

Fundamentals of Nanomedicine

The first introductory book on the subject, this volume will provide a complete grounding to this pioneering field for students and professionals across biomedical engineering, biology, and medicine. It features a comprehensive overview of original work in this revolutionary field. Topics discussed include drug delivery, cell–nanomaterial interaction, and gene therapy, accompanied by real-world examples and 149 illustrations. The book teaches readers how to design and test their own nanomedical systems for real-world applications in biomedical engineering, medicine, and pharmacy.

Presenting a thorough discussion of the science and engineering of nanomedicine, it discusses vital environmental, social, and ethical impacts of this revolutionary technology. With 250 thought-provoking study questions, allowing the reader to self-assess their understanding, this book is a rich source of information that will be of interest and importance in nanomedicine.

Professor James F. Leary is Professor Emeritus of Nanomedicine, Biomedical Engineering, and Basic Medical Sciences at Purdue University and President and Founder of Aurora Life Technologies, LLC.

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JAMES F. LEARY

Purdue University



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To my wife, Jill Norton, whose encouragement and support were essential to the completion of this book.

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Preface

A little perspective might be helpful to the reader to better understand the somewhat unusual professional circumstances that led to the writing of this book. This book has been a labor of love for over eight years, but the field of nanomedicine started for me in 2000 when I and others were invited by NASA (John Hines was my excellent program officer) to invent some nanomedicine for the Mars mission. I was then a professor at the University of Texas Medical Branch (UTMB) in Galveston, Texas, just down the road from Johnson Space Center. I became one of the first researchers in the United States to be funded for a grant on nanomedicine. The book's nanomedicine origins come from two funding sources – NASA and the National Cancer Institute – in what was a bold joint initiative at the time by those two funding entities.

While pursuing my PhD in biophysics at Penn State University, I was one of the first two graduate students in the USA to train in the field of flow cytometry. I knew all of the original inventors of this field personally. My dissertation work led to my postdoctoral fellowship at Los Alamos National Laboratory in Los Alamos, New Mexico, where I was immersed in one of the birthplaces of the field of flow cytometry. After I left Los Alamos and started my career as an assistant professor of pathology at the University of Rochester, I quickly became known as the “father of high-speed flow cytometry and rare-event analysis” for my early work in these areas, and many of my more than 100 flow cytometry publications in this field are cited in this book. My first research as a young assistant professor at the University of Rochester Medical School in Rochester, New York, was in kinetics of viral binding to single cells. For that work, I fluorescently labeled viruses to measure their interactions with single cells using flow cytometry. Viruses were my first nanoparticles – from nature! Viewing nanomedical drug delivery devices was inspired by my early work with virus–cell interactions. There are many allusions in this book to biomimicry designs of nanomedical devices based on viruses in nature.

Importantly, my background in flow cytometry and single-cell analysis prepared me for being receptive to approaching nanomedicine as “single-cell medicine,” which was definitely not the emphasis of medicine at the time! I was a medical school professor and researcher for the first 27 years, including 10 years as a professor of internal medicine within the Division of Infectious Diseases while at UTMB, among my many roles as professor there in five different departments and four research centers. When I moved to Purdue University in 2005, I became an endowed professor of nanomedicine where I first had my office and then my laboratories within the Birck

Nanotechnology Center. This allowed me to immerse myself in the diverse multi-disciplinary research areas of nanotechnology as well as enabling possibilities for interactions with many nanotechnology collaborators. I mainly focused on nanomedicine teaching and research, resulting in more than 40 scientific publications, thus far, in the field of nanomedicine.

At Purdue University, I instantly acquired four graduate students in the Weldon School of Biomedical Engineering. Those students needed to be quickly trained in nanomedicine, so within the next year I formulated what was presumably the world's first graduate-level nanomedicine course, Engineering Nanomedical Systems. There were no textbooks or other courses elsewhere in existence. I started teaching this course in 2007 at Purdue University as part of the graduate program in the Weldon School of Biomedical Engineering, the source of most of my graduate students in nanomedicine. By 2012, it had become sufficiently popular at Purdue that it went worldwide on the Internet; my lectures were videotaped and archived on Purdue's nanoHUB, as well as distributed as podcasts at Apple U. I taught the course every year from 2007 through 2014, my last full academic year at Purdue University before I retired in August 2015.

This actual book grew out of earlier interactions with Cambridge University Press starting in 2010. I was asked to review another nanomedicine book proposal for Cambridge University Press. It was an edited book on aspects of nanomedicine. I evaluated the book and told Cambridge University Press that I thought that at least 2 of the 12 or so chapters would be good because of the expertise of the authors of those chapters, but that the book (as is frequently the case for edited compilations involving diverse and unconnected chapters by different authors not communicating with each other) was disjointed since it was written entirely separately by different authors without any serious interaction. I had contributed over 20 chapters to other people's books before writing my own book. I made the offhand remark to Cambridge University Press (not realizing where it would lead!) that I thought I could write a better book, as a textbook, all by myself on the subject. Cambridge University Press quickly replied, asking me what would be the title of *my* book! After some serious thought, I finally accepted their challenge.

I had already realized, after teaching my course for over four years, that there was still an unmet need for a textbook on the subject, and that the course could serve as a template for a textbook. I then responded affirmatively to Cambridge University Press's request for a book proposal. My book proposal was reviewed by several experts in the field and very quickly accepted.

My original 2010 proposal to Cambridge University Press consisted of these same 14 chapters of this book. For several years, I proceeded to flesh out more details of the book in outline form, in many cases down to individual sections, but I had very little time to actually write. Although many sections needed updating over the years and new sections were added to satisfy new developments in this rapidly changing field, it is surprising how well that original vision for the book stood up! That is particularly the case since there were no other nanomedicine courses out there. I had to figure out

on my own what topics belonged in a textbook and how all of those many diverse topics should be linked together into something coherent.

Many friends, colleagues, and students have wondered what took me so long to finish the book. There were many reasons, some good and others not, but there were two major reasons. First, it is hard to find the time and energy to write a book with this level of breadth and depth across multiple scientific fields and medicine in the hours *after* working 65+ hours per week on other job-related activities. Second, I was constantly engaged in a steep learning curve to keep up with the work in nanomedicine fields of science and engineering that had technical half-lives of three to four years. Technical half-life means half of everything you learned, and thought you knew, would be superseded by new advances in the field. The science and engineering, in addition to the molecular biology and medicine, underlying nanomedicine is literally shifting under your feet, so that sections of the book needed to be updated or edited many times to reflect these advances. I like to say I have written this one book several times already!

Finally, I began writing again in earnest during 2020. The COVID-19 pandemic's forced isolation, as well as "semi-retirement", gave me an opportunity to partially escape the chaos of 2020. Throughout 2020, I frequently spent five to six (or more!) hours per day writing. Despite the pandemic, 2020 was a very good year for book writing – a silver lining in an otherwise dark year! I like to joke that when Isaac Newton escaped the plague to the countryside, he spent the year developing much of the field of physics. All I did with my year escaping to the countryside during the COVID-19 pandemic was to write this book!

This book was produced electronically – in every sense of the word! My lectures were digitally recorded at Purdue. I used those recordings and Dragon Naturally Speaking digital speech recognition software (originally invented by an MIT classmate of mine) to transcribe the video-recorded lectures to give partial content to the book. I made generous use of the lifetime digital library access given to me by Purdue upon my becoming an emeritus professor to give me access to many hundreds of scientific papers used in this book. I downloaded pdf versions of all papers cited and then organized all of the references within EndNote, a reference database software system. EndNote was then linked directly to Microsoft Word to allow insertion of all references into the text as citations. Microsoft Word was used for all writing, formatting, indexing, and automated generation of a table of contents for each chapter at the front of the book as well as a bibliography of all references used. Figures, those not taken from published literature, are all my own, mostly generated while teaching my course at Purdue ("Source: Leary teaching"). Many started out as PowerPoint slides used in my lectures and other scientific presentations at national and international meetings where I was a frequently invited speaker. I used a variety of graphic software programs, including PowerPoint, Adobe Photoshop, and Adobe Photoshop Elements. The book is complex not only due to the multidisciplinary nature of the field of nanomedicine, but also due to the complexity in terms of the many electronic pieces and how they all fit together!

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