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Book Review

Bioelectronics: From Theory to Applications. Edited by Itamar Willner and Eugenii Katz, John Wiley & Sons, Ltd. New York, 2005, Hardcover, $255, ISBN 3-527-30690-0, 492 pp.

Bioelectronics implies that there is meaningful transfer of electronic information between biomaterials and electrical elements. Since most biological systems involve transfer of electrons and ions, it would seem that integrating electronics with biological processes would be natural. However, practitioners have overcome numerous hurdles (especially during the last two decades) and many remain challenges even today.

Willner and Katz consider bioelectronics on a molecular scale. Hence, advances in prosthetics or electrical muscle stimulation for example are not covered. The preface lists the applications covered, which include specific biosensors, coupling neurons with electronic elements (information-processing devices), development of biofuel cells and biomolecule based motors. The book's objectives are to consider theoretical limitations in electronic coupling of biomolecules with electronic elements, list methods of immobilizing biomolecules on electronic transducers, apply systems as biosensors, and explore neural networks as information processing, storing, and computing systems. Chapters 1 and 15 summarize the remaining chapters and speculate on realistic bioelectronic applications in the near future.

Chapters 2 and 3 explore electron transfer. Chapter 2 investigates electron transfer through proteins and explores the theory of tunneling pathways. It also summarizes extensions and alternatives of this theory including variations on multiple pathways, and shortcomings of each approach. Chapter 3 investigates redox enzymes on electrodes and electron transfer at functionalized electrodes, and current challenges. Redox reactions are at the heart of traditional fuel cells, and this chapter extends its discussion to cover biofuel cell design.

Chapters 4, 5, and 8 focus on biosensors and their applications. As a standalone article, Chapter 4 provides an excellent historical overview of the development of biosensors, examples of biosensors today, and an extensive list of references for further study. A natural extension of biosensors would be sensor arrays, leading to miniaturization and biochips—all of which are discussed in this chapter. Chapter 5 starts with a summery of DNA's electronegativity and DNA labeling. Next, it provides an excellent state of the art on DNA sensors. For those readers who would like to gain more in depth knowledge, this chapter includes an extensive list of references.

Chapter 8 extends biosensing applications with functionalized nanoparticles. Its focus is electrical wiring of redox enzymes, integration of semiconductor nanoparticles with enzyme-driven biocatalytic transformations, use of biomaterial-nanoparticle conjugates in sensing, and application of magnetic particles during bioelectrochemical analysis.

Chapters 6, 7, and 10 explore working with a single biomolecule. Chapter 10 examines manipulating biomolecules using glass microneedles and laser traps. Chapter 7 investigates immobilizing biomolecules on silicon (as it is homogeneous and atomically flat). Silicon can be integrated with conventional silicon electronics for amplification and signal processing. This chapter also discusses using diamond thin films on silicon to provide the stability, selectivity, and sensitivity needed for biosensing applications.

Chapter 6 focuses on probing a single biomolecule. For this to happen, the biomolecule needs to be adsorbed on a conducting surface. It also needs to be ordered, biologically active and fully functional. In practice, this is difficult to achieve and most biomolecules are not in their "native" state once adsorbed. The chapter first explores chemical and physical methods of anchoring biomolecules on conducting surfaces followed by methods for controlled adsorption of biomolecules. Next Atomic Force Microscopy (AFM) and Scanning Tunneling Spectroscopy (STS) are discussed as tools for investigating biomolecules.

Molecular electronics does not have anything analogous to the integrated circuit in microelectronics. Chapters 9 and 13 report on work that draws inspiration from self-assembly based on recognition among molecular building blocks to construct templates for such applications. Chapter 9 discusses using DNA scaffolding with defined molecular addresses. One can then instill electronic functionality to the scaffold by localized electronic devices at the desired locations and connect them by DNA-template wires. This chapter presents the state of the art in DNA scaffolding and current challenges. It also outlines other biological mechanisms that could construct complex templates. Chapter 13 explores using S-layer proteins as nanotemplates since they form highly ordered lattices and can serve to insulate neighboring functional groups from unwanted electrical connectivity.

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Biocomputing has long captured the imagination of scientists and the public at large. Chapters 11, 12, and 14 provide current state of the art, existing challenges, and realistic expectations in the years ahead. Chapter 11 investigates using photosimulation to read and write information. The authors summarize it best as: "The optical signal "writes" information to the assembly by defining the state of the photoisomerizable component. This state is then preserved (stored) until another signal changes the state again. The information is "read" by the detection of the biocatalytic current, and thus signal transduction from optical through biological to electronic forms can be achieved." [p. 336].

Chapter 12 starts by listing near term applications of neuron-semiconductor interfaces. Each section then explores a facet of the ionic-electronic interface, and each section ends with a conclusion that summarizes current challenges in that specific area. The chapter ends by listing areas that need optimization for both neural networks and semiconductors, and speculating on future research directions. This chapter is well organized and easy to read for the general reader.

Chapter 14 summarizes the work done in computing with nucleic acids (DNA computation). This review excludes methods where proteins or cells display Boolean behavior and focuses exclusively on instances where some type of DNA hybridization procedure performs computation. It gives a good overview of what is already in the open literature starting with Adleman's experiment. The chapter states that while DNA computation is unlikely to replace silicon computers, some form of DNA computation will have implications on controlling chemical/biological systems (such as intelligent drug delivery systems). "In the absence of technical breakthrough, optimism regarding the creation of a molecular computer capable of computing with electronic computers on classical computational problems is not warranted." [p. 454]. It is difficult to argue with this less than optimistic conclusion given the somewhat narrow scope of this chapter.

Overall, chapters are well organized with subheadings and sub-subheadings making them easier to reference. Skimming the introduction and conclusion of any chapter provides one with that chapter's scope and a good idea of what is covered. References at the end of each chapter make it easier to pursue a more in depth review of the relevant literature. It is surprising to find a typographical error as the authors and editors would read their chapter, however it does not detract from the discussion.

Bioelectronics is a vast multidisciplinary field. *Bioelectronics: From Theory to Applications* does a good job of compiling the relevant topics that describe the state of the art, and challenges facing bioelectronics in the field of biology. The breadth of coverage within biology is not sacrificed, and enough depth is provided to show the complexity of the topic being discussed. This book is a handy reference for those working in the field of bioelectronics—regardless of their background. It is also a suitable text for an advanced graduate course in bioelectronics. This reviewer would strongly encourage those getting into the field of bioelectronics to read, at a minimum, the introductory and concluding chapters of this book.

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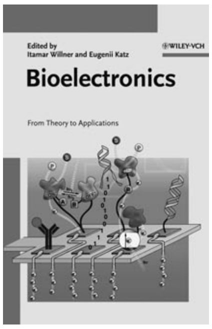
A vivid insight into the world of biolelectronics

Bioelectronics

From Theory to Applications. Edited By *Itamar Willner* and *Eugenii Katz*.

Wiley-VCH, Weinheim ***2005****. XVII + 475 pp., hardcover € 189.00.—ISBN 3-527-30690-0*

Itamar Willner has gained over 20 years of experience in molecular electronics, bioelectronics and related research areas. Since 1982 he has been Professor of Chemistry at the Hebrew University of Jerusalem, Israel. Eugenii Katz has a long-standing research record in electro-analytical chemistry, biosensors, bioelectronics and related fields. Since 1994 he is a Senior Research Associate at the Institute of Chemistry, Hebrew University of Jerusalem, Israel.



The combination of biological elements with electronic systems has recently emerged as a field of increasing importance which will open major scientific and technological avenues. Inspired by biological signal processes, scientists and engineers are exploring ways of manipulating, assembling and applying biomolecules and cells on integrated circuits, joining biology with electronic devices. The overall goal is to create bioelectronic devices for biosensing, drug discovery, and curing diseases, but also to build new electronic systems based on biologically inspired concepts. This research area called "bioelectronics" requires a broad interdisciplinary and transdisciplinary approach to biology and materials science. The challenges, belonging to research areas of a strongly multidisciplinary nature, are highly demanding requiring background in a diversity of classical disciplines such as physical chemistry, molecular and cellular biology, biophysics and solid-state electronics.

The book edited by I. Willner and E. Katz presents timely, convincing and appropriately weighted contributions of key players in this interdisciplinary research field, covering selected topics from bio- and immunosensors, neuronal and DNA computing, bioassays, or biochemical batteries. The contributions discuss the limitations in the coupling of biomolecules with electronics, the strategies to immobilize proteins or DNA on electronic transducers, and to apply the systems as biosensors. The advancement of nanotechnology is introduced by imaging methods of biomolecular structures on surfaces at the single-molecule level, the use of biomolecules for nano-objects and devices, and the use of biomolecule–nanoparticle hybrid systems. The interfacing of networks of neurons with electronic devices and the use of biomolecules as information storage and computing systems are further topics that are discussed in the book.

The book will be of interest to bioengineers and professionals working in the area of bioelectronics. The different contributions allow chemists, biologists, physicists, materials scientists and engineers to start forming a good knowledge base in order to better deal with this field and attract newcomers to these new themes.

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Analytical and Physical Electrochemistry

By *Hubert H. Girault.*

EDFP Press, Lausanne, ***2004****. 448 pp., hardcover, € 79.00.—ISBN 2-940222-03-7*

This text book is a welcome addition in an area of chemistry in which good text books are difficult to find. The author fulfills the promise of the title in 10 well organized chapters which deal with both the physical-chemical background of electrochemistry and also its important analytical applications. The first three chapters discuss fundamental thermodynamic concepts including the electrochemical potential, electrochemical equilibria, and the properties of electrolyte solutions. Chapter 4 describes non-equilibrium processes in solution including electrical conductivity and diffusion. The electrical double layer and associated thermodynamics are discussed in Chapter 5. Chapter 6 deals with electrokinetic phenomena and electrochemical separation methods. Most teachers will be very happy to find this important material in an electrochemistry text book. The last four chapters deal with electrode kinetics studied under a variety of potentiostated techniques. These include steady-state voltammetry, pulse voltammetry, impedance techniques, and cyclic voltammetry. Finally, there is an appendix with a review of vector analysis and some electrochemical data.

As an example of organization, one first reads about liquid junction potentials in Chapter 2 in a discussion of potentiometric methods of analysis. Then the reader is referred to Chapter 4, Section 5 where the Planck–Henderson equation, used to estimate the liquid junction potential, is derived. What is missing here is estimates of these quantities for important analytical applications such as the pH meter.

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BOOK REVIEWS

Cytochrome P450: Structure, Mechanism, and Biochemistry, 3rd ed. Edited by Paul R. Ortiz de Montellano (University of California, San Francisco). Kluwer Academic/Plenum Publishers: New York. 2005. xx + 690 pp. $149.00. ISBN 0-306-48324-6.

The three editions of *Cytochrome P450: Structure, Mechanism, and Biochemistry* have appeared at approximately ten-year intervals and present a snapshot of the field of cytochrome P450 at each decade, with some retrospective on the previous edition's unanswered questions. This edition continues the tradition established in the first two volumes and covers exactly what the title suggests. Eleven of the authors from the second edition contributed to the third, providing considerable continuity in their stories. The third edition focuses exclusively on P450, and two earlier chapters comparing P450s to peroxidases, chloroperoxidase, and nitric oxide synthase have been dropped. This has permitted the welcome addition of two excellent chapters on P450s in plants and the diversity of P450s in microbes, including bacteria and fungi.

This book is really two books in one. In 1959, C. P. Snow delivered his famous Rede Lecture on the "two cultures", meaning the humanities and the sciences, in which he discussed how practitioners of the two disciplines know little about each other and how communication between the two camps is difficult as a consequence (Snow, C. P. *The Two Cultures and the Scientific Revolution*; Cambridge University Press: New York, 1959). In much the same way, I think that the practitioners in the P450 field can be divided into chemists and molecular biologists, all of whom appear to suffer from the same difficulty. I find myself in the molecular biology camp. This made reading the chapters on models and mechanisms, computational approaches, substrate oxidation, and inhibition very challenging, but in the end quite rewarding. I gained a much greater appreciation for the elegant and difficult biochemistry that cytochrome P450 must experience without itself being destroyed with each turn of the catalytic cycle. I also learned how the subtleties of the active site architecture influence the "push effect" of the thiolate ligand and control uncoupling by providing thermodynamic barriers to undesired side reactions. These chapters especially emphasized the exquisite dependence of function on structure, down to the presence of water molecules at precise locations, the importance of hydrogen bond networks to fine-tune the electrical properties of the thiolate, and the effect of single side chains on substrate orientation and product formation. The richness of detail in these chapters was remarkable.

Every book has a particular emphasis, and scientific books are no different. One idea that is referred to multiple times in the book by several authors is the two-state reactivity model of Shaik. Chapter two by Shaik and De Visser describes this model in some detail. The basic idea is that the reactive iron–oxygen complex at the heart of the P450 mechanism can exist in two electronic configurations, with electrons occupying different orbitals of nearly the same energy. The outcome of the reaction depends on which state (high-spin or low-spin) is involved in completing the reaction. This model, based on computational studies of the mechanism, appears to explain many experimental results that were difficult to reconcile previously. This two-state model is certainly one of the scientific highlights presented in the third edition.

One take-home message from the chemistry and quantum chemistry chapters is that structure matters, and it matters both in terms of the physical 3D space as well as the electronic landscape. One comes away with a strong sense of the perfection of each active site and how key changes at the level of a few tenths of an angstrom would ruin a P450 enzyme. This realization has implications for P450 modelers who compute models based on the crystal structures of cytochrome P450 from bacteria, as in CYP102, or from mammals, as in CYP2C5. Usually these models are for other families of P450 proteins, and the sequence similarity is low, often less than 25%. Information in the chemically based chapters of the third edition would suggest that models of this type could never achieve the necessary accuracy needed to predict substrate binding or mechanism and may be pointless exercises.

The molecular biology side of the third edition also has some gems. The chapter by Guengerich on human P450s fills one-quarter of the book, and it is the most comprehensive detailing of these 57 enzymes that exists anywhere. It would be worth buying the book just to have this chapter with its 1500+ references. The chapter by Williams et al. on induction of P450 enzymes was the clearest exposition on this topic I have read. In another chapter, Poulos and Johnson, who have solved bacterial and mammalian P450 structures, provide a basic introduction to the structure of these enzymes, with emphasis on the bacterial structures.

In reading this book, I began at the back because I was very interested in the plant, bacterial, and fungal P450s, and I wanted to see what these chapters contained. Plant P450s are a huge topic in themselves, with over 300 different P450 genes in a single plant like rice or poplar. Nielsen and Møller provide a useful introduction covering brassinosteroid, flavonoid, alkaloid, and glucosinolate biosynthesis and additional topics. This chapter will be very helpful to those who need a summary of this broad area. The chapter on biodiversity in microbial CYPs spans many areas, including fusions to electron transport proteins, evolution of CYP51, mycobacterial, archaebacterial, and streptomycete CYPomes, and the basis of antifungal drug resistance.

In another chapter, Capdevila et al. cover P450s involved in arachidonic acid metabolism and the potential importance of P450s in hypertension and cardiovascular disease. The Cyp4a14 mouse knockout enhances this story by providing a novel mouse model. Waxman and Chang cover the sex-specific P450s CYP2C11 and CYP2C12 in the rat and the regulation of P450s by steroid hormones, growth hormones, thyroid hormones, and various drugs, chemicals, and diseases such as diabetes. Of course, none of these enzymes will run without a source of

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electrons. Chapter 4 on electron-transfer partners covers this quite thoroughly, including the enigmatic cytochrome b_5 that can enhance P450 activity, in some cases even in the apoenzyme form. The chapter on activation of molecular oxygen, though ostensibly aimed at the chemist, is very accessible to the molecular biologist. The authors, Makris, Denisov, Schlichting, and Sligar, should be commended for bridging the two cultures in their presentation. Current views are given on the P450 catalytic cycle, and this is related to the role of particular side chains, such as T252 and D251 in CYP101.

The whole book is of uniformly high quality. Even the appendix, which lists inducers, substrates, inhibitors, and noninvasive markers, including structures, will be very useful. There is much that can be learned even by experts in the field. I was surprised to find out that CYP17 and CYP19 (aromatase) have very similar three-step oxidations in their mechanisms that break a carbon−carbon bond, even though the substrates and products of these enzymes are very different. Such observations may provide clues to the origin of the aromatase enzyme, which does not resemble any other P450 in its sequence. This book may serve as a reference or as an introduction to specific areas. P450 researchers will want a copy within easy reach, while the nonspecialist will be grateful to have the book in the campus library.

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Bioelectronics: From Theory to Applications. Edited by Itamar Willner and Eugenii Katz (The Hebrew University of Jerusalem). Wiley-VCH Verlag GmbH & Co. KGaA: Weinheim, Germany. 2005. xviii + 476 pp. $255.00. ISBN 3-527-30690-0.

Bioelectrochemical sensing, defined as a part of bioelectronics in this book, has continued to grow over the last 40 years. The reviews in this book are an accurate reflection of the current state of the field, which is summarized in the cover's artwork, and future directions. While coverage of routine biomolecular attachment to surfaces is left to appropriate reviews cited in the book, the analytical advantages offered by hybrid materials are reviewed in detail. Both protein- and nucleic acid-based applications are reviewed with applications to electrochemical sensors, fuel cells, circuit fabrication, optically addressed electrochemistry, single molecule detection, and neuron stimulation. This approach makes *Bioelectronics* more valuable than the previous reviews written by the editors, who have integrated and expertly placed the diverse topics into context.

The bottom-up approach of this book helps position the wide range of experiments in a chemical context within the field of bioelectronics. Chapter 2 sets the groundwork with a discussion of electron transfer in natural or semisynthetic metalloprotein systems. Reviews of semisynthetic protein, metalloprotein, and DNA-based electrochemical sensors provide a current (as of 2004) and accurate picture of bioelectrochemistry. The first five chapters provide an excellent framework for an introduction to the bioelectronics field, whereas the remaining ones give insights into the future of this field. Chemistries associated with effecting attachments of biomolecules to silicon substrates are reviewed, presenting exciting opportunities. Deposition of S-layer proteins in 2-D lattices on bulk materials is also described as an alternative attachment strategy. The recent use of metallic and semiconducting nanoparticles in bioelectrochemical sensors is reviewed along with the application of these systems and organic analogues to optically activated bioelectrochemical sensing. The use of single biomolecule methods of detection is also discussed in the context of bioelectrochemical sensor characterization and patterning.

Two reviews highlight abiological uses for DNA: templated nanometer scale circuits with single-walled carbon nanotubes and DNA computing. The latter review contains a frank discussion of this field, in which the authors conclude that bioelectronics is a viable extension of this research. At the opposite end of the spectrum, the patterning of neurons on electrodes and associated electrochemical stimuli is reviewed. The more applied chapters (Chapters 6−14) highlight future applications for bioelectronics, identified as electrode-neuron interfacing and nanolithographic applications to the design of sensors.

This book provides an excellent introduction to and overview of bioelectronics with a focus on chemical and biochemical aspects. Although the quality of the different chapters is variable, the references at least point to leading reviews to acclimate additional researchers with this field. The strength of this book is clearly derived from the research and previous reviews of the editors. It would be a good addition to both personal and institutional libraries.

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