What is bioelectronics?

Sandro Carrara

Although the term was first proposed in 1968, the birth of *bioelectronics* as we know it today is much more recent. In fact, the first meaning of the word bioelectronics was the intermolecular electron transfer found in biological systems [1], while its modern meaning is quite different, as discussed in this chapter.

Tony Turner, founder and Editor-in-Chief of the Elsevier journal *Biosensors and Bioelectronics*, wrote in 2005: "Bioelectronics is a recently coined term for a field of research that works to establish a synergy between electronics and biology" [2]. Over the years, his journal became the main forum in the field of bioelectronics. The journal originally appeared in 1985 with the simple name of *Biosensors*, and the title was expanded to include the term *Bioelectronics* in 1992 [2]. The expressed scope of the journal [3] explains that a key aspect of bioelectronics is the interface between biological materials and electronics.

To better understand the modern state of the field, we can also consider the meaning of "advanced bioelectronics" as mentioned in April 2013 by the National Institute of Standards and Technology (NIST - an agency of the US Department of Commerce) and represented by the example of electronic DNA sequencing, as supported by singlemolecule mass spectrometry to develop innovative electronic devices for healthcare [4]. The authors [4] refer to devices in which an electric field drives individual molecules of single-stranded DNA through a nanometer-scale pore (Figure 1.1). That approach is a step toward applications for rapid sequencing of DNA [5] and DNA transcription complexes [6], and could lead to further developments in protein sequencing [7] too. The application is clearly focused on devices for healthcare and, more generally, includes both diagnostic and therapeutic tools.

We could briefly summarize bioelectronics as "the application of electronics in the field of biology", and, in fact, IUPAC accepts the definition of bioelectronics as "the application of biomolecular principles to microelectronics such as in biosensors and biochips" [8]. However, in the literature we actually have much more than that. It is easy to find extensions of bioelectronics into the area of electronic components and circuits that include proteins or other biological macromolecules. For example, it has been outlined that this field might include biotemplated circuitries [9]. To quote the Elsevier journal Biosensors and Bioelectronics, already mentioned above as a leader in the field: "The emerging field of bioelectronics seeks to exploit biology in conjunction with electronics in a wider context encompassing, for example, biological fuel cells, bionics and biomaterials for information processing, information storage, electronic components and actuators" [3].

Another historical pioneer of the field, Wolfgang Göpel, wrote in 1998: "Bioelectronics is aimed at the direct coupling of biomolecular function units of high molecular weight and extremely complicated molecular structure with electronic or optical transducer devices" (Figure 1.2) [10]. Two key points are introduced here: the "direct coupling" and the "high molecular weight". The first indicates an intimate integration between biomolecular principles and microelectronics. The second implies large biomolecules such as proteins or complex biological systems such as cells or bacteria. That means we need to integrate biomolecular functions with extremely complicated biological structures. However, "organic bioelectronics" has been introduced, too, by proposing, for example, organic polymers for drug delivery systems [11]. Now, we cannot say that "a polymer" can be seen as "an extremely complicated molecular structure" and, therefore, we need to

Handbook of Bioelectronics, Sandro Carrara and Krzysztof Iniewski. Published by Cambridge University Press. © Cambridge University Press 2015.



Figure 1.1 Single molecule spectroscopy at nanopores (reprinted from NIST website, courtesy of Jeffrey Aarons [4])



Figure 1.2 Schematic representation of a bioelectronic sensor device (redrawn from [10])

conclude that the field of bioelectronics has further expanded beyond the original definition of its pioneers. In fact, it has also been declared that "the fundamental element of molecular electronics is a molecular device or a supramolecular device, which is an organized molecular system constructed mainly by **organic molecules or biomolecules** that have some specific functions in signal detection, process, storage, and transmission through chemical or physical interactions at molecular or supramolecular levels" [12]. Very recently, this extension of the field toward organic molecules has been certified by a special issue in the journal *Biochimica et Biophysica Acta* dedicated to *organic bioelectronics* [13]. The field was presented there as an interdisciplinary field that "encompasses many different applications, including neural interfaces, tissue engineering, drug delivery, and biosensors" [13].



Figure 1.3 Redox enzymes electrically contacted by nanostructures such as gold nanoparticles or carbon nanotubes (redrawn from [9]). SWCNT, single-walled carbon nanotube

Going back to the original definition set in 1998 by W. Göpel, we can then say that the intimate integration with "extremely complicated molecular structure" may also lie in the interface between the realized inorganic device and the more complex biological system once the device has been implanted for use in an application. Göpel also agreed that "with increasing complexity and demands for future information technologies, a trend is to be seen towards the design of 'smart' nanostructures which will be interfaced to silicon or other substrates. These structures may consist [...] of chemically synthesized units such as molecules, supramolecules and biologically active (biomimetic) recognition centers" (Figure 1.3) [10]. This prediction made in 1998 has been confirmed by several developments that exploit nanotechnology for sensing [14], and has now reached the stage of a fundamental codesign of the interface between biological macromolecules, organic nanostructures, and CMOS circuitries [15].

Several books have been published over the last 20 years to cover the field of bioelectronics. However, these books usually only partially cover this vast field. For example, we can find books that mainly cover molecular devices [16], devices for sensing and computing [17], neural networks and biosensors [18], artificial retinas [19], interfaces for biosensing [20] [15], smart materials [21], biophysics of electron transfer [22], or low-power design [23]. We might find good introductory books [24] but nothing fully exhaustive. The aim of this book is, then, to address this gap and try to propose a comprehensive overview of the whole field of bioelectronics.

To be sure that we address the whole variety of different aspects of bioelectronics, we can look at the division of the field first made in a session of the main congress *Biosensors*, held in Bangkok in 1996 [10]:

- Biocompatible electronic devices
- In vivo sensors; sensors based on biological materials
- Biological materials for electronics and optics
- Materials for electronics synthesized by biological processes, including bacteriorhodopsin
- Concepts and materials inspired by biology and useful for electronics
- Algorithms inspired by biology
- Artificial senses
- Biological-inorganic hybrids
- Imaging and addressing of individual biomolecular function units

The book is organized into the following separate sections in order to address this aim.

- Bioelectronic components
- Biosensors
- Fuel cells
- Biomimetic systems
- Bionics
- Brain interfaces
- Lab-on-a-chip

Then the final section is:

Future perspectives

This last section of the book aims to show the trends in bioelectronics emerging at the frontiers of worldwide research in the field of electronics, and to indicate how these might meet our new needs for more advanced healthcare systems.

The book ends with a chapter on *distributed theranostics* as supported by *personal electronics*. In our daily lives, all of us carry personal electronic devices (such as smartphones, touch-screen tablets, laptops, and satellite navigators). The new frontier of bioelectronics is to integrate, expand, and transform part of these personal devices into new healthcare tools that can provide distributed diagnostics and personalized therapy: *theranostics*.

References

- A. Szent-Györgyi, "Bioelectronics," Science, vol. 161, pp. 988–990, 1968.
- [2] A. P. F. Turner, "Biosensors and bioelectronics 20 years on," Biosensors and Bioelectronics, vol. 20, p. 2387, 2005.
- [3] A. P. F. Turner, "Biosensors and Bioelectronics journal: aims and scope," available at http://www.journals.elsevier.com/ biosensors-and-bioelectronics/, July 17 2013.
- [4] J.W.F. Robertson, J.J. Kasianowicz, and A. Balijepalli, "Metrology for advanced bioelectronics," NIST web page available at http://www.nist.gov/pml/div683/grp06/nanobio.cfm, 2013.
- [5] D. Branton, D. W. Deamer, A. Marziali *et al.*, "The potential and challenges of nanopore sequencing," *Nature Biotechnology*, vol. 26, pp. 1146–1153, 2008.
- [6] C. Raillon, P. Cousin, F. Traversi et al., "Nanopore detection of single molecule RNAP-DNA transcription complex," Nano Letters, vol. 12, pp. 1157–1164, 2012.
- [7] Q. Zhao, R. S. S. de Zoysa, D. Wang, D. A. Jayawardhana, and X. Guan, "Real-time monitoring of peptide cleavage using a nanopore probe," *Journal of the American Chemical Society*, vol. **131**, pp. 6324-6325, 2009.
- [8] B. Nagel, H. Dellweg, and L. Gierasch, "Glossary for chemists of terms used in biotechnology (IUPAC Recommendations 1992)," *Pure and Applied Chemistry*, vol. 64, 1992.
- [9] E. Katz, "Bioelectronics," in *Encyclopedia of Condensed Matter Physics, B.* Editors-in-Chief: F. Bassani, L. L. Gerald, and W. Peter, Eds., Elsevier, 2005, pp. 85–98.

- [10] W. Göpel, "Bioelectronics and nanotechnologies," *Biosensors and Bioelectronics*, vol. 13, pp. 723–728, 1998.
- [11] K. Svennersten, K. C. Larsson, M. Berggren, and A. Richter-Dahlfors, "Organic bioelectronics in nanomedicine," *Biochimica et Biophysica Acta (BBA) – General Subjects*, vol. 1810, pp. 276–285, 2011.
- [12] Y. Wei, "Molecular electronics the future of bioelectronics," *Supramolecular Science*, vol. 5, pp. 723–731, 1998.
- [13] G. G. Malliaras, "Organic bioelectronics: A new era for organic electronics," *Biochimica et Biophysica Acta (BBA) – General Subjects*, vol. **1830**, pp. 4286–4287, 2013.
- [14] S. Carrara, Nano Bio Sensing, Springer, 2010.
- [15] S. Carrara, Bio/CMOS Interfaces and Co-design, Springer, 2012.
- [16] S. C. C. Nicolini, P. Facci, V. Sivozhelezov et al., Molecular Bioelectronics, World Scientific Publishing, 1996.
- [17] I. Willner and E. Katz, *Bioelectronics*, John Wiley & Sons, 2006.
- [18] M. Grattarola and G. Massobrio, Bioelectronics Handbook: MOSFETs, Biosensors, and Neurons, McGraw-Hill, 1998.
- [19] J. C. S. Martins, Leonel Augusto Bioelectronic Vision: Retina Models, Evaluation Metrics and System Design (Series on Bioengineering and Biomedical Engineering vol. 3), World Scientific, 2009.
- [20] J. J. Davis, Engineering the Bioelectronic Interface: Applications to Analyte Biosensing and Protein Detection, Royal Society of Chemistry, 2009.
- [21] D. Andreescu, S. Andreescu, and O. A. Sadik, New Materials for Biosensors, Biochips and Molecular Bioelectronics. Comprehensive Analytical Chemistry vol. 44, Amsterdam: Elsevier, 2005.
- [22] C. A. Nicolini, Biophysics of Electron Transfer and Molecular Bioelectronics, Plenum Press, 1998.
- [23] R. Sarpeshkar, Ultra Low Power Bioelectronics vol. 1, Cambridge University Press, 2010.
- [24] R. R. Pethig and S. Smith, Introductory Bioelectronics: For Engineers and Physical Scientists, Wiley, 2012.