



## Review

# Construction and control of bio-syncretic robots actuated by living materials

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## ABSTRACT

Bio-syncretic robots represent a novel class of robots that integrate biological and artificial materials. These robots combine the high energy efficiency and environmental adaptability of biological tissues with the precise control and programmability of traditional robots, making them a focal point in the field of robotics. This paper reviews the latest research progress in bio-syncretic robots. Initially, we classify and introduce bio-syncretic robots from the perspective of structural design, which incorporates both biological and artificial materials. Subsequently, we provide a detailed discussion of their fabrication techniques and control methodologies. Finally, to facilitate broader applications of bio-syncretic robots, this paper explores their potential applications and future development prospects.

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## 1. Introduction

With the rapid advancement of cutting-edge fields such as artificial intelligence, sensor technology, and mechanical engineering, robotic technology has been increasingly applied across industries. Against this backdrop, bio-syncretic robots have emerged. Their core lies in the full-chain collaborative innovation spanning design, manufacturing, and control. By leveraging the efficient actuation and environmental responsiveness of biological materials as a foundation, and combining the structural plasticity and intelligent control methods of artificial materials, bio-syncretic robots overcome the limitations of traditional robots in terms of flexibility, energy efficiency, and biocompatibility [1].

Bio-syncretic robotic systems have emerged as a significant research interest in robotics due to the deep integration of biological and electromechanical systems [2]. In the design and construction of bio-syncretic robots, the first step is to clarify the tasks they are expected to perform, such as walking [3,4], swimming [5–7], manipulation [8–10], transportation [11] and pumping [12,13]. Subsequently, the selection of appropriate biological and artificial materials is made based on specific functional and performance requirements for the design and construction (Fig. 1). For example, Gao et al. [14] proposed a skeletal muscle actuator by mimicking the non-joint structure of the tongue. It

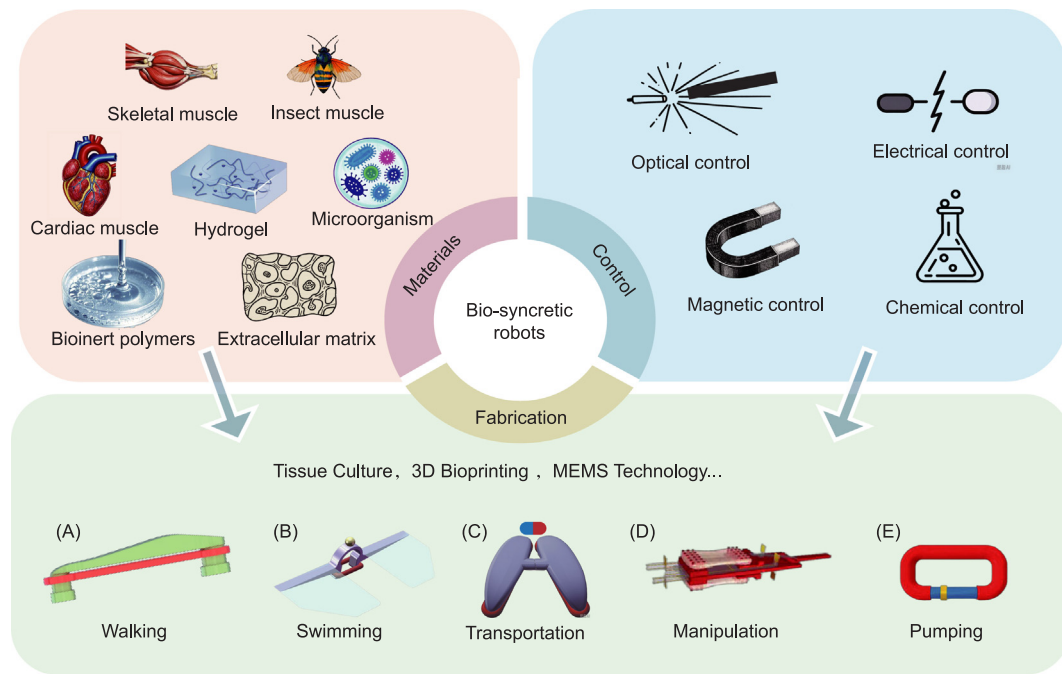
exhibits different motion patterns under varying stimulation conditions and can achieve complex movements. Bartolucci et al. [15] studied the contraction and bending mechanisms of skeletal muscles, and the fabricated actuator features a better bending angle and vertical displacement. Li et al. [16] realized the automatic control of magnetic diatom bio-microbots using deep learning technology, enabling them to autonomously avoid obstacles and accurately reach target cells for targeted drug delivery.

Such designs must follow the principle of collaborative optimization. Through techniques such as tissue engineering-based directed cultivation, Three-dimensional (3D) bioprinting of heterogeneous structures, and biomedical micro-electromechanical systems (Bio-MEMS) miniaturization, functional coupling across scales from the molecular to the macroscopic can be achieved, providing systematic solutions for task-oriented design of bio-syncretic robots.

Bio-syncretic robots have several significant advantages. First, biological muscles can directly utilize chemical energy and convert it into mechanical energy with high efficiency, achieving an energy conversion efficiency of over 50% [17]. Second, the rapid responsiveness of biological materials to environmental stimuli endows bio-syncretic robots with higher adaptability in complex environments. Moreover, the biological materials used in bio-syncretic robots, exhibit excellent biocompatibility and rarely elicit immune responses or adverse reactions when interacting with human tissues, providing a crucial guarantee for their application in the medical field. Shin et al. [18] developed a biohybrid chip robot with sensing function based on the nervous system. Through the transmission of electrophysiological signals between

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**Fig. 1.** Design, fabrication, and control of bio-syncretic robotic systems. (A) A bio-syncretic robot inspired by a caterpillar. Reproduced with permission from [4]. Copyright 2024, Wiley-VCH GmbH. (B) A manta ray-inspired bio-syncretic robot. Reproduced with permission from [7]. Copyright 2022, licensed under CC BY 4.0, AAAS. (C) The biped bio-syncretic robot. Reproduced with permission from [11]. Copyright 2024, Mary Ann Liebert, Inc. (D) A biohybrid robot with an antagonistic pair of skeletal muscle tissues. Reproduced with permission from [8]. Copyright 2018, The American Association for the Advancement of Science. (E) A biohybrid valveless pump-bot. Reproduced with permission from [12]. Copyright 2019, licensed under CC BY-NC-ND 4.0, PNAS.

the eye assembly, brain organoids, motor neuron spheres, and muscle bundles, it achieves muscle contraction induced by visual stimuli.

This paper focuses on the construction and control technologies of bio-syncretic robots. It provides a detailed review of how these robots integrate living and artificial materials to construct complex structures through advanced manufacturing techniques such as tissue engineering and 3D printing. It also discusses how they achieve precise control through multiple control methods, including optical, magnetic, electrical, and chemical control. Finally, the paper explores the potential applications faced by bio-syncretic robots and their future development prospects.

## 2. Development overview of bio-syncretic robots

Bio-syncretic robots have garnered significant scientific attention since the early 21st century (Fig. 2). This profound synergy between living and artificial systems not only redefines fundamental robotics design principles but also establishes a transformative research platform for interdisciplinary innovations in tissue engineering, flexible electronics, and artificial intelligence. The field has evolved rapidly, advancing from basic demonstrations of spontaneous motion to systems capable of complex tasks, intelligent feedback, and autonomous control (Table 1). These developments highlight the potential of multidisciplinary convergence and lay the groundwork for future innovations.

Early studies addressed challenges at the interface of biological and synthetic materials [19]. Xi et al. [20] introduced a microdevice fabrication technique based on the self-assembly of muscle cells. These devices achieved crawling motion with a maximum velocity of 38  $\mu\text{m/s}$ , thereby validating the feasibility of using biological tissues to actuate artificial components. Subsequently, Tanaka et al. [21] developed PDMS-based bio-microactuators that employed micropillar arrays to constrain

the contraction directionality of cardiomyocytes, the beat frequency was 1.4 Hz at 37 °C. However, their operation relied entirely on the inherent rhythmic contractions of biological tissues, lacking responsiveness to external environmental stimuli.

With advances in optogenetics and microfluidics, researchers have achieved precise control over bioactuators, enhancing motion controllability and enabling multimodal functionalities like steering and grasping. Park et al. [22] developed a bionic fish using cardiomyocytes. This device achieved phototactic swimming at 3.2 mm/s with turnable control, enabling obstacle-avoidance maneuvers. This work provides novel insights into biomimetic design and environmental adaptability for bio-syncretic robots. Kim et al. [23] created wireless optogenetic skeletal muscle robots via radiofrequency (RF)-powered micro-ILED arrays. A maximum walking speed of 0.83 mm/s was achieved when the eBiobot was stimulated at 4 Hz, 50-ms pulse width, and 10-W RF antenna power.

At the cutting edge of technology, bio-syncretic robot development has garnered significant attention, progressing towards intelligent feedback and autonomous control. Research teams are using reinforcement learning to enhance their autonomy, with self-healing materials and organoid intelligence as hotspots. These robots have advanced from “simple utilization” to “deep integration”, driving cross-innovation in regenerative medicine, micro-nano manufacturing, and artificial intelligence. With advances in synthetic biology and flexible electronics, they are expected to move from labs to industrial applications, bringing new opportunities.

## 3. Living materials for bio-syncretic robots

Living materials play an essential role in bio-syncretic robots. These materials not only provide robots with actuation and sensing capabilities but also endow them with biological-like characteristics, such as self-healing abilities and rapid responsiveness to environmental stimuli. These unique properties are the key

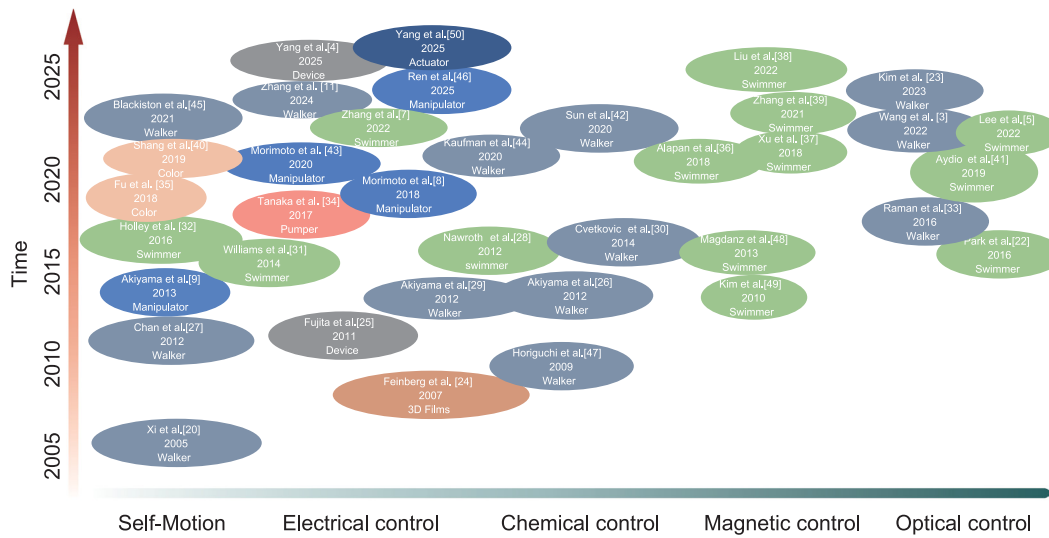
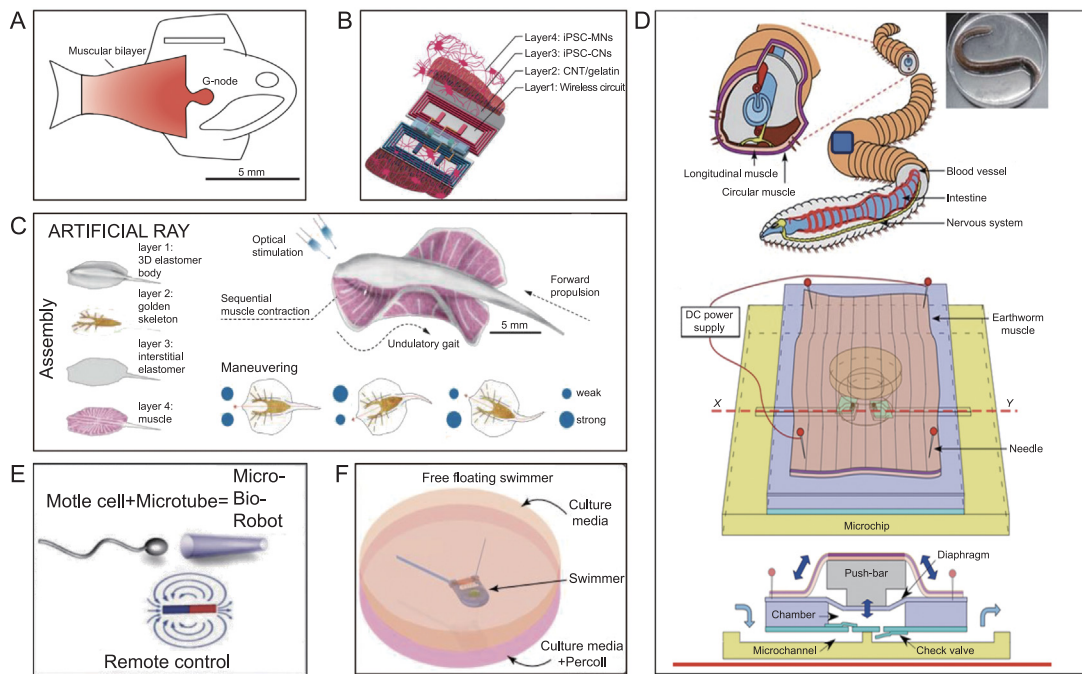


Fig. 2. The development overview of bio-syncretic robots. [3–5,7–9,11,20,22–50].

**Table 1**  
The evolution of bio-syncretic robotic systems.

Year	Living materials	Artificial materials	Fabrication technology	Control method	Performance	Function	Refs.
2005	Cardiomyocytes	Si; SiO <sub>2</sub>	Bio-MEMS	–	Speed: 38 μm/s	Walker	[20]
2007	Cardiomyocytes	PIPAAm; PDMS	Tissue culture	Electrical control	Speed: 24 mm/min	3D Films	[24]
2009	Cardiomyocytes	PDMS	Tissue culture	Chemical control	Frequency: 1.2 Hz	Walker	[47]
2010	Tetrahymena pyriformis	Fe <sub>3</sub> O <sub>4</sub>	Tissue culture	Magnetic control	Speed: 448.9 μm/s	Swimmer	[49]
2011	Skeletal muscle cells	Si; PNIPAAm	Bio-MEMS	Electrical control	–	Device	[25]
2012	Dorsal vessel	PTFE; PDMS	Tissue culture	Chemical control	Speed: 257 μm/s	Walker	[26]
2012	Cardiomyocytes	PEGDA	3D bioprinting Tissue culture	–	Speed: 236 mm/s Frequency: 1.5 Hz	Walker	[27]
2012	Cardiomyocytes	PDMS; fibronectin	Tissue culture Bio-MEMS	Electrical control	Propulsion: 0.4–0.7 BL/S	Swimmer	[28]
2012	Dorsal vessel	PDMS	Bio-MEMS	Electrical control	Speed: 3.5 mm/s	Walker	[29]
2013	Dorsal vessel	PDMS	Bio-MEMS	–	Frequency: 1.1 Hz	Manipulator	[9]
2013	Sperm cells	Ti; Fe	Bio-MEMS	Magnetic control	Speed: 5–10 μm/s	Swimmer	[48]
2014	Skeletal muscle cells	PEGDA	Tissue culture 3D bioprinting	Electrical control	Speed: 156.1 μm/s	Walker	[30]
2014	Cardiomyocytes	Pluronic F127	Tissue culture Bio-MEMS	–	Speed: 81 μm/s	Swimmer	[31]
2016	Cardiomyocytes	PDMS	Tissue culture Bio-MEMS	–	Speed: 142 μm/s	Swimmer	[32]
2016	Skeletal muscle cells	PEGDA	Tissue culture 3D bioprinting	Optical control	Speed: 312 ± 63 μm/s	Walker	[33]
2016	Cardiomyocytes	PDMS; fibronectin	Bio-MEMS	Optical control	Speed: 3.2 mm/s	Swimmer	[22]
2017	Earthworm muscle	PDMS	Bio-MEMS	Electrical control	Flow Rate: 5.0 μL/min	Pumper	[34]
2018	Skeletal muscle cells	PDMS	Tissue culture 3D printing	Electrical control	–	Manipulator	[8]
2018	Cardiomyocytes	GelMA; SiO <sub>2</sub>	Tissue culture	–	–	Color	[35]
2018	Red blood cells	PDMS; SPIONs	Tissue culture Bio-MEMS	Magnetic control	Speed: 10.2 ± 3.5 μm/s	Swimmer	[36]
2018	Sperm cells	PDMS; Fe; Ti	Tissue culture Bio-MEMS	Magnetic control	Speed: 41 ± 10 μm/s	Swimmer	[37]
2019	Cardiomyocytes	PVDF	Tissue culture Bio-MEMS	–	–	Color	[40]
2019	Skeletal muscle cells	Matrigel	Tissue culture Bio-MEMS	Optical control	Speed: 0.7 μm/s	Swimmer	[41]
2020	Cardiomyocytes	GelMA;CNT	Tissue culture Bio-MEMS	Chemical control	Speed: 20 μm/s	Walker	[42]
2020	Skeletal muscle cells	GelMA	Tissue culture	Electrical control	–	Manipulator	[43]
2020	Skeletal muscle cells	PEGDA	3D bioprinting Tissue culture	Chemical control	Frequency: 2.11 Hz	Walker	[44]
2021	Neutrophils	Fe <sub>3</sub> O <sub>4</sub>	Tissue culture Bio-MEMS	Magnetic control	Speed: 16.4 μm/s	Swimmer	[39]
2021	Xenopus laevis	EosFP; MMR	Tissue culture	–	Speed: 100 μm/s	Walker	[45]
2022	Chlorella pyrenoidosa	Fe <sub>3</sub> O <sub>4</sub>	Tissue culture Bio-MEMS	Magnetic control	Speed: 100 μm/s	Swimmer	[38]
2022	Skeletal muscle cells	PDMS; PI	Tissue culture	Electrical control	Speed: 1.49 mm/s	Swimmer	[7]
2022	Cardiomyocytes	PDMS	Tissue culture	Optical control	Speed: 15 mm/s	Swimmer	[5]
2022	Skeletal muscle cells	PEGDA	Tissue culture 3D bioprinting	Optical control	Speed: 13 mm/min	Walker	[3]
2023	Cardiomyocytes	PDMS; Cu	Tissue culture 3D printing Bio-MEMS	Optical control	Speed: 0.83 mm/s	Walker	[23]
2024	Skeletal muscle cells	PMMA;PDMS	Tissue culture	Electrical control	Speed: 0.8 mm/s	Walker	[11]
2025	Skeletal muscle cells	PDMS	Tissue culture 3D Printing	Electrical control	Speed: 2.38 mm/s	Device	[4]
2025	Skeletal muscle cells	PDMS	Tissue culture 3D printing	Electrical control	Lifetime: 178 day	Manipulator	[46]
2025	Skeletal muscle cells	PDMS; PE	Tissue culture 3D printing	Electrical control	Force: 2.92 ± 0.07 mN	Actuator	[50]



**Fig. 3.** Examples of living materials in bio-syncretic robots. (A) Biohybrid fish equipped with the muscular bilayer and the G-node. Reproduced with permission from [5]. Copyright 2022, The American Association for the Advancement of Science. (B) Wirelessly controllable bioelectronic neuromuscular robots for steering actuation behavior. Reproduced with permission from [52]. Copyright 2022, The American Association for the Advancement of Science. (C) Tissue-engineered ray with four layers of body architecture. Reproduced with permission from [22]. Copyright 2016, The American Association for the Advancement of Science. (D) Fluidic pump powered by an earthworm muscle. Reproduced with permission from [34]. Copyright 2016, Elsevier B.V. (E) A sperm-flagella driven micro-biorobot. Reproduced with permission from [53]. Copyright 2013, WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim. (F) Bio-syncretic robot actuated by neuromuscular tissue. Reproduced with permission from [41]. Copyright 2019, licensed under CC BY-NC-ND 4.0, PNAS.

distinguishing features of bio-syncretic robots from traditional robots. Specifically, living materials such as cardiomyocytes, skeletal muscle cells, insect muscle tissues, and microorganisms have garnered significant attention due to their ability to generate substantial output forces and achieve controllable actuation [51]. The diversity and functionality of these living materials have led to their widespread application in the research of bio-syncretic robots (Fig. 3), offering new insights and possibilities for the design and development of future robots.

### 3.1. Cardiomyocytes

Cardiomyocytes spontaneously generate rhythmic electrical activity, enabling the heart's autonomous beating. Though atrial and ventricular myocytes function independently, intercalated discs connect them into a network for rapid electrical conduction—supporting near-synchronous contraction to boost efficiency. Gap junctions (for ion/signal transfer) reinforce this coupling. These properties provide bio-syncretic robots with strong actuation, natural control, and high integration. The fatigue mechanism of cardiac muscle is closely related to calcium ion regulation. Continuous electrical stimulation may cause calcium overload, damage cardiomyocytes, and impair rhythmic contraction. Baron et al. [54] further revealed that high pacing frequencies (>1 Hz) lead to a progressive decline in myocardial contractility, while glucocorticoids (e.g., cortisol) can maintain myocardial function by stabilizing the extracellular matrix.

Traditional bio-syncretic robots often employ 2D cardiac tissues, which consist of a monolayer of cardiomyocytes with a thickness of only 3–5 micrometers, resulting in limited contractile force [55]. Morita et al. [56] developed a novel type of 3D cardiac muscle ring composed of human induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CMs). These rings not only exhibit higher contractile forces (with the maximum contractile force

of thick muscle rings reaching up to 850  $\mu\text{N}$ ) but can also be integrated into desired 3D structures.

Recent advances in bio-syncretic robotics have demonstrated remarkable improvements in durability and neural-muscular integration. Lee et al. [5] designed and tested a biohybrid fish whose spontaneous activity can last for up to 108 days (equivalent to 38 million heartbeats), making it 16–18 times more durable than previous bio-syncretic fish. In another study, Tetsuka et al. [52] developed a micro-swimming robot using human motor neurons and cultured cardiomyocytes to mimic muscle tissue (speed:  $0.52 \pm 0.22$  mm/s). Electrical synapses between human iPSC-derived motor neurons (MNs) and cardiomyocytes (CMs) enable rapid bidirectional signaling for this control.

The unique characteristics [57] of cardiomyocytes make them ideal materials for constructing bio-syncretic robots [58]. However, these characteristics also pose challenges in control. The precise regulation of cardiomyocyte contraction timing and amplitude is difficult to achieve, thereby complicating the precise control of the movement of bio-syncretic robots. Moreover, the electrophysiological properties of cardiomyocytes are also key factors influencing the motion control of bio-syncretic robots.

### 3.2. Skeletal muscle cells

Skeletal muscle, the largest muscle group in the body, plays a crucial physiological role [59]. The differentiation of myoblasts (e.g., C2C12) is a crucial step in the fabrication of skeletal muscle cell-driven robots [60]. In the field of bio-syncretic robots, early research primarily focused on the cultivation and manufacturing of muscle tissues. Researchers have continuously explored and optimized the culture methods and stimulation techniques for skeletal muscle cells to enhance the performance of robots [6,61–63]. This includes improving culture media and adding growth

factors to promote the growth and differentiation of skeletal muscle cells, thereby enhancing their contractile capabilities. In addition, new control technologies are being investigated to improve the precision of skeletal muscle contraction.

Maintaining the viability and functionality of skeletal muscle cells *in vitro* remains a challenge, requiring strict control of the culture environment, including temperature, pH, and nutrients [64]. Akiyama et al. [65] developed a maintenance-free culture system with electrical stimulation and medium exchange capabilities. Each tissue-engineered muscle potentially generating a force of up to approximately 10 mN. In recent years, hybrid stimulation techniques have also been explored. For example, Yang et al. [4] designed and constructed a spring-based electromechanical co-stimulation system (EMCSS) for enhanced cultivation and contractile force measurement of skeletal muscle. Results showed that the enhanced muscle exhibited superior performance, capable of driving robots at a maximum speed of 2.38 mm/s, which is faster than most currently reported robots. Further studies have confirmed that coordinated electrical and mechanical stimulation can induce the desired remodeling of the extracellular matrix (ECM) [66], thereby enhancing the contractile force of engineered skeletal muscle tissues.

Skeletal muscle fatigue under long-term electrical stimulation mainly stems from energy metabolism imbalance and disrupted excitation-contraction coupling regulation. For example, Arjunan et al. [67] noted that increased synchronization index of surface electromyogram (sEMG) is highly correlated with muscle fatigue and can serve as an evaluation indicator. Additionally, Lynch et al. [61] systematically analyzed the inhibitory effect of flexible components on skeletal muscle fatigue, finding they increased muscle contraction stroke by 5 times and reduced fatigue via frequency-independent regulation.

Moreover, given the inseparable connection between the nervous system and skeletal muscle cells, researchers have also conducted multiple studies on neuromuscular drivers. Aydin et al. [68] successfully developed a multi-target neuromuscular co-culture platform. Muscle bundles cultured alone and those co-cultured with neurospheres show significant differences: their contractile forces are 18.8  $\mu\text{N}$  and 102  $\mu\text{N}$ , respectively, on day 7.

Bio-syncretic robots based on skeletal muscle cells offer promising size scalability and can perform basic actuation functions through controllable contractions under external stimulation. However, current artificial stimulation methods remain limited in their ability to precisely regulate muscle cell actuation, hindering the realization of complex and flexible movements. Moreover, the efficient large-scale cultivation and fabrication of skeletal muscle tissue remains technically challenging. These obstacles collectively constrain the practical development of skeletal muscle-based bio-syncretic robots.

### 3.3. Insect muscle tissue

Unlike mammalian cardiomyocytes, which can only survive and contract optimally at around 37 °C, insect muscle cells can spontaneously contract within a temperature range of 5 °C to 35 °C without irreversible damage. This makes them highly suitable for temperature-tolerant bio-actuators that do not require complex temperature control devices [29]. Akiyama et al. [26] constructed a microrobot driven by dorsal vessel (DVT). They also demonstrated that insect muscle cells can survive and contract in culture medium for over 90 days without medium replacement. This makes insect muscle cells highly suitable for developing bio-actuators. Based on this, researchers [9] have designed and fabricated a bioactuator named AOB (Atmospheric-operable Bioactuator) with a lifespan of over five days.

Additionally, the team proposed a prototype of an autonomous micro-swimming robot [69] powered by insect muscle tissue. It was confirmed that the micro-swimming robot could autonomously swim at an average speed of 11.7  $\mu\text{m/s}$  using the spontaneous contractions of the intact DVT. However, variations in the contraction force of DVT among different individuals may lead to actual swimming speeds lower than the theoretical value. Future research needs to develop more effective control strategies, such as optogenetics or electrical stimulation, to achieve precise control of insect muscle tissue.

Currently, the establishment of stable insect myogenic cell lines remains a significant challenge, which limits the in-depth application of insect muscle tissue in the field of bio-syncretic robotics. However, with the continuous advancement of tissue engineering technologies, it is anticipated that insect muscle cell lines can be successfully developed in the future, thereby enhancing the environmental adaptability and application scope of bio-syncretic robots.

### 3.4. Microorganisms

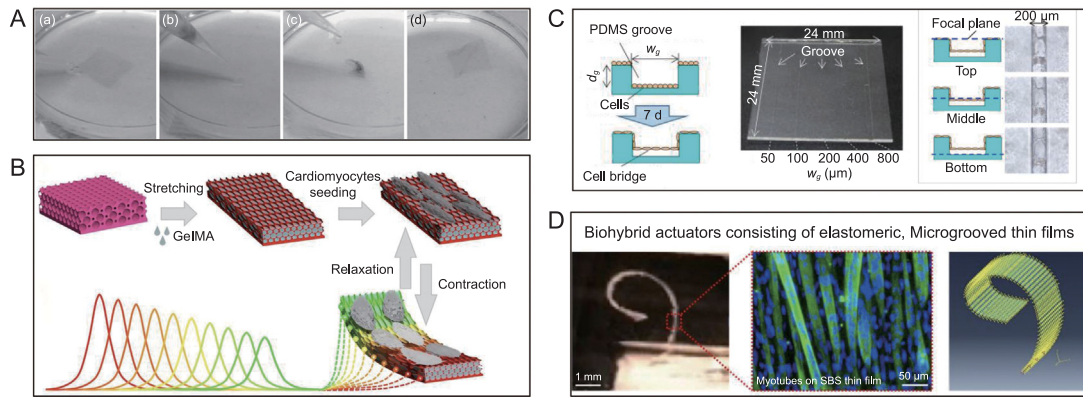
Microorganism-driven robots represent a novel type of robotic system that integrates the natural characteristics of microorganisms with artificial micro/nanostructures [70]. This emerging research field is a result of the interdisciplinary convergence of micro/nanotechnology and robotics [71]. These robots leverage the excellent environmental adaptability and sensing capabilities of microorganisms (e.g., magnetotaxis, electrotaxis, phototaxis, and chemotaxis) to achieve various functions at the microscale, including drug delivery [72], environmental monitoring [73], and microsurgery [73].

Different types of microorganism-driven robots possess unique characteristics. To overcome the non-Newtonian fluid properties of blood, Xu et al. [74] developed a sperm-based hybrid micromotor. Utilizing the strong propulsive force of the sperm's flagellum, which can reach up to 100 pN, the sperm micromotor achieves a swimming speed of 59–93  $\mu\text{m/s}$  in static blood, comparable to the speed of 75–103  $\mu\text{m/s}$  in sperm culture medium. Oda et al. [75] developed a basket-like microtrap structure that minimizes interference with the movement of *Chlamydomonas*. This structure enables *Chlamydomonas* to maintain a stable posture and rotate (Average speed of 21.2  $\mu\text{m/sec.}$ ), holding promise for environmental monitoring applications, such as detecting water pollution. Akolpoglu et al. [76] constructed a motile bio-hybrid microrobot using *Escherichia coli*, averaging a swimming velocity of 18.5  $\mu\text{m/s}$ . Under magnetic guidance, this microrobot can navigate through 3D biomaterials and deliver anti-cancer drugs specifically to tumors, providing a stimulus-responsive therapeutic solution for various medical applications.

Microorganism-driven bio-syncretic robots are promising, but practical use requires overcoming technical and safety challenges. Integrating artificial components into bacteria is non-trivial—complex reactions may harm them (e.g., impairing motility). Current systems lack high-throughput, easy-to-construct components, limiting microrobot performance (propulsion, payload, etc.). For swarms, internal communication, transformation, and individual control remain key challenges [77].

## 4. Artificial materials for bio-syncretic robots

In addition to living materials, artificial materials are also an essential component of bio-syncretic robots. These materials provide structural support, growth environments, and attachment substrates for living materials, ensuring that biological tissues can function properly within predefined shapes and dimensions [78]. Common artificial materials include bioinert polymers, hydrogels, and biomaterials harvested from tissues (Fig. 4). The following sections will systematically introduce these three types of artificial materials.



**Fig. 4.** Examples of artificial materials in bio-syncretic robots. (A) Ultrathin poly(lactic acid) films cultured with skeletal muscle cells. Reproduced with permission from [79]. Copyright 2018, Springer Science. (B) A bio-drive consisting of cardiomyocytes cultured in GelMA hydrogels. Reproduced with permission from [40]. Copyright 2019, American Chemical Society. (C) Formation of PDMS microgroove structures for cardiomyocyte microtissue bridging walls. Reproduced with permission from [80]. Copyright 2019, Elsevier B.V. (D) A biohybrid device formed by culturing C2C12 skeletal myocytes on SBS microgroove membranes. Reproduced with permission from [81]. Copyright 2019, American Chemical Society.

#### 4.1. Bioinert polymers

Bioinert polymers (e.g., PDMS, SBS) are stable and low-immunogenic in biological environments, eliciting minimal immune or inflammatory responses *in vivo*. Polydimethylsiloxane (PDMS) is particularly notable for its biodegradation resistance, biocompatibility, and mechanical/chemical properties, making it critical for bio-syncretic robots (e.g., flexible substrates, microactuators). For instance, He et al. [82] used PDMS/Teflon molds to develop a ring-shaped skeletal muscle actuator, integrating a 3D-printed PDMS skeleton with fins to create a swimming bio-syncretic robot (speed: approximately 0.8  $\mu$ m/s). Similarly, Li et al. [12] fabricated muscle rings via PDMS molds, combining them with hydrogel inserts in PDMS skeletons to develop a pumping robot (flow rate: 22.5  $\mu$ L/min).

PDMS is also widely used to fabricate microchannels for microfluidic chips [83–85]. By mixing PDMS with a crosslinker, pouring it into microstructured molds, and curing it under heat, highly detailed elastic replicas with microchannels can be obtained. This fabrication method offers high resolution, allowing for the molding of structures at the nanometer scale. Furthermore, by introducing tracer particles into PDMS chips and employing micro-particle image velocimetry (Micro-PIV) technology, high-precision measurements of microfluidic flows can be achieved.

However, due to its strong hydrophobicity [57], PDMS typically requires surface modification to transition from a hydrophobic to a hydrophilic state, thereby enhancing the cellular adhesion and growth environment. For example, plasma treatment or silanization can significantly increase the hydrophilicity of PDMS surfaces, making them more suitable for cell culture. These modified PDMS surfaces promote cell proliferation and differentiation and are widely applied in tissue engineering and cell biology research.

#### 4.2. Hydrogels

Hydrogels are 3D network structures composed of natural or synthetic polymers, characterized by their high-water content (typically exceeding 95%). These materials possess excellent biocompatibility and tunable mechanical properties, making them capable of mimicking the characteristics of biological tissues [86]. For example, researchers have developed a composite hydrogel based on Matrigel–fibrinogen–thrombin (MFT) [87], which, when combined with cardiomyocytes, can construct spontaneously contracting *in vitro* active muscle tissue. The MFT

hydrogel exhibits favorable elastic modulus and anti-swelling properties. At equilibrium swelling, its elastic modulus is approximately 1.51 kPa, sufficient to support the contraction of cardiomyocytes.

In recent years, hydrogel research for multimodal applications has attracted much attention [88,89]. Inspired by peripheral nerve structures, researchers developed a hydrogel with a multi-layer sandwich structure (oriented fibers–pores–fibers) [90]. It has excellent mechanical properties: even at  $-20$   $^{\circ}$ C, it maintains 88.6% fracture elongation and 1.1 MPa fracture strength, showing good antifreeze performance and low-temperature stability. As a sensor, it has great application potential. In another study inspired by planarian structures, a reprogrammable biomimetic hydrogel (FLH) was developed [91]. Via ultraviolet polymerization and graphene content regulation, it can exhibit multiple actuation modes under different programming conditions.

Overall, multimodal hydrogels, with diverse response mechanisms and functional integration, have great potential in smart materials [92–94]. Their versatility and adaptability make them a key direction for future smart materials, applicable to biomedical sensing, environmental monitoring, and smart robots.

In addition to mimicking the mechanical properties of biological tissues, the immune shielding function and anti-fatigue design of hydrogels are also critical for host integration. Unmodified synthetic material interfaces may trigger a foreign body reaction, leading to fiber encapsulation and functional degradation. Collagen–hyaluronic acid composite hydrogels [95] can reduce host foreign body reaction and support long-term implantation. Temperature-sensitive hydrogels (e.g., PIPAAm) [96] enable non-destructive cell stripping and reduce implantation damage. Carbon nanotube composite hydrogels [97] can enhance mechanical durability and reduce repeated deformation damage.

Other hydrogels have also been widely applied, such as PEG [98] and PEGDA [99,100]. Despite their many advantages, hydrogels have limitations. For instance, achieving both high water content and high toughness remains challenging. Traditional synthetic hydrogels – composed of a single non-uniform hydrophilic polymer network – typically have poor mechanical properties, with low fracture energy ( $<10$  J  $m^{-2}$ ), significantly limiting their applications. Besides toughness, key mechanical parameters include elastic modulus, fracture strength, elongation at break, and fatigue threshold. While strategies like double-network structures and nanocomposites have improved performance, most solutions sacrifice preparation convenience or increase cost, hindering large-scale application.

### 4.3. Tissue-harvested biomaterials

Tissue-harvested biomaterials refer to biological materials extracted from tissues, such as extracellular matrix (ECM), collagen, fibronectin, and laminin. These materials closely resemble the structure of human tissues, thereby facilitating cell acceptance and growth. They possess certain mechanical strength and toughness, providing structural support for cells. ECM proteins regulate cellular behaviors such as adhesion, migration, proliferation, and differentiation through their signaling functions. For instance, fibronectin interacts with integrins and activates them via its arginine–glycine–aspartic acid (RGD) sequence domain, thereby influencing cytoskeletal tension and gene expression. This property has been widely applied to the surface modification of biomaterials to enhance cell growth and differentiation on scaffolds. Cvetkovic et al. [30] combined mouse skeletal muscle myoblasts with extracellular matrix proteins (collagen I and fibrin) and hydrogel structures to construct a Bio-Syncretic Robot. Under electrical stimulation, the robot reliably moved at frequencies of 1 Hz, 2 Hz, and 4 Hz, with a maximum speed of approximately 156  $\mu\text{m/s}$ . Additionally, the team compared the effects of collagen and fibrin matrices on muscle strip function, finding that the fibrin-based muscle strips generated greater passive tension, likely due to their faster polymerization rate and greater deformability.

Overall, the applications of ECM, collagen, and fibronectin in bio-syncretic robots primarily lie in providing a supportive microenvironment for biological tissues, promoting cell growth and tissue repair, and surface modification. The biocompatibility and multifunctionality of these materials make them essential components in the field of bio-syncretic robots. With the emergence of new technologies, these biomaterials are expected to exhibit more systematic functions in the future and further expand their potential applications in the realm of smart biomaterials.

## 5. Fabrication technologies of bio-syncretic robots

Bio-syncretic robots represent a new generation of robots that integrate biological materials. Their fabrication involves a variety of sophisticated techniques, including biological tissue culture, 3D printing, and biomedical micro-electromechanical systems (Bio-MEMS) technology. The integration of these techniques provides robust support for the design and fabrication of bio-syncretic robots. As science and technology continue to advance, the manufacturing of bio-syncretic robots will become more efficient and precise. In the future, we can expect to see an increasing number of bio-syncretic robots with complex structures and functionalities.

### 5.1. Tissue culture technology

Tissue culture technology is a technique that involves isolating biological tissues from an organism and culturing them in an artificial medium under sterile conditions. It has extensive applications in the study of cell differentiation, tissue regeneration, and disease mechanisms. The basic steps of cell culture include cell thawing, medium exchange, cell passaging, and cryopreservation, with mammalian muscle cells requiring strictly controlled environmental conditions. To maintain cell viability, the culture conditions must be kept at 37 °C, pH 7.4, and 5%CO<sub>2</sub> in a sterile incubator. Additionally, to ensure adequate nutrition and a suitable liquid environment for the cells, the culture medium must be replaced every few days.

With continuous technological advancements, tissue culture technology has also been evolving. For example, optimizing culture conditions and developing new culture media can significantly improve the efficiency and quality of cell culture. In a

2025 study by Ren et al. [46], an “in-sheet” culture method was adopted. Through the design of rolled muscle tissue, oxygen utilization efficiency was improved, enabling the maintenance of maximum contractile force for 30 consecutive minutes and long-term operation for 178 days.

Combined with cutting-edge technologies such as optogenetics and magnetic materials, tissue culture technology can enable precise control of biohybrid robots. Raman et al. [33] utilized optogenetically modified cells to achieve light-controlled actuation. Yamamoto et al. [104,105] employed magnetically modified myoblasts using cationic liposomes to develop magnetically controlled soft robots, enabling complex deformations and multifunctional integration. Hiroyuki Tetsuka et al. [52] connected neurons to muscle tissues via electrical synapses to construct a neuromuscular control system, providing new insights for the intelligent control of biohybrid robots.

In recent years, microfluidic technology [106] has demonstrated significant advantages in the manufacturing of building blocks with diverse structures and compositions, thanks to its precise fluid manipulation capabilities. It has been widely applied in the field of tissue culture [107,108].

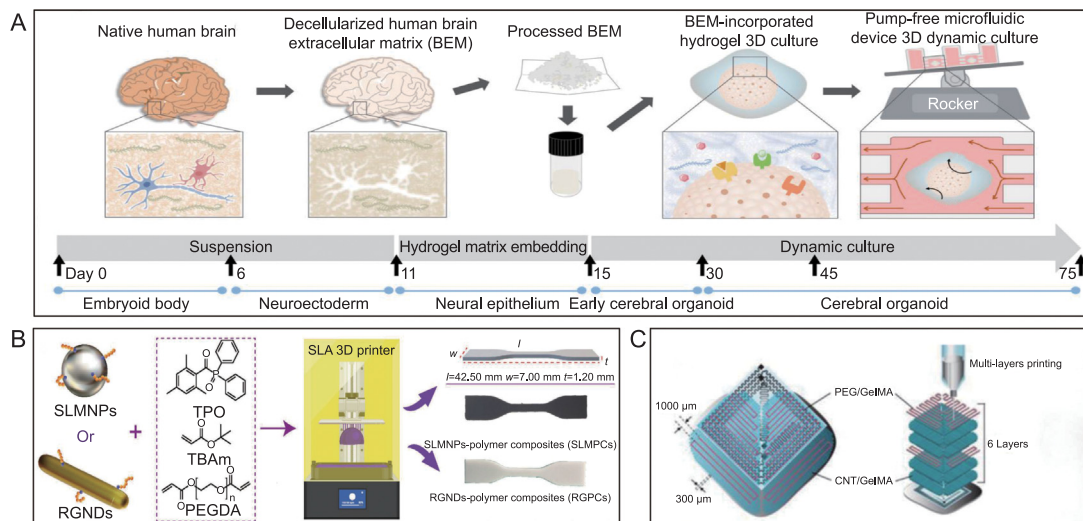
To address the issue that millimeter-scale biological tissues are prone to necrosis due to hypoxia, Pagan-Diaz et al. [109] proposed a “stepwise integration” strategy. This strategy enables cross-scale nutrient delivery through a microfluidic channel network, allowing the robot to exceed a length of 10 mm with a load capacity of 4.3 mN, surpassing the <5 mm limit of most bio-robots at that time. Bingchu et al. [110] fabricated and cultured cell-loaded GelMA constructs with channel networks of different densities using sacrificial materials. Experimental results showed that interconnected channel networks accelerated oxygen/nutrient supply and promoted cell growth, providing a practical method for 3D cell culture and the fabrication of highly bioactive tissues.

The integration of microfluidic technology and biological culture is an innovative approach that introduces the high precision, high throughput, and automation of microfluidics into cell culture and biological experiments, thereby creating cell culture systems that more closely mimic the *in vivo* environment. For example, Cho et al. [101] developed a microfluidic organoid culture system by integrating brain-specific signaling molecules into the extracellular matrix. This system supports three-dimensional organoid culture for up to 75 days (Fig. 5 A). After 75 days of culture, the organoids exhibit more mature functional characteristics, such as the generation of sodium currents, action potentials, and synaptic currents.

However, constructing biological tissues with complex structures and functions remains a challenging task. To enable cultured tissues to perform their intended functions in bio-syncretic robots, precise control over cell alignment, differentiation, and tissue morphogenesis is required. Currently, for some complex organoid tissues (e.g., liver tissues with intact vascular systems), it is still difficult to achieve their complete three-dimensional structure and functionality *in vitro*.

### 5.2. 3D bioprinting technology

3D bioprinting is an advanced technology that integrates 3D printing with biomedical applications. It constructs functional biological tissues and organs by depositing biomaterials (such as cells, biomolecules, and biocompatible scaffold materials) layer by layer [111]. This technique can significantly enhance the precision of structural fabrication and even replicate complex tissue architectures found in the human body, making it widely applicable for rapidly manufacturing complex bio-syncretic structures [112–114].



**Fig. 5.** The Integration of Advanced Manufacturing Technologies in bio-syncretic robots. (A) Schematic illustration of the cerebral organoid culture system with a combination of 3D BEM hydrogel culture and the microfluidic device. Reproduced with permission from [101]. Copyright 2021, licensed under CC BY 4.0, Springer Nature. (B) Three-dimensional (3D) printing design of the CNT/ GelMA and PEG/ GelMA hydrogel patterns on the soft robot with the embedded wireless device and schematic illustration of the soft robot with a scaffold composed of six-layered hydrogel pattern. Reproduced with permission from [102]. Copyright 2022 WILEY-VCH GmbH. (C) Fabrication of 3D-printed GNPPCs. Reproduced with permission from [103]. Copyright 2024, Wiley-VCH GmbH.

With advancing technology, vascularization [115,116] remains a key challenge: without an effective vascular network, printed tissues/organs struggle to get adequate nutrition and oxygen, hindering long-term survival and normal function. Zhang et al. [117] developed a six-axis robotic bioprinter and oil-bath cell printing system. This enables comprehensive cell printing on complex vascular scaffolds, with cell viability (>98%, comparable to manual operations). The printed cells maintain normal cycles and physiological functions, surviving *in vitro* for over six months.

Moreover, 3D bioprinting can customize structure and functionality as needed. Huang et al. [103] developed gallium-based nanoparticle/polymer composites (GNPPCs) with tunable mechanical properties by integrating variously shaped gallium-based nanoparticles (GNPs) into 3D-printed polymers (Fig. 5C). Traditional bio-syncretic robots usually rely on wired electrodes or light sources for control, restricting flexibility and application scenarios. Tetsuka et al. [102] developed a wirelessly powered bio-syncretic soft robot with a maximum swimming speed of approximately 580  $\mu\text{m/s}$ . By embedding wireless power-supply devices into carbon nanotube/gelatin methacrylamide (CNT/GelMA) layers and encapsulating them via photopolymerization, they achieved seamless integration of the wireless device with the scaffold (Fig. 5B).

Yang et al. [50] fabricated modular skeletal muscle actuators using 3D printing technology. Through bionic design and structural optimization for assembly into different shapes, the contractile performance of skeletal muscles was significantly improved, achieving a maximum contractile force of  $2.92 \pm 0.07$  mN.

To date, the precision and cell density achievable by bioprinting still require improvement. Current technologies often inflict damage to cells during the printing process, thereby reducing cellular viability. Moving forward, researchers will focus on developing higher-precision printing techniques to achieve cell densities comparable to those of natural tissues, with the goal of fabricating bio-syncretic robots with enhanced actuation capabilities.

### 5.3. Bio-MEMS technology

Bio-MEMS technology is a micro-electro-mechanical system that integrates microsensors, microactuators, microfluidic systems, micro-optical systems, and micromechanical components.

It has advantages such as strong specificity, high sensitivity, good accuracy, low power consumption, small size, and strong stability. Flexible electronic technology and implantable devices are commonly used in bio-syncretic robots.

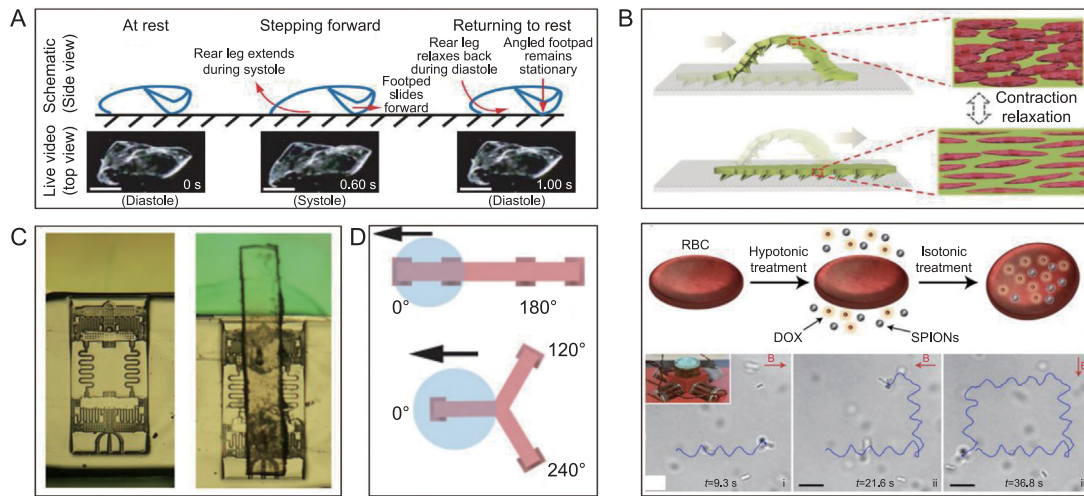
Flexible electrodes, noted for high deformability, light weight, and bendability, have gained significant attention. Compared to silicon-based electrodes, they can float freely with tissues, benefiting long-term biocompatibility. Park et al. [118] developed a flexible 3D bioelectrode platform, preparing bioelectrodes via liquid metal 3D printing. These electrodes, matching tissue softness, minimize damage to cardiac organoids. In addition, flexible electrodes can also enable modular operations. Webster et al. [119] used flexible electrode arrays to connect neural tissues with artificial joints, and this modular and standardized electrode interface realized “plug-and-play” unit replacement. Kim et al. [99] conducted integration research on graphene electrodes and three-dimensional skeletal muscle tissue models, which also utilized the repeated disassembly and assembly of skeletal muscles and flexible electrodes.

Verderber et al. [120] used EMIT (Electro-Mechanical Integration Technique), implanting microprobes and electronics into tobacco hornworm pupae for a tight electronic-tissue interface. The implants worked post-adulthood. In insect robot flight control, the microsystems were biocompatible with insect tissues, forming a reliable control interface.

Bio-MEMS is pivotal for bio-syncretic robots, providing key support. Its miniature sensors detect physical/chemical signals for high-resolution inputs. Micro-actuators and micropumps enable precise motion/substance transfer, letting robots mimic biological movements/functions for autonomous/semi-autonomous interaction. Soon, integrating artificial intelligence and big data will let researchers analyze bio-information from Bio-MEMS, giving robots intelligent perception, decision-making and control.

## 6. Control methods of bio-syncretic robots

The control method is a core element in realizing the functionality of bio-syncretic robots. Diverse control approaches endow these robots with a wide range of motion and operational capabilities (Fig. 6). In-depth investigation of these control methods is essential for advancing the development and application of



**Fig. 6.** Schematic illustration of control methods for bio-syncretic robots. (A) Myopod capable of autonomous or remote-controlled walking. Reproduced with permission from [24]. Copyright 2007, The American Association for the Advancement of Science. (B) The crawling process of the soft robot driven by cardiomyocytes. Reproduced with permission from [42]. Copyright 2019, WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim. (C) Integration of Si-MEMS device with collagen film. Reproduced with permission from [25]. Copyright 2010, Springer Science Business Media. (D) Optically controlled bio-robot with multiple actuators. Reproduced with permission from [3]. Copyright 2022, licensed under CC BY 4.0, AIP Publishing. (E) Magnetic steering of an RBC micro-swimmer. Reproduced with permission from [36]. Copyright 2018, The American Association for the Advancement of Science.

bio-syncretic robots. Currently, the primary control mechanisms for bio-syncretic robots include electrical, magnetic, optical, and chemical control. Each of these methods is based on distinct principles and mechanisms, and they all play significant roles in practical applications.

### 6.1. Electrical control

Electrical control involves the application of electrical stimuli to activate biological tissues (such as muscle cells) or neurons, thereby enabling the motion control of bio-syncretic robots. In living organisms, the contraction and relaxation of muscles rely on the conduction of bioelectrical signals. Kinjo et al. [121] designed a silicone rubber-skeletal muscle bio-syncretic robot to mimic human walking's alternating muscle usage. Alternating electrical stimulation every 5 s on its left/right legs enabled 5.4 mm/min movement. Electrical stimulation can also enable walking control of robots. Kai et al. [122] exploited the defensive behavior of crabs, which retract upon receiving noxious stimuli, to control the directional movement of a semi-aquatic crab in both terrestrial and underwater environments by electrically stimulating the sensory system of the crab's carapace. In the exploration of muscle-driven actuation mechanisms. These research examples demonstrate the potential of electrical stimulation in biohybrid robots, where precise control of muscle tissue contraction enables the realization of robotic motion functions.

Electrical control can precisely regulate muscle contraction frequency/force with high temporal resolution, showing promise in tissue engineering, disease modeling and drug screening. However, it has limitations: in liquid, electrical stimulation's spatial resolution is hard to control due to action potential propagation and depends on electrode-biological material gaps. Contact electrodes may damage biological materials. Medium electrolysis produces harmful substances, affecting cell viability/function. These limit its wide use in bio-syncretic robots.

### 6.2. Optical control

Optical control primarily relies on the response of light-sensitive biological materials or cells that have been genetically modified through optogenetics to achieve control of bio-syncretic

robots. Park et al. [22] developed a biohybrid fish with controllable movement by integrating optogenetically modified cardiomyocytes with soft materials. Upon stimulation with blue light (approximately 10 mW), The speed can reach 1.85 mm/s. Xiong et al. [123] constructed a biological microrobot (Ebot) using *Euglena gracilis*. By controlling the intensity and duration of light exposure, they could precisely regulate the beating of the flagella. Furthermore, by irradiating the cells with a 670 nm laser, reactive oxygen species (ROS) can be generated for photodynamic therapy against tumor cells, demonstrating significant potential for multifunctional biomedical applications.

Compared to electrical control, optical control offers extremely high spatiotemporal resolution, allowing precise control over the location and timing of light exposure to achieve accurate robot motion control [124]. Additionally, optical control is non-invasive, resulting in minimal damage to biological materials. However, optical control also has certain limitations. For instance, certain light sources used for stimulation, such as ultraviolet light, can damage DNA and proteins in biological materials, affecting the activity and functionality of the biological components. Moreover, the effective penetration depth of light is limited, restricting its application in deep tissues or opaque environments.

### 6.3. Magnetic control

Magnetic control leverages the interaction between magnetic fields and magnetic materials to achieve remote manipulation of bio-syncretic robots. For biological components containing magnetic materials, such as cells or microorganisms labeled with magnetic nanoparticles, movement can be precisely controlled in terms of speed and direction by applying external magnetic fields. This control method is characterized by its non-contact, non-toxic, and high-penetration properties, allowing remote operation without direct physical interference and enabling applications within biological tissues [125].

Most magnetic control systems rely on scalable magnetic field gradients and require active position feedback, which limits their suitability for diffusely distributed applications. To address this, Gwisai et al. [126] developed a hybrid control approach using magnetic torque for motion and autonomous navigation. They employed the magnetotactic bacterium AMB-1 strain as

a magnetic-responsive model organism and a covalently coupled liposome carrier to enhance permeability. Uniform rotating magnetic fields have been proposed for clinical applications to control dispersed microrobots without relying on visual feedback, effectively resolving some of these limitations.

With technological advancements, magnetic control robots [127–129] are expected to play significant roles across various fields. However, these robots typically require high-precision magnetic field sensors to monitor field strength and direction in real-time. The feedback data is then used by the control system to adjust the parameters of the magnetic field generator, ensuring precise control. This requirement significantly increases system complexity and cost.

#### 6.4. Chemical control

Chemical control leverages the natural responsiveness of biological components to specific chemicals to manipulate the behavior of bio-syncretic robots. Many biological cells and tissues exhibit reactions to certain chemical substances. For instance, the contraction frequency and force of muscle cells can be modulated by specific chemicals, and microorganisms can move directionally along chemical concentration gradients through chemotaxis. By introducing specific chemicals into the robot's environment, the behavior of biological components can be regulated, thereby controlling the robot's motion. Park et al. [130] demonstrated the chemotactic behavior of bacteria-driven microrobots using a microfluidic chamber. They showed that *Salmonella typhimurium* tends to aggregate towards chemotactic attractants (e.g., aspartate) and move away from chemotactic repellents (e.g., NiSO<sub>4</sub>), highlighting the potential of chemical control in guiding the directional movement of biohybrid robots.

However, chemical control has several limitations. Its spatiotemporal resolution is relatively low due to the slow diffusion of chemicals in the environment, making it challenging to achieve precise and rapid control of robot motion. Moreover, the concentration of chemicals diminishes with distance from the source, weakening the control effect. Additionally, some chemicals may exhibit potential toxicity to biological components, necessitating careful selection and application.

#### 6.5. Other control

In addition to the aforementioned control methods, the field of bio-syncretic robots has explored emerging control strategies to further enhance their adaptability, intelligence, and multifunctionality. For example, temperature-responsive materials [96] (such as thermosensitive hydrogels) or the response of biological tissues to temperature changes are used to regulate the deformation or movement of robots. Start-stop control of bio-syncretic robots is achieved through physical structures [131]. The aerotaxis of microorganisms (e.g., bacteria) is utilized for targeted drug delivery to tumors [132].

Current research tends to focus on single control modalities (such as optical or electrical control), making it difficult to achieve effective and flexible motion control of bio-syncretic robots. However, the complexity of biological systems requires multimodal collaboration. To improve the controllability of bio-syncretic robots, multiple control methods can be adopted for synergistic control. For instance, combining magnetic control with taxis-based control: first, a magnetic field is used to control the drug-delivery robot to approach the tumor area at a relatively fast speed, and then taxis-based control is employed to guide it into the deep tumor tissue for drug release, thereby achieving efficient and precise motion control. The synergistic control of neuromorphic interfaces and optogenetics also provides a new

technical path for the precise regulation of bio-actuated systems. This hybrid control strategy combines the advantages of rapid conduction of neural electrical signals and high spatiotemporal resolution of optogenetics, enabling the programming of complex motion patterns and real-time feedback adjustment. Furthermore, with the advancement of science and technology, new control strategies applicable to bio-syncretic robot research are yet to be developed, which will further promote the practical application of bio-syncretic robots.

## 7. Potential applications

With breakthroughs in the key technologies of bio-syncretic robots, their application fields are rapidly expanding from laboratory research to practical engineering applications. Based on the aforementioned biological material integration, advanced manufacturing processes, and intelligent control methods, bio-syncretic robots have demonstrated unique application advantages in the following directions. These technological breakthroughs not only open up new paths for application scenarios such as medical rehabilitation and environmental monitoring but also drive paradigm innovations in life sciences and human-machine interaction theories. A detailed discussion will be presented below.

### 7.1. Vascularized system design

Vascularization of bio-syncretic robots stands as one of the core challenges in constructing functional bio-mechanical hybrid systems. With advancements in tissue engineering and micro-nano manufacturing technologies, researchers have increasingly recognized that biomimetic vascular networks play a decisive role in sustaining the long-term survival and functional integration of biological components. Vascularized design aims to emulate the dynamic transport mechanisms of biological circulatory systems, achieving directional transport of oxygen, nutrients, and metabolic waste through biomimetic microfluidic networks. This facilitates collaborative optimization of the robot's energy supply and mechanical drive modules.

Researchers are exploring technical approaches for vascularization in bio-syncretic robots. A common method is constructing 3D vascular network scaffolds with biocompatible materials like hydrogels and fibrin, using 3D printing or micro-nano manufacturing for high-precision fabrication—this simulates biological vascular structures and supports cell growth. Bertasconi et al. [133] developed bio-printing-based microchannel network technology, creating 3D microchannels in hydrogels that mimic microvasculature and support cell survival.

Additionally, microfluidic technology is being tested for this purpose. “Lung-on-a-chip” model [134] offered key references: it used microfluidics to simulate alveolar-capillary interface mechanics, revealing that dynamic mechanical environments matter for vascular function simulation—insights for bio-syncretic robot design. Microfluidics enables precise control of fluid flow and distribution; via complex chip design, it can simulate microscopic vascular structures (e.g., branching) and processes like blood flow or material exchange, boosting vascularization precision and providing a platform to study vascular physiology and pathology.

### 7.2. Encapsulation technology

Encapsulation technology for bio-syncretic robots is a core challenge in their functionalization and practicalization. It involves issues like synergistic integration of biological and engineering materials, interface design optimization, and system stability maintenance. The encapsulation must ensure the activity

and functionality of biological components (e.g., cells, tissues) in complex environments while enabling efficient interaction with synthetic materials (e.g., sensors, actuators). This integration aims to build a hybrid system with autonomous responsiveness.

The biocompatibility and durability of encapsulation materials are also critical. Bio-syncretic robots often face biological component degradation, mechanical stress damage, and environmental interference, so novel flexible and functional encapsulation materials need to be developed. Roshanbinfar et al. [95] introduced a Collagen-hyaluronic acid composite hydrogel: when encapsulating human fibroblasts, traditional collagen hydrogels contracted over 90% within 7 days, while the 60% HAGA composite hydrogel contracted only 20% and maintained the 3D-printed cardiac ventricle chamber structure for up to 30 days. For practical use, encapsulation technology must further tackle scalable manufacturing and standardization challenges.

With the integration of artificial intelligence and flexible electronics, encapsulation systems hold the potential to incorporate real-time monitoring and dynamic adjustment capabilities. For instance, embedded sensors can provide real-time feedback on the physiological state of biological components, while machine learning algorithms optimize control strategies. Such “smart encapsulation” technologies will facilitate the transition of bio-syncretic robots from laboratory concepts to practical deployment, ultimately enabling transformative applications in fields such as medical rehabilitation and environmental remediation.

### 7.3. Integration of perception and intelligence

The integration of perception and intelligence in bio-syncretic robots represents the deep integration of biological and mechatronic systems at the molecular, cellular, and tissue levels. Its core lies in leveraging the inherent environmental responsiveness of biological materials and the computational advantages of artificial intelligence algorithms to construct intelligent closed-loop systems with lifelike characteristics.

The perception module serves as the foundation for interaction between bio-syncretic robots and the external environment, responsible for real-time environmental information acquisition and signal conversion. The unique advantages of biological materials in perception lie in their high sensitivity and multimodal sensing capabilities. Photosensitive biological materials can convert environmental light signals into electrical signals through electrophysiological responses, thereby enabling efficient environmental perception. The intelligence module processes and learns from the information acquired by the perception module through dynamic training of neural networks, thereby achieving intelligent control of robot behavior. The realization of this integrated technology typically relies on the integration of biological materials with artificial electronic systems.

The closed-loop integration of perception, intelligence, and actuation represents a core challenge in the systematization of bio-syncretic robots. Most current bio-hybrid intelligent systems rely on two-dimensional neural networks, which constrain the complexity and precision of information processing [135]. Cultivating three-dimensional neural networks can significantly enhance information processing capabilities and enable precise training of neural networks through multimodal stimulation (e.g., electrical, optical, and chemical stimuli). The closed-loop system of perception and intelligence not only facilitates efficient environmental interaction but also improves the functional performance and longevity of both perception and intelligence modules through the physiological connections of neurons.

### 7.4. Bioelectric interface

Bioelectronic interface is a key technology for bio-integrated robots to achieve efficient coupling between biological systems and artificial electromechanical systems. The core goal is to establish low-damage, high signal-to-noise ratio cross-scale signal transmission channels to coordinate the spontaneous activities of biological tissues with the precise execution of external control commands.

Mishra et al. [136] developed the mycelial electrical interface, which processes the electrical signals generated by mycelia through threshold detection and other methods, converts them into digital control signals, and can stably control the continuous movement of robots for dozens of minutes. Soliman et al. [137] explored the possibility of using yeast as the driving and sensing mechanism of soft robots. As a living organism, yeast is combined with micro-electromechanical systems (MEMS) to form a special biological interface. When used as a tactile sensor, in terms of force, the maximum resolution is  $7 \times 10^{-5}$  N; in terms of pressure, the maximum resolution is  $9 \times 10^{-6}$  bar.

Although the unique functions of biological tissues, such as muscle contraction, nerve signal transmission, and enzyme catalysis, enable robots to perform various functions, bioelectromechanical interface technology also faces many challenges. For example, biological materials and cells are sensitive to the chemical and physical environment of electronic devices, so it is necessary to develop more biocompatible electronic devices. Organisms exhibit complex dynamic behaviors, requiring the development of more effective control algorithms to regulate their activities. Additionally, the lifespan of organisms is limited, which necessitates the development of more efficient technologies for organism cultivation and maintenance.

## 8. Conclusion

This review summarizes the latest research progress in bio-syncretic robots, detailing their design elements, fabrication methods, and control technologies, while also discussing the potential challenges faced in their development. As a novel type of robot that integrates biological and artificial materials, bio-syncretic robots exhibit significant advantages, including high energy efficiency, self-healing capabilities, intrinsic safety, and multifunctional integration. Every aspect of their research relies on in-depth interdisciplinary collaboration, spanning robotics, biology, materials science, chemistry, and medicine. With the continuous advancement of interdisciplinary research, bio-syncretic robots are poised to achieve greater breakthroughs in the future. Despite numerous challenges, the study of bio-syncretic robots holds important scientific significance and broad application prospects. Through ongoing exploration and innovation, we anticipate that bio-syncretic robots will break through in more fields and make greater contributions to the development of human society.

### CRedit authorship contribution statement

**Yuyang Li:** Writing – original draft. **Chuang Zhang:** Writing – review & editing, Writing – original draft. **Qi Zhang:** Writing – review & editing. **Jiaduo Guo:** Writing – review & editing, Conceptualization. **Lianchao Yang:** Writing – review & editing. **Wenfeng Liang:** Writing – original draft. **Lianqing Liu:** Writing – original draft, Conceptualization.

### Declaration of competing interest

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

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