Guest Editorial
Bionic Organs and Tissues

I. Introduction

BIONICS has a twofold meaning. On the one hand, it refers to artificial devices/systems whose design and features are inspired by natural systems. On the other hand, bionics concerns artificial and bioartificial solutions that closely interact with human tissues and organs to restore lost function (items 1)–3) in the Appendix).

The term "cyborg," coined in the '60s and referring to a cybernetic organism, identifies the dream of incorporating exogenous components extending the self-regulatory control function of an organism, to adapt it to new environments. In the past decades, numerous science fiction novels and movies have driven a relatively negative public image of cyborgs, which often appeared as beings with supernatural abilities and power, frequently used to harm humanity, at least in the Western world. Today, a significant number of individuals are using intracorporeal medical devices, such as pacemakers, sophisticated prostheses, cochlea and retina implants, artificial pancreas, etc. It is increasingly evident that nowadays these technologies constitute an opportunity for humankind, rather than a threat. This field has made tremendous progress in the past 15 years (items 4)–7) in the Appendix).

The Focused Section on "Bionic Organs and Tissues" aimed at attracting original scientific and technological contributions on devices, hardware/software solutions and materials enabling the mimicking, substitution or enhancement of a human organ or tissue, for drug screening and/or for replacing functions compromised by traumas or degeneration processes.

These efforts can be pursued at different scales. For example, they can focus on milli- or micro-scale systems, not designed to be implanted, but aiming at reproducing on a chip the main features of a tissue or organ. This enables the screening of drug safety and efficacy, in the context of a personalized medicine approach. Other engineered artificial or bioartificial solutions, typically at larger scales (from a few mm to several cm), are thought to be implanted in the human body and to replace lost function or to support the residual functions of the native biological structure. Other artificial or bioartificial solutions can be used as organ and tissue simulators.

All these efforts require a highly interdisciplinary approach, in which engineering solutions must be coupled with a deep awareness of biological and physiological aspects of the target tissues and organs, as well as with advanced materials, which are used as both functional elements and as coatings to engineer cell functions. The categorization of the research efforts in this multi-disciplinary domain are graphically represented in Fig. 1.

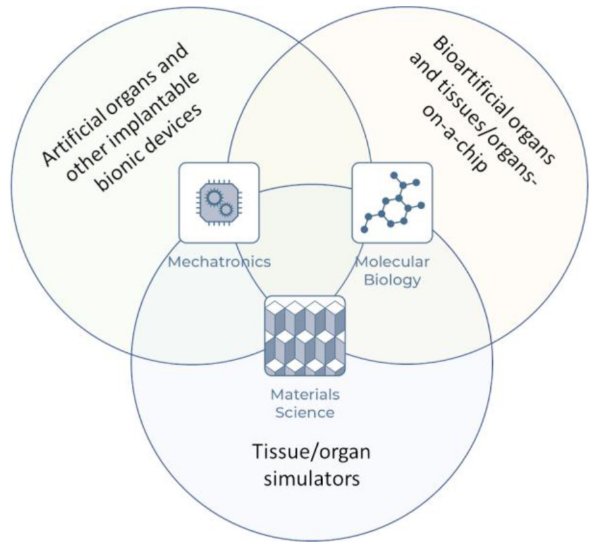

Fig. 1. Depiction of the three research domains addressed by the Focused Section on Bionic Organs and Tissues. In each of them, mechatronics, materials science and molecular biology play complementary roles.

II. Focused Section Content

This Focused Section includes six manuscripts, covering the three research themes depicted in Fig. 1.

A. Artificial Organs and Other Implantable Devices

Artificial organs and other implantable devices based on a bionic design are mainly based on mechatronic solutions, but they also often exploit advanced materials. The first two papers of this Focused Section deal with this research theme.

The paper "RhinoFit: A Bionic Nasal Device for Mitigating Post-Operative Complications After Rhinosurgery" by Campacci *et al.* addresses the bionic design of a device, which is based on standardized anatomical internal geometry of the natural nasal cavity. The authors also describe the fabrication and testing of such a system *in vitro*, taught to tamponade the surgical wounds after rhinoplasty, perform nasal washes draining residual fluids from the nostril and adjust the pressure on the lateral wall of the nasal cavity, thus preventing pain.

In the field of artificial pancreas substitutes, the proposed technologies typically consist of three key elements: a glucose sensor, an insulin pump and a control algorithm regulating the interplay between sensor and pump. In the paper "Artificial Pancreas: *In Silico* Study Shows No Need of Meal Announcement and Improved Time in Range of Glucose With Intraperitoneal vs. Subcutaneous Insulin Delivery," by Toffanin *et al.*, a novel control algorithm is proposed and validated *in silico*. The results shown by the authors demonstrate

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that delivering insulin in the peritoneal cavity is much more advantageous than subcutaneous release, highlighting the potential of fully implanted artificial pancreas systems exploiting this route for correcting glycemic levels.

B. Bioartificial Organs and Tissues/Organs-on-a-Chip

Bioartificial organs, as well tissues- and organs-on-a-chip, have molecular biology as a crucial component. However, properly engineered biomaterials and mechatronic set-ups for maintaining appropriate conditions (e.g., medium renewal, or adding actuation degrees of freedom) also have important roles. Two papers of this Focused Section deal with this research theme.

The paper "Exploring the Contribution of Thalamic and Hippocampal Input on Cortical Dynamics in a Brain-on-a-Chip Model" by Brofiga *et al.* describes a brain-on-a-chip based on thalamic and hippocampal neurons and micro-electrode arrays to record electrophysiological activity. The authors analyze the dynamics of cortical ensembles, paving the way to *in vitro* models to investigate how connectivity among different neuronal populations can be affected by neurodegenerative pathologies.

The paper "3D Printed Perfusable Renal Proximal Tubule Model With Different Extracellular Matrix Compositions" by Mazzeo *et al.* describes the design of a chip modeling the proximal renal tubule, that is targeted by drug toxicants. The authors demonstrated a tubule model based on a 3D convoluted geometry whose printing parameters were optimized to achieve a perfusion system. The obtained chip is promising as a means to test nephrotoxicity of drugs and other compounds, or for the use of transglutaminase-based extracellular matrix formulations as a basis for the development of engineered bioartificial kidneys.

C. Tissue/Organ Simulators

In tissue and organ simulators, materials science efforts allow mimicry of the characteristics of natural components; mechatronics plays a role in replicating motion and recording functional parameters, while molecular biology enables the development of bio-hybrid solutions. Two papers of this Focused Section deal with this research theme.

The paper "Conductive Silicone Vocal Folds Reproducing Electroglottographic Signal in Pathophysiological Conditions" by Conte *et al.* addresses the development of electrically conductive biorobotic simulators that can recapitulate an electroglottography (EGG) signal under pathophysiological conditions to monitor vibration of the vocal folds. They find an inverse correlation between resistance variation and contact area of the vocal folds. Their simulators replicate the vibratory characteristics of healthy and pathological vocal folds, and corresponding EGG signal. Utilization of the simulators developed herein may enable meaningful categorization of laryngeal disease which may lead to enhanced treatment and prevention programs.

The review paper "High-Fidelity Physical Organ Simulators: From Artificial to Bio-Hybrid Solutions" by Maglio *et al.* describes an insight into the current state-of-the-art high-fidelity physical organ simulators that are used for training purposes, biomechanical studies and preclinical device testing. In the paper, the authors highlighted the traditional approaches for static organ simulators using synthetic materials, and diverse approaches for dynamic organ simulators including soft robotic, *ex vivo* and biohybrid strategies, and finally discuss challenges and potential future avenues in the field of high-fidelity physical organ simulators.

III. Conclusion

The Focused Section on Bionic Organs and Tissues confirms the important progress made in the area of bionic medical devices, artificial and bioartificial organs and tissues, lab-on-a-chip and simulators, highlighting the importance of highly interdisciplinary efforts connecting advanced technologies with the clinical world. We hope that this Focused Section will contribute to the development of this research arena in the next years, as well as to the reinforcement of the "Bionic organs" area of this journal, which will hopefully attract an increasing number of high-quality scientific contributions.

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Editors of the Focused Section

Leonardo Ricotti, *Guest Editor*
The BioRobotics Institute
Department of Excellence in Robotics & AI
Scuola Superiore Sant'Anna
56127 Pisa, Italy

Toshinori Fujie, *Guest Editor*
School of Life Science and Technology
Tokyo Institute of Technology
Tokyo 226-8501, Japan

Ellen T. Roche, *Guest Editor*
Institute for Medical Engineering and Science
Department of Mechanical Engineering
Massachusetts Institute of Technology
Cambridge, MA 02139 USA

Appendix
Related Work

1) L. E. Lipetz, "Bionics," *Science*, vol. 133, no. 3452, pp. 588–593, Feb. 1961.
2) M. A. Arbib, H. E. Von Gierke, and H. L. Oestreicher, *Principles and Practice of Bionics*. Slough, U.K.: Technivis. Services, 1970.
3) P. Dario, "Editorial medical robotics and bionics: A new interdisciplinary adventure," *IEEE Trans. Med. Robot. Bionics*, vol. 1, no. 1, pp. 1–3, Feb. 2019.
4) L. Ricotti, T. Assaf, P. Dario, and A. Menciassi, "Wearable and implantable pancreas substitutes," *J. Artif. Org.*, vol. 16, no. 1, pp. 9–22, Mar. 2013.
5) E. T. Roche *et al.*, "Soft robotic sleeve supports heart function," *Sci. Transl. Med.*, vol. 9, no. 373, Jan. 2017, Art. no. eaaf3925, doi: 10.1126/scitranslmed.aaf3925.
6) R. Feiner and T. Dvir, "Tissue–electronics interfaces: From implantable devices to engineered tissues," *Nat. Rev. Mater.*, vol. 3, no. 1, pp. 1–16, Nov. 2017.
7) K. Yamagishi, S. Takeoka, and T. Fujie, "Printed nanofilms mechanically conforming to living bodies," *Biomater. Sci.*, vol. 7, no. 2, pp. 520–531, Jan. 2019.