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Computational Molecular Magnetic Resonance Imaging for Neuro-oncology

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Preface

Molecular imaging is promising for two main reasons. First, it enables human diseases to be detected early, that is, before noticeable symptoms manifest. Second, it makes precision drug delivery possible. This technique has the potential of demonstrating changes in tissue physiology, biochemistry, and biology on image scanners. The implication of this is that we can now perform patient-specific treatment, precise follow-up after treatment, and patient monitoring using computational techniques.

Noninvasive medical interventions that effectively increase physician performance in arresting or curing disease, that reduce risk, pain, complications, and reoccurrence for the patient, and that decrease healthcare costs are now within reach. What is yet required is focused reduction of recent and continuing advances in visualization technology to the level of practice, so that they can provide new tools and procedures for smarter healthcare. While magnetic resonance imaging (MRI) is one of the most developed of all the techniques of molecular imaging, it is also unfortunately one of the most expensive diagnostic tools anywhere. It is therefore necessary to develop mathematical concepts based on the fundamental Bloch nuclear magnetic resonance (NMR) flow equation for simple, cost-effective computational MRI to be used in the diagnosis and therapy of brain-related diseases at the molecular level.

The rapid development of innovations including Internet of Things (IoT), big data analysis techniques, and miniature wearable biosensors is generating new opportunities for healthcare systems. Many challenges in the emerging technology can be addressed by the development of consistent, suitable, safe, flexible, and real-time healthcare systems based on the Bloch NMR flow equation.

This book presents mathematical and computational concepts (generally applicable to the analysis of biological and non-biological systems) specifically applied for the analysis of brain tissues and neuro-oncology.

Brain tissues can be likened to complex systems and are often dominated by large numbers of processes. When deviations occur in these processes, human disease conditions are produced. Understanding these processes is important not just in

unraveling the causes of diseases, but also the manner of disease propagation and the best plan for treatment. The inadequate understanding of molecular dynamics of diseases is one reason why many diseases remain incurable and become life-threatening. Molecular MRI now provides new ways of visualizing molecular dynamics and their roles in human diseases.

However, current molecular imaging techniques suffer from low sensitivity as well as problems in temporal and spatial resolutions. The available imaging equipment no longer matches the increasing number of patients requiring diagnosis. The few available imaging machines are costly to maintain while financial difficulties are making acquisition of new ones nigh impossible. Obviously, experimental methods alone are no longer enough for efficient diagnosis, and these challenges may now require development of appropriate mathematical models and sophisticated computer simulations based on the Bloch NMR flow equations to complement laboratory and clinical observations. Such mathematical models have the potential to provide insight into the imaging of the molecular interactions through the analysis of the behavior of relaxation processes as observed on magnetic resonance (MR) scans.

The goal is to explore how patients or hospitals can benefit from using novel situation-aware technologies in real-world settings through the exploitation of big data technologies in the context of smart healthcare: wearable sensors, body area sensors, Internet of Things (IoT), machine learning, and artificial intelligence. Based on this theoretical innovation, it may be possible to develop training software to simulate MRI experiments and provide visual training tools to help understand MRI technology for future generations.

The book is organized as follows. Chapter 1 presents a general introduction to the molecular or cellular processes associated with disease conditions. The development of model solutions to the Bloch NMR flow differential equations which can be applied to describe specific clinical problems is presented in Chap. 2. Chapters 3 and 4 present mathematical analyses developed for radio frequency identification (RFID) systems for computational MRI, based on Bloch NMR flow equations and Hermite functions for detailed studies of processes taking place at molecular level in living tissues (particularly for MRI neuro-oncology).

Chapters 5–10 document analytical expressions obtained for the Bloch NMR flow equations and the solutions developed into the various computer programs used. The nuclei of general interest, hydrogen (proton), and fluorine are very abundant, and they have particularly strong NMR/MRI signals. Hence, Chap. 6 is devoted to quantum and classical mechanical analyses of Bloch NMR flow equations so that the wave function of hydrogen atom and hydrogen-like ions can be represented in terms of NMR/MRI parameters. Chapters 7, 8, and 9 present specific analytical methods and computer programs that may be needed to perform MRI tissue diagnosis and therapy at the molecular level, based on relaxometric data. Chapter 10 focuses on computational analysis of MRI contrast agents and their physico-chemical variables. This is considered very important because of the need to improve the sensitivity and specificity of MR imaging using new MR contrast agents designed to probe specific molecules or cells.

The final chapter, Chap. 11, presents general conclusions.

This book is intended for students, scientists, engineers, medical personnel, and researchers who are interested in developing new concepts for deeper appreciation of computational MRI for medical diagnosis, prognosis, therapy, and management of tissue diseases. Researchers who are interested in developing new concepts for the application of artificial intelligence, machine learning, deep learning, and radiomics to solve real-life biological and medical problems at the molecular level utilizing fundamental mathematical concepts will also find it useful. We hope that this book will help a new generation of researchers who want to be involved in this new field of science which is expected to become of great practical importance. We also expect that this book will provide a new and deeper appreciation of computational MRI.

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Acknowledgments

Due to the ability of magnetic resonance imaging (MRI) to probe right to the fundamental level, scientists may be able to image human cellular functions and such imaging modalities would definitely help in the understanding of human disease conditions and thus permit the physician to make more specific diagnosis, prognosis, and the appropriate therapy. The basic challenge in this direction is finding the right mathematical frameworks and the physics which appropriately describe the processes involved. This book was written to meet this challenge. Particularly essential to the development of the initial concepts of the book were the research meetings and seminars as well as the symposia, workshops, conferences, schools, and colleges held at the International Center for Theoretical Physics (ICTP), Trieste, Italy, that Awojoyogbe attended as an ICTP regular associate between the year 2000 and 2008. We would like to take this opportunity to thank the following senior academics: Professor D. K. De of Sustainable Green Power Technologies, USA, Professor P. Boesiger of the Institute of Biomedical Engineering and Medical Informatics, University and ETH, Zurich, Switzerland, Professor Paola Fantazzini of the University of Bologna, Italy, Professor Silvio Aime of University of Torino, Italy, Professor Bill Price of Western Sydney University, Australia, and Professor Julian Chela-Flores of ICTP, Trieste, Italy, for their academic guidance and encouragement. We thank Dr. Udunna Anazodo of Western University, Canada, for her determination to promote MRI training and research among younger scientists. We would like to thank our immediate past and present Vice Chancellors of our University: Professor M. A. Akanji and Professor Abdullahi Bala for providing the needed academic leadership and encouragement. We appreciate Professor Funmi O. Olubode-Sawe of Federal University of Technology, Akure, for her support on English language editing of this book. We thank the unanimous reviewers of this book and the editorial team of the distinguished Biological and Medical Physics/Biomedical Engineering series of Springer Nature for supporting the publication of this book. Finally, we thank the students, scientists, engineers, medical personnel, researchers, and research administrators from all over the world who are interested in reading this book for developing new concepts for

deeper appreciation of computational MRI for medical diagnosis, prognosis, therapy, and management of tissue diseases.

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Book Review

This book presents mathematical and computational concepts that can be applied to the analysis of brain tissues, to complement noninvasive imaging for efficient and early diagnosis of disease. The basis of these concepts is the Bloch NMR flow equations.

Chapter 1 establishes the biological bases of disease and the need for early diagnosis for prompt intervention. It highlights the drawbacks of invasive medical procedures which include tissue damage and false diagnosis. In Chap. 2, the authors describe how magnetic resonance works and how knowledge of the expected behavior of normal tissue helps to determine the presence of disease when abnormal behavior is noticed. Specifically, it describes the principles and physics of magnetic resonance imaging (MRI), the design of MRI equipment, and how images are acquired and enhanced for analysis. Then it goes on to show how Bloch's flow equations can mathematically model MRIs of different disease conditions. Chapter 3 presents a new mathematical formulation for diffusion MRI developed by solving the Bloch NMR flow equation. This would probably be the most opaque chapter for people without a strong grounding in physics and mathematics, but will be interesting to diffusion MRI specialists.

In Chap. 4, the Bloch NMR flow equation is developed into two second-order differential equations which can predict fluid flow at suction points analytically and precisely. The flow properties of the time-independent Bloch NMR flow equations describe the dynamics of blood flow under the influence of a radio frequency identification (RFID) system subject to the resonance condition at Larmor frequency. These equations depend on existing knowledge of fluid dynamics applied to predict analytically and precisely the blood flow behavior at suction points in the circulatory system.

Chapter 5 presents practical ways of using computational MRI to provide innovative data-driven algorithms to predict, simplify, and characterize brain tumors and delineate their mechanisms. The chapter first establishes the inadequacies of current imaging techniques to differentiate between primary and metastatic malignant brain tumors for better treatment planning. To address the problem, the chapter presents a computational MR model developed from Bloch's NMR flow equation to classify

brain tumors using MRF-derived relaxometric data. The performance of eight machine learning models as diagnostic tools was assessed. Developments in computational MRI could lead to the invention of interactive brain tumor classification apps and the design/development of wearable devices in the future.

Chapter 6 focuses on quantum and classical mechanical analyses of the Yukawa potential which is based on a differential equation developed from Bloch's NMR flow equations, with the wave function of hydrogen atoms and hydrogen-like ions being represented in terms of NMR parameters. As a method of analyzing hydrogen atom and hydrogen-like ions, three advantages put this model above others: its easier visualization, being based on the analytical solution of the fundamental Bloch NMR flow equations, the formulation of a weighting parameter as an interesting physical mechanism that provides a switch between classical and quantum mechanism, and the combination of the quantum and the classical models which can complement each other to provide an excellent innovation for the NMR study of atomic structure of hydrogen-like particles in general for patient-specific and time-unique solutions, an important aspect of personalized medicine. This would pave the way for the next generation of molecular medicine.

While previous chapters focused on solid tissue, Chap. 7 focuses on the flow of blood and presents methods of applying known quantum mechanical formulations and models to the Bloch NMR flow equations, providing a theoretical foundation that may enhance accurate understanding of the transport of nanodevices in microscopic blood vessels used in nanomedicine. Nanomachines can be developed to deliver specially designed quantum drugs carried by blood to the site of infections. The question is: "how much is known of how blood flows to these sites and how to exercise control over the nanomachines carrying the drugs?" The chapter answers these questions by presenting a mathematical algorithm to describe in detail the dynamical state of the hydrogen atom starting from the NMR flow equation, using basic quantum mechanical tools. The mathematical approach may be applied to any situation of restricted fluid flow in small blood vessels.

The premise of Chap. 8 is that experimental methods must be complemented by developing appropriate mathematical models and innovative computer simulation for efficient diagnosis. One method applied in the chapter is the use of R machine learning, which can be used for intensity visualization, intensity separation, and neighborhood information. The works of different researchers in the areas of noise removal and image enhancement were reviewed. Then, an algorithm to classify human brain tumors hierarchically is presented. Using R machine language with various classifiers, distinctions are made between glioblastoma multiforme, metastasis, and lower grade glioma. Chapter 9 demonstrates the use of Avizo, an imaging processing software for distinguishing between radiation necrosis and tumor progression. By the use of several computer images generated by the software, the differences between necrosis and tumor images are established.

Chapter 10 provides a detailed discussion of MR contrast agents GADOVIST, MULTIHANCE, and Gadomer, and their physicochemical basis, which had been previously mentioned in Chap. 2. For the various contrast agents, a Wolfram Mathematica computer program successfully distinguished between the

performances of the different MR contrast agents. Solutions to the time-independent NMR Bloch flow equation feature in the writing of the computer program, and the magnetization power of various contrast agents within various laboratory solvents or human tissues was compared quite easily. This can prepare the reader for future innovations in computational MRI.

Chapter 11 briefly highlights the overall goal of the book, especially to facilitate innovation in advanced MRI technologies that could be applied to fundamental basic and preclinical research problems in neuro-oncology and to develop training software that can simulate MRI experiments and provide visual training tools to help understand MRI technology. These might provide support for the development, maintenance, and operation of appropriate MRI devices.

The book will make an interesting read for its audience. The language is accessible, and the equations provide detailed and step-by-step procedures of the mathematical developments for the readers.

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