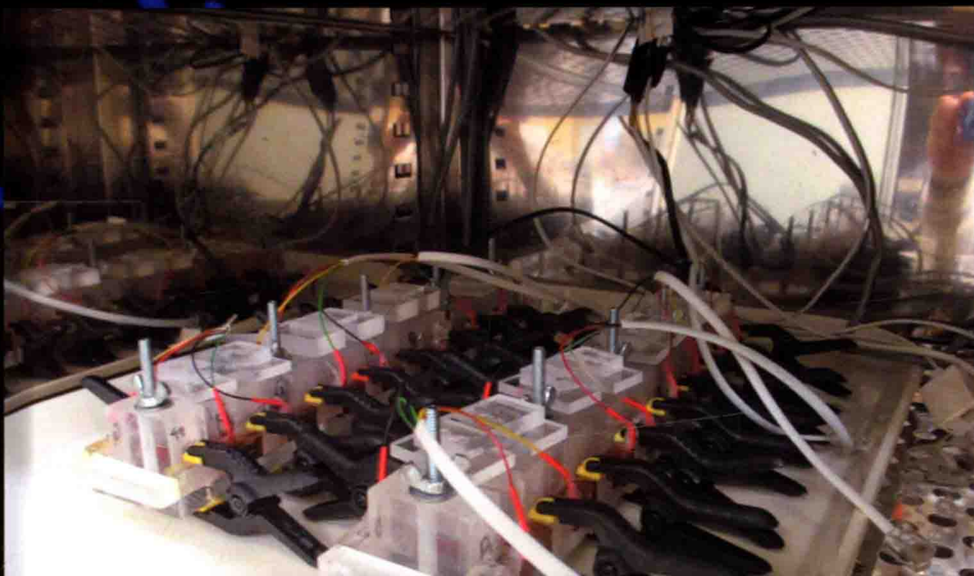
CONDUCTIVE POLYMERS

Electrical Interactions in Cell Biology and Medicine



edited by
Ze Zhang
Mahmoud Rouabhia
Simon E. Moulton

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MATERIALS SCIENCE

CONDUCTIVE POLYMERS

Electrical Interactions in Cell Biology and Medicine

This book is dedicated to the field of conductive polymers, focusing on electrical interactions with biological systems. It addresses the use of conductive polymers as the conducting interface for electrical communications with the biological system, both *in vitro* and *in vivo*. It provides an overview on the chemistry and physics of conductive polymers, their useful characteristics as well as limitations, and technologies that apply conductive polymers for medical purposes. This groundbreaking resource addresses cytotoxicity and tissue compatibility of conductive polymers, the basics on electromagnetic fields, and commonly used experimental methods. Readers will also learn how cells are cultured *in vitro* with conductive polymers, and how conductive polymers and living tissues interact electrically. Throughout the contents, chapter authors emphasize the importance of conductive polymers in biomedical engineering and their potential applications in medicine.

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To my parents, Li Zhang and Yanjun Tai,
my wife, Jin, and my children, Issan and Roger,
for their love, support, and understanding.

Ze Zhang

I would like to dedicate this book to my wife, Jamila,
to my daughter, Dounia, and my son, Réda, for their continued love, support,
patience, etc., and having made this edition possible and exciting.
I would also like to dedicate this book to my father and
my father-in-law for inspiration and guidance.
I am terribly missing both of you, but your inspiration
and guidance are with me forever.

Mahmoud Rouabhia

I wish to dedicate this book to my wife, Louise, and
my children, Aleida and Liam, who encourage me to aim high and
achieve my goals.
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for their silent but ever-present support.

Simon E. Moulton

Series Preface

The Series in Materials Science and Engineering publishes cutting-edge monographs and foundational textbooks for interdisciplinary materials science and engineering. It is aimed at undergraduate and graduate-level students, as well as practicing scientists and engineers.

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Foreword

The dramatic developments in microelectronics technology over the past generation or so have been nothing less than transformational for science, engineering, and society as a whole. The ability to rapidly design and manufacture on a large-scale solid-state components with ever-smaller, faster, inexpensive, and complex computational circuitry has now put simply incredible amounts of processing power into the hands of essentially everyone on the planet. What is perhaps most remarkable is that the platform substrates that drove this revolution are single crystals of semiconducting silicon, locally doped with different electron-rich or electron-poor elements (such as phosphorous or boron) to provide controlled variations in electron transport performance. These are then layered up with appropriate insulators (typically oxides) and metals (such as gold, copper, and tungsten) to provide the necessary means for interconnecting these ever-shrinking components with the external world.

In many instances, there is a need to directly integrate these engineered, typically inorganic electronic devices with living systems. This might be necessary to provide support for a function that no longer exists (such as for an auditory or visual prosthesis), or to directly communicate with the central or peripheral nervous system. In such instances, it is important to maintain efficient, stable interactions that will allow for the patient to establish and maintain an intimate interface with the technology. However, traditional electronic components are not typically designed to work well in this environment, since they are composed of solid, stiff, essentially flat, inorganic, and relatively inert metals, semiconductors, or dielectrics. Living tissue, on the other hand, is wet, soft, dynamic, articulated, mostly organic, and conducts charge predominantly by ionic transport.

Conjugated polymers have recently emerged as a class of organic materials that can work well at the interface between living systems and engineered components. Examples of these materials include functionalized poly(pyrroles) and poly(thiophenes) that have interesting chemical similarities to melanin, a natural conjugated polymer found in skin, hair, and certain electrically active organs, such as the ear and the brain. The mechanical and electrical properties of conjugated polymers are typically intermediate to those of the tissue and the solid-state devices, and they have the ability to efficiently transmit charge as both electrons and holes in the solid state, as well as ionically through their precisely controlled counterion and side-group chemistry.

This monograph focuses on this important biology-conducting materials interface. There have been considerable efforts to create mechanically stable, biocompatible interactions between implanted devices and living tissue. However, for an electrically active system, it is absolutely critical to maintain long-term, facile charge transport between the implanted device and the cells in the tissue of interest. Professors Zhang, Rouabhia, and Moulton have assembled a group of investigators who are working on issues ranging from materials synthesis to device characterization to analytical measurements of performance. Of particular interest and value are several reports from clinically inclined investigators that describe recent studies of electrically mediated cell response. These areas represent opportunities for future developments and collaborations between chemists, materials scientists, biomedical engineers, and physicians. Taken together, these chapters provide a comprehensive overview of issues related to the interface between active devices and biological systems, and emphasize the need to consider future opportunities in this area.

We of course never know for sure what the future will bring. However, by looking at the progress that is being made by the international collection of research groups included in this book, it is clear that there are many opportunities for creating ever-more intricate, sophisticated components that will effectively integrate advanced microelectronics technology with living systems. I am hopeful that this book will not only serve as a useful snapshot of the state of the art at this point in time but also help to guide future investigators as the field rapidly evolves into the unknown frontier.

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Preface

Research in the fields of conductive polymers (defined as intrinsically conducting polymers for most of this book) and cellular electrophysiology has been disconnected until the 1990s, when Masuo Aizawa's lab published electrochemical modulation of enzyme activities of yeast cells (Haruyama et al. 1993) and Robert Langer's lab published work on the noninvasive modulation of the shape and function of endothelial cells (Wong et al. 1994). In these two works, however, cells were found to be affected through the secondary effect of the electrical field, that is, because of redox-induced chemical or physical changes at the interface of the polypyrrole and cells. The first report on conductive polymer–mediated electrical stimulation to directly enhance mammalian cell performance is probably the work of Christine Schmidt et al. (1997), who found that neurite outgrowth in PC12 cells was doubled in the presence of electrical current. The work of Wong and Schmidt also brought tissue engineering into the context of electrical stimulation and conducive polymers.

Bioelectricity was first documented by Aristotle (350 BCE), who wrote, "The torpedo narcotizes the creatures that it wants to catch, … and the torpedo is known to cause a numbness even in human beings." This phenomenon was used to release pain in humans as early as 46 AD by Scribonius Largus, a court physician to the Roman Emperor Claudius (Kane and Taub 1975). Since Luigi Galvani, bioelectricity has been studied extensively in biosciences and medicine with many modern medical diagnostics and treatments based on electrical and electromagnetic phenomena in the human body, such as electrocardiography, magnetic resonance imaging, and pacemaker technology. Despite the wide recognition of bioelectrical phenomena in humans at the organ, tissue, and cellular levels, electrical and electromagnetic fields are yet to be widely accepted as effective tools to induce cell growth and treat diseases. One major obstacle is the lack of specificity. The size or range of a field generated by instruments currently used in most labs, either electrical or magnetic, is much larger than the size of cells, not to mention the much smaller membrane receptors. When the same field is applied to different cell populations, diseased and normal alike, the absence of specificity is expected. This is just an example of how cell biologists, material researchers, and electrical engineers can work together to address the outstanding challenges. Of course, how electrical or electromagnetic fields initiate cell signaling cascades remains the central issue that requires the collaboration of those with different expertise, including physicists, computational chemists, and cell biologists. Solving such issues will bring about truly exciting science and engineering advances in areas such as the brain–machine interface and field-assisted tissue engineering and regenerative medicine.

Compared with the long research records of bioelectricity in human history, research on conductive polymers has a much shorter registry, taking off only in the 1970s and peaking again following the awarding of the Nobel Prize in Chemistry in 2000 to the founders of conducting polymers. Most current industrial research on conductive polymers has focused on electrochromic, photovoltaic, energy storage, and anticorrosion applications. In fact, as a class of material, conductive polymers have natural advantages over most synthetic substances when it comes to their interaction with living systems. First, they are electrically conductive and ionically active, similar to biological tissues. All biological systems are made up of electrolytes, proteins, sugars, lipids, and so forth, which carry electrical charges and react to electrical and electromagnetic fields. In fact, when we talk about the basic force in molecular interactions, it boils down to electrical and electromagnetic fields. Conductive polymers can carry electrical current and generate electrical fields, facilitating their ease of "communicating" with living tissues (compared with insulating synthetic polymers). The second advantage of conductive polymers in interacting with living tissues stems from their functionality. As synthetic materials, conductive polymers can be modified to carry functional groups or biologically active molecules, making conductive polymers "friendlier" with living tissues. Biologically functional conductive polymers may confine electrical impact to specific molecular interactions such as adhesion. Third, with respect to metals and inorganic conductors, conductive polymers can be fabricated or modified to acquire mechanical properties similar to those of living tissue. Evidently, these advantages do not mean that conductive polymers can be used to substitute for natural tissues, but they do open a new dimension in conductive polymer research.

This book is intended to provide readers with a relatively comprehensive picture regarding conductive polymers and electrical modulation of cellular activities in the context of medicine. Different from traditional electrophysiology, which is more about diagnosis and recording, our objective is to treat, cure, and communicate using electrical and electromagnetic fields, with the help of conductive polymers as the interface, scaffold, substrate, guidance channel, and so forth. To achieve this objective, we need to see several changes, including better materials allowing us to perform electrical field intervention with high specificity; a more thorough understanding about how electrical and electromagnetic fields interact with electrolytes, ligands, and receptors; and improved awareness of safety issues related to electrically activated cells. Obviously, these challenges cannot be met without collaboration among scientists and engineers of different disciplines. Hopefully, the information and core messages in this book will contribute to the success of our objective.

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