



Review

Symbiotic bioelectronics: Toward energy-autonomous, bioabsorbable, and closed-loop therapeutic systems

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ABSTRACT

Implantable bioelectronic devices are developing from a single stimulation and recording tool to a long-term medical platform integrating perception, computing, communication and treatment. They are still limited by finite battery lifetime, permanent hardware residue and open-loop treatment mode. Symbiotic bioelectronics redefine the relationship between device and host from passive implantation to active coexistence, emphasizing the synergy of energy, materials and information: energy is harvested from heartbeat, respiration, gastrointestinal peristalsis and joint movement through triboelectric, piezoelectric and electromagnetic transduction, whereas ultrasound, radiofrequency and inductive coupling are treated as externally powered battery-free architectures rather than host-energy harvesting; Using transient electronic materials, bioabsorbable metals, silicon nanomembranes and biodegradable polymers to achieve safe exit after the completion of the task; The closed-loop treatment is realized through multimodal sensing, low-power decision-making and precise actuation. Based on the proposed symbiotic bioelectronics, combined with the representative work of self-powered pacemakers, symbiotic transcatheter pacemaker and degradable neuromodulation system, this paper systematically expounds the material basis, device architecture and translational challenges of self-powered implants, bioabsorbable therapeutic devices and self decision closed-loop systems. This review provides a summary of the current situation and future challenges for the next generation of implantable devices from in vivo tools to long-term collaborative therapy partners with the host.

1. Introduction

Implantable medical devices [1–3] have profoundly changed the management of chronic diseases. Cardiac Pacemaker, Implantable Cardioverter-Defibrillator (ICD), Deep Brain Stimulator (DBS), Spinal Cord Stimulator (SCS), Cochlear Implant, Vagus Nerve Stimulator (VNS) and capsule endoscopes can perform long-term stimulation, recording, monitoring and drug delivery tasks in complex physiological environments for a long time. However, with the evolution of devices from a single output module to a multifunctional platform integrating sensing, computing, communication and closed-loop control [4–6], traditional implantable electronic systems face three types of core contradictions: the energy system is difficult to support long-term autonomous operation [7–10], the device lifetime is difficult to match the limited

treatment window [3,11,12], and the fixed treatment parameters are difficult to adapt to the dynamic changes of disease status [4,13,14]. Fig. 1 summarizes the overall framework of symbiotic bioelectronics, showing the transformation of implantable devices from in vivo tools to host integrated treatment systems.

First, most of the existing implants still rely on finite battery lifetime [1,7]. The battery not only limits the service time, but also determines the device volume, stiffness, packaging method and surgical path. After the battery runs out, patients usually need to replace the whole pulse generator and implantation module, thus increasing infection, bleeding, bag complications, wire damage and hospitalization burden. Although high energy density batteries, rechargeable batteries and percutaneous wireless charging can extend the service life, they do not eliminate the dependence of equipment on preset chemical energy storage. The real

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breakthrough is to make the device not only bring energy into the body, but also continuously obtain energy in the body. Heartbeat, respiration, gastrointestinal peristalsis [15–17], blood flow and joint movement can be used as low-frequency biomechanical energy sources and converted into electrical energy through triboelectric, piezoelectric, electromagnetic and ultrasonic driving mechanisms [10,16,18,19]. Represented by the symbiotic cardiac pacemaker (SPM) proposed by Ouyang et al. [8] and the subsequent development of self-powered intracardiac pacemakers and symbiotic transcatheter pacemakers [10], the heart is no longer just a treatment object, but can also provide power for the operation of treatment equipment.

Second, many implantable electronic systems do not need to exist permanently. Postoperative monitoring, temporary pacing, short-term nerve stimulation, tissue repair and local drug release often require only a few days to months of functional windows; After the end of the mission, the residual devices may cause fibrotic encapsulation, chronic inflammation, device migration, tissue wear and the need for secondary removal. Material symbiosis requires devices to maintain electrical, mechanical and interface stability during service [20–22], and degrade, absorb and discharge at a predictable time scale after completing the task. Transient silicon electronics, bioabsorbable brain sensors [23–25], leadless absorbable temporary pacemakers [12,26], millimeter scale absorbable optoelectronic electrotherapy system [27] and transient closed-loop electrotherapy network [28] jointly prove that high-performance electronic functions and controllable disappearance can coexist in the same system.

Third, the disease state is not static but constantly fluctuates with time, behavior state, treatment response and external stimuli. Therefore, the treatment strategy should also shift from fixed output to state-dependent regulation. Traditional open-loop devices usually output stimulation and drugs continuously according to the preset frequency, amplitude and administration rate, which is difficult to adjust according to the real-time state of patients, so it is often difficult to achieve the optimal balance between efficacy, energy consumption and side effects. Through the continuous reading of electrophysiological, electrochemical, mechanical and optical signals, information symbiosis transforms the treatment output into a closed-loop process of "perception decision actuation feedback". Responsive neurostimulation for epilepsy [13], individualized closed-loop depression regulation [14], transient closed-loop electrotherapy network [28] and wearable facial spasm treatment system show that the device can intervene on demand according to the host state, rather than continuously executing fixed procedures.

1.1. Definition and conceptual boundary of symbiotic bioelectronics

In this review, symbiotic bioelectronics is defined as a system-level framework describing adaptive and functional coupling between electronic devices and biological hosts. Unlike conventional classifications based on a single technical attribute, a bioelectronic system is considered symbiotic when its operation establishes meaningful coupling with at least one host-related dimension: physiological energy exchange

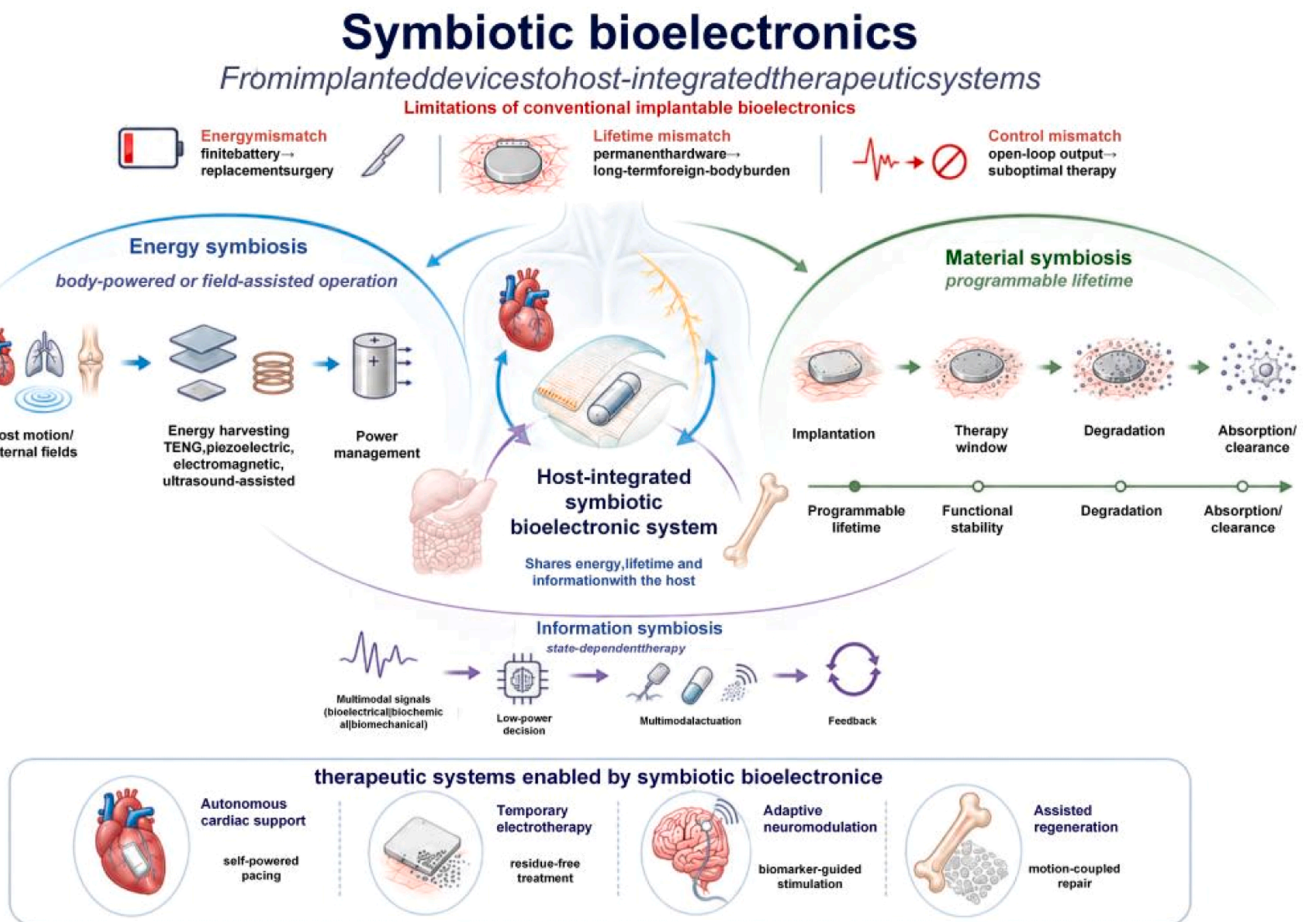


Fig. 1. | General framework of symbiotic bioelectronics. The Figure outlines the evolution path of implantable devices from passive implantable tools to host integrated treatment systems, focusing on three symbiotic mainlines: energy, materials and information. The equipment draws energy from heartbeat, breathing and movement, and safely disappears with the help of absorbable materials after the task is completed; At the same time, multimodal sensing, decision-making and actuation work together to achieve closed-loop treatment.

(energy symbiosis), task-matched material lifetime and safe exit (material symbiosis), or state-dependent sensing, decision-making and therapeutic feedback (information symbiosis). Systems that deliberately co-design all three dimensions are referred to here as fully symbiotic bioelectronics.

Importantly, a device that is merely battery-free, flexible, biodegradable or equipped with sensors does not automatically qualify as symbiotic. Self-powered, battery-free, transient, biointegrated and closed-loop bioelectronics describe specific device attributes or implementation strategies; they contribute to symbiosis only when those attributes create a functional host-device coupling. Table 1 summarizes these conceptual boundaries.

Therefore, symbiotic bioelectronics is not a specific device, but a set of systematic design ideas. It requires the equipment to cooperate with the host at three levels: energy to obtain power from the host and a safe external field; On the material, the lifetime of the device is matched with the disease process and treatment window; In terms of information, adaptive therapy is realized through perception, decision-making and feedback. Focusing on the three dimensions of energy symbiosis, material symbiosis and information symbiosis, this paper reviews the key progress of self-powered implants, bioabsorbable therapy systems and closed-loop self-decision-making platforms, and discusses their material selection, device architecture, system integration and transformation challenges.

2. Energy symbiosis: from battery dependence to host energy supply autonomy

2.1. Three energy architectures in symbiotic bioelectronics

Energy symbiosis should be distinguished from battery-free operation at the architectural level. For the purpose of this review, implantable bioelectronic energy systems are organized into three architectures. Only Type I directly represents host-energy symbiosis; Types II and III are adjacent or enabling architectures that reduce battery burden but have different translational implications.

Type I — Host-energy-autonomous systems. These systems harvest physiological energy generated by the host, including heartbeat, respiration, gastrointestinal motion and joint movement, and directly convert it into electrical energy for sensing or therapy.

Representative examples include the symbiotic cardiac pacemaker and other motion-driven self-powered implants.

Type II — Externally powered battery-free systems. These devices operate without an implanted battery but receive energy from an external transmitter through ultrasound, radiofrequency or inductive coupling. They can eliminate battery replacement, but the energy originates outside the host; therefore, battery-free operation should not be equated with host-energy symbiosis.

Type III — Energy-assisted hybrid storage systems. Host-derived or environmental energy harvesting supplements an implanted storage element such as a capacitor or rechargeable battery. A representative example is a TENG that recharges a lithium-ion battery used to support pacing. These systems reduce battery depletion but remain dependent on energy storage.

A quantitative head-to-head comparison of representative Type I–III systems is provided in Table 2, including average usable power where reported, conversion efficiency, operating frequency, implantation site/depth, device volume and demonstrated therapeutic load (Table 3–5).

2.2. Hybridization versus symbiosis

Hybrid energy strategies should be distinguished from the concept of symbiosis. Hybridization represents a device-level engineering strategy that combines multiple energy conversion mechanisms to improve output stability, power density, or operational reliability, whereas symbiotic bioelectronics describes a system-level relationship between the electronic device and the biological host. Therefore, combining triboelectric nanogenerators (TENGs), piezoelectric nanogenerators (PENGs), electromagnetic generators (EMGs), or other harvesting mechanisms does not establish a new symbiotic category; instead, it represents optimization within a specific energy architecture.

Accordingly, hybridization should be considered an implementation strategy within energy design rather than an independent symbiotic paradigm. The hierarchical relationship can be summarized as: Symbiotic bioelectronics → Energy symbiosis → Energy architecture → Single or hybrid mechanism → TENG/PENG/EMG/Hybrid systems. This distinction clarifies that hybrid devices improve energy performance while the symbiotic relationship is determined by the functional coupling between the device and the host.

2.3. Energy bottleneck of implantable devices

The long-term service capability of implantable bioelectronic devices [1–3] is first restricted by their own energy system. Cardiac pacemaker ICD, DBS, SCS, Cochlear implant and capsule endoscopy systems need to be stable, predictable and long-term operation in complex internal environment. However, most of the existing implantable devices still rely on finite battery lifetime, which forms a fundamental contradiction between "long-term disease management" and "limited chemical energy storage". With the gradual development of the device from a single stimulus output to a multi-functional platform integrating perception, communication, closed-loop control and intelligent regulation, the power consumption structure has also changed from a simple pulse output to a multi module coupling of "perception computing communication therapy", further amplifying the limitations of the energy system. Fig. 2 summarizes that symbiotic bioelectronics from respiratory drive energy supply, biodegradable power supply, symbiotic cardiac pacing to battery is not merely an auxiliary component, but a core module that directly affects the volume, stiffness, packaging method and clinical life of the device. The representative development path of closed-loop absorbable treatment system is shown in Fig. 2, which further summarizes the system transformation from battery dependent implants to energy symbiotic operation.

Traditional battery technology has laid the clinical foundation for implantable medical devices, but once the battery capacity is exhausted

Table 1
Conceptual boundaries of symbiotic bioelectronics and related paradigms.

Concept	Core feature	Host coupling?	Relation to symbiosis
Self-powered bioelectronics	Energy harvesting	Not necessarily	Only host-derived energy harvesting contributes to energy symbiosis
Battery-free bioelectronics	No implanted battery	No required host coupling	An energy architecture, but not sufficient to define symbiosis
Transient electronics	Designed disappearance	Material lifetime coupling	Can contribute to material symbiosis when lifetime matches therapy
Biointegrated electronics	Soft biological interface	Interface matching	Provides the basis for host-device integration
Closed-loop bioelectronics	Feedback control	Information interaction	Corresponds to information symbiosis
Symbiotic bioelectronics	Host-device co-adaptation	Multi-dimensional coupling	Umbrella framework integrating energy, material, and information interactions

As summarized in Table 1, these adjacent paradigms are complementary rather than mutually exclusive. The defining feature of symbiotic bioelectronics is not a particular material, power source or control algorithm, but whether that feature creates a purposeful functional relationship with the host.

Table 2

| Quantitative comparison of representative energy architectures in symbiotic bioelectronics.

Representative system	Energy architecture	Energy source / conversion	Average usable power	Conversion efficiency	Operating frequency	Implantation site / depth	Device volume	Therapeutic load / validation
Respiration-driven I-TENG pacing system	Type I	Respiratory motion; contact-separation TENG	Not reported; reported output at the μW level	Not reported	Respiration-coupled; exact value Not reported	Respiratory-motion implant interface; exact depth Not reported	Not reported	Direct powering of a prototype pacemaker; proof-of-concept validation
Symbiotic cardiac pacemaker (SPM)	Type I	Heartbeat; implantable TENG	Not reported; 0.495 μJ usable energy per cardiac cycle	Not reported	Heartbeat-synchronous; exact value Not reported	Porcine cardiac model; exact depth Not reported	Not reported	Cardiac pacing; harvested energy exceeded the endocardial pacing requirement
Self-rechargeable cardiac pacemaker system	Type III	In vivo inertial motion; stacked I-TENG + Li-ion battery	Not reported; maximum RMS volumetric power density 4.9 $\mu\text{W cm}^{-3}$	Not reported	Motion-dependent; exact value Not reported	Implantable cardiac pacing system; exact depth Not reported	Not reported	Battery recharging and VVI pacing; stable output after 30,000 cycles
Self-powered intracardiac pacemaker (SICP)	Type I	Cardiac motion; triboelectrification/electrostatic induction	Not reported; in vivo output $\approx 6.0\text{ V}$ and 0.2 μA	Not reported	Heartbeat-coupled; exact value Not reported	Right ventricle; transcatheter implantation	1.52 cm^3	Battery-free endocardial pacing in a porcine model; 3-week follow-up
Symbiotic transcatheter pacemaker (STPM)	Type I	Cardiac motion; electromagnetic induction with magnetic-levitation buffering	Hundreds-of- μW intracardiac output reported	Not reported	Heartbeat-coupled; exact value Not reported	Intracardiac, transcatheter; exact depth Not reported	Not reported	Porcine bradyarrhythmia pacing; 1-month autonomous operation
Implantable self-powered vagus nerve stimulator	Type I	Gastric peristalsis; flexible TENG	Not reported; biphasic stimulation pulses reported	Not reported	Gastrointestinal-motion coupled; exact value Not reported	Stomach surface coupled to vagus nerve; exact depth Not reported	Not reported	VNS for body-weight control in rats
Fully biodegradable triboelectric vagus nerve stimulator	Type I	Physiological mechanical motion; biodegradable TENG	Not reported; 9.07 $\pm 0.43\text{ V}$ and 4.19 $\pm 0.14\text{ }\mu\text{A}$ reported	Not reported	Physiological-motion coupled; exact value Not reported	Implantable vagus-nerve interface; exact depth Not reported	Not reported	Low-level VNS for cardiac remodeling; ≈ 4 -week stable stimulation
Rehabilitation-motion-driven symbiotic electrical stimulation system	Type I	Rehabilitation motion; hybrid piezoelectric/triboelectric generator	Not reported; motion-induced biphasic pulses reported	Not reported	Intermittent rehabilitation motion; exact value Not reported	Musculoskeletal/bone-defect interface; exact depth Not reported	Not reported	Electrical stimulation for bone-defect repair and regeneration
Porous TENG knee-joint implant load sensor	Type I	Knee-joint loading; porous silicone-rubber TENG	Not reported; maximum power $\approx 18\text{ }\mu\text{W}$	Not reported	Joint-loading dependent; exact value Not reported	Knee-joint/TKR interface; exact depth Not reported	Not reported	Self-powered load/pressure sensing; tolerates $\approx 2000\text{ N}$
Ultrasound-driven implantable TENG wireless power system	Type II	External ultrasound; ultrasound-driven capacitive TENG	Not reported; $\approx 11.50\text{ V}$ in water and $\approx 8.75\text{ V}$ in vivo	Not reported	Externally driven ultrasound; exact frequency Not reported	Deep implant in mice; ex vivo porcine tissue; exact depth Not reported	Not reported	Battery-free implantable neurostimulation; stable output > 300 min

Note: Type I, host-energy-autonomous; Type II, externally powered battery-free; Type III, energy-assisted/self-recharging. Not reported indicates that the metric was not explicitly reported in the cited study or in the source information summarized in this review. Peak voltage, current, power density or energy-per-cycle values are retained when average usable power was unavailable, because these quantities are not interchangeable. TENG, triboelectric nanogenerator; SPM, symbiotic cardiac pacemaker; SICP, self-powered intracardiac pacemaker; STPM, symbiotic transcatheter pacemaker; VNS, vagus nerve stimulation; TKR, total knee replacement.

[1,7], it is usually necessary to replace the whole pulse generator and re-implant the module in clinic, which greatly increases the medical cost and risk. For patients with pacemaker dependence, children and patients who need high-frequency nerve stimulation, equipment replacement may run through the whole life cycle, and bring infection, bleeding, bag complications, wire damage and hospitalization burden. Ryu reported a self-charging cardiac pacing system based on the in vivo inertia driven triboelectric Nanogenerator (I-TENG) [7]. (Fig. 3a) it is precisely for this pain point that the five layer stacked I-TENG can produce 136 V peak voltage and 2 $\mu\text{A cm}^{-3}$ peak current density under experimental conditions, with a maximum RMS volumetric power density of 4.9 $\mu\text{W cm}^{-3}$, and maintain a stable output after 30000 cycles; In large-animal model, the system can record the output in real time through Bluetooth and charge the lithium-ion battery. After integration with the pacemaker, the ventricular pacing ventricular sensing inhibitory

response mode (VVI) operation was verified. The work shows that the battery can be recharged through energy collection in the body, but it also highlights that if the battery is still retained, the system still needs to face problems such as battery aging, packaging and capacity degradation.

The battery also imposes multiple constraints on the material and shape design of devices. Firstly, the battery is usually one of the parts with the highest volume and mass in the implantation system, which limits the miniaturization of devices and minimally invasive implantation. Secondly, the rigidity of battery and metal packaging is high, and there is a mechanical mismatch with myocardium, nerves, blood vessels and soft tissues. Long term implantation may induce chronic inflammation, fibrotic encapsulation and signal attenuation. Thirdly, the battery must rely on high reliability airtight packaging to isolate body fluids, which will increase the thickness of the system and the

Table 3
Representative Transient Materials and Biodegradable Therapeutic Systems in Material Symbiosis.

Category	Representative system/ material	Key material composition	Function and validation scenario	Degradation/resorption features	Significance for material symbiosis
Material platform	Transient silicon electronics	Ultrathin Si, Mg interconnects, MgO insulating layers, silk fibroin encapsulation, etc.	Demonstrates dissolvable electronic circuits and transient device architectures.	Gradually dissolves in aqueous or physiological environments; device lifetime can be tuned by material thickness and encapsulation.	Proposed the core idea of a "designable material lifetime," shifting implantable electronics from permanent stability toward service periods defined by therapeutic tasks.
Sensor	Bioabsorbable brain pressure/temperature sensor	Si nanomembranes, Mg/MgO, PLGA, silk fibroin, and other bioresorbable materials.	Monitoring of intracranial pressure and temperature during the acute period.	Gradually resorbs after the monitoring window, avoiding long-term foreign-body retention.	Combines high-performance postoperative sensing with extraction-free operation, reflecting the clinical value of material symbiosis in short-term monitoring.
Neural repair	Wireless bioresorbable nerve stimulator	Bioresorbable circuits, substrate, electrodes, and wireless powering structure.	Programmable electrical stimulation after peripheral nerve injury to promote nerve regeneration.	Gradually resorbs after the nerve repair window.	Converts material transience from passive disappearance into an active therapeutic function, matching device service life with the tissue regeneration process.
Therapeutic device	Bioabsorbable temporary pacemaker	Bioresorbable metals, electrodes, polymer encapsulation, and wireless inductive powering structure.	Leadless, battery-free temporary cardiac pacing.	Dissolves and is cleared through biological processes after the predetermined working window.	Reduces risks related to temporary pacing leads, infection, and secondary handling by disappearing after task completion; a representative paradigm of material symbiosis in cardiac electrotherapy.
Semiconductor material	Silicon nanomembranes	Single-crystalline Si nanomembranes and related SiO ₂ /SiN _x thin layers.	Active sensing, signal amplification, logic circuits, and microelectronic structures.	Hydrolyzes into soluble silicic acid products; thickness and effective interfacial area determine degradation lifetime.	Combines microelectronic performance, flexibility, and degradability, serving as a foundational semiconductor platform for transient active devices.
Conductor material	Dissolvable metals	Mg, Zn, Fe, Mo, W, etc.	Transient interconnects, electrodes, antennas, and energy-transfer structures.	Dissolution rates are jointly regulated by metal type, thickness, grain structure, morphology, and encapsulation environment.	Provides conductive functional layers for bioresorbable electronics and enables tuning of service time and mechanical/electrochemical behavior through material selection.
Material/therapy interface	Biodegradable piezoelectric/self-electrifying materials	PLLA, collagen, silk fibroin, cellulose, amino acids/peptides, etc.	Convert mechanical stimuli into local electrical signals to support bone, nerve, and soft-tissue repair.	Gradually degrade together with scaffolds, conduits, patches, or tissue-engineering interfaces.	Embodies the design logic of "material as function": the material simultaneously serves as an interface, energy converter, and therapeutic regulator.
Self-powered neuromodulation	Fully biodegradable triboelectric vagus nerve stimulator	Biodegradable TENG materials such as PVA/Fe, PVA, Mo, and PCL/PLA.	Low-level VNS for intervention in heart-failure-related cardiac remodeling.	Works stably for approximately 4 weeks and can undergo ultrasound-triggered accelerated degradation.	Connects energy symbiosis and material symbiosis, enabling therapeutic devices to operate self-powered during service and exit controllably after treatment.
Drug delivery	Self-powered, light-controlled bioresorbable drug-delivery platform	Bioresorbable electronic/photothermal actuators and drug-release structures.	Programmed local drug release.	Materials gradually resorb after task completion.	Integrates an energy source, actuator, and therapeutic payload into a disappearing system, extending material symbiosis to on-demand drug therapy.
Cardiac electrotherapy	Millimeter-scale bioresorbable optoelectronic cardiac electrotherapy system	On-chip power source, wireless optical-control unit, bioresorbable encapsulation, and electrodes.	Minimally invasive cardiac pacing/electrotherapy.	Resorbs biologically after service.	Moves from a single stimulator toward a "bioresorbable device - epidermal controller - closed-loop algorithm" architecture, reflecting the intersection of material and information symbiosis.
Closed-loop system	Transient closed-loop wireless body-integrated electrotherapy network	Wearable/implantable wireless nodes, sensing modules, and stimulation modules.	Autonomous detection and triggering of short-term electrotherapy.	Can be removed, deactivated, or disappear when no longer needed, depending on node material design.	Connects material symbiosis with information symbiosis, enabling short-term therapy with autonomous sensing, decision-making, and treatment capability.

Note: PLGA, poly(lactic-co-glycolic acid); PVA, poly(vinyl alcohol); PCL, polycaprolactone; PLA, polylactic acid; TENG, triboelectric nanogenerator. In this table, "significance for material symbiosis" emphasizes that materials are no longer merely inert encapsulation and structural supports. Instead, through designable service life, bioresorbable conductors/semiconductors, biodegradable actuators, and task-completion exit mechanisms, device life cycles can be matched with disease-treatment windows and tissue-repair processes.

Table 4
Information-symbiosis characteristics of representative closed-loop and self-decision bioelectronic systems.

System/platform	Development stage/evidence level	Sensed signals and sensing interface	Decision architecture	Actuation mode	Application scenario	Information-symbiosis features and three-dimensional cross-over significance	Major limitations and future directions
NeuroPace RNS responsive neurostimulation system	Clinically approved; long-term follow-up.	Intracranial EEG (iEEG); long-term recording of epileptiform discharges with cortical and depth electrodes.	Detection of seizure-like activity based on preset features and thresholds; parameters can be optimized over time.	Brief bursts of cortical electrical stimulation.	Drug-resistant focal epilepsy.	A nine-year follow-up showed an approximately 75% median reduction in seizure frequency.	Limited channel count and spatial coverage; network-level recording, predictive algorithms, and individualized parameter updating are needed.
Personalized closed-loop depression neuromodulation system	Single-case clinical validation.	Multi-day intracranial electrophysiological recordings; identification of patient-specific neural biomarkers related to mood symptoms.	Triggered by patient-specific biomarkers; shift from universal thresholds to individualized state recognition.	Local brain-area electrical stimulation / closed-loop deep brain stimulation.	Severe treatment-resistant depression.	Stimulation triggered by patient-specific neural biomarkers, reflecting personalized information symbiosis.	Single-case clinical validation; larger cohorts and evaluation of long-term stability and algorithm transferability are needed.
WAND wireless closed-loop neuromodulation platform	Nonhuman-primate experimental platform.	Multichannel local field potentials and neural activity recording; 128-channel recording/stimulation capability.	On-board real-time processing; stimulation-artifact cancellation, biomarker detection, and adaptive adjustment of stimulation parameters.	Multichannel cortical/brain-region electrical stimulation.	Nonhuman-primate closed-loop neuromodulation research.	Integrates multichannel recording, stimulation-artifact cancellation, and real-time closed-loop control, validating the feasibility of low-latency hardware closed loops.	High system complexity; further miniaturization, low-power packaging, and long-term implantation validation are needed.
Adaptive deep brain stimulation (adaptive DBS)	Clinical research/early clinical validation.	Subthalamic nucleus local field potentials; beta-band pathological oscillations as representative feedback signals.	Dynamically adjusts stimulation output according to neural biomarker intensity.	Deep brain stimulation.	Regulation of Parkinsonian motor symptoms.	Dynamically regulates DBS output based on subthalamic beta oscillations, reducing unnecessary stimulation and related side effects.	Feedback signals remain relatively singular; complex states such as movement, mood, sleep, and medication cycles need to be covered.
Millimeter-scale bioresorbable optoelectronic cardiac electrotherapy system	Multispecies preclinical models.	Paired with an epidermal wireless interface; treatment initiated according to arrhythmia detection.	Autonomous closed-loop pacing triggered by arrhythmia detection in the epidermal system.	Wireless optical electrotherapy; single-point or multipoint cardiac pacing.	Temporary cardiac electrotherapy; mouse, rat, pig, dog, and human-heart models.	Couples rhythm detection, wireless control, and bioresorbable actuators, showing the intersection of information and material symbiosis.	Mainly intended for temporary electrotherapy; multimodal sensing and long-term rhythm-control capability need enhancement.
Transient closed-loop wireless body-integrated electrotherapy network	Preclinical/system-level proof of concept.	Distributed epidermal and flexible nodes collect physiological states.	Networked closed-loop control; collaborative decision-making among multiple nodes.	Distributed electrotherapeutic stimulation.	Temporary electrotherapy and multinode autonomous treatment.	Enables short-term autonomous electrotherapy through distributed nodes, advancing from single-point stimulation to networked closed-loop treatment.	Node communication, synchronized control, powering efficiency, and life-cycle matching still need optimization.
Eyeglass-based closed-loop therapy system for hemifacial spasm	Preliminary clinical validation.	Electrostatic-induction sensor captures abnormal facial muscle contractions; eyeglass-style everyday-wear interface.	Threshold detection and event recognition; treatment triggered when spasms occur.	tissue-conformal interfaces electrical stimulation.	Hemifacial spasm.	The eyeglass-based platform integrates noninvasive sensing, event recognition, and on-demand tissue-conformal interfaces electrical stimulation, with an identification accuracy of approximately 98.0%.	Limited sample size and follow-up; stability during real-life wear, false-trigger rate, and individualized parameter optimization need validation.
Self-decision bioelectronic system (conceptual framework)	Conceptual framework / review synthesis.	Multimodal signals including electrophysiological, electrochemical, mechanical, and optical signals.	Hierarchical decision-making from threshold logic and machine learning to neuromorphic computing.	Multimodal actuation including electrical stimulation, drug release, mechanical modulation, and optical modulation.	Chronic disease, neuromodulation, metabolic control, tissue repair, etc.	Provides a general autonomous therapeutic architecture of "sensing - decision-making - actuation - feedback".	Low-power computing, material stability, algorithm safety, clinical interpretability, and regulatory pathways must be addressed.

Table note: Information symbiosis emphasizes bidirectional information exchange between the device and host: the device continuously and intermittently reads the host's electrophysiological, chemical, mechanical, or optical state and delivers electrical stimulation, drug release, mechanical modulation, and optical modulation according to state changes. Unlike simple closed-loop control, information symbiosis also requires co-design among sensing, computing, and actuation modules with energy-supply mode and material life cycle. Long-term implantable systems place greater emphasis on low power consumption, low inflammation, and algorithm updatability; temporary therapeutic systems emphasize wireless powering, bioresorbable materials, and safe exit after task completion. Abbreviations: RNS, responsive neurostimulation; DBS, deep brain stimulation; WAND, wireless artifact-free neuromodulation device; iEEG, intracranial electroencephalography.

Table 5
| Design matrix for fully symbiotic bioelectronics.

Clinical task	Energy requirement	Energy architecture	Material lifetime	Sensing modality	Decision strategy	Actuation	Main constraint
Lifelong pacing	Low, repetitive, safety-critical	Host-energy autonomous with redundancy	Permanent	ECG/hemodynamics	Threshold-based rhythm detection	Electrical pacing	Long-term reliability
Temporary pacing	Low-moderate	Externally powered battery-free or transient systems	Days-weeks, programmed degradation	ECG	Rhythm recognition	Electrical stimulation	Controlled lifetime and safety
Epilepsy therapy	Moderate, intermittent	Battery/hybrid wireless architecture	Years	iEEG/LFP biomarkers	Closed-loop abnormal activity detection	Neural stimulation	Signal stability and specificity
Peripheral nerve repair	Low-moderate	Self-powered or hybrid systems	Weeks-months	Neural/electrophysiological signals	Adaptive stimulation control	Electrical/chemical stimulation	Interface compatibility
Bioelectronic drug delivery	Intermittent demand-driven	Battery-assisted or biodegradable systems	Task-matched	Physiological biomarkers	Stimulus-responsive control	Drug release	Dose precision and degradation

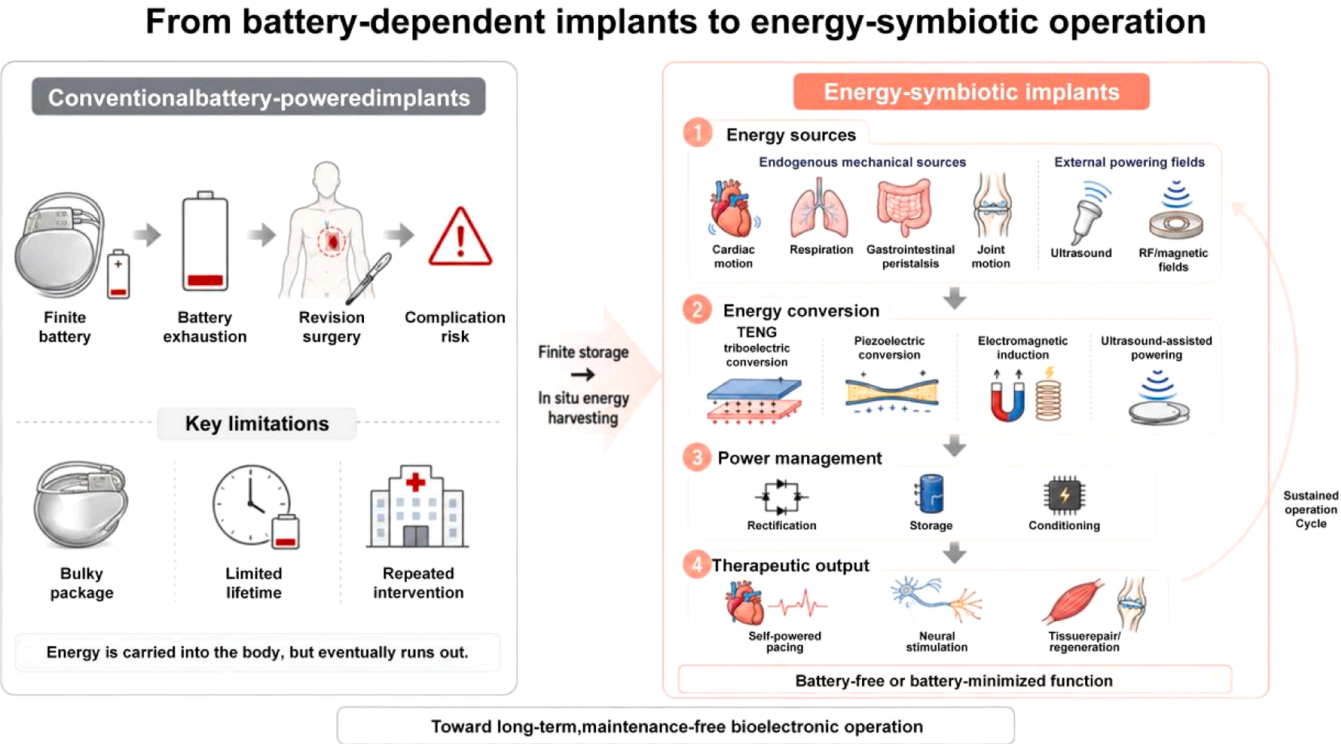


Fig. 2. | From battery-dependent implants to differentiated energy architectures. The left side depicts the limitations of traditional battery-powered implants, including finite battery life, replacement procedures and associated complications. The right side distinguishes host-energy-autonomous harvesting from externally powered battery-free operation and energy-assisted/self-recharging architectures. Host-derived mechanical sources such as cardiac, respiratory, gastrointestinal and limb motion can directly support energy symbiosis, whereas ultrasound, radiofrequency and inductive coupling provide external battery-free power and should not be equated with host-energy harvesting.

complexity of the device structure, and contradict the next generation implantable electronics goals such as flexibility, extensibility and bio-absorbability [29–34]. Rogers' team reported full implantation, leadless, battery-free, bioabsorbable temporary cardiac pacemaker (Fig. 3b) [26], which shows that for short-term treatment tasks such as postoperative temporary pacing, a more ideal strategy is not to continue to extend the battery life, but to remove the burden of batteries, leads and permanent hardware as much as possible. The system relies on inductive wireless energy transmission, which can achieve effective pacing in mouse, rat, rabbit, dog and human heart tissue lamp model experiments, and dissolve and clear through biological processes after a predetermined working window.

In order to alleviate battery dependence, researchers also explored

strategies such as percutaneous wireless charging, RF/inductive coupling energy supply, ultrasonic energy supply and in vivo energy collection. External energy supply can reduce the capacity of airborne battery, but it still depends on external equipment, spatial alignment between transmitter and receiver and patient compliance; Rechargeable batteries can extend the service life, but cannot eliminate battery aging and capacity degradation. In contrast, in vivo energy collection provides a more fundamental solution: instead of pre encapsulating energy into devices, energy is extracted in situ from the persistent physiological activities of the host. The flexible PZT piezoelectric energy collector (Fig. 3c) demonstrated by Rogers in the early stage proved that the natural movement of the heart, lungs and diaphragm can be used for power generation and energy storage in the body; The strategy of

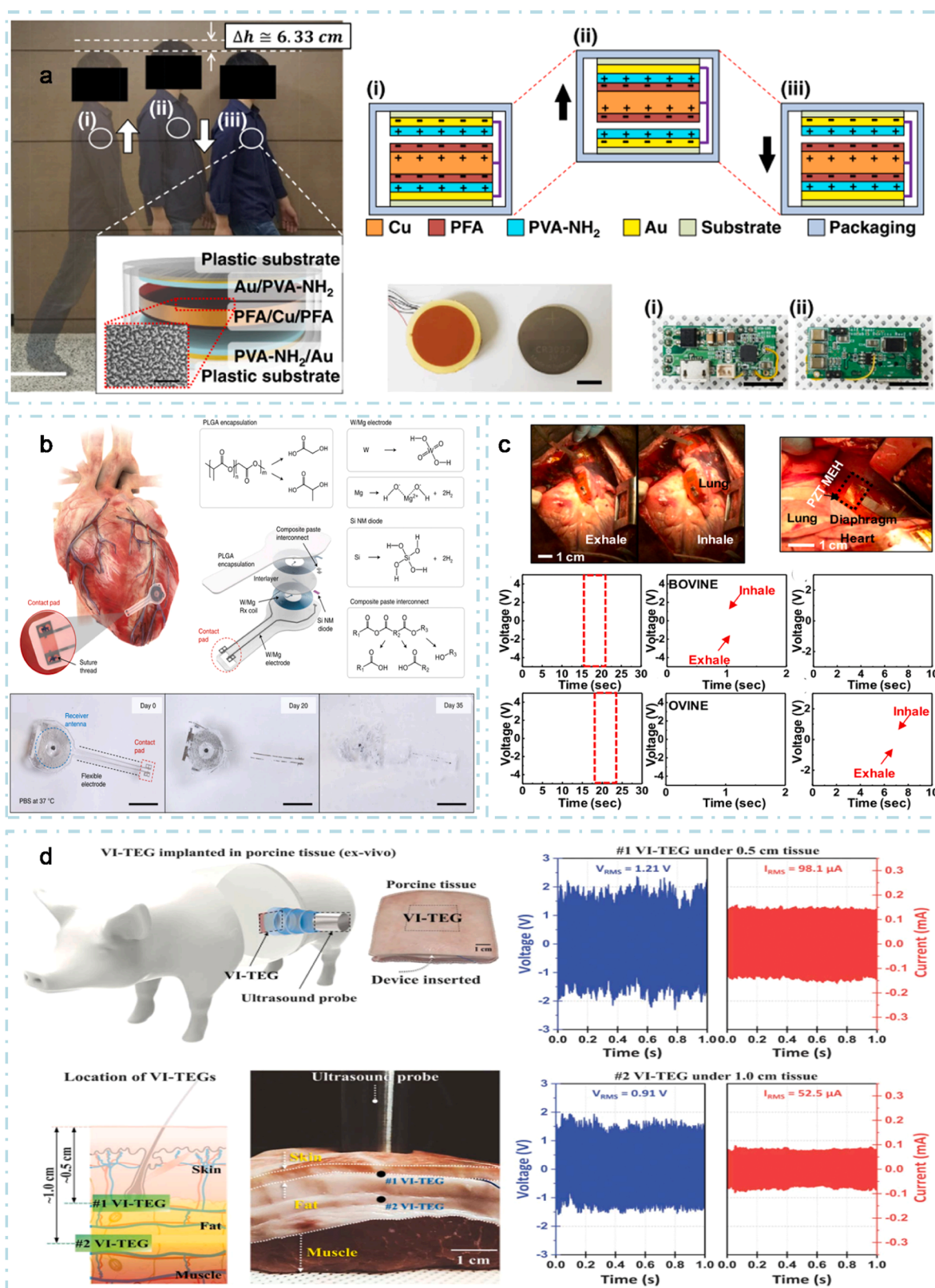


Fig. 3. | Energy bottleneck and battery-free strategies of implantable devices. **a**, The inertia driven I-TEG self-charging pacemaker system shows the path of battery recharging by internal movement. Copyright 2021, Springer. **b**, The fully implanted, bioabsorbable, leadless and battery-free temporary pacemaker can realize short-term cardiac electrotherapy through inductive wireless power transfer, and is bioresorbed after service. Copyright 2021, Springer. **c**, Flexible PZT piezoelectric devices collect and store energy from the movement of the heart, lungs and diaphragm. Copyright 2014, National Academy of Sciences. **d**, Percutaneous ultrasound driven capacitive TENG provides acoustic-field-assisted power delivery for deep implants. The Figure emphasizes that battery-free operation is not a single route, but a continuous spectrum from battery energy supplement, wireless energy supply to energy collection in the host, laying the technical foundation for energy symbiosis. Copyright 2019, American Association for the Advancement of Science.

percutaneous ultrasound driven capacitive triboelectric energy collection [16] proposed by Hinchet et al. (Fig. 3d) provides a battery-free energy supply path assisted by external sound field for deep implants in vivo.

Therefore, the energy bottleneck of implantable devices is not only "insufficient battery capacity", but also the deeper problem is that the limited chemical energy storage is difficult to meet the long-term independent treatment needs of patients. Innovative breakthroughs need

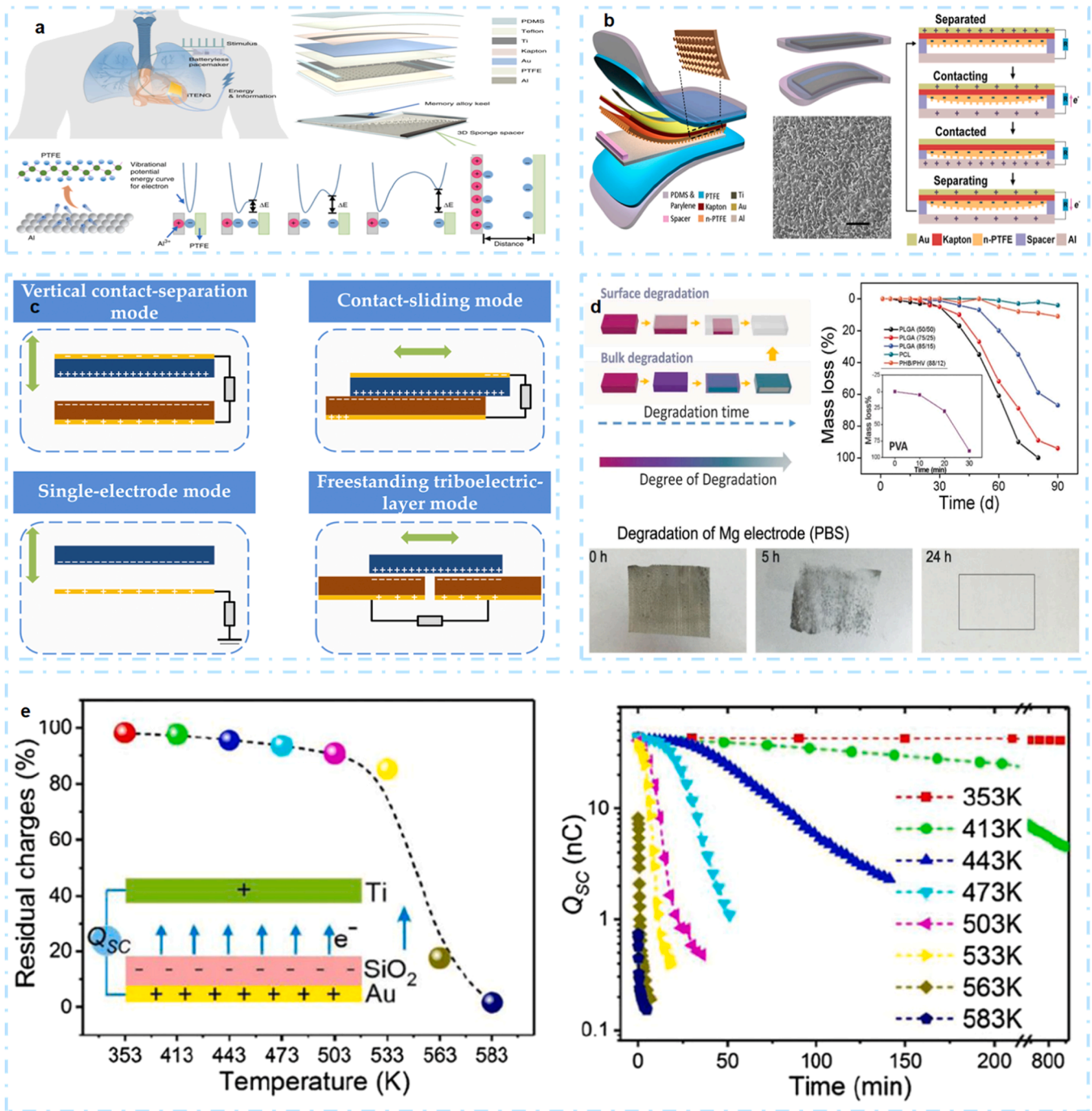


Fig. 4. | Working mechanism, material design and implantable adaptation of the TENG. **a.** The overall architecture and charge transfer path of the symbiotic cardiac pacemaker system. Copyright 2019, Springer. **b.** An example of the material and device structure of an I-TENG, and how the triboelectric layer, conductive layer, elastic support and packaging structure work together, is shown in the Figure. Copyright 2016, American Chemical Society. **c.** The four basic working modes of TENG—vertical contact separation, horizontal sliding, single electrode and independent triboelectric layer mode—are applicable to slightly different scenarios. Copyright 2021, Elsevier. **d.** The tissue-conformal interfaces/overall degradation behavior of biodegradable TENG materials and the dissolution process of the Mg electrode reveal that the life cycle of implantable energy devices is designable. Copyright 2016, American Association for the Advancement of Science. **e.** Thermal stability and time decay behavior of the friction charge in the Ti/SiO₂/Au structure. Copyright 2015, Wiley-VCH. The ratio of residual charge decreases with the increase of temperature; Under different temperature conditions, the short-circuit transferred charge (QSC) shows different degrees of attenuation with time. The tissue-conformal interface charge retention and thermal stability directly affect the long-term output level of TENG. In summary, The Figure shows the adaptability of TENG in low-frequency, small-amplitude and irregular motion energy extraction in vivo, and also points out how the surface charge density, interface morphology, mechanical compliance and biocompatibility of the material work together on the implantable output.

to transform the energy system from "carrying energy into the human body" to "continuously obtaining energy in the human body". This is the core of energy symbiosis: the device obtains energy from the host's heartbeat, respiration, blood flow and limb movement, and maintains the host's function through pacing, nerve stimulation and physiological monitoring. The stability of host function in turn ensures the persistence of energy sources. Thus, the implant is no longer an isolated electronic system relying on a preset battery, but an autonomous treatment platform dynamically coupled with the host's life activities.

2.4. Friction Nano Generator: Mechanism, Material and Optimization

Among various in vivo energy collection technologies, TENG [18, 35–37] has become one of the most representative device platforms in energy symbiosis due to its high adaptability to low-frequency, small-amplitude and irregular mechanical motion [38–40]. TENG was first proposed by Wang's team. Its basic principle is the coupling of contact electrification and electrostatic induction [18,37,41]: two materials with different triboelectric polarities have interfacial charge transfer after contact, and then separate and slide relatively, forming a potential difference and driving the flow of electrons in the external circuit (Fig. 4a). This mechanism enables TENG to obtain electrical energy from low-frequency physiological movements such as heartbeat, respiration, blood vessel pulsation, muscle contraction and joint activity, which is particularly suitable for microwatt to milliwatt implantable devices.

Unlike piezoelectric power generation, which depends on crystal polarization inside the material, TENG output is more determined by the surface charge density, effective contact area, interface morphology and motion mode of the material. Therefore, TENG has a high degree of freedom in material selection and interface design [37,42,43], and can realize diversified construction through polymers, elastomers, biomaterials, biodegradable materials and composite films [44–46] (Fig. 4b). Wang's team and Ouyang et al. have jointly promoted the application path of TENG in implantable scenarios. For example, the I-TENG driven by respiratory movement [47] can directly supply energy for pacemakers, the degradable TENG [48] can be used as an implantable power supply that can be designed in the life cycle (Fig. 4d), and the I-TENG can also be used for wireless heart monitoring and multifunctional active sensing [49]. The efforts jointly promote TENG from flexible energy devices to implantable treatment and diagnosis systems. Furthermore, a more extensive design principle is proposed: implantable energy devices should not only pursue the highest output of a single material and mechanism, but should be designed according to the specific organ movement, tissue interface and treatment load.

TENG usually includes four working modes of vertical contact separation, horizontal sliding, single electrode and independent triboelectric layer [36,50,51] (Fig. 4c). The vertical contact separation mode is suitable for periodic compression of myocardium, diaphragm and soft tissue; The horizontal sliding mode is suitable for joint movement, intestinal peristalsis and tangential displacement of tissue tissue-conformal interfaces; The single electrode mode is easy to integrate with the skin and organ tissue-conformal interfaces; The free-standing triboelectric-layer mode is suitable for irregular and multi-directional mechanical input. For symbiotic bioelectronics, the key is not to pursue the highest output of a single working mode, but to make the device operation mode accurately match the host motion characteristics. For example, TENG powered by breathing emphasizes the stable capture of large displacement and low-frequency motion, while TENG powered by intracardiac pacing emphasizes the low threshold response in a small volume, and the orthopedic rehabilitation system emphasizes the fatigue resistance output under heavy load and intermittent exercise.

The material selection of the triboelectric layer is the core of TENG performance and implantation applicability. Traditional high-performance TENG often use PTFE, FEP, PDMS, Kapton and other materials as triboelectric layers, which have clear friction polarity and high

charge retention ability. However, I-TENG should not only pursue output, but also meet the requirements of biocompatibility, mechanical flexibility, body fluid stability and necessary biodegradability. Fig. 4e further illustrates that whether the friction charge can be retained for a long time is directly related to the continuous output capacity of TENG. Taking the triboelectric layer of the Ti/SiO₂/Au structure as an example, the increase in temperature will significantly reduce the proportion of residual charge [52]; At the same time, the short-circuit transferred charge (QSC) will also decay with time, and the higher the temperature, the faster the decay. Therefore, the material design of I-TENG should not only improve the initial surface charge density, but also enhance the charge retention ability, and reduce the charge loss through interface optimization and packaging design [53]. Taking 2019 symbiotic cardiac pacemaker [8] as an example, nanostructured PTFE film, corona polarization, EVA elastic interlayer and flexible packaging jointly improve the output of I-TENG. The open-circuit voltage, transfer charge and short-circuit current of PTFE-based TENG increased from 67.5 V, 24.8 nC and 5.9 μ A to 187 V, 80.2 nC and 19.5 μ A, respectively, due to corona polarization; The average output of the encapsulated implantable triboelectric nanogenerator (I-TENG) in vitro was 97.5 V, 49.1 nC and 10.1 μ A, and the peak power density was 110 mW m⁻². The data show that the effective output of implanted TENG is determined by the interface charge density, micro-nano structure and mechanical support.

The in vivo environment further changed the evaluation criteria of TENG. Wet ion environment will lead to tissue-conformal interface charge decay and leakage risk, and long-term periodic deformation will lead to material fatigue and encapsulation failure. Therefore, I-TENG should not only take the open circuit voltage and short circuit current as the evaluation index, but also pay attention to the average effective power, energy management efficiency, long-term stability and tissue safety in the real physiological environment. In 2019, the symbiotic cardiac pacemaker system further showed that I-TENG was no longer just an energy demonstration at the large animal scale, but began to approach the actual pacing needs.

From the system level, TENG usually outputs high voltage, low current and pulsed AC signals, which cannot fully match the stable low-voltage DC power supply required by implantable circuits. Therefore, the collaborative design of rectification, impedance matching, energy storage, power management and stimulation circuit is a necessary link for TENG to move towards clinical application. Ryu's I-TENG self-charging pacing system [7] combines TENG with a power management IC, energy storage capacitor and lithium-ion battery energy supplement, which shows that TENG can not only be used as an instantaneous generator, but also as an energy supplement module in the implantable energy management chain. In the future, the collaborative design of TENG with micro supercapacitors, degradable energy storage devices and low-power integrated circuits will determine whether it can support truly long-term, stable and autonomous symbiotic electronic devices.

2.5. From Proof of Concept to Preclinical Transformation: Symbiotic self-powered Pacemaker

Cardiac pacemaker is the most representative implantable platform to verify energy symbiosis. The heart is not only a therapeutic target, but also a stable source of mechanical energy; Every myocardial contraction is accompanied by periodic deformation, displacement and pressure changes. If a small part of the mechanical energy can be converted into electrical energy and fed back to maintain the heart rhythm, a clear reciprocal closed loop can be formed: the device obtains energy from the heart movement, and the pacing function will maintain the continuous and effective beating of the heart. This relationship makes self-powered pacemaker a core model for the transformation of energy symbiosis from concept to clinical practice.

Early studies on TENGs mainly proved the feasibility of the "host mechanical energy–electrical energy–therapeutic output" chain. In

2014, Ouyang et al. and Wang's team reported that the I-TENG driven by respiratory movement directly supplied energy for pacemakers, which connected physiological movement in vivo with pacemaker function for the first time. In the same year, Rogers' team showed a flexible piezoelectric energy collection system attached to the surfaces of the heart,

lung and diaphragm, proving that soft piezoelectric devices can generate electricity and store energy from the natural movement of organs. Although there is still a gap between the works and clinical morphology, they jointly break the default assumption that pacemakers must completely rely on preset batteries.

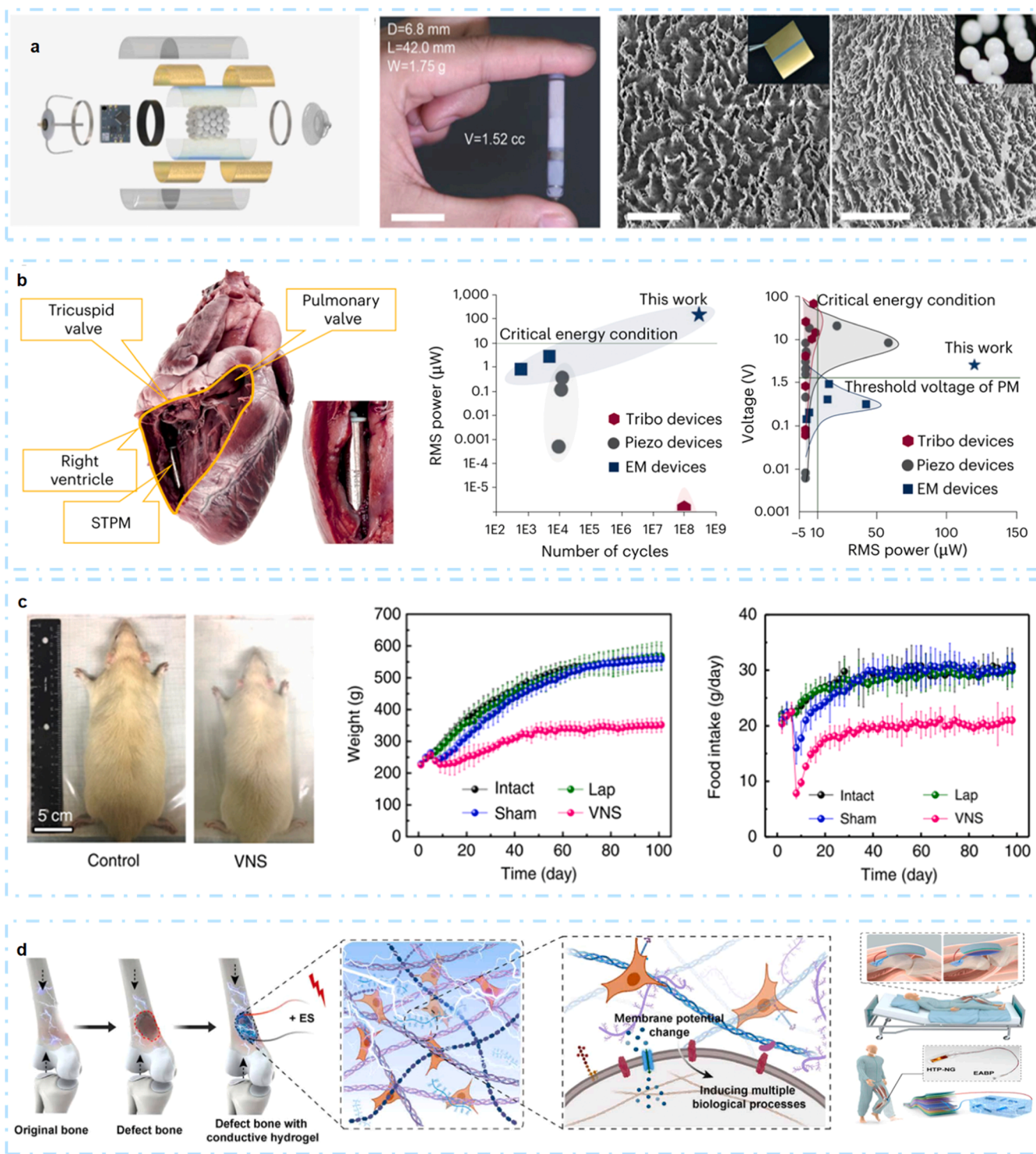


Fig. 5. | transformation path of symbiotic self-powered systems from cardiac pacing to neuromodulation and tissue regeneration. a, Structure and material design of self-powered intracardiac pacemaker SiCp. Copyright 2024, Springer. b, The working principle of the symbiotic transcatheter pacemaker STPM and the pig model validation. Copyright 2026, Springer. c, self-powered vagus nerve stimulation system is used for weight control. Copyright 2018, Springer. d, The symbiotic electrical stimulation system driven by rehabilitation exercise [55] is used for bone regeneration. Copyright 2024, American Association for the Advancement of Science. The Figure shows the extrapolation of energy symbiosis from cardiac rhythm regulation to gastrointestinal neuromodulation and musculoskeletal regeneration therapy [55,56].

In 2019, Ouyang et al. reported a "symbiotic cardiac pacemaker" on the scale of large animals, and formally defined the relationship between equipment and host as a symbiotic system. The system is composed of I-TENG, power management unit and pacing unit, which can collect energy from heart movement and use it for cardiac rhythm regulation. In the pig model, I-TENG can charge the 100 μF capacitor to 3.55 V in 190 min, and realize energy capture synchronized with the ECG signal; 0.495 μJ per cardiac cycle, which was higher than the endocardial pacing threshold. After triggered by an external magnet, the symbiotic cardiac pacemaker outputs a pacing pulse of 3 V, 0.5 ms, 130 beats per minute (bpm), which increases the heart rate from about 90 bpm to about 130 bpm, and can restore rhythm in the arrhythmia model induced by sinoatrial node hypothermia [5]. The important significance of this research is that the research focus will shift from "whether the device can generate electricity" to "whether the system can stabilize the treatment", so that the self-powered implants will move from a single energy collection device to a closed-loop system with clear treatment function. More importantly, symbiotic cardiac pacemaker defines the heart as a therapeutic target and energy source at the same time, demonstrating the reciprocal relationship between "host movement energy conversion pacing intervention" for the first time on a large animal scale. Therefore, the symbiotic cardiac pacemaker not only verified the feasibility of self-powered pacing, but also laid a systematic foundation for the development of subsequent endocardial, minimally invasive and long-term energy regenerative symbiotic pacemakers.

Subsequently, the research on cardiac pacemakers further turned to miniaturization, minimally invasive and clinical pathway adaptation [9, 10]. In 2021, Ryu team reported a self-charging pacemaker system based on I-TENG, which recharged lithium-ion batteries by driving I-TENG through internal motion and gravity, and verified the operation in VVI mode. This work emphasizes the complete chain of "energy harvesting–energy storage–pacing circuitry", but still retains the battery. In 2024, Ouyang et al., together with Hua's team, reported the self-powered intracardiac pacemaker (SICP) [9] in the pig model adopted a capsule shape and a transcatheter implantation path [54] (Fig. 5a). The device has a mass of only 1.75 g, a volume of 1.52 cm^3 , a diameter of 6.8 mm, and a length of 42 mm. It can be delivered intravenously and fixed in the right ventricle; the in vitro open circuit voltage, short-circuit current and transferred charge were about 21.8 V, 0.25 μA and 6.4 nC, respectively, and the in vivo output was about 6.0 V and 0.2 μA . the endocardial pacing function was maintained during the three-week follow-up.

In 2026, Ouyang et al. and Hua's team further reported on the symbiotic transcatheter pacemaker (STPM) (Fig. 5b). Different from TENG route, STPM regenerates electric energy from heart movement through electromagnetic induction [10], and proposes a maglev energy buffer structure to reduce startup threshold, mechanical collision and friction loss. The device is suitable for interventional delivery, has good biocompatibility and blood compatibility, and has completed a month of autonomous operation and treatment function verification in the porcine bradyarrhythmia model. This shows that the development of a symbiotic pacemaker is not limited to the TENG mechanism, but can choose the most appropriate technical route among the triboelectric, piezoelectric and electromagnetic mechanisms according to the implantable space, energy conditioning requirements and clinical safety. This study has achieved the therapeutic effect of the energy collection and power supply device in vivo for the first time, reaching a level comparable to that of battery-powered devices. A microscale energy regeneration module (ERM), an ultra-simplified circuit, and a minimal number of components were integrated into the transcatheter pacemaker. The above characteristics have improved the reliability of ERM in STPM, and it has also successfully passed the long-term stability test of 300 million cycles (converted by heart rate of 60 bpm, equivalent to about 10 years) [10]. The output performance can be further enhanced by increasing the number of coil turns, improving the remanence of magnet and optimizing the structure of the ERM module.

At the same time, the fully implanted, bioabsorbable, leadless and battery-free temporary pacemaker developed by Rogers and Efimov's teams provides another important path for "temporary pacing": power supply through wireless energy transmission and natural degradation after the task is completed. This work does not belong to the self-powered movement of the host, but it emphasizes the importance of battery-free operation, leadless and absorbable for the next generation of pacemaker devices. It can be seen that in the future, symbiotic pacemakers may develop in parallel along two paths: one is for lifelong treatment, which pursues host energy supply, long-term stability and safety redundancy; The other is for short-term treatment, emphasizing battery-free, absorbable and disappearing after the task is completed.

2.6. Extend symbiosis paradigm to other applications

The significance of symbiotic self-powered pacemaker is not limited to the regulation of cardiac rhythm, but to provide a set of extrapolatable design paradigms: identify the stable and predictable energy source in the host, determine the power consumption window according to the treatment task, and then convert the physiological energy into treatment and monitoring function through the collaborative design of material, structure, interface and power management. Along this logic, the application of energy symbiosis is expanding from cardiac pacing to neuromodulation, bone repair, rehabilitation monitoring, deep stimulation and transient treatment systems. Among them, the symbiotic electrical stimulation system driven by rehabilitation exercise represents the extrapolation path of "exercise participation–energy acquisition–bone regeneration therapy" coupling in the musculoskeletal scenarios [57–60].

As summarized in Table 2, it can be found that the core difference of the symbiotic self-powered systems lies not only in the energy conversion mechanism, but also in whether there is a stable match between the energy source, tissue interface and treatment load [61,62]: the cardiac system emphasizes continuous energy supply and safety redundancy, the gastrointestinal and nervous systems emphasize rhythm coupling, the musculoskeletal system emphasizes movement participation and regeneration of the microenvironment, and the ultrasonic drive system provides an external energy supplement path for the deep implantation scene with insufficient host movement.

Breathing, gastrointestinal peristalsis and other visceral rhythmic movements [63] are important sources of mechanical energy other than heart beat. The implanted self-powered vagus nerve stimulator reported by Yao et al. Fixed the flexible TENG on the tissue-conformal interfaces of the stomach and transmitted the biphasic electric pulse [17] generated by gastric peristalsis to the afferent fibers of the vagus nerve (Fig. 5c). In the rat model, the system can control the average body weight at about 350 g within 100 days, which is about 38% lower than the control group. This work shows that physiological movement can not only provide energy for implantable devices, but also serve as a physiological coupling signal between disease status and treatment trigger.

In 2026, Ouyang et al. and Tang's team further reported that VNS was used for heart failure related cardiac remodeling intervention. This study integrated physiological and mechanical energy collection, low-level vagus nerve stimulation and degradable withdrawal after treatment into the same system, indicating that energy symbiosis can be further combined with material symbiosis to support short-term, task limited neuromodulation.

The musculoskeletal system of the human body provides high amplitude, intermittent mechanical energy source with outstanding clinical value. In 2024, the Zheng's team reported that the symbiotic electrical stimulation system driven by rehabilitation exercise [32,64, 65] was used for bone regeneration (Fig. 5d). The system combines the composite piezoelectric/triboelectric nano generator with conductive bioactive hydrogel [66], generates biphasic electrical pulses through active and passive rehabilitation movement, and couples electrical

stimulation with bone defect repair, stem cell osteogenic differentiation and local regeneration microenvironment regulation. The design reflects the unique symbiotic logic in the orthopedic scene: rehabilitation exercise is not only a source of energy, but also a trigger signal for treatment, and electrical stimulation intensity is naturally coupled with exercise participation.

For deep nerve stimulation, antibacterial, tumor treatment and tissue repair [67], the host's own mechanical energy may be insufficient and unstable. At this time, the battery-free system driven by external fields [16,68] can be used as an important supplement to energy symbiosis. The capacitive triboelectric energy collection driven by percutaneous ultrasound reported by Hinchet et al. Provides a wireless energy supply route that can penetrate tissues for deep implants [16]. Although such systems do not rely entirely on host movement, they are also in line with the symbiotic direction of reducing the burden of long-term foreign bodies and improving treatment autonomy by avoiding built-in batteries, reducing implantation volume and achieving on-demand activation. Therefore, the expansion of the symbiotic paradigm should not be understood as simply transplanting the same TENG to different organs, but should be designed around the triad of "energy source–tissue interface–treatment load." Cardiac pacing emphasizes continuity and safety redundancy, vagus nerve stimulation emphasizes rhythm matching and nerve interface stability, bone repair emphasizes motion response and tissue regeneration microenvironment, and ultrasound driven implants emphasize acoustic safety and deep positioning. Future symbiotic bio-electronic systems need to develop multimodal energy collection such as triboelectric, piezoelectric, electromagnetic and ultrasonic drives at the energy level, build a flexible, stable and low-inflammatory tissue-coupling structure at the interface level, and integrate energy management, sensing, therapeutic stimulation, wireless communication and closed-loop algorithms into a low-power platform at the system level [6, 69–72]. Only when the device can be customized according to specific organ movement [73] and treatment tasks, can energy symbiosis really expand from the landmark case of cardiac pacing to the important design principle of the next generation of implantable and wearable medical devices.

3. Material symbiosis: the necessity of bioabsorbability

3.1. Problems with legacy equipment

Energy symbiosis solves the problem of "how to operate" implantable devices, while material symbiosis further focuses on: does the device need to remain in the body after completing the treatment or monitoring tasks? For life-long implants such as cardiac pacemakers, DBS and cochlear implants, the long-term existence of devices in the body is usually part of the treatment demand; However, a large number of implantable electronic systems do not need permanent service. Applications such as postoperative pain management, acute inflammation monitoring, fracture healing evaluation, tissue regeneration stimulation, short-term neuromodulation, local drug release and wound repair [74,75] often only need a functional window of several days to months. Once the window ends, the originally beneficial electronic devices may turn into nonfunctional residual foreign bodies, and even cause potential mechanical and biological damage to human tissues. Therefore, the essence of the material persistence [3,11,12] does not lie in whether the device can still work, but in the mismatch between its functional life and material retention time. By comparing the permanent residual hardware and the material symbiosis absorbable system, the life cycle mismatch problem that the material symbiosis attempts to solve. Its significance is that the design endpoint of the implanted device should not only stay in "whether it can work stably for a long time", but also further turn to "whether it can reliably serve when needed and withdraw from the body as expected after the task is completed".

Traditional implantable electronic devices usually follow the engineering logic of "long-term stable existence". Silicon chip, metal wire,

polyimide substrate, epoxy packaging, titanium shell and non-degradable battery are widely used because they can resist hydrolysis, oxidation, corrosion and mechanical fatigue. However, this stability may become a burden for temporary implants. The more inert the material is, the more likely it will remain for a long time after completing the task; The firmer the package, the harder it is to be removed by the body; The more complex the structure, the more likely it is to cause difficulty in removal, tissue damage and a chronic foreign body reaction in the later stage. In other words, what the temporary implantable device needs is not permanent stability, but stability within the mission period and controllable disappearance after the mission is completed [76].

Long-term residual implants may affect host tissue through a variety of mechanisms. First, the presence of foreign bodies will induce protein adsorption, macrophage recruitment, fibroblast activation and collagen deposition, and finally form fibrotic encapsulation [3,5]. For sensors and stimulation electrodes, fibrosis is not only a histological response, but also increases interface impedance, weakens signal acquisition, increases cardiac electrical stimulation threshold and reduces long-term reliability. Secondly, residual devices may migrate, break and wear in dynamic tissues such as the heart, lung, gastrointestinal activity, muscle and joints, causing local mechanical stimulation. Third, there is a mechanical mismatch between hard electronic materials and soft tissue, which may lead to microinjury, pain, scar formation and chronic inflammation. For children and patients at the stage of tissue remodeling, permanent residual hardware may also interfere with tissue growth and subsequent treatment pathways [77].

Fig. 6a illustrates through the time-dependent dissolution process that the key to transient electronics is not to reduce the performance of the device, but to design the material thickness, packaging structure and moisture entry path to maintain the electronic function within the predetermined window and disappear according to the design path after the task is completed. Rogers' team's work on transient silicon electronics provides an early example of "designable material life" [78]. The circuit based on ultra-thin silicon, magnesium interconnection, magnesium oxide insulation layer and silk fibroin encapsulation can gradually dissolve in the aqueous environment, making the electronic devices from "long-term stable existence" to "task-defined lifetime" (Fig. 7a). Subsequently, Rogers' team promoted the concept to the postoperative monitoring scenario and developed a bioabsorbable silicon-based brain sensor for intracranial pressure and temperature monitoring [23], which was degraded after the completion of acute phase monitoring. The importance of such studies is that they do not simply show that materials can be dissolved, but prove that high-performance electronic functions and controllable disappearance can coexist in the same system, which provides a key basis for material symbiosis from conceptual judgment to device engineering [11,12,23,78].

There are usually two ways to deal with temporary implantation devices in the clinic. Long term retention and secondary removal [23,26, 27]. The former avoids reoperation, but makes patients continuously exposed to potential risks such as late-onset infection, chronic inflammation, device migration and imaging interference; The latter can remove nonfunctional devices, but requires additional anesthesia, incision, tissue separation and perioperative management, which increases the potential risk of infection, bleeding, scar and medical costs. The fully implantable, leadless, battery-free, bioabsorbable temporary pacemaker developed by the team provides a more direct medical answer to this question: driven by wireless energy transmission, the device does not need percutaneous leads and external hardware, and can achieve effective pacing in mice, rats, rabbits, dogs and human heart models. Compared with the traditional temporary pacing lead, the key advantage of such devices is not just "pacing", but the ability to dissolve and remove the lead through natural biological processes after the defined working time, reducing the risk of lead removal, infection and secondary treatment from the source.

Fig. 6b summarizes the life cycle of an ideal material symbiotic

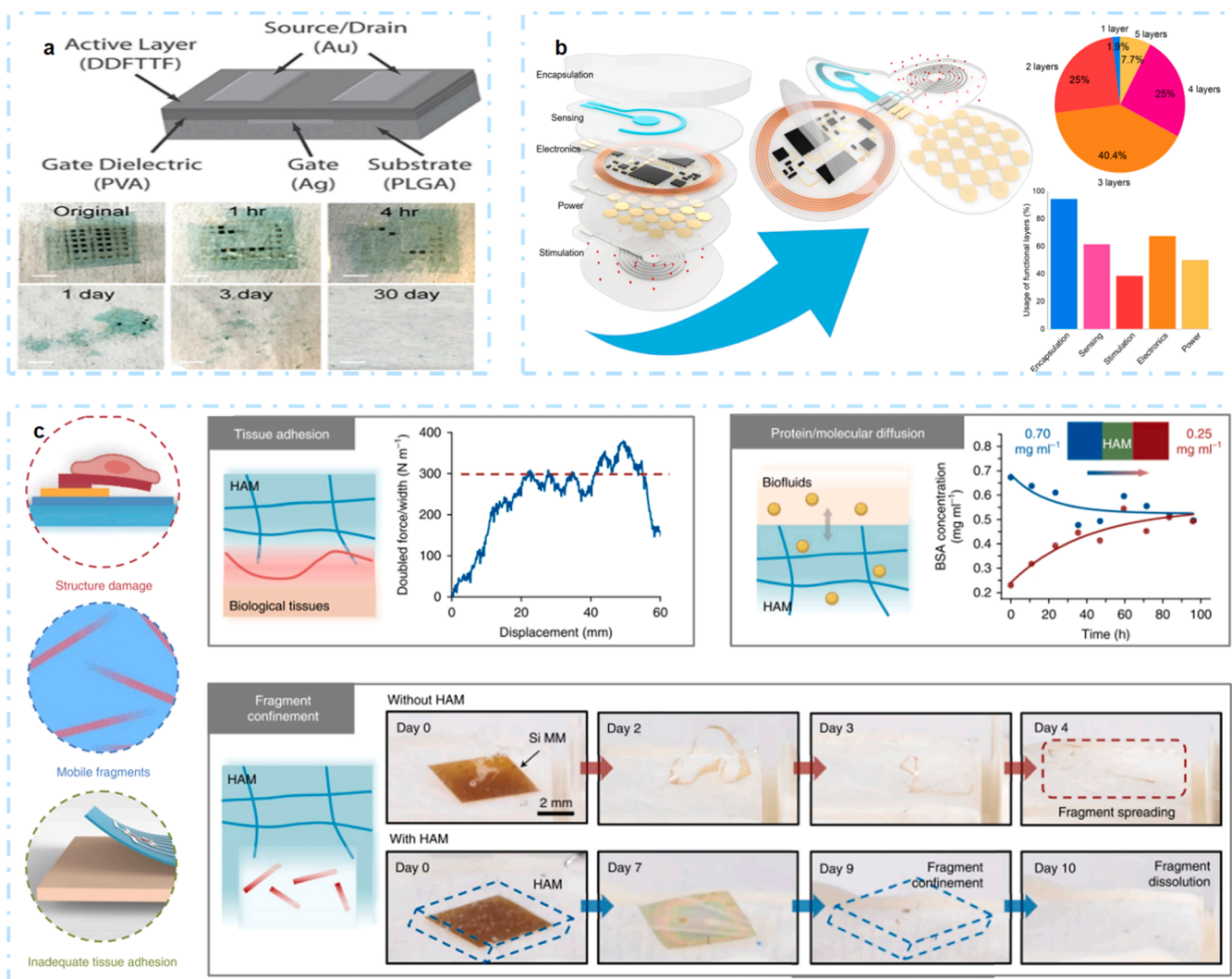


Fig. 6. | Residual device problem and the lifecycle of material symbiosis. **a**, The time-dependent dissolution process of biodegradable electronic devices shows that electronic function and controllable disappearance can coexist in the same system. Copyright 2010 Wiley-VCH. **b**, The ideal implantable bioabsorbable electronic system should work stably in the treatment and monitoring window, and reduce the burden of long-term foreign bodies by degradation, absorption and clearance after the task is completed. Copyright 2025, Springer. **c**, Key challenges and solutions in biointegrated applications include mechanical mismatch, encapsulation failure, device migration, fragment residues and tissue reaction. Copyright 2022, Springer. The Figure reflects the core idea of material symbiosis: the device life should be determined by the clinical task and tissue repair process, rather than by default permanent residence.

device [3,11,12]. Maintain the function in the treatment and monitoring window, and enter the controllable degradation, absorption and clearance stage after the task is completed; Fig. 6c summarizes the mechanical mismatch, encapsulation failure, device migration, fragment residues and tissue reaction problems that still need to be solved for symbiotic devices. Material symbiosis does not sacrifice electronic functions, but requires devices to gradually disappear according to the design path after completing the task. The ideal material symbiosis equipment should maintain sufficient electrical, mechanical and interface stability in the treatment window, degrade in accordance with a predictable time scale after the end of the task, and produce non-toxic, metabolizable and excretable by-products in the degradation process. Thus, the end point of the implant is no longer "permanent residue" and "secondary removal," but "natural disappearance after the function is completed". This also means that the design problem of implantable electronics is changing from "how to stay in the body for a long time" to "how to exit the body at the right time".

3.2. Material library of transient bioelectronics

The development of bioabsorbable electronics requires a fundamental reconstruction of the traditional electronic material system. The material selection of traditional electronic devices aims at long-term stability, corrosion resistance and high reliability, while transient bioelectronics needs to establish design principles in the opposite direction: the device must maintain its function within the predetermined treatment window, and degrade, dissolve or be metabolized and absorbed by the human body after the task is completed. Therefore, the design of transient electronic materials is not to simply replace the traditional materials with "biodegradable materials" [79,80], but to design the electrical properties, mechanical properties, biocompatibility and degradation dynamics for substrates, conductors, semiconductors, dielectrics, encapsulation layers and energy storage units respectively.

Substrate and packaging materials determine the structural integrity and service life of devices. PLGA, PLA, PLLA, PCL [3,11,12], poly-anhydrides, silk fibroin, chitosan, gelatin, cellulose and other natural polymers are commonly used as biodegradable substrates and packaging materials in transient electronics. PLGA can regulate the degradation

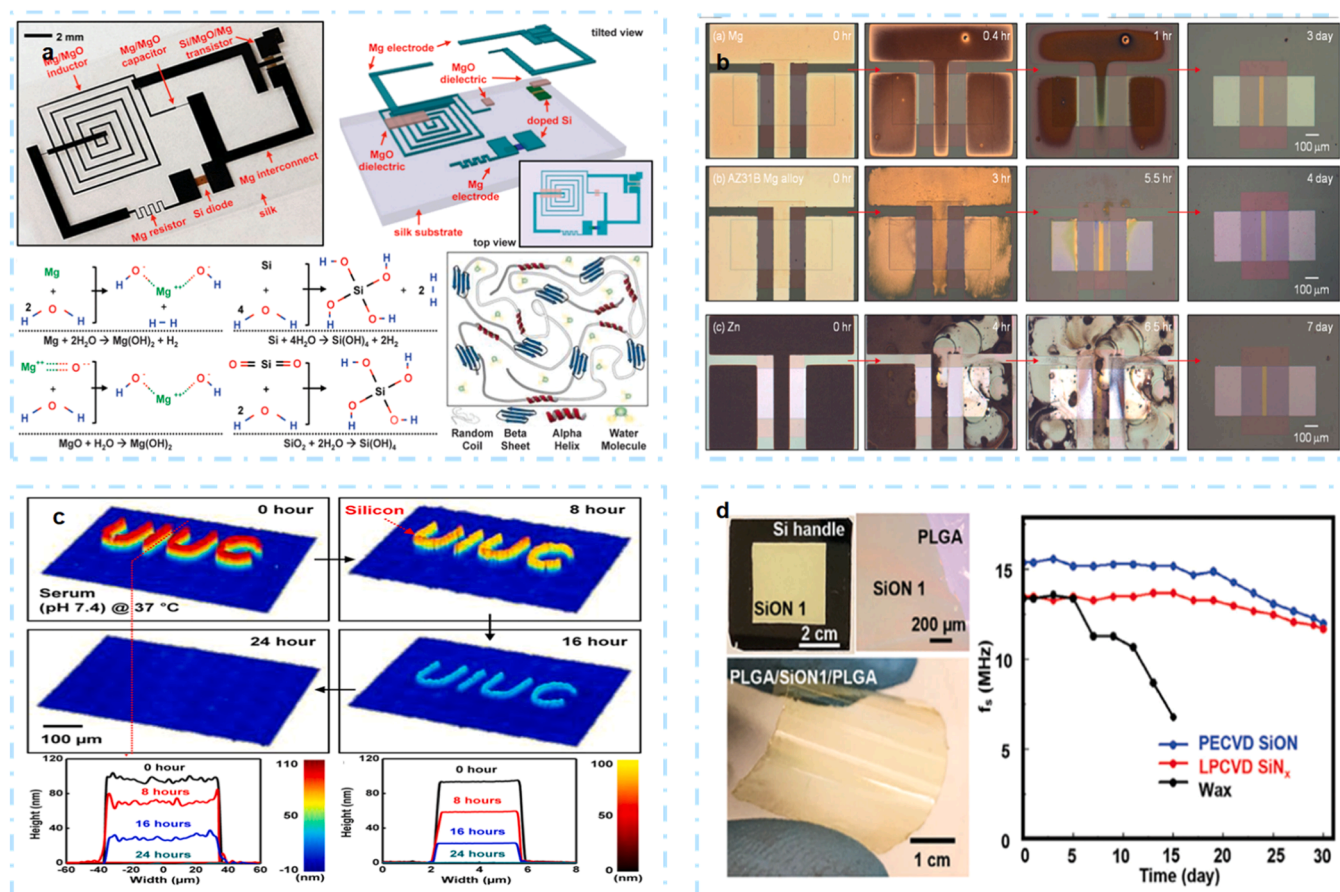


Fig. 7. | Material basis of transient electronics and bioabsorbable devices. a, Transient silicon electronics demonstrates dissolvable device architectures such as ultra-thin Si, Mg interconnects, MgO dielectric layers and silk fibroin encapsulation. Copyright 2012, American Association for the Advancement of Science. b, Soluble metal electrodes are used in transient interconnects, electrodes and antennas, and their dissolution behavior is controlled by material type, thickness, grain size and morphology. Copyright 2013, Wiley-VCH. c, Si nanomembranes and related materials are gradually hydrolyzed to soluble silicic acid products in a physiological environment, which shows the bioabsorbable potential of active semiconductor devices. Copyright, 2014 American Chemical Society. d, Transient packaging and programmable barrier strategy are used to adjust water entry, function maintenance and device degradation time. Copyright 2024, Wiley-VCH. The Figure summarizes the conductor, semiconductor, dielectric layer and encapsulation material library required for material symbiosis, and emphasizes "programmable lifetime" rather than simple rapid degradation.

cycle through the ratio of lactic acid/glycolic acid, which is suitable for the treatment window of weeks to months; PCL degradation is slow, which is suitable for systems requiring longer mechanical support; Silk fibroin and chitosan have good biocompatibility and interface modifiability, which are suitable for soft tissue contact. For transient devices, the task of the encapsulation layer is not to permanently block body fluids [67,79,81], but to provide "programmable barriers" [11,12,82,83], delay the entry of water during the service period, gradually lose the barrier function after the task, and degrade the internal functional layer according to the design path.

Conductor material is one of the most challenging parts of transient electronic devices. Traditional gold, platinum, copper and other conductors have excellent electrical properties, but they are difficult to degrade in vivo. Absorbable metals such as magnesium, zinc, iron, molybdenum and tungsten provide alternatives to transient interconnects, electrodes and antennas [11,83]. Rogers' team systematically studied the role of soluble metals in transient electronics, indicating that the thickness, morphology and chemical composition of metals can adjust their dissolution time (Fig. 7b). Magnesium metal has high conductivity and fast hydrolysis, which is suitable for short-life interconnection; The degradation of zinc and iron metals is slow, which is suitable for the conductive function window for a long time; Molybdenum and tungsten can be dissolved in thin film scale, which is suitable for high-precision conductive materials of microelectronic

structures. It should be emphasized that conductor materials can not only be "soluble" for implanted electrodes, but also meet the requirements of charge injection ability, electrochemical stability, interface impedance and degradation product safety. Otherwise, ions, gases and local pH changes released during the degradation of conductor materials may in turn affect the tissue microenvironment.

Semiconductor materials determine whether transient devices can realize active sensing, signal amplification, logic operation and wireless communication. single-crystalline silicon nanomembranes are the most mature transient semiconductor platforms at present [23,78,83]. Rogers' team proved that the nanoscale silicon film can not only maintain good electronic properties, but also gradually hydrolyze to soluble silicic acid products in an aqueous environment (Fig. 7c); Kang et al. further clarified the dissolution behavior of silicon oxides and nitrides in transient electronics, providing a chemical basis for regulating life through thickness, doping and packaging structure (Fig. 7d). Previous studies have shown that the dissolution rate of silicon nanofilms in phosphate buffer at 37 °C is about $2.9 \times 10^{-5} \text{ nm d}^{-1}$, which means that silicon nanofilms with a thickness of 100–300 nm can provide a working window of weeks to months. Unlike bulk silicon materials, nano film silicon can be flexible, processable and degradable at the same time [33,78,83], and can be conformally contacted with soft tissue and reduce mechanical mismatch.

The dielectric and insulation also need to have transient

characteristics. Inorganic dielectric materials such as silica, silicon nitride and magnesium oxide can be gradually dissolved by hydrolysis and ion exchange. For example, silica is finally converted into orthosilicic acid, which can be tolerated and excreted by the body. Organic dielectric materials such as silk fibroin, chitosan, polyvinyl alcohol, PLGA and gelatin have better flexibility and biocompatibility. The

evaluation criteria for transient dielectrics should not only be based on dielectric constant and breakdown strength, but also on water penetration, ion migration, degradation by-products and interface stability. For sensors that need long-term stable signal acquisition, premature water absorption in the dielectric layer will lead to the increase of leakage current and signal drift; For devices that need to disappear on

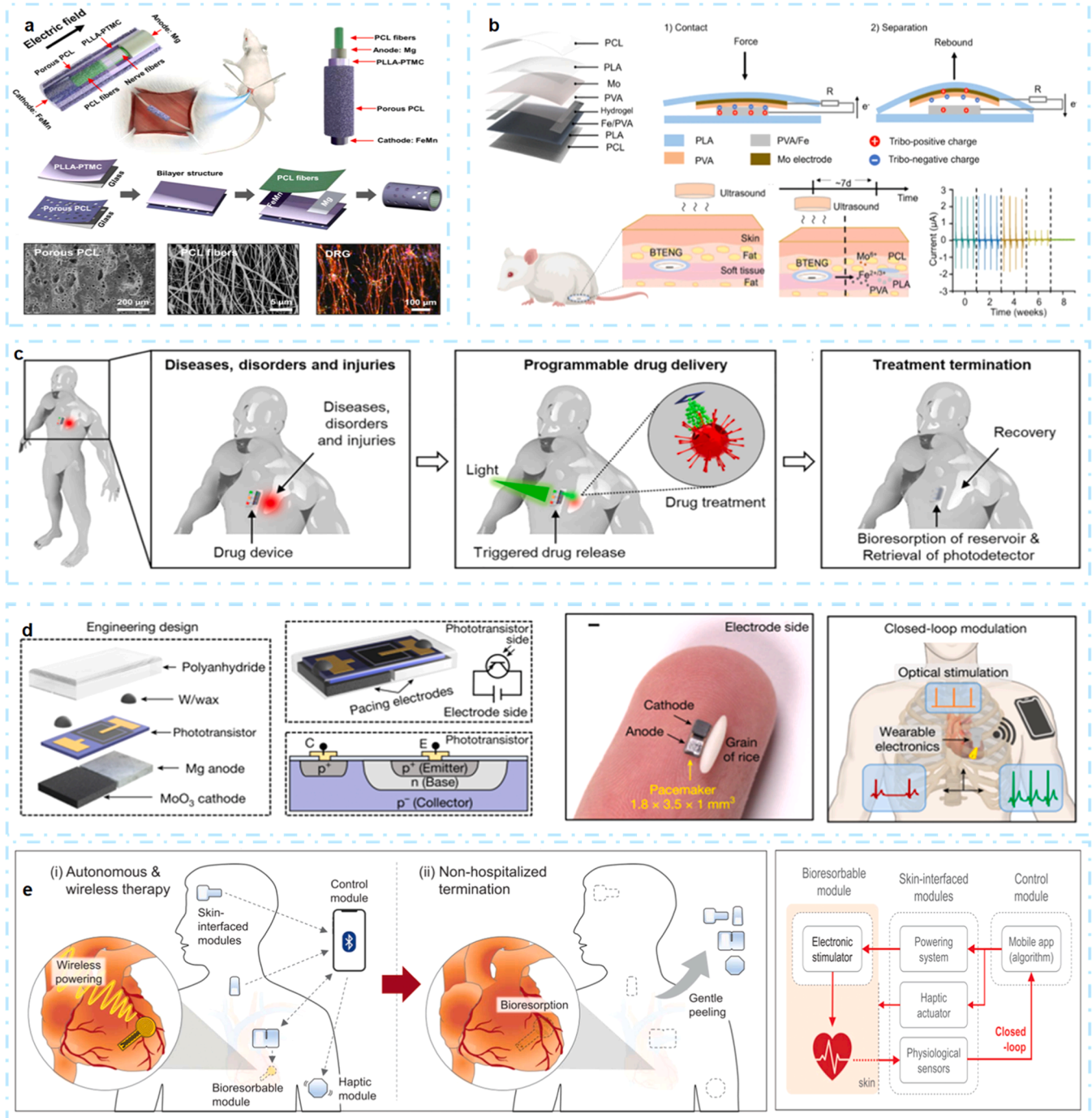


Fig. 8. | biodegradable self-powered therapy system and transient closed-loop electrotherapy platform. a, Biodegradable self-powered nerve regeneration device couples absorbable materials, electrical stimulation output and nerve repair function. Copyright 2020, American Association for the Advancement of Science. b, The fully degradable triboelectric vagus nerve stimulator can produce low-level VNS through degradable TENG, which can be used for heart failure related cardiac remodeling intervention, and can accelerate degradation after treatment. Copyright 2026, Springer. c, Self-powered, light controlled and bioabsorbable platforms realize programmed local drug release [84]. Copyright 2023, National Academy of Sciences. d, Millimeter scale absorbable optoelectronic electrotherapy system supports minimally invasive delivery, wireless light control and cardiac electrotherapy. Copyright 2025, Springer. e, The transient closed-loop wireless skin-interfaced electrotherapy network integrates sensing, control and stimulation into a short-term autonomous therapeutic system. Copyright 2022, American Association for the Advancement of Science. The Figure shows the system evolution of material symbiosis from "material degradability" to "functional transience".

time, the dielectric layer should not be too inert, otherwise it will delay the overall degradation.

The core of the material library design of transient bioelectronics is to match the degradation time of different functional layers. If the package fails prematurely, the device may lose its function before the end of the treatment window; If the degradation of the conductor and semiconductor is too slow, residual fragments may be left in the body; If different degradation products interact, it may also change the local pH and inflammatory response. Therefore, the pursuit of transient electronics is not the fastest degradation, but "programmable lifetime". Different clinical scenarios require different time scales: postoperative pressure and temperature monitoring may take only a few days, nerve repair and tissue regeneration may take weeks to months, and bone healing monitoring may require a longer cycle. The goal of material symbiosis is to match the device life with the disease process, tissue repair speed and treatment task.

3.3. Biodegradable self-powered therapeutic system: from material transients to functional transients

In the material system of transient Bioelectronics, the meaning of degradable energy devices is not only "power generation", but also the direct connection between energy symbiosis and material symbiosis. Traditional self-powered implantable devices emphasize the collection of mechanical energy from human movement, respiration, heartbeat and organ deformation; The symbiosis of materials further requires that energy collectors, stimulation electrodes, encapsulation layers and interconnection structures themselves should not become permanent foreign bodies. For applications such as postoperative monitoring, short-term nerve stimulation, tissue repair, heart failure intervention and local drug release, the device only needs to provide electrical energy, electrical stimulation and control signals in a limited treatment window; After the task is completed, the system should be degraded gradually like an absorbable suture to avoid secondary removal.

The concept of "biodegradable TENG as an implantable power supply" has been discussed earlier. This section will focus on the development of "biodegradable self-powered therapy system". One of the representative directions is the direct coupling of degradable energy converters to neuromodulation and tissue repair tasks. The fully biodegradable and self-powered nerve regeneration device reported by Wang et al. Combines biodegradable materials, electrical stimulation output and tissue repair functions, indicating that the transient electronic system can not only disappear, but also actively participate in the nerve repair process before disappearance (Fig. 8a). This kind of work has promoted degradable electronics from "material display" to "treatment intervention", so that the degradable properties of materials really serve the treatment function.

Furthermore, the fully degradable triboelectric VNS [85] reported by Ouyang et al. and Tang and other collaborators provides a more complete system case for material symbiosis. The device uses a degradable triboelectric structure to generate nerve stimulation signals for low-level vagus nerve stimulation to intervene in different stages of heart failure and cardiac remodeling. Its output reaches 9.07 ± 0.43 V open-circuit voltage and 4.19 ± 0.14 μ A short-circuit current, which can support 4 weeks of stable electrical stimulation and accelerate degradation through ultrasound triggering (Fig. 8b). The data are of great significance: on the one hand, the microampere output matches the low-level vagus nerve stimulation demand; On the other hand, the 4-week stable work covered the key intervention window in the small animal heart failure model; More importantly, ultrasound triggered degradation [85] makes the device life no longer completely determined by the passive hydrolysis process of the material, but can be actively terminated according to the treatment process.

Therefore, the evaluation criteria of degradable energy devices should be further extended from the conventional open circuit voltage, short circuit current and power density of TENG to the treatment related

indicators. For vagus nerve stimulation, whether the output current falls within the safe and effective range, whether the stimulation frequency matches the neuromodulation target, and whether long-term peripheral nerve electrical stimulation changes the heart rate variability and myocardial remodeling process are far more important than simply pursuing higher voltage. For nerve regeneration and tissue repair, whether the device can maintain peripheral nerve electrical stimulation within the regeneration window, whether it can disappear after repair, and whether degradation products affect local inflammation and cell behavior are the core issues of material symbiosis.

Another meaningful direction to incorporate material symbiosis is self-powered, light controlled and wireless triggered absorbable treatment platforms. The self-powered, light controlled and bioabsorbable platforms reported by Zhang's team. are used for programmed drug delivery [4,86], suggesting that the transient system is not limited to electrical stimulation, but can also control the drug release process through energy conversion and external triggers (Fig. 8c). The value of this kind of platform is to integrate the "energy-actuator-therapeutic load" into a disappearable system, so that the device can gradually exit after completing a specific task in the body. Compared with traditional drug delivery stents and long-term implantable pumps, absorbable platforms are more suitable for short-term, local and programmable intervention scenarios.

In this regard, the degradable self-powered therapeutic system should not be understood as the replacement of traditional TENG materials with simple degradable materials, but as a "functional transient" system engineering. The fully degradable self-powered nerve repair device, fully degradable triboelectric vagus nerve stimulator and self-powered optically controlled absorbable drug delivery platform jointly show that the key to material symbiosis is not to let the material degrade passively, but to treat the device as a degradation system, and its functional life, treatment window and material degradation cycle are designed in the same system.

3.4. Wireless power supply, closed-loop control and transient electrical stimulation for degradable systems

If the degradable self-powered device answers the question of "how to generate energy and therapeutic stimulation signals in the body", then the wireless energy supply, closed-loop control and transient electrical stimulation system further answers the question of "how to convert the energies into controllable treatments". Mechanical energy in the body is often intermittent and fluctuating, and respiration, heartbeat, gastrointestinal peristalsis and limb movement do not always provide stable input. Nerve stimulation, cardiac pacing, tissue repair and drug delivery usually require more controllable timing, amplitude and frequency. Therefore, a complete material symbiosis system needs not only biodegradable materials, but also collaborative design schemes of wireless energy supply, power management, signal control and treatment feedback.

The wireless absorbable electronic system developed by Rogers' team provides an important demonstration for transient peripheral nerve electrical stimulation in nerve repair. The system is composed of fully bioabsorbable and biocompatible circuit elements and substrates, which can perform wireless and programmable peripheral nerve electrical stimulation, and enhance nerve regeneration and functional recovery through multiple peripheral nerve electrical stimulation in rodent models [87]. The significance of this work is that it promotes the degradable electronic system from the "passive monitoring" to the "active treatment" stage: the device provides electrical stimulation in the nerve damage repair window, and then gradually absorbs it to avoid the residue of permanent electrodes and wires.

Since then, the transient electrical stimulation system has further expanded to miniaturization, closed-loop and multi scene electrotherapy. The millimeter scale bioabsorbable optoelectronic electrotherapy system reported by Zhang's team. Integrates on-chip power

supply, wireless optical control and absorbable materials. It can achieve minimally invasive delivery through percutaneous injection and intravascular delivery, and demonstrate effective pacing in mouse, rat, pig, dog and human heart models. The system can also be paired with skin interface wireless devices to realize autonomous closed-loop operation after detecting arrhythmia (Fig. 8d) [88]. Compared with the early wireless pacemaker, the key progress of this kind of system lies in its smaller size and more minimally invasive implantation path, and it has begun to move from a single stimulator to the system architecture of "absorbable device absorbable device-skin-interfaced controller-closed-loop algorithm architecture".

The above closed-loop trend is particularly important for symbiotic electronic equipment. Material symbiosis is to solve when the equipment disappears, while information symbiosis is to solve how the equipment adjusts the treatment according to the host state. If the absorbable electrical stimulator can only have a fixed output, its clinical adaptability is still limited, but if it can be combined with tissue-conformal interfaces sensing, wireless control and algorithm decision-making, it can dynamically adjust the stimulation according to the heart rhythm, nerve activity, muscle state and tissue repair process in the treatment window. For example, the transient, closed-loop, wireless body skin-interfaced electrotherapy network reported by Choi's team. Provides an important reference for this direction: multiple wireless, wearable and implantable nodes can work together during the short-term treatment process and exit and remove when they are not needed (Fig. 8e). The significance of this work is that it promotes the transient electrotherapy from a single absorbable stimulator to a multi node collaborative system, so that the short-term treatment has the system capability of on-demand startup, spatial distribution regulation and exit after the task is completed.

Therefore, this section focuses on several types of technical routes for material symbiosis to systematic treatment: wireless absorbable nerve stimulation, leadless absorbable temporary pacing, millimeter scale absorbable optoelectronic electrotherapy, and transient closed-loop electrotherapy network. All the works show that material symbiosis is not an isolated material problem, but a system engineering of collaborative design of energy, control, electrotherapy stimulation and degradation behavior.

3.5. biodegradable piezoelectric electrical materials and self-powered regeneration: material is the treatment interface

Although TENG occupies an important position in self-powered biodegradable implants, piezoelectric and self-powered materials are becoming another important frontier of material symbiosis. Piezoelectric materials can generate charge under mechanical strain [89,90], and can also generate mechanical response under an applied electric field, which has the functions of energy collection, sensing and therapeutic stimulation. Bones, tendons, myocardium, nerves and other tissues have complex electrical mechanical coupling characteristics. Cells can also sense local electric fields and mechanical stimulation. Therefore, the introduction of the piezoelectric effect and self-powered functions into biodegradable biomaterials is expected to form a treatment method closer to the physiological process of tissues. The material generates local electrical signals under tissue movement, rehabilitation training and external mechanical stimulation to promote bone regeneration, nerve repair, wound healing and myocardial regulation. After treatment, the material is degraded with the device.

Traditional high-performance piezoelectric materials mainly include PZT, barium titanate and other inorganic ceramics. They have high voltage coefficients and stable output, but they are usually rigid and non-degradable, and some systems have heavy metals and long-term biosafety problems. For bioabsorbable implants, non-degradability and mechanical mismatch are fundamental limitations. Therefore, the development goal of biodegradable piezoelectric materials is not to simply replace PZT, but to establish a new balance between piezoelectric

properties, flexibility, biocompatibility and degradation behavior. What this field pursues is not the highest piezoelectric constant, but an absorbable piezoelectric platform that can meet the needs of bioelectrical stimulation and sensing.

Biodegradable piezoelectric materials can be divided into natural piezoelectric materials and synthetic biodegradable piezoelectric and biodegradable piezoelectric polymers. Natural materials include collagen, gelatin, silk fibroin, cellulose, chitin, amino acids and peptides. Many natural polymers exhibit measurable piezoelectric responses due to chain orientation, hydrogen bond networks and non-centrosymmetric structures. Although its piezoelectric coefficient is usually lower than that of inorganic ceramics, it is attractive for soft tissue interfaces and low-power biological stimulation. In particular, collagen and bone tissue have piezoelectric properties. Electrical signals induced by mechanical load are considered to be involved in bone remodeling and cell behavior regulation. Therefore, the use of natural piezoelectric and self-powered materials for bone repair and soft tissue regeneration has clear biomimetic rationale.

PLLA material is particularly important in the synthesis of degradable and degradable electrical polymers [90]. PLLA has good biocompatibility, processability and clinical basis. Its molecular chain can be oriented in the process of stretching, annealing and electrospinning, resulting in a stable piezoelectric response. Although the piezoelectric property of PLLA is lower than that of high-performance ceramics, it is sufficient for flexible sensing, low-power energy collection and local electrical stimulation. By adjusting the molecular weight, crystallinity, orientation and device structure of PLLA, its mechanical properties, piezoelectric output and degradation time can be adjusted at the same time. Compared with non-biodegradable piezoelectric electroceramics, polymers such as PLLA are more suitable for the construction of absorbable scaffolds, patches, nerve conduits and tissue engineering interfaces.

The application of biodegradable piezoelectric and self-powered systems is first focused on bone and nerve repair. Human bone is a typical force sensitive tissue. Mechanical loading can regulate osteogenic behavior through piezoelectric, electrochemical and cellular mechanical transduction pathways. In the bone defect model repair experiment, if the implanted material can produce local electrical stimulation and local therapeutic electrical stimulation during the patient's exercise and rehabilitation training, it may couple mechanical rehabilitation with electrical therapy. Nerve tissue is also highly sensitive to electrical signals. Moderate peripheral nerve electrical stimulation can affect neurite growth, Schwann cell behavior and axon regeneration. The fully degradable and self-powered nerve regeneration device reflects this idea: the material is not only a passive scaffold, but provides local electrical therapeutic stimulation in the repair window, and then gradually degrades.

Piezoelectric and self-powered materials also have potential for wound healing and drug delivery. Absorbable electroactive dressings can generate a weak electric field by body movement and external mechanical pressing to regulate cell migration, angiogenesis and inflammatory reactions. The self-powered and light controlled absorbable drug delivery platform shows that the material system can achieve programmed treatment through external triggers and endogenous energy. The directions indicate that the "material" in material symbiosis is not only the substrate for carrying the circuit, but can also directly become the treatment interface, energy conversion interface and biological signal regulation interface.

However, biodegradable piezoelectric electrical materials are still in the early stage of development. First of all, there is often a contradiction between piezoelectric properties and degradability: This is because higher piezoelectric response usually requires materials with high crystallinity, strong orientation and stable crystal structure, and the factors may reduce the degradation rate of materials. Secondly, the water, ions and proteins in body fluids will affect the piezoelectric output and polarization state. Third, material safety should not only

evaluate the initial material, but also systematically study degradation products, local pH changes and long-term tissue reactions. Fourth, there are great differences in piezoelectric coefficient, output voltage, mechanical loading conditions and degradation test methods among different studies, so it is urgent to establish a standardized evaluation system.

From the perspective of symbiotic bioelectronics, the greatest value of degradable and self-powered materials lies in "material is function" [90]. They do not necessarily rely on complex circuits to transform tissue movement into local electrical signals, and can also be used as scaffolds, dressings, electrodes and energy units, and participate in tissue repair. They can also degrade naturally at the end of the mission to avoid permanent residue. In the future, if we can combine biodegradable piezoelectric electrical materials, self-powered electrical stimulation, wireless energy supply and closed-loop sensing, it is possible to build a more complete material symbiosis platform, so that the material itself can be transformed from a passive support structure to an active biological interface that can be capable of sensing, powering, therapy, and task-defined disappearance according to the task.

4. Information symbiosis: closed loop and self decision system

4.1. From open-loop treatment to information symbiosis

Most traditional implantable and wearable treatment devices operate in open-loop mode. For example, the cardiac pacemaker outputs electrical pulses at a preset frequency, the deep brain stimulator continues electrical stimulation according to fixed parameters, and the drug pump releases drugs at a set rate. Such methods can play a therapeutic role in scenarios with relatively stable physiological needs and a wide treatment window. However, for epilepsy, Parkinson's disease, chronic pain, heart failure, neuromuscular spasm and other diseases with obvious fluctuations, fixed treatment parameters are often difficult to take into account the efficacy, energy consumption and side effects at the same time. The fundamental issue with open-loop therapy is that the absence of real-time device feedback may result in overtreatment, high energy consumption, and side effects associated with therapeutic stimulation.

The core of closed-loop treatment is to transform "treatment output" into "state dependent regulation". The system first senses the key physiological signals of the tissue, then identifies the disease status and the degree of treatment demand through the algorithm, and finally delivers therapeutic agents in a specific dose, time sequence and spatial location. Electrophysiological signals, electrochemical signals and mechanical signals are used as multimodal inputs [91], which are transformed into precise treatment output schemes through state identification and decision-making algorithms, and enter the next round of perception learning analysis state through treatment feedback. Thus, the device is no longer just an electronic tool for one-way execution of instructions, but an intelligent system that can continuously read the host state [92, 93] and dynamically adjust the treatment strategy [94–96].

Neuropace responsive neurostimulation system (RNS) monitors EEG activity through intracranial electrodes for a long time, and delivers a short string of electrical stimulation when detecting paroxysmal abnormal discharges. It is a representative system of closed-loop neuromodulation for clinical application. The long-term follow-up results show that the system can significantly reduce the attack burden of patients with drug-resistant focal epilepsy, indicating that the equipment does not need continuous intervention, but can intervene on demand when pathological activities occur, so as to reduce ineffective electrical stimulation and energy consumption.

Similar ideas have also been extended to mental illness and cardiovascular electrotherapy. The individualized closed-loop neuromodulation system reported by Chang and Krystal's team identifies biomarkers related to patients' specific depressive symptoms through multi-day intracranial electrophysiological records and converts them

into trigger signals of chronic implantable devices [14]. Although this study is a single case study, it proves to a certain extent that closed-loop treatment can move from "universal threshold" to "patient-specific biomarker-driven". Rogers and Efimov's teams further introduced the closed-loop idea into absorbable cardiac electrotherapy: millimeter scale bioabsorbable optoelectronic systems can achieve single and multi-point pacing in a variety of animal and human heart models through percutaneous injection and intravascular delivery, and can pair with skin interface wireless devices to automatically start closed-loop pacing after detecting arrhythmia. The work together show that closed-loop treatment is moving from a single threshold trigger patient-specific biomarkers, scene specificity and system integrated regulation.

Therefore, information symbiosis is not simply to add auxiliary sensors to the device, but to establish a two-way information exchange between the device and the host. The electrophysiological, chemical and mechanical states of the host are continuously read by the device, and the device then adjusts the electrotherapy stimulation, electrotherapy, drug release and other intervention methods according to the states. More importantly, devices should be designed together from three dimensions: information symbiosis, energy and materials: sensing and computing will increase power consumption, which must be matched with self-powered and wireless power supply strategies. The closed-loop interface requires long-term stability of the equipment and must rely on materials with low impedance, low inflammation and mechanical matching. If the equipment is used for temporary treatment, its perception, calculation and actuation modules also need to match the material degradation cycle. Thus, the closed-loop treatment has changed from a simple control strategy to an intelligent layer of symbiotic electronic equipment, enabling the symbiotic electronic equipment to change from a passive treatment to an active treatment platform that continuously adapts to the host state [97–100].

4.2. Sensing Materials: Capture High-quality Physiological Signals

The upper limit of the performance of any closed-loop system depends first on the sensor. If the input signal is unstable, nonspecific and the noise is too high, the complex algorithm can only amplify the error. Therefore, the first layer of information symbiosis is based on sensing materials [101–103]. Different from traditional diagnostic neuromodulation, sensors in closed-loop bioelectronic systems must work in motion, humidity, complex ion environment and long-term tissue contact, and meet the requirements of high sensitivity, low drift, biocompatibility, mechanical matching and low power consumption.

Fig. 9 summarizes the representative sensing materials and device interfaces that can be used in the information symbiosis system. Fig. 9a shows the flexible bioelectronic materials for chronic neural interfaces, including flexible electrodes [104–106], soft substrates and tissue-conformal interfaces that can be used for long-term recording and peripheral nerve electrical stimulation of the brain and peripheral nervous system [107–109]. The materials together show that the key to electrophysiological perception is not only conductivity, but also thickness, flexibility, interface impedance, chronic inflammatory reaction and long-term mechanical stability [110,111]. Conductive polymers, carbon nanotube networks, graphene [112,113], MXene, liquid metals and metal nanogrids and other materials can form a continuous conductive path in the flexible substrate and maintain electrical connection during tissue movement. Their significance is that they transform the abrupt contact between the traditional rigid electrode and the soft tissue into a more stable and less damaging long-term information exchange interface, so as to provide reliable high-quality input signals for the closed-loop system.

In addition to planar flexible electrodes, one-dimensional soft bioelectronic fibers [103,115] are becoming an important material choice for multimodal sensing and electrical stimulation. The high-density soft bioelectronic fibers shown in Fig. 9b can integrate a variety of functional

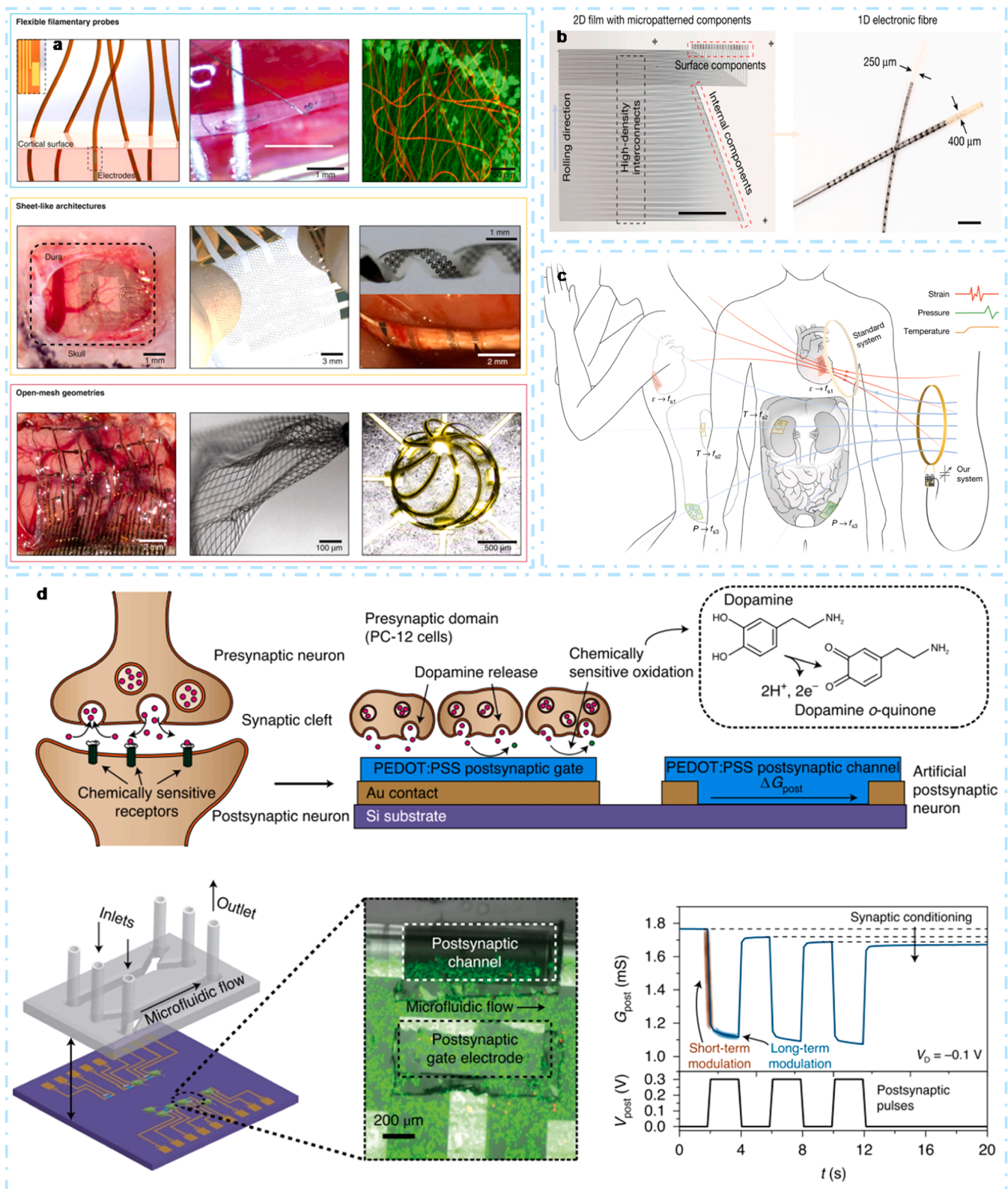


Fig. 9. | Sensing materials and multimodal signal interfaces of information symbiosis system. **a**, Flexible chronic neural interfaces materials are used for long-term brain and peripheral nerve recording/peripheral nerve electrical stimulation, emphasizing low impedance, flexibility and tissue conformal contact [29]. Copyright 2020, Springer. **b**, High density soft bioelectronic fibers can integrate multimodal sensing and therapeutic stimulation units, which are suitable for soft tissue and dynamic organ interfaces [34]. Copyright 2025, Springer. **c**, Soft biodegradable wireless implanted sensors support deep tissue signal reading and can be bioabsorbed after task completion [35]. Copyright 2026, Springer. **d**, Neurotransmitter mediated biological mixed synaptic devices display the coupling of electrochemical signals and organic neural morphological devices [114]. Copyright 2020, Springer. The Figure indicates that the input layer of information symbiosis should be expanded from a single electrical signal to multi-modal states such as electrophysiology, mechanical signals, electrochemistry and neurotransmitters.

units for continuous motion monitoring and nerve electrical stimulation. This kind of fiber structure has smaller implantation volume, higher channel density and better tissue adaptability, which is expected to be used for long-term multimodal real-time monitoring in the intestine, nerve, muscle and soft tissue. Compared with traditional chip devices, the fibrous interface is more suitable for coupling with slender [25], dynamic and curved structures, and also provides richer spatial sampling capabilities for future closed-loop systems.

For temporary monitoring tasks, biodegradable wireless sensors further connect information symbiosis and material symbiosis [3,23]. The soft biodegradable implantable sensor can enable wireless readout of sensor responses over a long distance and a wide angle range for monitoring deep physiological signals such as pressure, temperature and strain (Fig. 9c) [116]. The important significance of the system is that the sensor can provide a stable signal in the treatment and monitoring window, and realize degradation after the task is completed, so as to reduce the burden of long-term foreign bodies in the body. For the scenarios of postoperative monitoring, tissue repair and short-term functional evaluation, this "perceptible, readable and disappearable" sensing platform especially meets the cross needs of material symbiosis and information symbiosis.

Electrochemistry and neurotransmitter perception provide another kind of key evidence for closed-loop treatment [117–123]. The biological mixed synaptic devices shown can couple organic electronic devices with dopaminergic cells to achieve neurotransmitter mediated synaptic plasticity (Fig. 9d). This shows that in the future, the reading of closed-loop systems should not be limited to potential and impedance changes, but can also be extended to molecular states such as dopamine, glutamate, glucose, lactic acid, pH and inflammatory factors [117–121]. For Parkinson's disease, epilepsy, metabolic diseases and inflammatory diseases, electrochemical signals may reflect disease status and treatment response more intuitively than single electrophysiological signals. In contrast, traditional closed-loop systems rely on potential, impedance, local field potential, EEG, ECG and myoelectric and other electrophysiological signals to indirectly judge disease status, and rely on intermittent clinical indicators such as symptom score, imaging examination and blood/body fluid detection to evaluate treatment response. The methods can capture nerve discharges, abnormal rhythms and changes in muscle activity, but it is often difficult to reflect the dynamic changes of neurotransmitters, metabolites, inflammatory factors and the local microenvironment in time. Therefore, the introduction of electrochemistry and molecular sensing into the closed-loop system is expected to make the neuromodulation move from "feedback control driven by electrical activity" to "precise regulation assisted by molecular state".

Therefore, the evaluation of sensing materials should not only focus on sensitivity, but also focus on the systematic optimization of closed-loop treatment tasks. Epilepsy requires high spatiotemporal resolution and low-noise EEG and local field potential recording [104,105,124]; Cardiovascular closed-loop regulation requires continuous assessment of ECG [61], hemodynamics and autonomic nerve status; Facial spasm requires accurate identification of transient, local and involuntary muscle activity; Tissue repair requires low drift mechanical and inflammatory signal monitoring. The future information symbiosis system is likely to adopt multimodal sensing, combining electrophysiological, electrochemical, mechanical and optical signals [125]. The accuracy of comprehensive judgment can be improved through redundant information and AI learning, which can reduce the misjudgment caused by signal drift when using a single sensor.

4.3. Decision Making Framework: From Threshold Logic to neuromorphic computing

If the sensing material determines what the closed-loop system "sees", then the decision-making architecture determines how the system understands the signal and takes action. Early closed-loop treatment

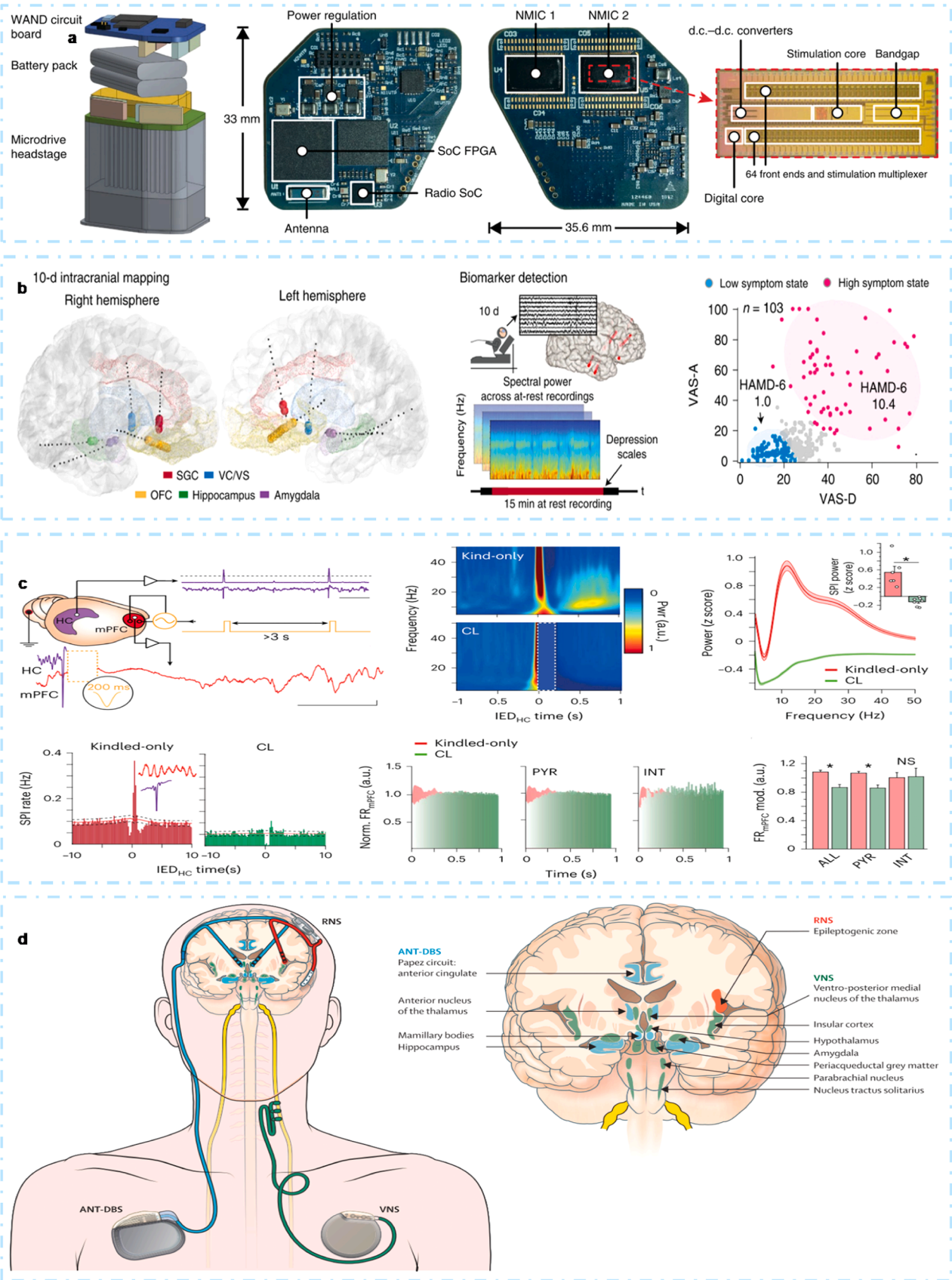
usually uses threshold logic [4,6], and pacing when the heart rate is lower than a certain value; Intracranial electrical stimulation when a specific waveform appears in the intracranial EEG; The intervention is triggered when the EMG amplitude exceeds the preset level. The three strategies are simple, stable and low power consumption, and are suitable for scenarios where the relationship between signal and treatment needs is clear. The neural intracranial electrical stimulation of responsive neurostimulation for epilepsy, implantable defibrillator and some closed-loop functional intracranial electrical stimulation systems are all based on similar logic. The advantages of the threshold algorithm are strong interpretability, simple hardware implementation, and easier to be understood, supervised and evaluated by doctors. But its limitations are also obvious. Complex disease states cannot be defined by a single variable and a fixed threshold.

Fig. 10 shows the representative path of the closed-loop decision-making architecture from the experimental platform to clinical treatment. The wireless artifact-free neuromodulation device (WAND) is an important engineering demonstration of closed-loop neuromodulation hardware (Fig. 10a) [126]. The platform can record and multi-channel electrical nerve stimulation on 128 channels, eliminate the artifacts of multi-channel electrical nerve stimulation, detect nerve biomarkers and automatically adjust the parameters of multi-channel electrical nerve stimulation through on-board processing. In the awake non-human primate model, WAND verified the feasibility of wireless long-term local field potential recording, real-time multi-channel neural electrical stimulation artifact elimination and closed-loop multi-channel neural electrical stimulation [126]. The system shows that the key of the closed-loop device is not only the algorithm itself, but also the low-power and low latency hardware that can execute the algorithm in the implanted and semi implanted scenario.

Fig. 10b corresponds to the study of individualized closed-loop neuromodulation of depression. The system first searches for biomarkers related to patients' specific symptoms through multi-day intracranial electrophysiological records and local intracranial electrical stimulation, and then converts them into trigger signals of implantable devices. This study reflects the transformation of closed-loop decision-making from "general threshold" to "patient-specific brain-network state recognition" [14,92]. For epilepsy, Parkinson's disease and mental illness, this kind of individualized decision-making ability may be more important than simply increasing the number of sensing channels.

Fig. 10c shows the new application of closed-loop intracranial electrical stimulation in the intervention of epilepsy progression. Related studies have shown that the closed-loop triggering of intracranial electrical stimulation for the network activities related to epileptiform discharges can prevent pathological cortical reactions and improve long-term memory damage. The results suggest that closed-loop intracranial electrical stimulation should not only be understood as a reactive treatment after symptom onset, but also can be developed as a predictive and preventive intervention to block the progress of the disease network [6,13]. Fig. 10d summarizes the approved neuromodulation therapies in the field of epilepsy, including vagus nerve stimulation, anterior thalamic nucleus deep brain stimulation and reactive nerve stimulation. The clinical applications show that neuromodulation has clear indications for disease, nerve electrical stimulation targets and long-term management basis, and the significance of a closed-loop strategy is to further improve the matching degree between therapeutic stimulation timing, dose and patient status.

Machine learning and neuromorphic computing further promote closed-loop decision-making to low power consumption and adaptive direction [71,72,127,128]. Machine learning can recognize the onset precursor, motor state, pain level and treatment response by long-term recording of individualized physiological data [72,129,130], and adjust nerve electrical stimulation parameters according to different states. Neural morphology circuit imitates the event-driven processing with sparse coding of the biological nervous system [71,127,128], and



(caption on next page)

Fig. 10. | Closed loop decision architecture in information symbiosis. a. The WAND wireless closed-loop neuromodulation platform triggers intracranial electrical stimulation based on motor cortex activity and beta wave characteristics during delayed reach tasks, demonstrating hardware execution capabilities for real-time recording, stimulation artifact cancellation, and closed-loop control. Copyright 2019, Springer. b. Individualized closed-loop depression neuromodulation converts patient-specific neural states into treatment trigger signals through intracranial electrode localization and symptom related biomarker detection. Copyright 2021, Springer. c. Medial prefrontal cortex (mPFC) intracranial electrical stimulation responds to hippocampal interictal epileptiform discharges (IEDs), hippocampal IED-related pathological activity, and inhibits epileptic related cortical responses, suggesting that closed-loop systems can move from reactive therapy to disease progression intervention. Copyright 2025, Springer. d. The approved neuromodulation therapies in the field of epilepsy provide a clinical basis for closed-loop treatment. Copyright 2021, Elsevier. The Figure summarizes the evolution path of threshold logic, patient-specific biomarkers, and network level regulation.

only consumes energy when signal changes and events occur, which is more suitable for processing continuous streaming data such as EEG, EMG, ECG and neural discharge. This is particularly critical for self-powered symbiotic devices: if the power required for sensing and electrical stimulation is close to the limit of the energy collector, the computing module must have very low power consumption. In future research, the more feasible architecture is hierarchical decision-making: the low-level threshold logic guarantees the security boundary, the middle-level machine learning classifies the state, and the high-level doctor and remote system defines the treatment objectives and parameter range. This method can not only achieve customized treatment, but

also retain the clinical interpretability and manual intervention channel.

4.4. Actuator platforms: delivering precise therapy

The final loop of the closed-loop system is the actuator, which is the functional module that converts decision results into therapeutic actions. The actuator determines the form, spatial range, and safety boundary of the therapeutic output. The main actuation methods of current closed-loop bioelectronic systems include electrical stimulation, on-demand drug delivery, mechanical actuation, and optical modulation. Among them, electrical stimulation technology is the most mature

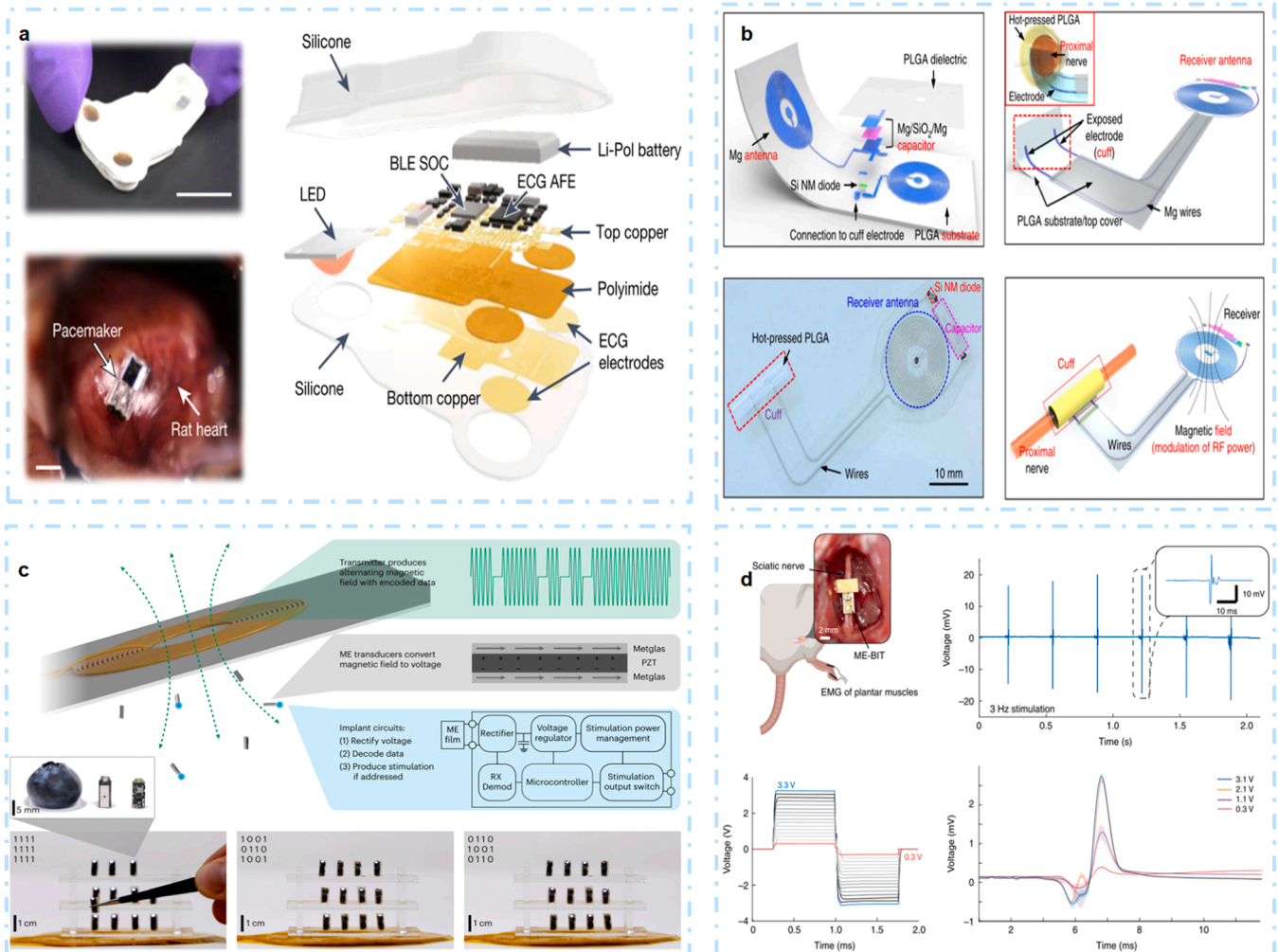


Fig. 11. | The actuator platform in the information symbiosis system. a. The millimeter scale bioabsorbable optoelectronic electrotherapy system achieves minimally invasive cardiac electrotherapy through wireless optical control and can be paired with tissue-conformal interfaces electronic interfaces for closed-loop pacing [27]. Copyright 2025, Springer. b. The wireless bioabsorbable neural stimulator delivers programmable electrical stimulation within the neural repair window and gradually absorbs it after treatment [87]. Copyright 2018, Springer. c. A distributed battery-free implant network based on magnetoelectric coupling achieves collaborative therapy through multi node wireless power supply and stimulation [131,132]. Copyright 2026, Springer. d. The intravascular millimeter level magnetoelectric nerve stimulator can be minimally invasive delivered to the vicinity of peripheral nerves through the vascular pathway [132]. Copyright 2022, Springer. This diagram emphasizes the evolution of actuators from traditional single point stimulation modules to minimally invasive, wireless, absorbable, and networked treatment platforms.

and has been widely used for cardiac pacing, defibrillation, deep brain stimulation, spinal cord electrical stimulation, vagus nerve stimulation, and peripheral neuromodulation; Drug delivery is suitable for molecular therapy scenarios such as metabolism, inflammation, and tumors; Mechanical actuation is suitable for soft tissue traction, rehabilitation assistance, and mechanical microenvironment regulation; Optical modulation has high spatial selectivity in optogenetics and local electrotherapy.

Fig. 11 shows a representative actuator platform in the information symbiosis system. The millimeter scale bioabsorbable optoelectronic electrotherapy system shown can serve as a representative of the absorbable actuator platform in information symbiosis (Fig. 11a). The system combines minimally invasive delivery, wireless control, cardiac electrotherapy, and material absorption characteristics, indicating that the actuator is no longer just a single stimulus output module, but can become the execution end in the "absorbable device-skin-interfaced controller-closed-loop algorithm architecture" system architecture.

The wireless absorbable neural stimulator shown represents the transient electrical stimulation actuator in neural repair scenarios (Fig. 11b) [87,133,134]. The significance lies not in repeatedly proving that absorbable materials can degrade, but in matching the therapeutic output, tissue regeneration window, and material lifespan.

Figs. 11c and 11d show the magnetoelectric coupling wireless power supply and electrical stimulation platform. Distributed battery-free bioelectronic implants can achieve wireless energy and data transmission through magnetoelectric mechanisms and support multiple millimeter level nodes to form a network [109,131,132]. The intravascular millimeter level magnetoelectric implant provides a minimally invasive delivery pathway for peripheral nerve stimulation. This type of platform indicates that future actuators may not necessarily be single implanted modules, but may be collaborative devices of multiple wearable, implantable, absorbable, and replaceable nodes. For information on symbiotic systems, multi node actuators can advance therapy from "single point therapeutic stimulation" to "distributed control" [109, 135].

The core of the electric stimulation actuator is still the electrode material and tissue interface. Ideal electrodes require high charge injection capacity, low impedance, good electrochemical stability, and long-term biocompatibility. Traditional platinum, platinum-iridium alloys, and iridium oxide materials have good stability but high rigidity. Conductive polymers such as PEDOT have lower modulus and higher volumetric capacitance, making them more suitable for flexible neural interfaces. Carbon based materials and metal nanostructures can reduce interfacial impedance by increasing the effective interfacial area. Low impedance interfaces are particularly important for closed-loop electrical stimulation because high impedance not only increases energy consumption, but also amplifies stimulation artifacts and thermal effects. Low impedance interfaces [62,136,137], leading to abnormal temperature rise, electrochemical side reactions, and local inflammation in the tissue around the electrode, thereby affecting the safety and long-term recording quality of electrical stimulation.

Therefore, the evaluation of closed-loop actuators should not only focus on output strength, but also analyze treatment accuracy, tissue safety, energy efficiency, and lifecycle matching. High intensity electrical stimulation may improve short-term efficacy, but it can also increase side effects and energy consumption. Continuous therapeutic stimulation is simple and reliable, but it may lead to decreased tissue adaptability and unnecessary burden. Active on-demand stimulation is more precise, but relies on real-time, stable, and disease-specific state perception, as well as low latency, interpretable, and safe closed-loop decision-making. In the future, actuators will develop towards multi-modality, low power consumption, and programmability [53,138]: the same platform can select electrical stimulation, drug release, mechanical adjustment, and optical modulation based on the disease state; The same stimulator can dynamically adjust the waveform and spatial distribution based on feedback; For temporary treatment, neuromodulation

actuators should also be symbiotic with the material and degrade and safely exit after completing the treatment.

4.5. Case study: Closed loop neural stimulation in epilepsy and motor disorders

Closed loop neural stimulation is one of the most mature and clinically convincing directions for information symbiosis. Diseases such as epilepsy, Parkinson's disease, muscle tone disorders, and chronic pain all have fluctuating and networked characteristics, and pathological activity is not constant, but dynamically appears in specific brain regions, time windows, and neural circuits. Traditional open-loop neural stimulation can alleviate symptoms through long-term output of fixed parameters, but it often suffers from problems such as excessive battery consumption, side effects, and complex parameter adjustment. Closed loop neural stimulation involves real-time monitoring of neural activity, delivering stimulation upon detecting pathological conditions, and continuously adjusting treatment intensity based on neural biomarkers. This model is closer to the dynamic characteristics of the disease itself and is more in line with the cyclical logic of information symbiosis "perception decision intervention re perception."

For example, the responsive neurosimulation system in drug-resistant focal epilepsy is a representative of clinical closed-loop neuromodulation. The system monitors brain electrical activity through intracranial electrodes for a long time and delivers short-term intracranial electrical stimulation to block abnormal discharge expansion when seizure-like discharges are identified. Compared with continuous intracranial electrical stimulation, reactive intracranial electrical stimulation reduces unnecessary energy consumption and tissue exposure, and provides a data basis for personalized treatment. A 9-year follow-up showed that the median frequency of seizures decreased by about 75%, with about 73% of patients achieving at least 50% reduction in seizures, and about 35% of patients experiencing a reduction in seizure frequency of 90% and more [13]. This case proves that a closed-loop system is not only a therapeutic device, but also a long-term disease phenotype recording platform: it gradually shifts treatment from group experience to individualized regulation by continuously collecting patient-specific biomarkers neural data.

Movement disorders provide another typical scenario for closed-loop neural stimulation. Deep brain stimulation has been widely used in Parkinson's disease, but traditional open-loop deep brain stimulation usually involves continuous electrical stimulation of the subthalamic nucleus and the inner part of the globus pallidus, which can lead to speech disorders, sensory abnormalities, excessive movement, and accelerated battery consumption. The adaptive deep brain stimulation (aDBS) proposed by the Brown team utilizes the β -band oscillations in the subthalamic nucleus local field potential as feedback signals to regulate the output of deep brain electrical stimulation based on the strength of pathological oscillations. This study preliminarily shows that adaptive DBS can reduce therapeutic stimulation time and energy consumption while maintaining and improving control of motor symptoms in patients with advanced Parkinson's disease, and is expected to reduce the side effects related to deep brain electrical stimulation. The significance of this strategy is that it transforms DBS from fixed deep brain electrical stimulation to dynamic therapy based on neural biomarkers: increasing neural electrical stimulation when pathological beta oscillations are enhanced, and reducing therapeutic stimulation when symptoms are relieved and physiological states change.

Although the systems have demonstrated the clinical potential of closed-loop neural electrical stimulation, existing devices still face three types of limitations. Firstly, the recording channels are limited, making it difficult to fully capture the spatial spread of disease-related networks. Secondly, most algorithms still rely on thresholds and manually set features, which lack adaptability to long-term changes in patients' states, sleep cycles, and medication cycles. Thirdly, energy consumption, packaging, and electrode stability still limit the miniaturization and

long-term reliability of equipment. Future systems require more channels, lower power data processing [139–142], more complex pattern recognition, and more flexible multi-channel neural electrical stimulation strategies. In other words, closed-loop neural electrical stimulation is moving from "reactive" to "predictive" and "adaptive": devices not only respond after pathological events occur, but also identify risk states and intervene in advance before symptoms occur.

This trend also puts forward higher requirements for symbiotic electronic devices. The sensing interface must be stable for a long time, the algorithm must be low-power and upgradable, the stimulation electrode must be safe and reliable, and the communication module must support remote monitoring and doctor supervision. If the device still needs to combine energy symbiosis and material symbiosis, further control of power consumption and lifecycle is necessary. For example, long-term epilepsy and Parkinson's disease devices may emphasize low inflammation [143–145], low power consumption [146], and upgradable algorithms [144,146–152], while postoperative and short-term neural repair devices may emphasize absorbable materials and post task degradation. Therefore, closed-loop peripheral nerve electrical stimulation is not only a clinical proof of information symbiosis, but also a testing ground for the future integration of three-dimensional symbiotic systems.

4.6. Progress in closed-loop systems and prospects for three symbiotic dimensions

The representative progress of Ouyang et al. in the field of information symbiosis is the extension of closed-loop neuromodulation from traditional implantable brain computer interfaces to lighter and more everyday wearable therapy systems. The glasses style facial spasm closed-loop system uses a flexible facial spasm sensor based on triboelectric/electrostatic induction sensing mechanism to capture abnormal muscle contractions in the face, and triggers tissue-conformal interfaces electrical stimulation upon detecting spasm events. This design is logically very suitable for information symbiotic narrative: Facial spasm is an intermittent, localized, non-autonomous movement disease, and continuous tissue-conformal interfaces electrical stimulation can increase discomfort and side effects, while on-demand therapeutic stimulation can intervene during episodes and remain silent during non-episodes. In preliminary human/clinical validation, the system achieved a spasm recognition accuracy of approximately 98.0%, indicating that non-invasive, wearable closed-loop neuromodulation has high reliability in specific disease scenarios.

From the perspective of materials and systems, the significance of the glasses based closed-loop system is not only for treating facial spasms. Firstly, glasses are a highly socialized, stable to wear, and widely accepted form by patients, avoiding the problem of many wearable devices relying on skin adhesives, headbands, and complex fixed structures. Secondly, electrostatic induction sensing has the advantages of passivity, low power consumption, and high sensitivity, making it suitable for capturing brief, localized, and non-autonomous muscle movements. Thirdly, the system forms a complete closed-loop chain: sensors capture spasm signals, decision modules perform threshold recognition, actuators deliver tissue-conformal interfaces electrical stimulation, and treatment results are fed back into subsequent signals. Although the closed-loop chain is relatively simple, it embodies the basic structure of information symbiosis, indicating that closed-loop therapy can start from peripheral neuromuscular scenarios with clear disease characteristics, easy signal capture, and low intervention risk.

In order to enhance international comparability, Ouyang et al.'s glasses based system will be understood in the context of wearable closed-loop therapy and personalized neuromodulation. Scangos et al.'s closed-loop depression treatment emphasizes "patient-specific biomarkers", Rogers et al.'s millimeter scale optoelectronic electrotherapy system emphasizes "absorbable devices and tissue-conformal interfaces closed-loop control," while the glasses based system emphasizes "low-

power closed-loop recognition and on-demand stimulation in daily form. The three represent the three directions of information symbiosis: individualized neural network regulation in the brain, an absorbable cardiac electrotherapy system, and wearable peripheral neuromodulation that is more easily accepted by patients on a daily basis. In contrast, the advantages of glasses based systems lie in wearing compliance and low invasiveness; Its limitation is that currently it mainly relies on threshold recognition, and in the future, multimodal sensing and personalized algorithms need to be introduced to improve robustness in complex life scenarios.

At a higher level, information symbiosis should be integrated with energy and material symbiosis. Energy symbiosis emphasizes that the device obtains power from the host's movement and the external environment, material symbiosis emphasizes that the device safely disappears after completing the task, and information symbiosis enables the device to perceive the host's state and deliver state dependent therapy. The three are not independent modules, but interdependent system entities [34,153]: closed-loop perception and computation require energy support; Sensors and stimulators require stable, low impedance, and biocompatible interfaces; If the device is used for temporary treatment, its material lifespan must also match the treatment window. Ouyang et al.'s fully biodegradable self-powered vagus nerve stimulator has demonstrated a combination of energy symbiosis and material symbiosis; If electrocardiogram, heart rate variability, respiratory rhythm, and neural activity feedback are further incorporated in the future, it is expected to move from preset stimuli to true information symbiosis.

Therefore, the next generation of symbiotic neural regulatory systems can be envisioned as a coupling of five functional layers [154–158]: flexible multimodal sensors continuously collect electrophysiological, mechanical, and biochemical signals [159]; The low-power decision-making module identifies pathological states through threshold logic, machine learning, and neuromorphic computation; The energy harvesting module utilizes triboelectric electricity, piezoelectric, electromagnetic, and wireless power supply to maintain operation; The actuator delivers electrical stimulation, drug release, mechanical regulation, and optical modulation based on the decision results; The material system is determined by the disease progression to exist stably for a long time and gradually degrade after completing the task. Such a system will no longer be a therapeutic tool that executes instructions in a one-way manner, but will be able to form dynamic collaborative therapy with the host in terms of energy supply, material lifespan, and physiological feedback.

5. Outlook: the path toward fully symbiotic bioelectronics

The previous chapters indicate that symbiotic bioelectronics has gradually evolved from a conceptual vision to an emerging direction with clear material foundations, device prototypes, and preclinical validation pathways. Energy symbiosis proves that implanted devices can obtain operational energy from heartbeat, respiration, gastrointestinal peristalsis, joint load, and external sound fields; Material symbiosis proves that high-performance electronic functions can be combined with controllable degradation, absorption, and ex vivo after task completion; Information symbiosis further demonstrates that devices can achieve state dependent therapy through multimodal sensing, low-power decision-making, and precise actuation. However, true 'fully symbiotic' devices do not simply add up the three dimensions, but require collaborative optimization of energy sources, material lifespan, perceptual quality, decision algorithms, actuation outputs, and clinical tasks in the same system [160,161]. The core issue in the future will shift from "whether a certain function is feasible" to "whether multi-dimensional symbiotic systems can operate in a long-term, safe, and predictable manner in the real in vivo environment".

5.1. System Level Integration: Major Challenges

At present, the development of energy symbiosis, material symbiosis, and information symbiosis is still on a relatively independent technological path. Energy harvesting research focuses on conversion mechanisms such as triboelectric electricity, piezoelectric, electromagnetic, and ultrasonic driving; Materials research focuses on absorbable metals, silicon nanofilms, degradable polymers, and transient packaging; Research on closed-loop systems focuses on sensing, algorithms, actuation, and wireless communication. Importantly, the next major challenge is system level integration [162–169], which involves achieving stable power supply, controllable lifecycle, and adaptive therapy in a device that meets clinical needs.

This integration method is not simply additive, but will bring new system constraints. Firstly, biodegradable materials must simultaneously meet the requirements of biocompatibility, mechanical stability, and energy conversion. For example, the triboelectric layer used for degradable TENG needs to form a sufficient potential difference in the triboelectric electric sequence and safely degrade after the treatment window. The metal used for absorbable electrodes should have sufficient charge injection capability [170,171], and should not cause local toxicity, gas accumulation, and drastic pH changes during degradation. Secondly, the sensing, computing, and communication of closed-loop systems will significantly increase the energy burden. Early self-powered devices were mainly powered by therapeutic stimulation pulses and energy storage units, while fully symbiotic systems must also support signal acquisition, filtering, feature extraction, event detection, wireless transmission, and parameter updates. Thirdly, the material degradation curve must be accurately matched with the treatment task: the device cannot fail before the end of the treatment window, nor can it leave functional fragments that are difficult to absorb after the task is completed.

The fully degradable triboelectric electric VNS reported by Ouyang et al. has demonstrated a two-dimensional integration of energy symbiosis and material symbiosis: the degradable TENG generates low-level vagus nerve stimulation driven by mechanical movement in the body, and can degrade after treatment and be accelerated by external triggering [85]. Similarly, millimeter scale absorbable optoelectronic electrotherapy systems and transient closed-loop wireless skin-interfaced electrotherapy networks connect material symbiosis and information symbiosis [27,28], demonstrating the prototype of the "absorbable device-skin-interfaced controller-closed-loop algorithm architecture" system [172,173]. The key to the future is to further merge the two types of pathways: devices can obtain energy from the host and a safe external field, as well as perform closed-loop perception and precise intervention within the treatment window, and can be controlled to exit after the task is completed.

5.1.1. Design matrix for fully symbiotic bioelectronics

To translate the concept of symbiotic bioelectronics into practical design principles, a design matrix is proposed to correlate clinical tasks with energy requirements, energy architectures, material lifetime, sensing modalities, decision strategies, actuation modes and dominant constraints Table 5. This framework emphasizes that different clinical objectives require different combinations of energy, material and information symbiosis rather than a universal device configuration.

5.2. Multimodal energy harvesting

A fully symbiotic system requires a more stable and predictable energy budget compared to a single stimulator. Currently, most self-powered implant devices still rely on a single energy conversion mechanism, such as TENG contact electrification and electrostatic induction, strain polarization of piezoelectric materials, magnetic flux changes in electromagnetic power generation, and ultrasound driven acoustic mechanical coupling. Different mechanisms are adapted to

different physiological energy sources: low heart movement frequency, small displacement but stable cycle, suitable for high-sensitivity TENG and low threshold electromagnetic structures; Respiratory movement displacement is large but the frequency is lower, suitable for flexible large deformation energy harvesters; Gastrointestinal peristalsis and joint activity have clear rhythms and high loads, but are intermittent and strong; The temperature gradient exists continuously, but the power density is usually low. A single mechanism is difficult to cover all energy requirements in complex clinical scenarios.

Therefore, multimodal energy harvesting and hybrid power supply will become the future direction [69,145,174–177]. TENG - Electromagnetic hybrid systems can simultaneously capture the kinetic energy generated by contact/separation and relative displacement from the same mechanical motion; Piezoelectric triboelectric composite devices can balance deformation response and interface charge transfer; Thermoelectric mechanical hybrid systems can utilize temperature gradients to provide baseline power and pulse energy from heartbeat, breathing, and motion events; External fields such as ultrasound, magnetic fields, and near-infrared light can be used as a safe way to supplement energy when the host's movement is insufficient. For high-power scenarios such as deep brain stimulation, tumor therapy, anti-infective electrotherapy, and complex closed-loop monitoring, relying solely on host mechanical motion may result in energy shortages. Hybrid energy supply will be more clinically feasible than "pure self-supply".

The evaluation of energy systems also needs to shift from single output indicators to task related indicators [178,179]. The open circuit voltage, short-circuit current, and peak power density are not sufficient to determine whether the symbiotic equipment is usable. More importantly, the average effective power, energy management efficiency, energy storage stability, start-up threshold, tissue motion disturbance, long-term fatigue life, and the degree of matching with the therapeutic load. For example, cardiac pacing focuses on whether the energy available for each cardiac cycle exceeds the pacing threshold and retains sufficient safety redundancy; Neural stimulation focuses on whether the output current and frequency meet the safe and effective window; Closed loop monitoring requires the energy system to support continuous and intermittent sampling, low-power computing, and wireless communication [180,181]. The future symbiotic energy module should be designed as a system level power management platform [80], rather than an isolated energy harvesting unit.

5.3. Artificial intelligence and self-decision-making bioelectronic implants

The next stage of information symbiosis is to move from closed-loop response to self-decision therapy. Traditional closed-loop systems typically trigger therapy based on thresholds and preset features, such as detecting epileptic like EEG activity, abnormal heart rhythm, and delivering intracranial electrical stimulation after abnormal muscle contractions. This strategy has advantages such as strong interpretability, simple hardware implementation, and relatively clear regulatory pathways, but it is difficult to capture the multivariate, nonlinear, and time-dependent characteristics of complex disease states. Artificial intelligence and machine learning (AI) [63,95,147,182] can learn patient-specific biomarkers patterns through long-term physiological records [183], identify risk states before symptoms appear, and dynamically optimize electrical stimulation parameters, drug release timing, and electrical therapy intensity.

For epilepsy, Parkinson's disease, chronic pain, heart failure, and mental illness, a truly valuable closed-loop system should not only respond after pathological events occur, but gradually develop into a predictive and preventive system. Long term recordings of electroencephalography, local field potentials, electrocardiography, electromyography, respiration, hemodynamics, metabolites, and inflammatory signals can form a patient-specific biomarkers multimodal disease map [184,185]. Algorithms can identify premonitory symptoms, medication cycles, sleep states, exercise states, and treatment responses, and adjust

intervention strategies within the safety boundaries set by doctors. As a result, treatment has shifted from "fixed parameter output" to a continuous process of "state recognition risk prediction precise intervention efficacy feedback".

However, implanting bioelectronic devices with AI algorithms and edge intelligence into the body is different from cloud and desktop AI. Its hardware must meet extremely low power consumption, low latency, high reliability, and biosafety requirements. Neuromorphic computing is particularly suitable for processing continuous stream signals such as electroencephalography [145,186–189], electromyography, electrocardiography, and neural discharges due to its event driven, sparse coding, and proximity sensing computing characteristics. Therefore, closed-loop decision-making for symbiotic electronic devices should not only pursue algorithm complexity, but also strike a balance between safety boundaries, state recognition, energy consumption, and clinical interpretability.

5.4. Remaining challenges

Although symbiotic bioelectronics has made significant progress in self-powered pacing, degradable neural stimulation, transient electrical therapy networks, and closed-loop neuromodulation, there are still multiple challenges to its widespread clinical adoption [147,189]. Firstly, there is still a gap between power output and the demand for high-power therapy. A hundred microwatts level output can already cover some cardiac pacing and low-level neural stimulation scenarios, but deep brain stimulation, multi-channel neural recording, continuous wireless communication, and complex closed-loop computing often require higher power budgets. In the future, materials that improve energy conversion, transmission, storage, and stimulation efficiency while meeting biocompatibility/degradability requirements as much as possible will be needed.

The low start-up threshold structure, multimodal energy harvesting, energy storage management, and ultra-low power circuits jointly improve the energy utilization efficiency of the system.

Secondly, degradation control is still not precise enough. The human environment is highly heterogeneous, pH, and there are significant differences in enzyme activity, ion strength, protein adsorption, mechanical stress, blood flow shear, and immune response among different patients and implantation sites. The degradation curve in vitro PBS and animal models cannot accurately predict human behavior. More complexly, real implanted devices are typically composed of multiple materials such as substrates, wires, electrodes, dielectric layers, and encapsulation layers, which are not independent of each other when degraded in vivo. For example, metal ions, acidic products of polymers, silicates, and residual encapsulation materials may interact to collectively alter local pH, ion strength, protein adsorption, and immune responses. Therefore, in the future, it is necessary to establish a standardized and cross scale degradation evaluation system to assess safety from four levels: material chemistry, device structure, local tissue reactions, and systemic metabolism.

Thirdly, the long-term biocompatibility and safety of degradation products still need to be systematically validated. There have been many studies on single materials such as Mg, Zn, PLGA, PLLA, PCL, and silicon nanofilms, but the degradation behavior of composite devices is more complex. Conductors, semiconductors, dielectric layers, packaging materials, and drug/stimulus modules degrade at different time points, which may result in local pH changes, osmotic pressure changes, inflammatory reactions, and residual small fragments. Future research should not only evaluate the biocompatibility of initial devices, but also track tissue reactions, metabolic pathways, and long-term safety throughout the entire service life and degradation period.

Fourthly, system level miniaturization and reliable packaging remain common bottlenecks. Energy harvesters typically require sufficient deformation space and contact area, closed-loop sensing requires stable electrodes and sensing interfaces [190–195], computing and

wireless communication require integrated circuits and antennas, and actuators require sufficient charge injection capability and drug/light/mechanical output capability. The modules coexist within the same small implant, resulting in conflicts in space, thermal management, packaging, and interconnection. Capsule sized self-powered intracardiac pacemakers and symbiotic transcatheter pacemakers have demonstrated the feasibility of miniaturized self-powered systems in large animal hearts, but higher levels of microfabrication, flexible hybrid integration, and 3D packaging technology are still needed for neural recording, pediatric implantation, dense sensing arrays, and multi node distributed therapy.

Fifthly, relevant comments and reviews indicate that the regulatory path is still immature. Traditional implants typically focus on long-term mechanical stability [110,196], electrical safety, packaging reliability, and biocompatibility; self-powered and absorbable closed-loop devices require additional proof of sustainable energy sources, predictable material degradation, interpretable algorithmic decisions, and definable treatment endpoints. For a device that actively degrades and disappears, regulatory issues are particularly complex: how to prove complete and safe degradation? How to define task completion? How to confirm that there is no functional residue after the device disappears? How to evaluate the electrical failure modes and tissue risks during the degradation process? The issues need to be jointly defined with clinical doctors and regulatory agencies in the early stages of device design.

5.5. Future Vision

The complete symbiosis of bioelectronics ultimately leads to a new mode of medical practice. Future heart failure patients may receive a self-powered, degradable vagus nerve stimulation system: the device obtains energy from respiration and cardiac movement, adjusts stimulation based on real-time electrocardiogram, heart rate variability, and hemodynamic signals [197–201], and gradually degrades after the cardiac remodeling intervention window ends. Epilepsy patients may receive a low-power closed-loop neural stimulation system: the device learns individual seizure patterns for a long time, identifies risk states before seizures, and delivers preventive stimuli, while supporting remote monitoring and parameter updates by doctors through external devices. Orthopedic patients may receive degradable sensing stimulation arrays: the system monitors fracture load transfer and the healing process, generates electrical stimulation during rehabilitation exercises to promote regeneration, and exits the body after imaging and mechanical indicators indicate healing.

In the scenarios, devices are no longer just implanted therapeutic tools [202–209], but dynamic partners that share energy, information, and lifecycle with the host. It obtains power from host activity, adapts disease progression with material lifespan [28,210–213], adjusts treatment through physiological feedback, and reduces and eliminates long-term foreign body burden after task completion. However, this does not mean that all devices must simultaneously be self-powered, biodegradable, and fully autonomous. On the contrary, the true clinical value lies in selecting appropriate symbiotic combinations based on specific diseases [214–219]: lifelong pacing may prioritize energy symbiosis and long-term reliability; Postoperative monitoring may prioritize material symbiosis [24,179]; Dynamic neurological disorders may prioritize information symbiosis; Short term neural repair, heart failure intervention, and tissue regeneration may become the earliest application scenarios where three symbiotic dimensions intersect.

From the concept of respiratory motion driven self-powered pacing, to symbiotic cardiac pacemaker, to encapsulated self-powered intracardiac pacemakers, symbiotic transcatheter pacemakers, fully degradable triboelectric electric VNS, and closed-loop wearable therapy systems, Ouyang et al. together with relevant international research, has promoted the field from a single point breakthrough to a systemic paradigm. The future challenge is to transform high-level prototypes into truly verifiable, manufacturable, regulated, and patient serving

medical technologies [220–225]. The ultimate goal of symbiotic bioelectronics is not to make devices more complex, but to make them closer to the logic of the body itself: to obtain the minimum necessary energy, perform the most precise intervention, exit at the most appropriate time, and always maintain dynamic coordination with the host state.

CRedit authorship contribution statement

Chunlin Liu: Writing – review & editing, Writing – original draft, Formal analysis, Data curation, Conceptualization. **Yukun Mao:** Validation, Investigation, Data curation, Conceptualization. **Kunyang Fan:** Methodology, Formal analysis. **Yu Chen:** Validation, Supervision. **Xulin Hu:** Writing – review & editing, Writing – original draft, Conceptualization. **Zhou Li:** Writing – review & editing, Writing – original draft, Conceptualization.

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Data availability

Data will be made available on request.

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