1126/science.aao6750.
28. Chang, D., Wang, Z., Flynn, C.D., Mahmud, A., Labib, M., Wang, H., Geraili, A., Li, X., Zhang, J., Sargent, E.H., and Kelley, S.O. (2023). A high-dimensional microfluidic approach for selection of aptamers with programmable binding affinities. Nat. Chem. *15*, 773–780. https://doi.org/10.1038/s41557-023-01207-z.
29. Landry, M.P., Ando, H., Chen, A.Y., Cao, J., Kottadiel, V.I., Chio, L., Yang, D., Dong, J., Lu, T.K., and Strano, M.S. (2017). Single-molecule detection of protein efflux from microorganisms using fluorescent single-walled carbon nanotube sensor arrays. Nat. Nanotechnol. *12*, 368–377. https://doi.org/10.1038/nnano.2016.284.
30. Lee, Y., Buchheim, J., Hellenkamp, B., Lynall, D., Yang, K., Young, E.F., Penkov, B., Sia, S., Stojanovic, M.N., and Shepard, K.L. (2024). Carbon-nanotube field-effect transistors for resolving single-molecule aptamer-ligand binding kinetics. Nat. Nanotechnol. *19*, 660–667. https://doi.org/10.1038/s41565-023-01591-0.
31. Choi, Y.S., Jeong, H., Yin, R.T., Avila, R., Pfenniger, A., Yoo, J., Lee, J.Y., Tzavelis, A., Lee, Y.J., Chen, S.W., et al. (2022). A transient, closed-loop network of wireless, body-integrated devices for autonomous electrotherapy. Science *376*, 1006–1012. https://doi.org/10.1126/science.abm1703.
32. Kang, S.K., Murphy, R.K.J., Hwang, S.W., Lee, S.M., Harburg, D.V., Krueger, N.A., Shin, J., Gamble, P., Cheng, H., Yu, S., et al. (2016). Bioresorbable silicon electronic sensors for the brain. Nature *530*, 71–76. https://doi.org/10.1038/nature16492.
33. Yang, Q., Liu, T.L., Xue, Y., Wang, H., Xu, Y., Emon, B., Wu, M., Rountree, C., Wei, T., Kandela, I., et al. (2022). Ecoresorbable and bioresorbable microelectromechanical systems. Nat. Electron. *5*, 526–538. https://doi.org/10.1038/s41928-022-00791-1.
34. Yu, K.J., Kuzum, D., Hwang, S.W., Kim, B.H., Juul, H., Kim, N.H., Won, S.M., Chiang, K., Trumpis, M., Richardson, A.G., et al. (2016). Bioresorbable silicon electronics for transient spatiotemporal mapping of electrical activity from the cerebral cortex. Nat. Mater. *15*, 782–791. https://doi.org/10.1038/nmat4624.
35. Hong, G., Fu, T.M., Qiao, M., Viveros, R.D., Yang, X., Zhou, T., Lee, J.M., Park, H.G., Sanes, J.R., and Lieber, C.M. (2018). A method for single-neuron chronic recording from the retina in awake mice. Science *360*, 1447–1451. https://doi.org/10.1126/science.aas9160.
36. Liu, J., Fu, T.M., Cheng, Z., Hong, G., Zhou, T., Jin, L., Duvvuri, M., Jiang, Z., Kruskal, P., Xie, C., et al. (2015). Syringe-injectable electronics. Nat. Nanotechnol. *10*, 629–636. https://doi.org/10.1038/nnano.2015.115.
37. Zhang, A., Mandeville, E.T., Xu, L., Stary, C.M., Lo, E.H., and Lieber, C.M. (2023). Ultraflexible endovascular probes for brain recording through micrometer-scale vasculature. Science *381*, 306–312. https://doi.org/10.1126/science.adh3916.
38. Sorgenfrei, S., Chiu, C.Y., Gonzalez, R.L., Jr., Yu, Y.J., Kim, P., Nuckolls, C., and Shepard, K.L. (2011). Label-free single-molecule detection of

DNA-hybridization kinetics with a carbon nanotube field-effect transistor. Nat. Nanotechnol. *6*, 126–132. https://doi.org/10.1038/nnano.2010.275.

39. Xie, P., Xiong, Q., Fang, Y., Qing, Q., and Lieber, C.M. (2011). Local electrical potential detection of DNA by nanowire-nanopore sensors. Nat. Nanotechnol. *7*, 119–125. https://doi.org/10.1038/nnano.2011.217.
40. Dai, X., Zhou, W., Gao, T., Liu, J., and Lieber, C.M. (2016). Three-dimensional mapping and regulation of action potential propagation in nanoelectronics-innervated tissues. Nat. Nanotechnol. *11*, 776–782. https://doi.org/10.1038/nnano.2016.96.
41. Duan, X., Gao, R., Xie, P., Cohen-Karni, T., Qing, Q., Choe, H.S., Tian, B., Jiang, X., and Lieber, C.M. (2011). Intracellular recordings of action potentials by an extracellular nanoscale field-effect transistor. Nat. Nanotechnol. *7*, 174–179. https://doi.org/10.1038/nnano.2011.223.
42. Qing, Q., Jiang, Z., Xu, L., Gao, R., Mai, L., and Lieber, C.M. (2014). Free-standing kinked nanowire transistor probes for targeted intracellular recording in three dimensions. Nat. Nanotechnol. *9*, 142–147. https://doi.org/10.1038/nnano.2013.273.
43. Yang, X., Zhou, T., Zwang, T.J., Hong, G., Zhao, Y., Viveros, R.D., Fu, T.M., Gao, T., and Lieber, C.M. (2019). Bioinspired neuron-like electronics. Nat. Mater. *18*, 510–517. https://doi.org/10.1038/s41563-019-0292-9.
44. Bonaccini Calia, A., Masvidal-Codina, E., Smith, T.M., Schäfer, N., Rathore, D., Rodríguez-Lucas, E., Illa, X., De la Cruz, J.M., Del Corro, E., Prats-Alfonso, E., et al. (2022). Full-bandwidth electrophysiology of seizures and epileptiform activity enabled by flexible graphene microtransistor depth neural probes. Nat. Nanotechnol. *17*, 301–309. https://doi.org/10.1038/s41565-021-01041-9.
45. Gu, Y., Wang, C., Kim, N., Zhang, J., Wang, T.M., Stowe, J., Nasiri, R., Li, J., Zhang, D., Yang, A., et al. (2022). Three-dimensional transistor arrays for intra- and inter-cellular recording. Nat. Nanotechnol. *17*, 292–300. https://doi.org/10.1038/s41565-021-01040-w.
46. Tringides, C.M., Vachicouras, N., de Lázaro, I., Wang, H., Trouillet, A., Seo, B.R., Elosegui-Artola, A., Fallegger, F., Shin, Y., Casiraghi, C., et al. (2021). Viscoelastic surface electrode arrays to interface with viscoelastic tissues. Nat. Nanotechnol. *16*, 1019–1029. https://doi.org/10.1038/s41565-021-00926-z.
47. Fang, Y., Prominski, A., Rotenberg, M.Y., Meng, L., Acarón Ledesma, H., Lv, Y., Yue, J., Schaumann, E., Jeong, J., Yamamoto, N., et al. (2021). Micelle-enabled self-assembly of porous and monolithic carbon membranes for bioelectronic interfaces. Nat. Nanotechnol. *16*, 206–213. https://doi.org/10.1038/s41565-020-00805-z.
48. Xie, C., Lin, Z., Hanson, L., Cui, Y., and Cui, B. (2012). Intracellular recording of action potentials by nanopillar electroporation. Nat. Nanotechnol. *7*, 185–190. https://doi.org/10.1038/nnano.2012.8.
49. Abbott, J., Ye, T., Qin, L., Jorgolli, M., Gertner, R.S., Ham, D., and Park, H. (2017). CMOS nanoelectrode array for all-electrical intracellular electrophysiological imaging. Nat. Nanotechnol. *12*, 460–466. https://doi.org/10.1038/nnano.2017.3.
50. Robinson, J.T., Jorgolli, M., Shalek, A.K., Yoon, M.H., Gertner, R.S., and Park, H. (2012). Vertical nanowire electrode arrays as a scalable platform for intracellular interfacing to neuronal circuits. Nat. Nanotechnol. *7*, 180–184. https://doi.org/10.1038/nnano.2011.249.
51. Dipalo, M., Melle, G., Lovato, L., Jacassi, A., Santoro, F., Caprettini, V., Schirato, A., Alabastri, A., Garoli, D., Bruno, G., et al. (2018). Plasmonic meta-electrodes allow intracellular recordings at network level on high-density CMOS-multi-electrode arrays. Nat. Nanotechnol. *13*, 965–971. https://doi.org/10.1038/s41565-018-0222-z.
52. Hai, A., Shappir, J., and Spira, M.E. (2010). In-cell recordings by extracellular microelectrodes. Nat. Methods *7*, 200–202. https://doi.org/10.1038/nmeth.1420.
53. Ojovan, S.M., Rabieh, N., Shmoel, N., Erez, H., Maydan, E., Cohen, A., and Spira, M.E. (2015). A feasibility study of multi-site,intracellular recordings from mammalian neurons by extracellular gold mushroom-shaped microelectrodes. Sci. Rep. *5*, 14100. https://doi.org/10.1038/srep14100.
54. Kozai, T.D.Y., Langhals, N.B., Patel, P.R., Deng, X., Zhang, H., Smith, K.L., Lahann, J., Kotov, N.A., and Kipke, D.R. (2012). Ultrasmall implantable composite microelectrodes with bioactive surfaces for chronic neural interfaces. Nat. Mater. *11*, 1065–1073. https://doi.org/10.1038/nmat3468.
55. Abidian, M.R., Ludwig, K.A., Marzullo, T.C., Martin, D.C., and Kipke, D.R. (2009). Interfacing Conducting Polymer Nanotubes with the Central Nervous System: Chronic Neural Recording using Poly(3,4-ethylenedioxythiophene) Nanotubes. Adv. Mater. *21*, 3764–3770. https://doi.org/10.1002/adma.200900887.
56. De Belly, H., Yan, S., Borja da Rocha, H., Ichbiah, S., Town, J.P., Zager, P.J., Estrada, D.C., Meyer, K., Turlier, H., Bustamante, C., and Weiner, O.D. (2023). Cell protrusions and contractions generate long-range membrane tension propagation. Cell *186*, 3049–3061.e15. https://doi.org/10.1016/j.cell.2023.05.014.
57. Shi, Z., Graber, Z.T., Baumgart, T., Stone, H.A., and Cohen, A.E. (2018). Cell Membranes Resist Flow. Cell *175*, 1769–1779.e13. https://doi.org/10.1016/j.cell.2018.09.054.
58. Li, Q., Lin, Z., Liu, R., Tang, X., Huang, J., He, Y., Sui, X., Tian, W., Shen, H., Zhou, H., et al. (2023). Multimodal charting of molecular and functional cell states via in situ electro-sequencing. Cell *186*, 2002–2017.e21. https://doi.org/10.1016/j.cell.2023.03.023.
59. Lee, S., Sasaki, D., Kim, D., Mori, M., Yokota, T., Lee, H., Park, S., Fukuda, K., Sekino, M., Matsuura, K., et al. (2019). Ultrasoft electronics to monitor dynamically pulsing cardiomyocytes. Nat. Nanotechnol. *14*, 156–160. https://doi.org/10.1038/s41565-018-0331-8.
60. Li, Q., Nan, K., Le Floch, P., Lin, Z., Sheng, H., Blum, T.S., and Liu, J. (2019). Cyborg Organoids: Implantation of Nanoelectronics via Organogenesis for Tissue-Wide Electrophysiology. Nano Lett. *19*, 5781–5789. https://doi.org/10.1021/acs.nanolett.9b02512.
61. Kalmykov, A., Huang, C., Bliley, J., Shiwarski, D., Tashman, J., Abdullah, A., Rastogi, S.K., Shukla, S., Mataev, E., Feinberg, A.W., et al. (2019). Organ-on-e-chip: Three-dimensional self-rolled biosensor array for electrical interrogations of human electrogenic spheroids. Sci. Adv. *5*, eaax0729. https://doi.org/10.1126/sciadv.aax0729.
62. Yang, X., Forró, C., Li, T.L., Miura, Y., Zaluska, T.J., Tsai, C.-T., Kanton, S., McQueen, J.P., Chen, X., Mollo, V., et al. (2024). Kirigami electronics for long-term electrophysiological recording of human neural organoids and assembloids. Nat. Biotechnol. https://doi.org/10.1038/s41587-41023-02081-41583.
63. Zhao, Z., Zhu, H., Li, X., Sun, L., He, F., Chung, J.E., Liu, D.F., Frank, L., Luan, L., and Xie, C. (2023). Ultraflexible electrode arrays for months-long high-density electrophysiological mapping of thousands of neurons in rodents. Nat. Biomed. Eng. *7*, 520–532. https://doi.org/10.1038/s41551-022-00941-y.
64. Le Floch, P., Zhao, S., Liu, R., Molinari, N., Medina, E., Shen, H., Wang, Z., Kim, J., Sheng, H., Partarrieu, S., et al. (2024). 3D spatiotemporally scalable in vivo neural probes based on fluorinated elastomers. Nat. Nanotechnol. *19*, 319–329. https://doi.org/10.1038/s41565-023-01545-6.
65. Lu, Y., Yang, G., Wang, S., Zhang, Y., Jian, Y., He, L., Yu, T., Luo, H., Kong, D., Xianyu, Y., et al. (2023). Stretchable graphene-hydrogel interfaces for wearable and implantable bioelectronics. Nat. Electron. *7*, 51–65. https://doi.org/10.1038/s41928-023-01091-y.
66. Choi, H., Kim, Y., Kim, S., Jung, H., Lee, S., Kim, K., Han, H.S., Kim, J.Y., Shin, M., and Son, D. (2023). Adhesive bioelectronics for sutureless epicardial interfacing. Nat. Electron. *6*, 779–789. https://doi.org/10.1038/s41928-023-01023-w.
67. Deng, J., Yuk, H., Wu, J., Varela, C.E., Chen, X., Roche, E.T., Guo, C.F., and Zhao, X. (2021). Electrical bioadhesive interface for bioelectronics. Nat. Mater. *20*, 229–236. https://doi.org/10.1038/s41563-020-00814-2.

68. Guyot, M., Simon, T., Ceppo, F., Panzolini, C., Guyon, A., Lavergne, J., Murris, E., Daoudlarian, D., Brusini, R., Zarif, H., et al. (2019). Pancreatic nerve electrostimulation inhibits recent-onset autoimmune diabetes. Nat. Biotechnol. *37*, 1446–1451. https://doi.org/10.1038/s41587-019-0295-8.

69. Lee, D.M., Kang, M., Hyun, I., Park, B.J., Kim, H.J., Nam, S.H., Yoon, H.J., Ryu, H., Park, H.M., Choi, B.O., and Kim, S.W. (2023). An on-demand bioresorbable neurostimulator. Nat. Commun. *14*, 7315. https://doi.org/10.1038/s41467-023-42791-5.

70. Liu, Y., Li, J., Song, S., Kang, J., Tsao, Y., Chen, S., Mottini, V., McConnell, K., Xu, W., Zheng, Y.Q., et al. (2020). Morphing electronics enable neuromodulation in growing tissue. Nat. Biotechnol. *38*, 1031–1036. https://doi.org/10.1038/s41587-020-0495-2.

71. Simon, D.T., Kurup, S., Larsson, K.C., Hori, R., Tybrandt, K., Goiny, M., Jager, E.W.H., Berggren, M., Canlon, B., and Richter-Dahlfors, A. (2009). Organic electronics for precise delivery of neurotransmitters to modulate mammalian sensory function. Nat. Mater. *8*, 742–746. https://doi.org/10.1038/nmat2494.

72. Jiang, Y., Carvalho-de-Souza, J.L., Wong, R.C.S., Luo, Z., Isheim, D., Zuo, X., Nicholls, A.W., Jung, I.W., Yue, J., Liu, D.J., et al. (2016). Heterogeneous silicon mesostructures for lipid-supported bioelectric interfaces. Nat. Mater. *15*, 1023–1030. https://doi.org/10.1038/nmat4673.

73. Jiang, Y., Parameswaran, R., Li, X., Carvalho-de-Souza, J.L., Gao, X., Meng, L., Bezanilla, F., Shepherd, G.M.G., and Tian, B. (2019). Nongenetic optical neuromodulation with silicon-based materials. Nat. Protoc. *14*, 1339–1376. https://doi.org/10.1038/s41596-019-0135-9.

74. Jiang, Y., and Tian, B. (2018). Inorganic semiconductor biointerfaces. Nat. Rev. Mater. *3*, 473–490. https://doi.org/10.1038/s41578-018-0062-3.

75. Parameswaran, R., Koehler, K., Rotenberg, M.Y., Burke, M.J., Kim, J., Jeong, K.Y., Hissa, B., Paul, M.D., Moreno, K., Sarma, N., et al. (2019). Optical stimulation of cardiac cells with a polymer-supported silicon nanowire matrix. Proc. Natl. Acad. Sci. USA *116*, 413–421. https://doi.org/10.1073/pnas.1816428115.

76. Tian, B. (2019). Nongenetic neural control with light. Science *365*, 457. https://doi.org/10.1126/science.aay4351.

77. Sahasrabudhe, A., Rupprecht, L.E., Orguc, S., Khudiyev, T., Tanaka, T., Sands, J., Zhu, W., Tabet, A., Manthey, M., Allen, H., et al. (2023). Multifunctional microelectronic fibers enable wireless modulation of gut and brain neural circuits. Nat. Biotechnol. *42*, 892–904. https://doi.org/10.1038/s41587-023-01833-5.

78. Samir, A., Ashour, F.H., Hakim, A.A.A., and Bassyouni, M. (2022). Recent advances in biodegradable polymers for sustainable applications. npj Mater. Degrad. *6*, 68. https://doi.org/10.1038/s41529-022-00277-7.

79. Han, H.-S., Loffredo, S., Jun, I., Edwards, J., Kim, Y.-C., Seok, H.-K., Witte, F., Mantovani, D., and Glyn-Jones, S. (2019). Current status and outlook on the clinical translation of biodegradable metals. Mater. Today *23*, 57–71. https://doi.org/10.1016/j.mattod.2018.05.018.

80. Koo, J., MacEwan, M.R., Kang, S.K., Won, S.M., Stephen, M., Gamble, P., Xie, Z., Yan, Y., Chen, Y.Y., Shin, J., et al. (2018). Wireless bioresorbable electronic system enables sustained nonpharmacological neuroregenerative therapy. Nat. Med. *24*, 1830–1836. https://doi.org/10.1038/s41591-018-0196-2.

81. Artzi, N., Oliva, N., Puron, C., Shitreet, S., Artzi, S., bon Ramos, A., Groothuis, A., Sahagian, G., and Edelman, E.R. (2011). In vivo and in vitro tracking of erosion in biodegradable materials using non-invasive fluorescence imaging. Nat. Mater. *10*, 704–709. https://doi.org/10.1038/nmat3095.

82. Li, C., Guo, C., Fitzpatrick, V., Ibrahim, A., Zwierstra, M.J., Hanna, P., Lechtig, A., Nazarian, A., Lin, S.J., and Kaplan, D.L. (2019). Design of biodegradable, implantable devices towards clinical translation. Nat. Rev. Mater. *5*, 61–81. https://doi.org/10.1038/s41578-019-0150-z.

83. Park, J., Jin, K., Sahasrabudhe, A., Chiang, P.H., Maalouf, J.H., Koehler, F., Rosenfeld, D., Rao, S., Tanaka, T., Khudiyev, T., et al. (2020). In situ electrochemical generation of nitric oxide for neuronal modulation. Nat. Nanotechnol. *15*, 690–697. https://doi.org/10.1038/s41565-020-0701-x.

84. Acarón Ledesma, H., Li, X., Carvalho-de-Souza, J.L., Wei, W., Bezanilla, F., and Tian, B. (2019). An atlas of nano-enabled neural interfaces. Nat. Nanotechnol. *14*, 645–657. https://doi.org/10.1038/s41565-019-0487-x.

85. Jiang, S., Wu, X., Yang, F., Rommelfanger, N.J., and Hong, G. (2023). Activation of mechanoluminescent nanotransducers by focused ultrasound enables light delivery to deep-seated tissue in vivo. Nat. Protoc. *18*, 3787–3820. https://doi.org/10.1038/s41596-023-00895-8.

86. Yang, F., Wu, X., Cui, H., Jiang, S., Ou, Z., Cai, S., and Hong, G. (2022). Palette of Rechargeable Mechanoluminescent Fluids Produced by a Biomineral-Inspired Suppressed Dissolution Approach. J. Am. Chem. Soc. *144*, 18406–18418. https://doi.org/10.1021/jacs.2c06724.

87. Hong, G. (2020). Seeing the sound. Science *369*, 638. https://doi.org/10.1126/science.abd3636.

88. Karatum, O., Kaleli, H.N., Eren, G.O., Sahin, A., and Nizamoglu, S. (2022). Electrical Stimulation of Neurons with Quantum Dots via Near-Infrared Light. ACS Nano *16*, 8233–8243. https://doi.org/10.1021/acsnano.2c01989.

89. Wu, X., Jiang, Y., Rommelfanger, N.J., Yang, F., Zhou, Q., Yin, R., Liu, J., Cai, S., Ren, W., Shin, A., et al. (2022). Tether-free photothermal deep-brain stimulation in freely behaving mice via wide-field illumination in the near-infrared-II window. Nat. Biomed. Eng. *6*, 754–770. https://doi.org/10.1038/s41551-022-00862-w.

90. Donahue, M.J., Ejneby, M.S., Jakešová, M., Caravaca, A.S., Andersson, G., Sahalianov, I., Đerek, V., Hult, H., Olofsson, P.S., and Głowacki, E.D. (2022). Wireless optoelectronic devices for vagus nerve stimulation in mice. J. Neural. Eng. *19*, 066031. https://doi.org/10.1088/1741-2552/aca1e3.

91. Silverå Ejneby, M., Jakešová, M., Ferrero, J.J., Migliaccio, L., Sahalianov, I., Zhao, Z., Berggren, M., Khodagholy, D., Đerek, V., Gelinas, J.N., and Głowacki, E.D. (2022). Chronic electrical stimulation of peripheral nerves via deep-red light transduced by an implanted organic photocapacitor. Nat. Biomed. Eng. *6*, 741–753. https://doi.org/10.1038/s41551-021-00817-7.

92. Bethel, N.P., Borst, A.J., Parmeggiani, F., Bick, M.J., Brunette, T.J., Nguyen, H., Kang, A., Bera, A.K., Carter, L., Miranda, M.C., et al. (2023). Precisely patterned nanofibres made from extendable protein multiplexes. Nat. Chem. *15*, 1664–1671. https://doi.org/10.1038/s41557-023-01314.

93. Li, Z., Wang, S., Nattermann, U., Bera, A.K., Borst, A.J., Yaman, M.Y., Bick, M.J., Yang, E.C., Sheffler, W., Lee, B., et al. (2023). Accurate computational design of three-dimensional protein crystals. Nat. Mater. *22*, 1556–1563. https://doi.org/10.1038/s41563-023-01683-1.

94. Watson, J.L., Juergens, D., Bennett, N.R., Trippe, B.L., Yim, J., Eisenach, H.E., Ahern, W., Borst, A.J., Ragotte, R.J., Milles, L.F., et al. (2023). De novo design of protein structure and function with RFdiffusion. Nature *620*, 1089–1100. https://doi.org/10.1038/s41586-023-06415-8.

95. Gu, Y., Srikanth, V., Salazar-Morales, A.I., Jain, R., O'Brien, J.P., Yi, S.M., Soni, R.K., Samatey, F.A., Yalcin, S.E., and Malvankar, N.S. (2021). Structure of Geobacter pili reveals secretory rather than nanowire behaviour. Nature *597*, 430–434. https://doi.org/10.1038/s41586-021-03857-w.

96. Terrell, J.L., Tschirhart, T., Jahnke, J.P., Stephens, K., Liu, Y., Dong, H., Hurley, M.M., Pozo, M., McKay, R., Tsao, C.Y., et al. (2021). Bioelectronic control of a microbial community using surface-assembled electrogenetic cells to route signals. Nat. Nanotechnol. *16*, 688–697. https://doi.org/10.1038/s41565-021-00878-4.

97. Xu, X., Duan, G., Li, Y., Liu, G., Wang, J., Zhang, H., Dai, Z., and Cai, W. (2014). Fabrication of gold nanoparticles by laser ablation in liquid and their application for simultaneous electrochemical detection of Cd2+, Pb2+, Cu2+, Hg2+. ACS Appl. Mater. Interfaces *6*, 65–71. https://doi.org/10.1021/am404816e.

98. Zhou, L., Xiong, W., and Liu, S. (2014). Preparation of a gold electrode modified with Au–TiO2 nanoparticles as an electrochemical sensor for the detection of mercury(II) ions. J. Mater. Sci. *50*, 769–776. https://doi.org/10.1007/s10853-014-8636-y.

99. Bernalte, E., Arévalo, S., Pérez-Taborda, J., Wenk, J., Estrela, P., Avila, A., and Di Lorenzo, M. (2020). Rapid and on-site simultaneous electrochemical detection of copper, lead and mercury in the Amazon river. Sensor. Actuator. B Chem. *307*, 127620. https://doi.org/10.1016/j.snb.2019.127620.

100. Wang, B., Yang, D., Chang, Z., Zhang, R., Dai, J., and Fang, Y. (2022). Wearable bioelectronic masks for wireless detection of respiratory infectious diseases by gaseous media. Matter *5*, 4347–4362. https://doi.org/10.1016/j.matt.2022.08.020.

101. Adeel, M., Cotur, Y., Naik, A., Gonzalez-Macia, L., and Güder, F. (2022). Face masks as a platform for wearable sensors. Nat. Electron. *5*, 719–720. https://doi.org/10.1038/s41928-022-00871-2.

102. Kim, J.H., Marcus, C., Ono, R., Sadat, D., Mirzazadeh, A., Jens, M., Fernandez, S., Zheng, S., Durak, T., and Dagdeviren, C. (2022). A conformable sensory face mask for decoding biological and environmental signals. Nat. Electron. *5*, 794–807. https://doi.org/10.1038/s41928-022-00851-6.

103. Lee, K., Park, J., Lee, M.S., Kim, J., Hyun, B.G., Kang, D.J., Na, K., Lee, C.Y., Bien, F., and Park, J.U. (2014). In-situ synthesis of carbon nanotube-graphite electronic devices and their integrations onto surfaces of live plants and insects. Nano Lett. *14*, 2647–2654. https://doi.org/10.1021/nl500513n.

104. Cao, B., Zhao, Z., Peng, L., Shiu, H.Y., Ding, M., Song, F., Guan, X., Lee, C.K., Huang, J., Zhu, D., et al. (2021). Silver nanoparticles boost charge-extraction efficiency in Shewanella microbial fuel cells. Science *373*, 1336–1340. https://doi.org/10.1126/science.abf3427.

105. Fu, T., Liu, X., Fu, S., Woodard, T., Gao, H., Lovley, D.R., and Yao, J. (2021). Self-sustained green neuromorphic interfaces. Nat. Commun. *12*, 3351. https://doi.org/10.1038/s41467-021-23744-2.

106. Smith, R.S.H., Bader, C., Sharma, S., Kolb, D., Tang, T.C., Hosny, A., Moser, F., Weaver, J.C., Voigt, C.A., and Oxman, N. (2020). Hybrid Living Materials: Digital Design and Fabrication of 3D Multimaterial Structures with Programmable Biohybrid Surfaces. Adv. Funct. Mater. *30*, 1907401. https://doi.org/10.1002/adfm.201907401.

107. Haseeb, K., Ud Din, I., Almogren, A., and Islam, N. (2020). An Energy Efficient and Secure IoT-Based WSN Framework: An Application to Smart Agriculture. Sensors *20*, 2081. https://doi.org/10.3390/s20072081.

108. Steeneken, P.G., Kaiser, E., Verbiest, G.J., and ten Veldhuis, M.C. (2023). Sensors in agriculture: towards an Internet of Plants. Nat. Rev. Methods Primers *3*, 60. https://doi.org/10.1038/s43586-023-00250-x.

109. Giraldo, J.P., Wu, H., Newkirk, G.M., and Kruss, S. (2019). Nanobiotechnology approaches for engineering smart plant sensors. Nat. Nanotechnol. *14*, 541–553. https://doi.org/10.1038/s41565-019-0470-6.

110. Jung, Y., Min, J., Choi, J., Bang, J., Jeong, S., Pyun, K.R., Ahn, J., Cho, Y., Hong, S., Hong, S., et al. (2022). Smart paper electronics by laser-induced graphene for biodegradable real-time food spoilage monitoring. Appl. Mater. Today *29*, 101589. https://doi.org/10.1016/j.apmt.2022.101589.

111. Yue, C., Wang, J., Wang, Z., Kong, B., and Wang, G. (2023). Flexible printed electronics and their applications in food quality monitoring and intelligent food packaging: Recent advances. Food Control *154*, 109983. https://doi.org/10.1016/j.foodcont.2023.109983.

112. Lv, M., Liu, Y., Geng, J., Kou, X., Xin, Z., and Yang, D. (2018). Engineering nanomaterials-based biosensors for food safety detection. Biosens. Bioelectron. *106*, 122–128. https://doi.org/10.1016/j.bios.2018.01.049.

113. Song, Y., Mukasa, D., Zhang, H., and Gao, W. (2021). Self-Powered Wearable Biosensors. Acc. Mater. Res. *2*, 184–197. https://doi.org/10.1021/accountsmr.1c00002.

114. Yu, Y., Nassar, J., Xu, C., Min, J., Yang, Y., Dai, A., Doshi, R., Huang, A., Song, Y., Gehlhar, R., et al. (2020). Biofuel-powered soft electronic skin with multiplexed and wireless sensing for human-machine interfaces. Sci. Robot. *5*, eaaz7946. https://doi.org/10.1126/scirobotics.aaz7946.

115. Ryu, H., Park, H.M., Kim, M.K., Kim, B., Myoung, H.S., Kim, T.Y., Yoon, H.J., Kwak, S.S., Kim, J., Hwang, T.H., et al. (2021). Self-rechargeable cardiac pacemaker system with triboelectric nanogenerators. Nat. Commun. *12*, 4374. https://doi.org/10.1038/s41467-021-24417-w.

116. Ouyang, H., Liu, Z., Li, N., Shi, B., Zou, Y., Xie, F., Ma, Y., Li, Z., Li, H., Zheng, Q., et al. (2019). Symbiotic cardiac pacemaker. Nat. Commun. *10*, 1821. https://doi.org/10.1038/s41467-019-09851-1.

117. Yao, G., Kang, L., Li, J., Long, Y., Wei, H., Ferreira, C.A., Jeffery, J.J., Lin, Y., Cai, W., and Wang, X. (2018). Effective weight control via an implanted self-powered vagus nerve stimulation device. Nat. Commun. *9*, 5349. https://doi.org/10.1038/s41467-018-07764-z.

118. Liu, Z., Hu, Y., Qu, X., Liu, Y., Cheng, S., Zhang, Z., Shan, Y., Luo, R., Weng, S., Li, H., et al. (2024). A self-powered intracardiac pacemaker in swine model. Nat. Commun. *15*, 507. https://doi.org/10.1038/s41467-023-44510-6.

119. Sim, K., Ershad, F., Zhang, Y., Yang, P., Shim, H., Rao, Z., Lu, Y., Thukral, A., Elgalad, A., Xi, Y., et al. (2020). An epicardial bioelectronic patch made from soft rubbery materials and capable of spatiotemporal mapping of electrophysiological activity. Nat. Electron. *3*, 775–784. https://doi.org/10.1038/s41928-020-00493-6.

120. Chen, Y.J., Groves, B., Muscat, R.A., and Seelig, G. (2015). DNA nanotechnology from the test tube to the cell. Nat. Nanotechnol. *10*, 748–760. https://doi.org/10.1038/nnano.2015.195.

121. Matange, K., Tuck, J.M., and Keung, A.J. (2021). DNA stability: a central design consideration for DNA data storage systems. Nat. Commun. *12*, 1358. https://doi.org/10.1038/s41467-021-21587-5.

122. Anees, P., Saminathan, A., Rozmus, E.R., Di, A., Malik, A.B., Delisle, B.P., and Krishnan, Y. (2023). Detecting organelle-specific activity of potassium channels with a DNA nanodevice. Nat. Biotechnol. https://doi.org/10.1038/s41587-023-01928.

123. Saminathan, A., Devany, J., Veetil, A.T., Suresh, B., Pillai, K.S., Schwake, M., and Krishnan, Y. (2021). A DNA-based voltmeter for organelles. Nat. Nanotechnol. *16*, 96–103. https://doi.org/10.1038/s41565-020-00784-1.

124. Organick, L., Ang, S.D., Chen, Y.J., Lopez, R., Yekhanin, S., Makarychev, K., Racz, M.Z., Kamath, G., Gopalan, P., Nguyen, B., et al. (2018). Random access in large-scale DNA data storage. Nat. Biotechnol. *36*, 242–248. https://doi.org/10.1038/nbt.4079.

125. Farzadfard, F., and Lu, T.K. (2018). Emerging applications for DNA writers and molecular recorders. Science *361*, 870–875. https://doi.org/10.1126/science.aat9249.

126. Zhuravel, R., Huang, H., Polycarpou, G., Polydorides, S., Motamarri, P., Katrivas, L., Rotem, D., Sperling, J., Zotti, L.A., Kotlyar, A.B., et al. (2020). Backbone charge transport in double-stranded DNA. Nat. Nanotechnol. *15*, 836–840. https://doi.org/10.1038/s41565-020-0741-2.

127. Chen, Y., Zhao, M., Ouyang, Y., Zhang, S., Liu, Z., Wang, K., Zhang, Z., Liu, Y., Yang, C., Sun, W., et al. (2023). Biotemplated precise assembly approach toward ultra-scaled high-performance electronics. Nat. Protoc. *18*, 2975–2997. https://doi.org/10.1038/s41596-023-00870-3.

128. English, M.A., Soenksen, L.R., Gayet, R.V., de Puig, H., Angenent-Mari, N.M., Mao, A.S., Nguyen, P.Q., and Collins, J.J. (2019). Programmable CRISPR-responsive smart materials. Science *365*, 780–785. https://doi.org/10.1126/science.aaw5122.

129. Jung, J.K., Archuleta, C.M., Alam, K.K., and Lucks, J.B. (2022). Programming cell-free biosensors with DNA strand displacement circuits. Nat. Chem. Biol. *18*, 385–393. https://doi.org/10.1038/s41589-021-00962-9.

130. Marković, D., Mizrahi, A., Querlioz, D., and Grollier, J. (2020). Physics for neuromorphic computing. Nat. Rev. Phys. *2*, 499–510. https://doi.org/10.1038/s42254-020-0208-2.

131. Sangwan, V.K., and Hersam, M.C. (2020). Neuromorphic nanoelectronic materials. Nat. Nanotechnol. *15*, 517–528. https://doi.org/10.1038/s41565-020-0647-z.

132. van de Burgt, Y., Melianas, A., Keene, S.T., Malliaras, G., and Salleo, A. (2018). Organic electronics for neuromorphic computing. Nat. Electron. *1*, 386–397. https://doi.org/10.1038/s41928-018-0103-3.

133. Bartolozzi, C., Indiveri, G., and Donati, E. (2022). Embodied neuromorphic intelligence. Nat. Commun. *13*, 1024. https://doi.org/10.1038/s41467-022-28487-2.

134. Li, T., Miao, J., Fu, X., Song, B., Cai, B., Ge, X., Zhou, X., Zhou, P., Wang, X., Jariwala, D., and Hu, W. (2023). Reconfigurable, non-volatile neuromorphic photovoltaics. Nat. Nanotechnol. *18*, 1303–1310. https://doi.org/10.1038/s41565-023-01446-8.

135. Grollier, J., Querlioz, D., Camsari, K.Y., Everschor-Sitte, K., Fukami, S., and Stiles, M.D. (2020). Neuromorphic spintronics. Nat. Electron. *3*, 360–370. https://doi.org/10.1038/s41928-019-0360-9.

136. Li, C., Zhao, Y.F., Vera, A., Lesser, O., Yi, H., Kumari, S., Yan, Z., Dong, C., Bowen, T., Wang, K., et al. (2023). Proximity-induced superconductivity in epitaxial topological insulator/graphene/gallium heterostructures. Nat. Mater. *22*, 570–575. https://doi.org/10.1038/s41563-023-01478-4.

137. Ladd, T.D., Jelezko, F., Laflamme, R., Nakamura, Y., Monroe, C., and O'Brien, J.L. (2010). Quantum computers. Nature *464*, 45–53. https://doi.org/10.1038/nature08812.

138. Maring, N., Fyrillas, A., Pont, M., Ivanov, E., Stepanov, P., Margaria, N., Hease, W., Pishchagin, A., Lemaître, A., Sagnes, I., et al. (2024). A versatile single-photon-based quantum computing platform. Nat. Photonics *18*, 603–609. https://doi.org/10.1038/s41566-024-01403-4.

139. Prabhathan, P., Sreekanth, K.V., Teng, J., Ko, J.H., Yoo, Y.J., Jeong, H.H., Lee, Y., Zhang, S., Cao, T., Popescu, C.C., et al. (2023). Roadmap for phase change materials in photonics and beyond. iScience *26*, 107946. https://doi.org/10.1016/j.isci.2023.107946.

140. Kim, J., Campbell, A.S., de Ávila, B.E.F., and Wang, J. (2019). Wearable biosensors for healthcare monitoring. Nat. Biotechnol. *37*, 389–406. https://doi.org/10.1038/s41587-019-0045-y.

141. Chen, J., Huang, Y., Zhang, N., Zou, H., Liu, R., Tao, C., Fan, X., and Wang, Z.L. (2016). Micro-cable structured textile for simultaneously harvesting solar and mechanical energy. Nat. Energy *1*, 16138. https://doi.org/10.1038/nenergy.2016.138.

142. Sun, H., Zhang, Y., Zhang, J., Sun, X., and Peng, H. (2017). Energy harvesting and storage in 1D devices. Nat. Rev. Mater. *2*, 17023. https://doi.org/10.1038/natrevmats.2017.23.

143. Zeng, S., Pian, S., Su, M., Wang, Z., Wu, M., Liu, X., Chen, M., Xiang, Y., Wu, J., Zhang, M., et al. (2021). Hierarchical-morphology metafabric for scalable passive daytime radiative cooling. Science *373*, 692–696. https://doi.org/10.1126/science.abi5484.

144. Zhang, Z., Guo, K., Li, Y., Li, X., Guan, G., Li, H., Luo, Y., Zhao, F., Zhang, Q., Wei, B., et al. (2015). A colour-tunable, weavable fibre-shaped polymer light-emitting electrochemical cell. Nat. Photonics *9*, 233–238. https://doi.org/10.1038/nphoton.2015.37.

145. An, B., Wang, Y., Huang, Y., Wang, X., Liu, Y., Xun, D., Church, G.M., Dai, Z., Yi, X., Tang, T.C., and Zhong, C. (2023). Engineered Living Materials For Sustainability. Chem. Rev. *123*, 2349–2419. https://doi.org/10.1021/acs.chemrev.2c00512.

146. Philipp, L.A., Bühler, K., Ulber, R., and Gescher, J. (2024). Beneficial applications of biofilms. Nat. Rev. Microbiol. *22*, 276–290. https://doi.org/10.1038/s41579-023-00985-0.

147. Rodrigo-Navarro, A., Sankaran, S., Dalby, M.J., del Campo, A., and Salmeron-Sanchez, M. (2021). Engineered living biomaterials. Nat. Rev. Mater. *6*, 1175–1190. https://doi.org/10.1038/s41578-021-00350-8.

148. Balasubramanian, S., Yu, K., Meyer, A.S., Karana, E., and Aubin-Tam, M.E. (2021). Bioprinting of Regenerative Photosynthetic Living Materials. Adv. Funct. Mater. *31*, 2011162. https://doi.org/10.1002/adfm.202011162.

149. Liu, Y., Xia, X., Liu, Z., and Dong, M. (2023). The Next Frontier of 3D Bioprinting: Bioactive Materials Functionalized by Bacteria. Small *19*, 2205949. https://doi.org/10.1002/smll.202205949.

150. Wangpraseurt, D., You, S., Sun, Y., and Chen, S. (2022). Biomimetic 3D living materials powered by microorganisms. Trends Biotechnol. *40*, 843–857. https://doi.org/10.1016/j.tibtech.2022.01.003.

151. Zhou, J.W., Barati, B., Giaccardi, E., and Karana, E. (2022). Habitabilities of Living Artefacts: A Taxonomy of Digital Tools for Biodesign. Int. J. Des. *16*, 57–73. https://doi.org/10.57698/v16i2.05.