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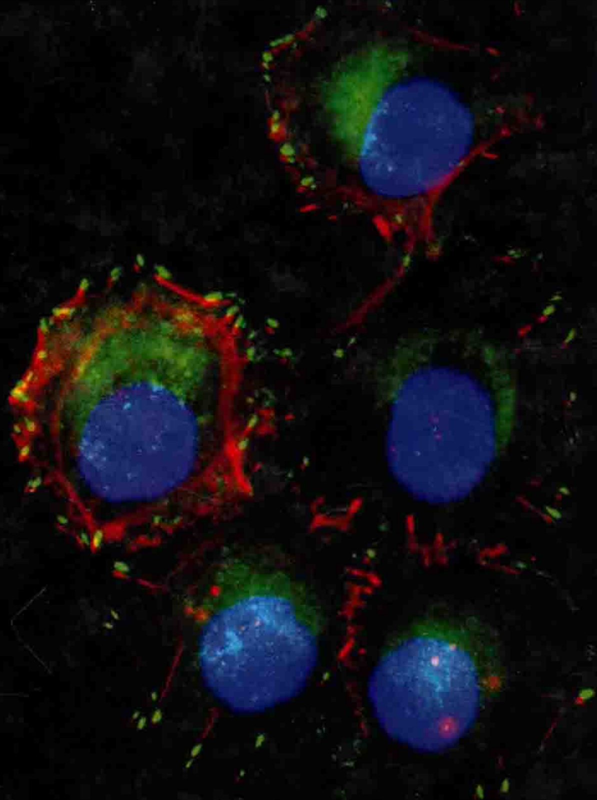

Silicon Carbide Biotechnology

A Biocompatible Semiconductor for Advanced Biomedical Devices and Applications

Edited by
Stephen E. Saddow

SILICON CARBIDE BIOTECHNOLOGY

A BIOCOMPATIBLE SEMICONDUCTOR FOR ADVANCED BIOMEDICAL DEVICES AND APPLICATIONS

FIRST EDITION

STEPHEN E. SADDOW

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FIRST EDITION

Dedication

This book is dedicated to Luca Edward Saddow—may you always respect those around you, question conventional wisdom, seek to make this world a better place, and, above all, live a happy, healthy, long, and productive life under the eyes of God.

Preface

The twenty-first century has long been hailed as the century of biology, since the extremely complex nature of the biological system is only now beginning to be more fully understood through the use of technology and the scientific tools that allow mankind to observe biological processes at the nano-scale. This has resulted in the ever pressing need to develop advanced "smart materials" for biomedical applications, and this important field of research has taken center stage worldwide as the new frontier of advanced scientific research. Although biocompatible materials have been in use for decades, the quest to merge smart materials, such as those used in modern computer integrated circuits, with the biological system, has proven to be much more difficult than originally imagined. If we take the brain–machine interface, or BMI, as an example, which was first reported in the early 1970s and was based on silicon probes, we learn that mankind is not much closer to the prospect of long-term (multiple years or even decades) implantation of these devices. Why? Simply put most "smart materials" such as semiconductors are typically poisonous to the biological system, and silicon is no exception. What is needed is therefore a material with the "smart properties"of silicon and the "biocompatible" properties of polymers. In this book such a candidate material, silicon carbide, is presented and the evidence that has been amassed, mostly over the last decade, indicates that this material system may prove to be the dream material for biomedical devices that must do more than simply provide structural support.

Silicon carbide has a long history as a robust and hard material, first used as a cutting material in the nineteenth century and later as a high-temperature semiconductor for advanced applications in the twentieth century. Indeed, the first solid-state blue light emission was observed from SiC in 1907, and this material has been under study ever since that time. It is best to consult the literature to fully understand all of the many aspects of SiC, from how it is formed to its myriad crystal properties, and finally to the large number and types of applications it is being used in. Fortunately it is sufficient here to provide a brief overview of SiC so that the reader can understand why this material is so compelling for biomedical applications and may become one of the most used biomaterials in the future. Indeed, the purpose of this book is to lay the foundation for exactly this—to introduce silicon carbide to biomedical engineers, medical professionals, and scientists, thus bringing together technologists from across many disciplines to help develop SiC as one of the next generation of smart biomaterials to realize advanced biomedical devices.

The organization of this book follows a logical sequence from an introduction of SiC, with a particular emphasis on biomedical applications, to the growth of thin SiC films and coatings (Chapter 2). Since the actual interface between any material and the biological system involves the atomic-scale interface between atoms in the material and the biomolecules (proteins at the microscopic scale to cells and then tissue), an overview of the SiC surface properties is given, so that the reader can understand how biocompatible SiC surfaces are prepared. Chapter 3 discusses the biofunctionalization of SiC surfaces that is the key to control the chemical properties of the material and optimize the SiC bio-interface for implants, sensors, and so on. This concludes the first section of the book which serves the purpose of introducing SiC as a biomedical material, touching upon some basic technology that applies to many biomedical devices and systems. The next section of the book focuses on establishing SiC as a biocompatible material: skin and connective tissue (Chapter 4), cardiovascular (Chapter 5), and the central nervous system (Chapter 6). The last section of the book is dedicated to biomedical devices that are enabled by the use of SiC materials. Chapter 7 discusses the potential of SiC for brain–machine interfaces (BMIs) that are one of the important chronic applications for semiconductor-based materials that will be implanted for not just years but decades in patients. Chapter 8 discusses novel work using porous SiC as a filtering media for such critical applications as micro-dialysis, followed by the use of porous SiC for bone implants (Chapter 9). A review of SiC for bio-micro-electromechanical systems (bioMEMs), which is the basis for sensors and advanced implants in SiC, is discussed in Chapter 10. One of the areas where SiC can greatly assist in disease detection and diagnosis is in the area of photoluminescent dye markers as discussed in Chapter 11. Finally we come full circle, back to the biocompatibility of materials and discuss a very new and exciting topic—the biocompatibility of carbon-based materials for electrodes in Chapter 12. The discussion focuses on pyrolyzed photoresist films (PPF) and graphene. Graphene is a carbon-based thin film that has extremely high electron conductivity and could serve as an ideal conductive layer for numerous biomedical devices that require an electrical interface to the biological applications. Photoresist, when pyrolyzed at high temperatures in an inert atmosphere, results in a durable carbon film that is easily patterned. In both cases the obvious benefit is to remove any possibility of metal contamination from the biomedical device, thus enhancing the biocompatibility while improving device performance. Hence this chapter "ties it all together" leaving only the bibliographical section where all of the references cited in the book are provided.

The authors listed at the beginning of each chapter provided the content, including figures and text that comprise the majority of this book. The Editor both solicited these chapters and edited the content in an effort to achieve a uniform and consistent text. This was done so that the reader could both focus on the very interesting subject matter contained within and see the connection that many of the chapters have with each other. The editor hopes that this endeavor was successful and that you, the reader of this book, will find this work both informative and enjoyable to read. Indeed, it was an extremely rewarding experience putting together this book and the editor hopes that this will be similarly felt by you, the reader.

At Academic Press/Elsevier Science, the project was coordinated by Louisa Hutchins and the editor is grateful to her for all of her support and kind assistance throughout the project. In addition, Parvathy Bala very capably coordinated the production of the book and is gratefully acknowledged for all of her hard work in making sure galley proof corrections were made, copyright approvals completed, and for her overall help in pulling this book together. The editor of *Silicon Carbide Biotechnology* hopes that users of this book, and especially the students who will become the next generation of biomedical practitioners and technologists, will find the subject matter of *Silicon Carbide Biotechnology* as interesting and exciting as the editor does.

Prof. Stephen E. Saddow, Editor
University of South Florida
Tampa, FL, USA

Acknowledgments

This project was made possible by so many people that it is difficult to thank everyone sufficiently and completely, and if I forget to include anyone in this acknowledgment, it is truly inadvertent. I am first grateful to my family who raised me to have real values—those of honest work and to always respect and appreciate others. To them I remain ever grateful. None of this would not have been possible had it not been for all of the teachers and professors in my life, most notably my Ph.D. advisor, Prof. Chi Lee at the University of Maryland, who taught me that no matter how successful one is, or how famous one becomes, the true measure of a colleague is kindness and respect. Naturally none of this would have been possible without the dedicated students that I have had the good fortune to work with and advise over the past 15 years. It is upon the shoulders of many of these fine students that this work rests upon. A few deserve a special note of recognition since they were the SiC biomaterials pioneers who laid the foundation for this book. They are Dr. C. Coletti for her pioneering work on the *in-vitro* biocompatibility of SiC and upon whose work Dr. N. Schettini (hemacompatibility) and Dr. C. Frewin (neuronal biocompatibility) directly followed. In addition Ms. A. Oliveros, my current Ph.D. student, has continued this tradition and has begun to develop SiC biosensors along with exploring the biocompatibility of graphene and carbon-based conductors. This core cadre of students made this work possible and I am eternally indebted to them. I wish to also thank Dr. C. Locke for his nonwavering support of all of the research in my group, mostly notably by growing and processing the needed SiC films. In addition, I wish to thank all of the present and former students of the USF SiC Group, as well as my close colleagues Dr. A. Hoff and Dr. S. Thomas of the Department of Electrical Engineering at USF. Dr. Hoff was my inspiration to enter the biomedical engineering field and introduced me to Dr. M. Jaroszeski of the Chemical and Biomedical Engineering Department who opened his laboratory to my students thus making the work of the Bio-SiC group possible. Dr. Thomas provides consistent encouragement and new ideas that continue to move the group forward into new areas of Bio-SiC research, currently with our joint student Ms. S. Afroz who is pioneering SiC *in-vivo* glucose sensors. I wish to thank the USF NREC staff for their support and kind assistance to my students as well as my department chairman Dr. S. Morgera who has always been extremely supportive of my research activity and group. I especially want to thank Dr. E. Weeber of the Byrd Alzheimer Center for our very fruitful collaboration in neuroscience and neuroengineering that has led to many of the recent breakthroughs in my group. None of this would have been possible without the support of Dr. C. Wood, formerly of the Office of Naval Research, who had the vision to encourage me to devote some resources to start the biomaterials research of Dr. Coletti. Finally, and most dear to my heart, is the ever present love and support of my wife Vaine Angelo, with whom we just had a son, little Luca Edward, who provides all of the incentive that anyone needs to continue to strive for scientific and technological excellence—in some small way I hope that all of this work will allow for his quality of life to be the best that man on earth can provide.

Prof. Stephen E. Saddow, Editor
Tampa, FL

Contents

CHAPTER

1

Silicon Carbide Materials for Biomedical Applications

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1.1 INTRODUCTION

Silicon carbide (SiC) has a long history as a robust and hard material, first used as a cutting material in the nineteenth century and later as a high-temperature semiconductor for advanced applications in the twentieth century. The history of SiC is quite interesting and the reader is referred to the first chapter in a book dedicated to this subject [1]. It is best to consult the literature to fully understand all of the many aspects of SiC, from how it is formed, to its myriad crystal properties, and finally to the large number and types of applications it is being used in. Fortunately, it is sufficient here to provide a brief overview of SiC so that the reader can understand why this material is so compelling for biomedical applications and may become one of the most used biomaterials in the twenty-first century. Indeed, the purpose of this book is to lay the foundation for this—to introduce SiC to biomedical engineers, medical professionals, and scientists, thus bringing together technologists from across many disciplines to help realize the ultimate use of SiC as one of the next generation of smart biomaterials for advanced biomedical devices.

The organization of this book follows a logical sequence from an introduction of SiC, with a particular emphasis on biomedical applications, to the growth of thin SiC films and coatings (Chapter 2). Since the actual interface between any material and the biological system involves the atomic-scale interface between atoms in the material and the neighboring biomolecules (proteins at the microscopic scale to cells and then, ultimately, tissue), an overview of the SiC surface properties is given, so that the reader can understand how biocompatible SiC surfaces are prepared. Chapter 3 discusses the biofunctionalization of SiC surfaces that is the key to controlling the chemical properties of the material and optimizing the SiC biointerface for implants, sensors, and so on. This concludes the first section of the book that serves the purpose of introducing SiC as a biomedical material, touching upon some basic technology that applies to many biomedical devices and systems. The next section of the book focuses on establishing SiC as a biocompatible material: skin and connective tissue (Chapter 4), cardiovascular system (Chapter 5), and the central nervous system (Chapter 6). The last section of the book is dedicated to biomedical devices that are enabled by the use of SiC materials. Chapter 7 discusses the potential of SiC for brain–machine interfaces (BMIs). The BMI is one of the most important chronic applications for semiconductor-based materials as they will be implanted for not only years but for decades in patients. Chapter 8 discusses novel work using porous SiC as a filtering media for critical applications such as microdialysis, followed by the use of porous SiC for bone implants (Chapter 9). SiC for biomicroelectromechanical systems (bioMEMS), which is the basis for sensors and advanced implants in SiC, is reviewed in Chapter 10. One of the areas where SiC can greatly assist in disease detection and diagnosis is the area of photoluminescent dye markers as discussed in Chapter 11. Finally, we come full circle, back to the biocompatibility of materials and discuss a very new and exciting topic—the biocompatibility of carbon-based materials for advanced electrodes in Chapter 12. The discussion focuses on pyrolyzed photoresist films (PPFs) and graphene. Graphene is a carbon-based thin film that has extremely high electron conductivity and serves as an ideal conductive layer for numerous biomedical devices that require an electrical interface to the biological system. Photoresist, when pyrolyzed at high temperatures in an inert atmosphere, results in a durable carbon film that is easily patterned. In both cases, the obvious benefit is to remove any possibility of metal contamination from the biomedical device, thus enhancing the biocompatibility while improving device performance. Hence, this chapter "ties it all together" leaving only the bibliography section where all of the references cited in the book are provided.

1.2 SILICON CARBIDE—MATERIALS OVERVIEW

SiC is first and foremost a material that consists of the covalent bonding of Si and C atoms, typically in biatomic layers as shown in Figure 1.1. These form tetrahedrally oriented molecules of Si–C, with a very short bond length and, hence, a very high bond strength. This is the origin of the extremely high chemical and mechanical stability of SiC [2,3].

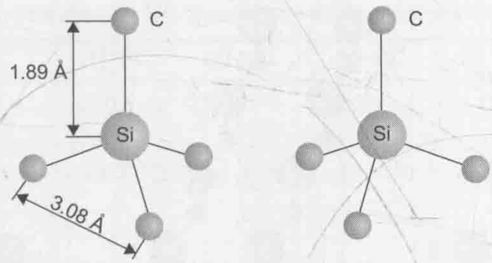

FIGURE 1.1 All SiC crystals are formed via bilayers of C and Si, covalently bonded to form a tetrahedron. Four carbon atoms are covalently bonded with a silicon atom in the center (conversely four Si atoms are covalently bonded with a C atom as this arrangement is crystallographically identical and represents the next atomic layer in the crystal). Two types exist—one is rotated 180° around the *c*-axis with respect to the other, as shown. This tetrahedrally bonded molecule then forms the basic building block of all SiC materials [1].

SiC can be formed in amorphous, polycrystalline, and monocrystalline solid forms, and because of the high bond strength and high-temperature operating capabilities of SiC, synthesis of SiC materials normally requires high temperatures (>1,000 °C). The material can be grown in bulk (boule) crystal form, currently with diameters up to 150 mm (6 in.), and can be heteroepitaxially grown on Si substrates (details of how this is accomplished are provided in the next chapter).

One of the important characteristics of SiC is that the bilayers of Si and C (Figure 1.1) can be stacked one upon the other in different crystal orientations: cubic, hexagonal, and rhombohedral. With more than 200 known polytypes reported in the literature, the three technologically relevant forms are one purely cubic form (β-SiC) and two hexagonal forms that actually have some cubic symmetry (α-SiC). These three polytypes are shown in Figure 1.2. The cubic form has the designation 3C-SiC, where the "3" delineates that 3 bilayers of Si–C are needed to form the basic structure and the "C" indicates that the crystal form is cubic. The hexagonal forms are 4H-SiC and 6H-SiC, where the "4" and "6" delineate that 4 and 6 bilayers are needed, while the "H" indicates that the crystal form is hexagonal. While interesting in their own right, these various forms of SiC actually have varying application, where the dominant power electronic device crystal of choice is 4H-SiC because of it having the highest bandgap (3.2 eV), while 6H-SiC is ideally suited for solid-state lighting (LEDs), as its lattice constant is close to the GaN family of alloys used in advanced LEDs that have enabled DVD and blue ray technology, not to mention the solid-state lighting revolution that is currently leading to dramatic reductions in power consumption worldwide.[1] A comparison of the properties of SiC relative to Si is shown in Table 1.1 for reference.

[1] <http://www.forbes.com/2008/02/27/incandescent-led-cfl-pf-guru_in_mm_0227energy_inl.html> (accessed 08.05.11)