NANOTECHNOLOGY IN BIOLOGY AND MEDICINE

Methods, Devices, and Applications

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Edited by **Tuan Vo-Dinh**

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Dedication

To the

Pioneers whose visions have

Sailed to the outer edges of the universe,

Pierced into the inner world of the atom, and

Unlocked the mysteries of the human cell

Preface

Nanotechnology in Biology and Medicine is intended to serve as an authoritative reference for a wide audience involved in research, teaching, learning, and practice of nanotechnology in life sciences. Nanotechnology, which involves research on and the development of materials and species at length scales between 1 to 100 nm, has been revolutionizing many important scientific fields ranging from biology to medicine. This technology, which is at the scale of the building blocks of the cell, has the potential of developing devices smaller and more efficient than anything currently available. The combination of nanotechnology, material sciences, and molecular biology opens the possibility of detecting and manipulating atoms and molecules using nanodevices, which have the potential for a wide variety of biological research topics and medical applications at the cellular level.

The new advances in biotechnology, genetic engineering, genomics, proteomics, and medicine will depend on how well we master nanotechnology in the coming decades. Nanotechnology could provide the tools to study how the tens of thousands of proteins in a cell (the so-called proteome) work together in networks to orchestrate the chemistry of life. Specific genes and proteins have been linked to numerous diseases and disorders, including breast cancer, muscle disease, deafness, and blindness. Protein misfolding processes are believed to cause diseases such as Alzheimer's disease, cystic fibrosis, "mad cow" disease, an inherited form of emphysema, and many cancers.

Nanotechnology has also the potential to dramatically change the field of diagnostics, therapy, and drug discovery in the postgenomic area. The combination of nanotechnology and optical molecular probes are being developed to identify the molecular alterations that distinguish a diseased cell from a normal cell. Such technologies will ultimately aid in characterizing and predicting the pathologic behavior of diseased cells as well as the responsiveness of cells to drug treatment.

The combination of biology and nanotechnology has already led to a new generation of devices for probing the cell machinery and elucidating molecular-level life processes heretofore beyond the scope of human inquiry. Tracking biochemical processes within intracellular environments can now be performed in vivo with the use of fluorescent and plasmonic molecular probes and nanosensors. Using near-field scanning microscopy and other nanoimaging techniques, scientists are now able to explore the biochemical processes and submicroscopic structures of living cells at unprecedented resolutions. It is now possible to develop nanocarriers for targeted delivery of drugs that have their shells conjugated with DNA constructs and fluorescent chromophores for in vivo tracking.

This monograph presents the most recent scientific and technological advances of nanotechnology, as well as practical methods and applications, in a single source. Included are a wide variety of important topics related to nanobiology and nanomedicine. Each chapter provides introductory material with an overview of the topic of interest; a description of methods, protocols, instrumentation, and applications; and a collection of published data with an extensive list of references for further details.

The goal of this book is to provide a comprehensive overview of the most recent advances in materials, instrumentation, methods, and applications in areas of nanotechnology related to biology and medicine, integrating interdisciplinary research and development of interest to scientists, engineers, manufacturers, teachers, and students. It is our hope that this book will stimulate a greater appreciation of the usefulness, efficiency, and potential of nanotechnology in biology and in medicine.

Tuan Vo-Dinh
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Editor

Dr. Tuan Vo-Dinh is the director of the Fitzpatrick Institute for Photonics and professor of biomedical engineering and chemistry at the Duke University. Before joining Duke University in 2006, Dr. Vo-Dinh was the director of the Center for Advanced Biomedical Photonics, group leader of Advanced Biomedical Science and Technology Group, and a Corporate Fellow, one of the highest honors for distinguished scientists at Oak Ridge National Laboratory (ORNL), Oak Ridge, Tennessee. A native of Vietnam and a naturalized U.S. citizen, Dr. Vo-Dinh completed his high school education in Saigon (now Ho-Chi Minh City) and went on to pursue his studies in Europe, where he received a Ph.D. in biophysical chemistry in 1975 from ETH (Swiss Federal Institute of Technology) in Zurich, Switzerland. His research has focused on the development of advanced technologies for the protection of the environment and the improvement of human health. His research activities involve laser spectroscopy, molecular imaging, medical diagnostics, cancer detection, chemical sensors, biosensors, nanosensors, and biochips.

Dr. Vo-Dinh has published over 350 peer-reviewed scientific papers, is an author of a textbook on spectroscopy, and is the editor of six books. He is the editor-in-chief of the journal *NanoBiotechnology*, associate editor of the *Journal of Nanophotonics*, *Plasmonics* and *Ecotoxicology and Environmental Safety.* He holds over 30 patents, 6 of which have been licensed to environmental and biotech companies for commercial development. Dr. Vo-Dinh is a fellow of the American Institute of Chemists, a fellow of the American Institute of Medical and Biological Engineering, and a fellow of SPIE, the International Society for Optical Engineering. He serves on the editorial boards of various international journals on molecular spectroscopy, analytical chemistry, biomedical optics, and medical diagnostics. He has also served the scientific community through his participation in a wide range of governmental and industrial boards and advisory committees.

Dr. Vo-Dinh has received seven R&D 100 Awards for Most Technologically Significant Advance in Research and Development for his pioneering research and inventions of innovative technologies; these awards were for a chemical dosimeter (1981), an antibody biosensor (1987), the SERODS optical data storage system (1992), a spot test for environmental pollutants (1994), the SERS gene probe technology for DNA detection (1996), the multifunctional biochip for medical diagnostics and pathogen detection (1999), and the Ramits Sensor (2003). He received the Gold Medal Award from the Society for Applied Spectroscopy (1988); the Languedoc-Roussillon Award (France) (1989); the Scientist of the Year Award from ORNL (1992); the Thomas Jefferson Award from Martin Marietta Corporation (1992); two Awards for Excellence in Technology Transfer from Federal Laboratory Consortium (1995, 1986); the Inventor of the Year Award from Tennessee Inventors Association (1996); and the Lockheed Martin Technology Commercialization Award (1998); the Distinguished Inventors Award from UT-Battelle (2003), and the Distinguished Scientist of the Year Award from ORNL (2003). In 1997, Dr. Vo-Dinh was presented the Exceptional Services Award for distinguished contribution to a healthy citizenry from the U.S. Department of Energy.

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Table of Contents

SECTION II Applications in Biology and Medicine

1

Nanotechnology in Biology and Medicine: The New Frontier

Tuan Vo-Dinh
Duke University

1.1 Introduction

The meter, a dimension unit closest to everyday human experience, is often considered as the basic dimension of reference for human beings. Let us look up in the dimension scale, up to the outer edges of our "local universe," the Milky Way, a galaxy of 100–400 billion stars. This universe revealed to us has a dimension of 50,000 light-years from the outer edges to its center. A light-year is the distance that light travels in 1 y at the speed of approximately 300 million (300,000,000) m/s, which corresponds to approximately 10,000,000,000,000,000 (16 zeros) or 10^{16} m. Therefore, the distance from the center to the outer edge of the Milky Way is 500,000,000,000,000,000,000 or 5×10^{20} m. Let us now look down in the other direction of the dimensional scale, down to a nanometer, which is a billion (1,000,000,000) times smaller than a meter (i.e., 10^{-9} m). The word *nano* is derived from the Greek word meaning "dwarf." In dimensional scaling *nano* refers to 10^{-9}—i.e., one billionth of a unit. A human hair has a diameter of approximately 10 μm, which is 10,000 nm. Diameters of atoms are in the order of tenths (10^{-1}) of nanometers, whereas the diameter of a DNA strand is about a few nanometers. Thus, *nanotechnology* is a general term that refers to the techniques and methods for studying, designing, and fabricating devices at the level of atoms and molecules. The initial concept of investigating materials and biological systems at the nanoscale dates to more than 40 years ago, when Richard Feynman presented a lecture in 1959 at the annual meeting of the American Physical Society at the California Institute of Technology. This lecture, entitled "There's Plenty of Room at the Bottom," is generally considered to be the first look into the world of materials, species, and structures at the nanoscale levels. Thinking small, however, is not a new idea. Thousands of years ago, the Greek philosophers Leucippus and Democritus have suggested that all matter was made from tiny particles like atoms. Only now, the advent of nanotechnology will lead to the development of a new generation of instruments capable of revealing the structure of these tiny particles conceived since the Hellenic Age.

It is now generally accepted that nanotechnology involves research and development on materials and species at length scales from 1 to 100 nm. Nanotechnology is very important to biology since many biological species have molecular structures at the nanoscale levels. These species comprise a wide variety of basic structures such as proteins, polymers, carbohydrates (sugars), and lipids, which have a great variety of chemical, physical, and functional properties. Individual molecules, when organized into controlled and defined nanosystems, have new structures and exhibit new properties. This structural variety and the versatility of these biological nanomaterials and systems have important implications for the design and development of new and artificial assemblies that are critical to biological and medical applications. The development of a next-generation nanotechnology tool-kit is critical to understand the inner world of complex biological nanosystems at the cellular level. Since nanotechnology involves technology on the scale of molecules it has the potential of developing devices smaller and more efficient than anything currently available. Traditionally defined disciplines, such as chemistry, biology, and materials science, also deal with atoms and molecules, which are of nanometer sizes. But nanotechnology differs from traditional disciplines in a very fundamental aspect. For example, chemistry (or biology and materials science) deals with atoms and molecules at the bulk level (we do not see the molecules in chemical solutions), whereas nanotechnology seeks to actually "manipulate" individual atoms and molecules in very specific ways, thus creating new materials having new properties and new functions. It is this "bottom-up" capability that makes nanotechnology a unique new field of research of undreamed possibilities and potential. Our mastering of nanotechnology could unleash breakthroughs in genetic engineering, genomics, proteomics, and medicine in the coming decades. If we can assemble biological systems and devices at the atomic and molecular levels, we will achieve versatility in design, a precision in construction, and a control in operation heretofore hardly imagined.

1.2 Cellular Nanomachines and the Building Blocks of Life

Nanotechnology is of great importance to molecular biology and medicine because life processes are maintained by the action of a series of biological molecular nanomachines in the cell machinery. By evolutionary modification over trillions of generations, living organisms have perfected an armory of molecular machines, structures, and processes. The living cell, with its myriad of biological components, may be considered the ultimate "nano factory." Figure 1.1 shows a schematic diagram of a cell with its

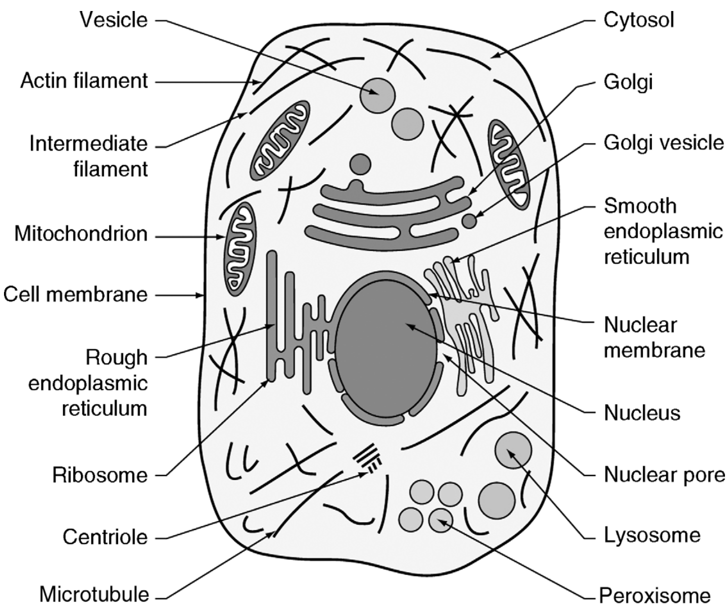

FIGURE 1.1 Schematic diagram of a cell and its components.

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