This is the accepted version of a paper presented at the 55th Annual Meeting of the 55th Italian Electronics Society - SIE, held in Genova, Italy, on June 26–28, 2024

When citing this work, please cite the original published paper:
Collu, R. et al. (2025). A Modular Portable Current Stimulator for Electrical Stimulation of Excitable Tissues. In: Valle, M., Gastaldo, P., Limiti, E. (eds) Proceedings of SIE 2024. SIE 2024. Lecture Notes in Electrical Engineering, vol 1263, p. 448-455. Springer, Cham. https://doi.org/10.1007/978-3-031-71518-1_54

Metadata of the chapter that will be visualized in SpringerLink

Book Title	Proceedings of SIE 2024
Series Title	
Chapter Title	A Modular Portable Current Stimulator for Electrical Stimulation of Excitable Tissues
Copyright Year	2025
Copyright HolderName	The Author(s), under exclusive license to Springer Nature Switzerland AG

Corresponding Author	Family Name	**Collu**
	Particle	
	Given Name	**Riccardo**
	Prefix	
	Suffix	
	Role	
	Division	
	Organization	University of Cagliari
	Address	090123, Cagliari, Italy
	Email	riccardo.collu@unica.it
	ORCID	http://orcid.org/0000-0001-7895-5956
Author	Family Name	**Lai**
	Particle	
	Given Name	**Stefano**
	Prefix	
	Suffix	
	Role	
	Division	
	Organization	University of Cagliari
	Address	090123, Cagliari, Italy
	Email	
	ORCID	http://orcid.org/0000-0002-2359-1865
Author	Family Name	**Mascia**
	Particle	
	Given Name	**Antonello**
	Prefix	
	Suffix	
	Role	
	Division	
	Organization	University of Cagliari
	Address	090123, Cagliari, Italy
	Email	
	ORCID	http://orcid.org/0000-0002-4185-7225
Author	Family Name	**Paolini**
	Particle	

	Given Name	**Roberto**
	Prefix	
	Suffix	
	Role	
	Division	
	Organization	Università Campus Biomedico di Roma
	Address	00128, Rome, Italy
	Email	
	ORCID	http://orcid.org/0009-0005-7327-3143
Author	Family Name	**Ferrazzano**
	Particle	
	Given Name	**Elena**
	Prefix	
	Suffix	
	Role	
	Division	
	Organization	University of Cagliari
	Address	090123, Cagliari, Italy
	Email	
	ORCID	http://orcid.org/0000-0002-9449-3680
Author	Family Name	**Zollo**
	Particle	
	Given Name	**Loredana**
	Prefix	
	Suffix	
	Role	
	Division	
	Organization	Università Campus Biomedico di Roma
	Address	00128, Rome, Italy
	Email	
	ORCID	http://orcid.org/0000-0002-8015-010X
Author	Family Name	**Cosseddu**
	Particle	
	Given Name	**Piero**
	Prefix	
	Suffix	
	Role	
	Division	
	Organization	University of Cagliari
	Address	090123, Cagliari, Italy
	Email	
	ORCID	http://orcid.org/0000-0003-4896-504X
Author	Family Name	**Barbaro**
	Particle	
	Given Name	**Massimo**

Prefix	
Suffix	
Role	
Division	
Organization	University of Cagliari
Address	090123, Cagliari, Italy
Email	
ORCID	http://orcid.org/0000-0001-6136-7664

Abstract

Electrical stimulation can be applied to excitable tissues to obtain sensory feedback, as in the case of stimulation of the peripheral nervous system, or mechanical actuation, as in the case of the stimulation of muscle tissues. In this study, a current stimulator for the stimulation of excitable tissues is proposed. The stimulator, created using a "stacked" approach, is made up of three separable units, namely a microcontroller unit, a stimulation frontend unit, and a power unit. The stimulator, made with Components-Off-the-Shelf (COTS), guarantees a working voltage of up to ±90 V and a stimulation current of up to 18 mA. The system has been tested for the stimulation of the peripheral nervous system on healthy volunteers, making it capable of inducing distinguishable sensations in the lower limb and on the upper limb, both through the use of conventional electrodes and ultra-conformable tattoo electrodes. Furthermore, the stimulator was tested for the control of a biohybrid actuator made up of muscle tissues showing the possibility of inducing twitch and tetanic contraction.

Keywords (separated by '-')

Neurostimulator - COTS - portable electronic system - tattoo electrodes - haptic feedback - biohybrid machines

A Modular Portable Current Stimulator for Electrical Stimulation of Excitable Tissues

Riccardo Collu[1](✉), Stefano Lai[1], Antonello Mascia[1], Roberto Paolini[2], Elena Ferrazzano[1], Loredana Zollo[2], Piero Cosseddu[1], and Massimo Barbaro[1]

[1] University of Cagliari, 090123 Cagliari, Italy
riccardo.collu@unica.it
[2] Università Campus Biomedico di Roma, 00128 Rome, Italy

Abstract. Electrical stimulation can be applied to excitable tissues to obtain sensory feedback, as in the case of stimulation of the peripheral nervous system, or mechanical actuation, as in the case of the stimulation of muscle tissues. In this study, a current stimulator for the stimulation of excitable tissues is proposed. The stimulator, created using a "stacked" approach, is made up of three separable units, namely a microcontroller unit, a stimulation frontend unit, and a power unit. The stimulator, made with Components-Off-the-Shelf (COTS), guarantees a working voltage of up to ±90 V and a stimulation current of up to 18 mA. The system has been tested for the stimulation of the peripheral nervous system on healthy volunteers, making it capable of inducing distinguishable sensations in the lower limb and on the upper limb, both through the use of conventional electrodes and ultra-conformable tattoo electrodes. Furthermore, the stimulator was tested for the control of a biohybrid actuator made up of muscle tissues showing the possibility of inducing twitch and tetanic contraction.

Keywords: Neurostimulator · COTS · portable electronic system · tattoo electrodes · haptic feedback · biohybrid machines

1 Introduction

Electrical stimulation of excitable tissues has been widely explored over the years [1], thus outlining the main stimulation paradigms that control muscle tissues' contractile activity or convey information through neurons. In the field of sensory feedback, the use of electrical stimulation has proven effective in allowing the restoration of tactile information in amputee subjects [2]. However, the main studies on sensory feedback are focused on the use of invasive technologies, such as implantable electrodes [3–6], which, as such, require surgery to be used, therefore limiting their field of applicability. Another substantial limitation is the need for more portable technology that can be integrated into the prosthetic system or the user's clothing, thus leading to benchtop use and the execution of tests mainly within laboratories [7]. The potential of non-invasive technologies to revolutionize the widespread use of electrical stimulation for sensory feedback is a promising development. Several studies have already demonstrated the effectiveness of transcutaneous electrical stimulation in inducing electrical sensations in peripheral limbs [8–10], thereby presenting a viable alternative to invasive technologies. The control of biohybrid actuators, and biohybrid machines in general, can be achieved through various methods, including magnetic, optical, chemical, and electrical actuation [11, 12]. Electrical stimulation offers several advantages over other methods, such as remote control, rapid activation of the actuator, and the ability for parallel and selective stimulation, making it a compelling choice. In this regard, however, electrical stimulation is usually performed under voltage and using benchtop instruments, even if this strategy does not guarantee optimal control over the injected charge, thus leading to the establishment of hydrolysis reactions.

The use of current electrical stimulation is the safest electrical stimulation strategy, both for sensory stimulation and for controlling biohybrid actuators. This work discusses the development of a portable and modular current stimulator designed to stimulate excitable tissues. The simulator has been tested in three different case tests: stimulation of peripheral nervous systems via commercial and tattoo electrodes, stimulation of biohybrid actuator, and evaluation of intracortical electrode.

2 The Designed Stimulator

To ensure the portable stimulator system remains small enough, the circuit has been designed as a stacked system measuring 59 mm × 28 mm × 25 mm (length × width × height). It consists of two custom Printed Circuit Boards (PCBs) and a commercial microcontroller unit, as shown in Fig. 1. This setup separates the power management units from the stimulation Frontend (FE), creating a modular device that can be easily adjusted for voltage compliance and stimulation current characteristics. Each PCB is a 59 mm × 28 mm, two-layer board designed to stack neatly on the commercial development microcontroller unit (MCU) board ESP32-WROOM-32UE. This MCU is a dual-core 32-bit microprocessor with a built-in Bluetooth module and USB peripheral.

2.1 Stimulation Frontend

The FE unit PCB is positioned in the middle of the stack. It receives the high-voltage bipolar supply from the power management unit and the 5 V supply from the MCU. It contains a four-channel 16-bit bipolar digital-to-analog converter (DAC) ADC, Analog Devices LTC2664, which is connected to the four stimulating channels. Each output channel consists of a voltage programmable voltage-to-current converter that delivers the current to the load using two amplifiers. One is a low voltage rail-to-rail amplifier from Analog Devices (Massachusetts, USA) AD8519ARTZ, and the other is a high voltage amplifier from Texas Instruments (Dallas, Texas, USA) OPA462IDDA. The MCU utilizes the SPI protocol to program the DAC, enabling users to turn ON or OFF any of the four channels. The low voltage amplifier serves as a buffer to sink/source the stimulation current, which is determined by the DAC output voltage and resistor Rstim. The load requiring stimulation is connected in feedback to the high-voltage amplifier to ensure the flow of the stimulation current as described in [7, 13]:

$$I_{stim} = \frac{V_{DAC}}{R_{stim}} \tag{1}$$

2.2 Power Management Unit

The power management unit PCB is situated at the bottom of the stack. It consists of two booster circuits utilizing switching voltage regulators from Analog Devices Inc. (Wilmington, MA, USA) LT8365, and a voltage inverting circuit using components from Maxim Integrated (San Jose, CA, USA) MAX889RESA to produce the required −5 V for the stimulation FE. The LT8365 is a voltage converter used to boost or invert voltages, ensuring low quiescent current and minimal output ripple. It is responsible for generating the ±90 V voltage compliance necessary for the stimulation output channel from the 5 V supply provided by the MCU.

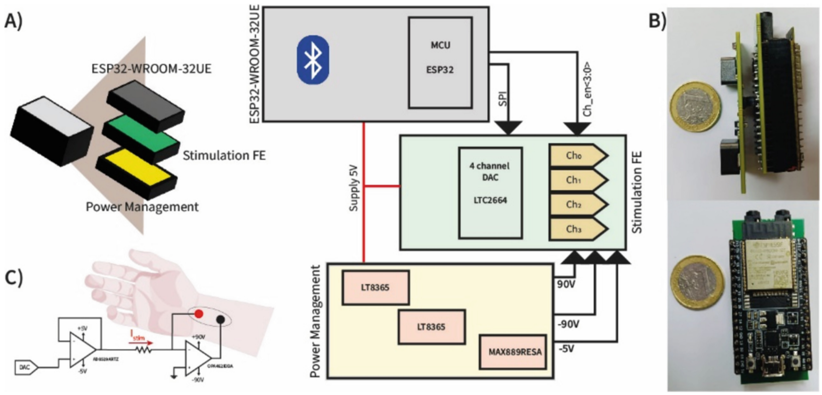

Fig. 1. The proposed prototype. **A)** The system is composed of three different mod-ules, a MCU, a frontend unit and a Power management unit. **B)** Front and lateral view of the prototype. **C)** Stimulation FE schematic.

2.3 Electrical Stimulation

The device can be fully programmed to provide stimulation with various waveforms, allowing for custom stimulation protocols. The capability to generate stimulation waveform is limited by the SPI to 2 ksps. The resolution of the current can be programmed between 381 nA and 762 nA.

3 System Evaluation

The power consumption of the device has been measured to be 1.3 W. The proposed system has been tested for three tasks: electrical stimulation of peripheral nerves in healthy volunteers, electrical stimulation of biohybrid actuator, and evaluation of intracortical electrode for invasive stimulation.

3.1 Electrical Stimulation of Peripheral Nervous System

The stimulation of peripheral nerves has been performed on ten healthy volunteers using commercial electrodes and three volunteers using ultra-conformable tattoo electrodes [13–15]. Commercial electrodes were positioned on the leg of the volunteers to target the tibial nerve. Stimulation was performed at different frequency and different amplitudes, modulating the injected charge. The maximum frequency employed was 500 Hz. The descriptions of sensations in terms of quality and naturalness were collected, as shown in Fig. 2.

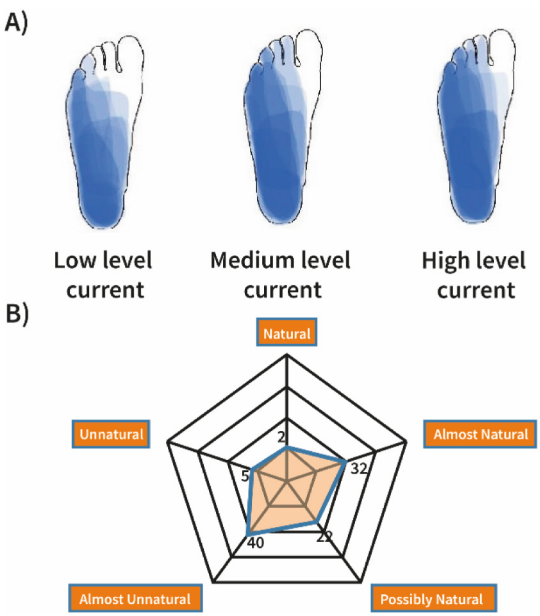

Fig. 2. Electrical stimulation of the tibial nerve in 10 healthy subjects. Following the stimulation, the projection areas of the induced sensation were collected based on the level of current applied (A) and the qualities of the sensations in terms of naturalness (B).

Ultra-conformable tattoo electrodes were used to stimulate the upper limb. The electrodes were positioned in correspondence of the median nerve. The reported sensations were collected in terms of position on the hand and quality, as shown in Fig. 3.

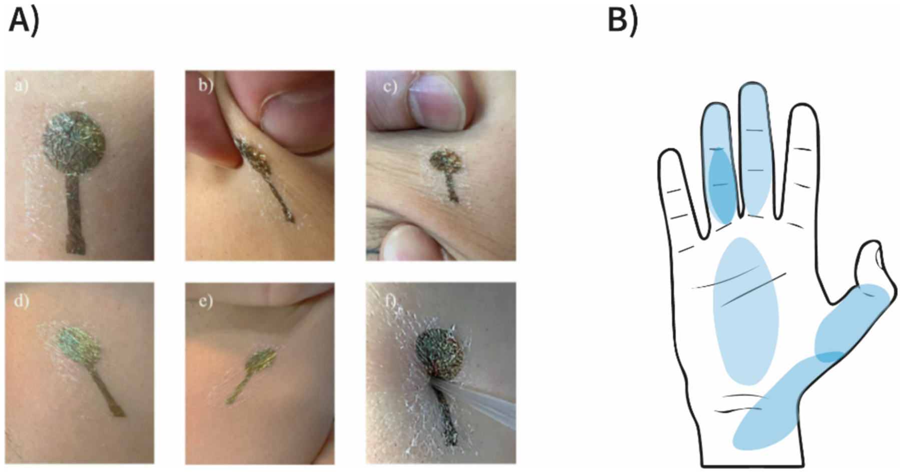

Fig. 3. Electrical stimulation using Tattoo electrodes. A) Tattoo electrodes allow high adhesion to tissues, ensuring they follow the skin's natural folds and remain adherent even following mechanical bending. B) Sensations collected following stimulation of the median nerve in three healthy subjects

3.2 Electrical Stimulation of Biohybrid Actuator

The soft robotics field has also verified the ability to stimulate and control excitable tissues by including biohybrid actuators based on skeletal muscle tissue [16]. In order to use biohybrid actuators, such as muscle tissues, in the robotic field, it is essential to control the actuator's contractions to control and maintain the flexions of the joints to be controlled. In particular, to create a structure such as a catheter, it would be necessary for the actuator to maintain the contraction to guarantee the routing of the catheter inside the blood vessels while still guaranteeing a rapid and precise contraction. Skeletal muscle tissue was selected to verify the suitability of the stimulator in the soft robotics sector, as shown in Fig. 4A-B. Skeletal muscle tissue was stimulated using symmetrical biphasic waveforms to induce tetanic contraction, as shown in Fig. 4C, or short contractions, as shown Fig. 4D. The tetanic contraction was obtained using stimulation trains between 20 and 35 Hz, while twitch was induced at 1 Hz.

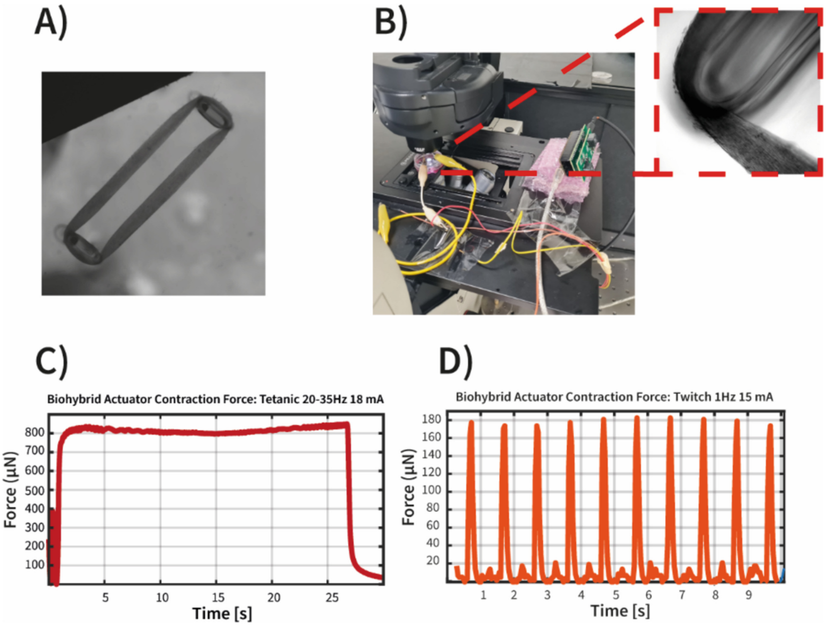

Fig. 4. The stimulator has been employed in the electrical stimulation of a biohybrid actuator for soft robotics applications. A) View of the biohybrid actuator. B) Stimulation setup. The setup is composed by the Leica Thunder Imaging system and the stimulator. C) The stimulator was capable of inducing controllable tetanic contraction on the actuator leading to contraction forces up to 800 µN. D) The stimulator was capable of inducing controllable twitch contraction on the actuator.

3.3 Evaluation of Intracortical Electrodes for Invasive Stimulation

The system was also used in the preliminary evaluation of implantable electrodes for intracortical electrical stimulation. An example of the electrodes used is shown in Fig. 5A. The impedance was evaluated by immersing the electrodes in a physiological solution and imposing electrical stimuli using the stimulator. The voltage across the active stimulation sites was recorded and used to estimate the resistive part of the impedance. The resulting impedance is shown in Fig. 5B. The impedance of the active sites is always higher than 25 kΩ, showing how it is necessary to have a high voltage compliance to be able to stimulate effectively. Considering the voltage compliance of ±90 V of the proposed device, an impedance of 25 kΩ leads to a maximum stimulation current equal to 3.6 mA, which is adequate for intracranial stimulation. However, in many cases, the impedance reaches values higher than 100 kΩ, a value that would limit the current to a maximum of 900 µA.

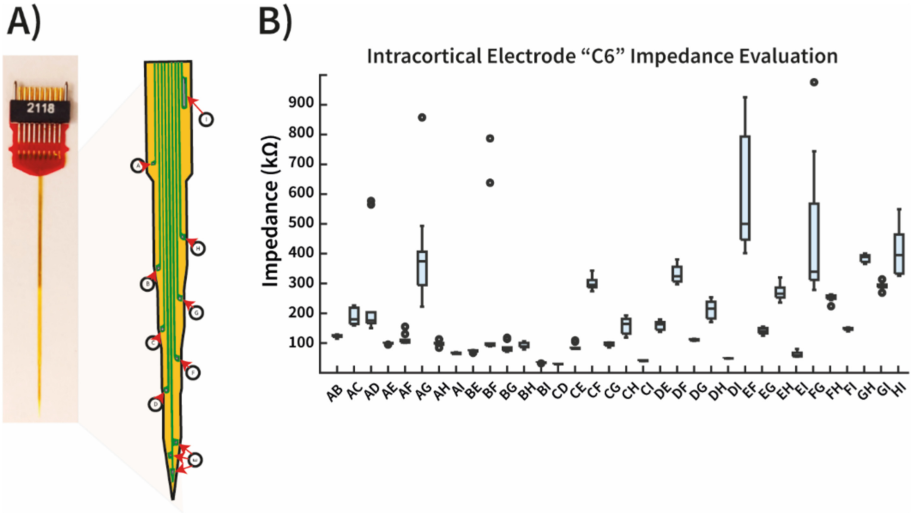

Fig. 5. Evaluation of intracortical electrodes for invasive stimulation. A) The electrode used is based on the TIME structure and is made up of nine different active stimulation sites B) The impedances of the active sites of the intracortical electrode were measured through the prototype. Stimulation sites have a minimum impedance of 25 kΩ (CI) but can reach more than 500 kΩ, making high voltage compliance necessary for proper stimulation of nerve tissue.

4 Conclusions

The power consumption of the device has been measured to be 1.3 W. The device has been tested on healthy volunteers, showing the capability to stimulate the peripheral nervous system properly and induce referred sensations on the leg and the hand through commercial and ultra-conformable tattoo electrodes. The stimulator was employed to control and induce contractions on a biohybrid actuator based on skeletal muscle tissue, showing the capability to induce twitch and tetanic contraction, reaching huge contraction forces up to 800 µN. The high voltage range also makes the stimulator suitable for working with intracortical electrodes, where the impedance of the stimulation sites can reach several hundreds of kΩ. To verify this, the prototype was used to evaluate the impedance of the stimulation channels of an intracortical electrode and will soon be used for intracortical neural stimulation of rodents.

Acknowledgment. This project has received funding from the European Union’s Horizon Europe research and innovation programme under grant agreement No. 101070328.

References

1. Zhao, S., Mehta, A.S., Zhao, M.: Biomedical applications of electrical stimulation. Cellular and Molecular Life Sciences **77**(14). Springer, pp. 2681–2699 (2020). https://doi.org/10.1007/s00018-019-03446-1

2. Pasluosta, C., Kiele, P., Stieglitz, T.: Paradigms for restoration of somatosensory feedback via stimulation of the peripheral nervous system. Clinical Neurophysiology **129**(4), 851–862. Elsevier Ireland Ltd. (2018). https://doi.org/10.1016/j.clinph.2017.12.027
3. Raspopovic, S., et al.: Restoring natural sensory feedback in real-time bidirectional hand prostheses. Sci. Transl. Med. **6**(222), 222ra19 (2014). https://doi.org/10.1126/scitranslmed.3006820
4. Zollo, L., et al.: Restoring tactile sensations via neural interfaces for real-time force-and-slippage closed-loop control of bionic hands (2019). http://robotics.sciencemag.org/
5. Tyler, D.J.: Neural interfaces for somatosensory feedback: Bringing life to a prosthesis. Current Opinion in Neurology **28**(6), 574–581. Lippincott Williams and Wilkins (2015). https://doi.org/10.1097/WCO.0000000000000266
6. Tan, D.W., et al.: A neural interface provides long-term stable natural touch perception. Sci. Transl. Med. **6**(257), 257ra138–257ra138 (2014). https://doi.org/10.1126/scitranslmed.3008669
7. Collu, R., et al.: Wearable high voltage compliant current stimulator for restoring sensory feedback. Micromachines (Basel) **14**(4) (2023). https://doi.org/10.3390/mi14040782
8. Collu, R., Earley, E.J., Barbaro, M., Ortiz-Catalan, M.: Non-rectangular neurostimulation waveforms elicit varied sensation quality and perceptive fields on the hand. Sci. Rep. **13**(1), 1588 (2023). https://doi.org/10.1038/s41598-023-28594-0
9. Scarpelli, A., Demofonti, A., Terracina, F., Ciancio, A.L., Zollo, L.: Evoking apparent moving sensation in the hand via transcutaneous electrical nerve stimulation. Front Neurosci. **14** (2020). https://doi.org/10.3389/fnins.2020.00534
10. Demofonti, A., Scarpelli, A., Cordella, F., Zollo, L.: Modulation of sensation intensity in the lower limb via Transcutaneous Electrical Nerve Stimulation. In: Proceedings of the Annual International Conference of the IEEE Engineering in Medicine and Biology Society, EMBS. Institute of Electrical and Electronics Engineers Inc. (2021). pp. 6470–6474. https://doi.org/10.1109/EMBC46164.2021.9630871
11. Ricotti, L., et al.: Biohybrid actuators for robotics: A review of devices actuated by living cells (2017). https://www.science.org
12. Ricotti, L., Menciassi, A.: Bio-hybrid muscle cell-based actuators. Biomed. Microdevices **14**(6), 987–998 (2012). https://doi.org/10.1007/s10544-012-9697-9
13. Collu, R., et al.: A microcontroller-based portable transcutaneous electrical nerve stimulator via ultra-comfortable tattoo electrodes for haptic feedback. In: Lecture Notes in Electrical Engineering, 385–395. Springer Science and Business Media Deutschland GmbH (2024). https://doi.org/10.1007/978-3-031-48711-8_47
14. Collu, R., et al.: A wearable electronic system for EEG recording. In: PRIME 2022 - 17th International Conference on Ph.D Research in Microelectronics and Electronics, Proceedings (2022). https://doi.org/10.1109/PRIME55000.2022.9816817
15. Mascia, A., et al.: Wearable system based on ultra-thin Parylene C tattoo electrodes for EEG recording. Sensors **23**(2) (2023). https://doi.org/10.3390/s23020766
16. Guix, M., et al.: Biohybrid soft robots with self-stimulating skeletons. Sci. Robot. **6**, 7577 (2020)