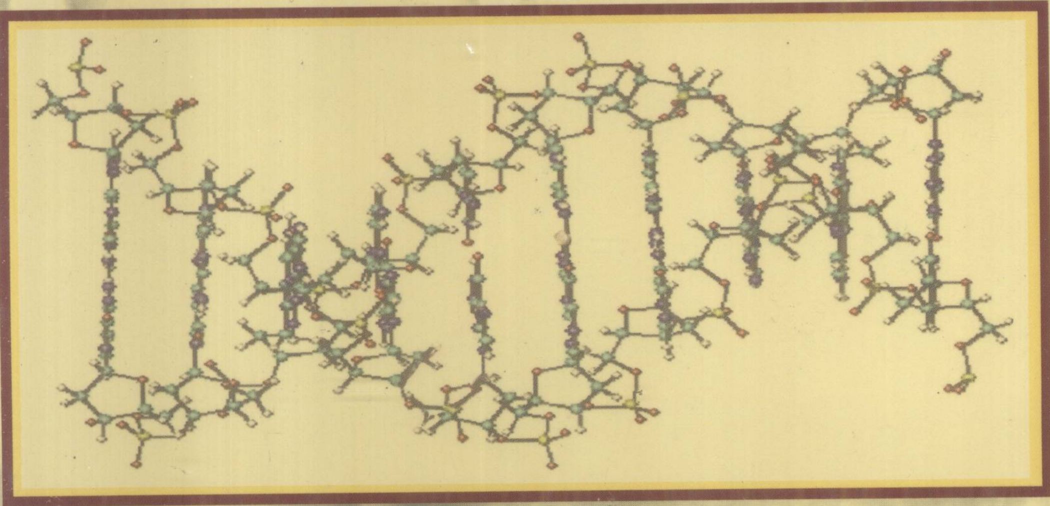
NanoBioTechnology

BioInspired Devices and Materials of the Future



Edited by

Oded Shoseyov
Ilan Levy

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BioInspired Devices and Materials of the Future

Edited by

Oded Shoseyov

The Institute of Plant Science and Genetics in Agriculture and The Otto Warburg Center for Agricultural Biotechnology, The Hebrew University of Jerusalem, Rehovot, Israel

and

Ilan Levy

Intel Research Israel, Intel Electronics, Jerusalem, Israel

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NanoBioTechnology

PREFACE

Research and applied science, as we see it today, has advanced to a place in which, instead of manipulating substances at the molecular level, we can control them at the atomic level. This exciting operational space, where the laws of physics shift from Newtonian to quantum, provides us with novel discoveries, which hold the promise of future developments that, until recently, belonged to the realm of science fiction.

Nanobiotechnology is a multidisciplinary field that covers a vast and diverse array of technologies from engineering, physics, chemistry, and biology. It is expected to have a dramatic infrastructural impact on both nanotechnology and biotechnology. Its applications could potentially be quite diverse, from building faster computers to finding cancerous tumors that are still invisible to the human eye. As nanotechnology moves forward, the development of a 'nano-toolbox' appears to be an inevitable outcome. This toolbox will provide new technologies and instruments that will enable molecular manipulation and fabrication via both 'top-down' and 'bottom-up' approaches.

This book is organized into five major sections; 1. Introduction, 2. Bio-templating, 3. Bionanoelectronics and Nanocomputing, 4. Nanomedicine, Nanopharmaceuticals and Nanosensing, and 5. *De Novo* Designed Structures.

Section 1 is an introductory overview on nanobiotechnology, which briefly describes the many aspects of this field, while addressing the reader to relevant sources for broader information overviews.

Biological materials can serve as nanotemplates for 'bottom-up' fabrication. In fact, this is considered one of the most promising 'bottom-up' approaches, mainly due to the nearly infinite types of templates available. This approach is demonstrated in Section 2.

The convergence of nanotechnology and biotechnology may combine biological and man-made devices for the design and fabrication of bio-nanoelectronics and for their use in nanocomputing. This area is addressed in Section 3, which covers the use of biological macromolecules for electron transfer and computation.

One of the main reasons nanobiotechnology holds so much promise is that it operates at the biological size scale. Biological molecules (such as enzymes, receptors, DNA), microorganisms and individual cells in our bodies are all nano-sized. Engineered ultrasmall particles that are made in the exact size needed to perform specific tasks, such as drug release in particular locations in the body, drug delivery into the blood stream, or to pinpoint malfunctioning tissues (cancerous tissue, for example), are examples of the new medical discipline termed 'nanomedicine'. Section 4 gives a brief look at this extensive and rapidly growing field.

The fact that nanobiotechnology embraces and attracts many different disciplines, encompassing both researchers and business leaders, has produced many examples of bio-inspired *de novo* designed structures. Each scientific group approaches the molecular level with unique skills, training, and language, and a few examples are presented in Section 5. Cross-talk and collaborative research among academic disciplines, and between the researchers and their counterparts in business, are critical to the advancement of nanobiotechnology and constitute the foundation for the new material generation.

Working at the molecular or atomic level allows researchers to develop innovations that will dramatically improve our lives. The new territory of bionanotechnology holds the promise of improving our health, our industry, and our society in ways that may even surpass what computers and biotechnology have already achieved.

Ilan Levy and Oded Shoseyov

CONTRIBUTORS

KENJI ARINAGA, *Walter Schottky Institut, Technische Universitaet Muenchen, Garching, Germany, and Fujitsu Laboratories Ltd., Atsugi, Japan*

LANE A. BAKER, *Departments of Chemistry and Anesthesiology, University of Florida, Gainesville, FL*

ROBERT R. BIRGE, *Department of Molecular and Cell Biology, and Department of Chemistry University of Connecticut, Storrs, CT*

STEFAN H. BOSSMANN, *Kansas State University, Department of Chemistry, Manhattan, Kansas*

JIN-HO CHOY, *Center for Intelligent NanoBio Materials (CINBM), Department of Chemistry and Division of Nanoscience, Ewha Womans University, Seoul 120-750, Korea*

GIANAURELIO CUNIBERTI, *Molecular Computing Group, Institute of Theoretical Physics, University of Regensburg, Regensburg, Germany*

ROSA DI FELICE, *National Center on nanoStructures and bioSystems at Surfaces (S3) of INFM-CNR, Modena, Italy*

EVA-M. EGELSEER, *Center for NanoBiotechnology, University of Natural Resources and Applied Life Sciences, Vienna, Austria*

JOSEPH FARFEL, *Department of Computer Science, Duke University, Durham, NC*

ERAN GABBAI, *Do-Coop Technologies Ltd, Or Yehuda, Israel*

EHUD GAZIT, *Department of Molecular Microbiology and Biotechnology, Tel Aviv University, Tel Aviv, Israel*

RAFAEL GUTIERREZ, *Molecular Computing Group, Institute of Theoretical Physics, University of Regensburg, Regensburg, Germany*

TETSUYA HARUYAMA, *Department of Biological Functions and Engineering, Kyushu Institute of Technology, Fukuoka, Japan*

JASON R. HILLEBRECHT, *Department of Molecular and Cell Biology, University of Connecticut, Storrs, CT*

KEWAL K. JAIN, *PharmaBiotech, Basel, Switzerland*

TAPAN K. JAIN, *Department of Pharmaceutical Sciences, College of Pharmacy, University of Nebraska Medical Center, Omaha, NE*

KATHARINE JANIK, *Kansas State University, Department of Chemistry, Manhattan, Kansas*

NATAŠA JONOSKA, *University of South Florida, Department of Mathematics, Tampa, FL*

Andreas Kage, *Charité Universitätsmedizin Berlin, Zentralinstitut für Laboratoriumsmedizin und Pathobiochemie, Berlin, Germany*

Jeremy F. Koscielecki, *Department of Chemistry, University of Connecticut, Storrs, CT*

Mark P. Krebs, *Department of Ophthalmology, College of Medicine, University of Florida, Gainesville, FL*

Vinod Labhasetwar, *Department of Biomedical Engineering, Lemer Research Institute, Cleveland Clinic, Cleveland, OH*

Katarzyna Lamparska-Kupsik, *City of Hope National Medical Center and Beckman Research Institute, Duarte, CA*

Ilan Levy, *Intel Research Israel, Intel Electronics, Jerusalem, Israel*

Loren Limberis, *Department of Engineering, East Carolina University, Greenville, NC*

Charles R. Martin, *Departments of Chemistry and Anesthesiology, University of Florida, Gainesville, FL*

Michael Niederweis, *University of Alabama at Birmingham, Department of Microbiology, Bevill Biomedical Research Building, Birmingham, AL*

Jae-Min Oh, *Center for Intelligent NanoBio Materials (CINBM), Department of Chemistry and Division of Nanoscience, Ewha Womans University, Seoul 120-750, Korea*

Man Park, *Center for Intelligent NanoBio Materials (CINBM), Department of Chemistry and Division of Nanoscience, Ewha Womans University, Seoul 120-750, Korea*

Megh Raj Pokhrel, *Central Department of Chemistry, Tribhuvan University, Kirtipur, Kathmandu, Nepal*

Danny Porath, *Physical Chemistry Department and Center for Nanoscience and Nanotechnology, The Hebrew University of Jerusalem, Israel*

Dietmar Pum, *Center for NanoBiotechnology, University of Natural Resources and Applied Life Sciences, Vienna, Austria*

Ulrich Rant, *Walter Schottky Institut, Technische Universitaet Muenchen, Garching, Germany*

Maram K. Reddy, *Department of Biomedical Engineering, Lemer Research Institute, Cleveland Clinic, Cleveland, OH*

Jennifer Sager, *Department of Computer Science, University of New Mexico, Albuquerque, NM*

Sanjeeb K. Sahoo, *Institute of Life Sciences, Nalco Square, Bhubaneswar, Orissa, India*

MARGIT SÁRA, *Center for NanoBiotechnology, University of Natural Resources and Applied Life Sciences, Vienna, Austria*

BERNHARD SCHUSTER, *Center for NanoBiotechnology, University of Natural Resources and Applied Life Sciences, Vienna, Austria*

ODED SHOSEYOV, *The Institute of Plant Science and Genetics in Agriculture and The Otto Warburg Center for Agricultural Biotechnology, Faculty of Agricultural, Food and Environmental Quality Sciences, The Hebrew University of Jerusalem, Rehovot, Israel*

UWE B. SLEYTR, *Center for NanoBiotechnology, University of Natural Resources and Applied Life Sciences, Vienna, Austria*

STEVEN S. SMITH, *City of Hope National Medical Center and Beckman Research Institute, Duarte, CA*

DARKO STEFANOVIC, *Department of Computer Science, University of New Mexico, Albuquerque, NM*

RUSSELL J. STEWART, *Department of Bioengineering, University of Utah, Salt Lake City, UT*

JEFFREY A. STUART, *W. M. Keck Center for Molecular Electronics, Syracuse University, Syracuse, NY*

MARC TORNOW, *Institute of Semiconductor Technology, Technical University of Braunschweig, Braunschweig, Germany*

HANS-ACHIM WAGENKNECHT, *University of Regensburg, Institute of Organic Chemistry, Regensburg, Germany*

KEVIN J. WISE, *Department of Molecular and Cell Biology, University of Connecticut, Storrs, CT*

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I
INTRODUCTION

1
Nanobiotechnology Overview

Oded Shoseyov and Ilan Levy

Summary

Nanobiotechnology is a multidisciplinary field that covers a vast and diverse array of technologies coming from engineering, physics, chemistry, and biology. It is the combination of these fields that has led to the birth of a new generation of materials and methods of making them. The scope of applications is enormous and every day we discover new areas of our daily lives where they can find use. This chapter aims to provide the reader with a brief overview of nanobiotechnology by describing different aspects and approaches in research and application of this exciting field. It also provides a short list of recently published review articles and books on the different topics in nanobiotechnology.

Key Words: Nanobiotechnology; nanocomputing; nanoelectronics; nanofabrication; nanomedicine; nanotechnology.

1. INTRODUCTION TO NANOSCIENCE AND NANOTECHNOLOGY

The prefix *nano* is derived from the Greek word *nanos* meaning "dwarf," need and today it is used as a prefix describing 10^{-9} (one billionth) of a measuring unit. Therefore, nanotechnology is the field of research and fabrication that is on a scale of 1 to 100 nm. The primary concept was presented on December 29, 1959, when Richard Feynman presented a lecture entitled "There's Plenty of Room at the Bottom" at the annual meeting of the American Physical Society, the California Institute of Technology (this lecture can be found on several web sites; *see* ref. *1*). Back then, manipulating single atoms or molecules was not possible because they were far too small for available tools. Thus, his speech was completely theoretical and seemingly far-fetched. He described how the laws of physics do not limit our ability to manipulate single atoms and molecules. Instead, it was our lack of the appropriate methods for doing so. However, he correctly predicted that the

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time for the atomically precise manipulation of matter would inevitably arrive. Today, that lecture is considered to be the first landmark of science at the nanolevel.

The first 30 yr or so of the nanosciences were devoted mainly to studying and fabricating materials at the nanolevel. In those studies, much effort was devoted to shrinking the dimension of fabricated materials. It was also a time when the two basic fabrication approaches were defined: "bottom-up" and "top-down." The bottom-up approach seeks the means and tools to build things by combining smaller components such as single molecules and atoms, which are held together by covalent forces. Theoretically, it can be exemplified by molecular assemblers, where nanomachines are programmed to build a structure one atom or molecule at a time or by self-assembly, where these structures are built spontaneously. The advantage of the bottom-up design is that the covalent bonds holding a single molecule together are far stronger than the weak interactions that hold more than one molecule together. The top-down approach refers to the molding, carving, and fabricating of small materials and components by using larger objects such as mechanical tools and lasers, such as is used today in current photolithographic approaches in silicon chip fabrication. Currently, techniques using both approaches are evolving, and many applications are likely to involve combination approaches. However, the bottom-up approach, at least theoretically, holds far more practical and applicative future potential.

Nanoscience is therefore a multidisciplinary field that seeks to integrate mature nanoscale technology of fields such as physics, biology, engineering, chemistry, computer science, and material science.

2. THE "NANO"–"BIO" INTERFACE

Biosystems are governed by nanoscale processes and structures that have been optimized over millions of years. Biologists have been operating for many years at the molecular level, in the range of nanometers (DNA and proteins) to micrometers (cells). A typical protein like hemoglobin has a diameter of about 5 nm, the DNA's double helix is about 2 nm wide, and a mitochondrion spans a few hundred nanometers. Therefore, the study of any subcellular entity can be considered "nanobiology." Furthermore, the living cell along with its hundreds of nanomachines is considered, today, to be the ultimate nanoscale fabrication system.

On the other hand, countless exciting questions in biology can be addressed in new ways by exploiting the rapidly growing capabilities of nanotechnological research approaches and tools. This research will form and shape the foundation for our understanding of how biological systems operate. We are exploiting nanofabrication to perform individual molecule analyses in biological systems, to study cellular responses to structured interfaces, and to explore dynamic life processes at reduced dimensions. Our research has advanced the ability to structure materials and pattern surface chemistry at subcellular and molecular dimensions.

The groundwork of each and every biological system is nanosized molecular building blocks and machinery that cooperate to produce living entities. These elements have ignited the imagination of nanotechnologists for many years and it is the combination of these two disciplines (nano and biotechnology) that has resulted in the birth of the new science of nanobiotechnology. Nanotechnology provides the tools and technology platforms for the investigation and transformation of biological systems, and biology offers inspirational models and bio-assembled components to nanotechnology. The difference between "nanobiology" to "nanobiotechnology" resides in the technology part of the term. Anything that is "man-made" falls into the technology section of nanobiotechnology. Nearly any molecular machinery that we can think of has its analog in biological systems and as for now, it appears that the first revolutionary application of nanobiotechnology will probably be in computer science and medicine. Nanobiotechnology will lead to the design of entirely new classes of micro- and nanofabricated devices and machines, the inspiration for which will be based on bio-structured machines, the use of biomolecules as building blocks, or the use of biosystems as the fabrication machinery.

3. NANOBIOTECHNOLOGY

Unlike nonbiological systems that are fabricated top-down, biological systems are built up from the molecular level (bottom-up). They do this via a collection of molecular tool kits of atomic resolution that are used to fabricate micro- and macrostructure architectures. Biological nanotechnology, or nanobiotechnology, can be viewed in many ways: one way is the incorporation of nanoscale machines into biological organisms for the ultimate purpose of improving the organism's quality of life. To date, there are a few methods for synthesizing nanodevices that have the potential to be used in an organism without risk of being rejected as antigens; another way is the use of biological "tool kits" to construct nano- to microstructures. However, the broad perspective is probably the one that will include both and will be defined as: **the engineering, construction, and manipulation of entities in the 1- to 100-nm range using biologically based approaches or for the benefit of biological systems**. The biological approaches can be either an inspired way of mimicking biological structures or the actual use of biological building blocks and building tools to assemble nanostructures. In a way, the first example of a nanobiotechnology system might be the production of recombinant proteins. Recombinant DNA technology can direct the ribosomal machinery to produce designed proteins both in vivo and in vitro that can serve as components of larger molecular structures.

As already mentioned, there are two basic fabrication approaches to creating nanostructures: bottom-up and top-down. The bottom-up approach exploits biological structures and processes to create novel functional materials, biosensors, and bioelectronics for different applications. This field encompasses many disciplines, including material science, organic chemistry, chemical engineering, biochemistry, and molecular biology. In the top-down approach, nanobiotechnology applies tools and processes of nano/microfabrication to build nanostructures and nanodevices. The tools that are used often involve optical and electron beam lithography and the processing of large materials into fine structures with defined surface features. One of the major differences between nanotechnology and nanobiotechnology is that in the former, the dominant approach is top-down, whereas in the latter, it is bottom-up.

An example of the bottom-up approach is the pioneering work of two leading groups on biomolecular motor proteins *(2–7)*. In these studies, naturally occurring motor proteins were engineered for compatibility with artificial interfaces to create new ways of joining proteins to synthetic nanomaterials. Biomolecular motors can provide chemically powered movement to micro- and nanodevices. Nanodevices utilizing motor proteins such as kinesin or F_1-ATPase can be used as nanoscale transporters, as probes for surface imaging, to control the movement of target substances, and to support the controlled assembly of nanostructures.

Structural properties that enable DNA to serve so effectively as genetic material can also be exploited to produce target materials with predictable three-dimensional (3D) structures in the bottom-up approach. Pioneering work using this approach is presented in studies performed by the group of Nadrian Seeman *(8–12)*. He uses DNA motifs with specific, structurally well defined, cohesive interactions involving hydrogen bonding or covalent interactions ("sticky ends") to produce target materials with predictable 2D and 3D structures. The complementarity that leads to the pairing of the DNA strands is the driving force for the complex assemblies with their branched structures. These efforts have generated a large number of individual species, including polyhedral catenanes, such as a cube and a truncated octahedron, a variety of single-stranded knots, and Borromean rings. The combination of these constructions with other chemical components is expected to contribute to the development of nanoelectronics, nanorobotics, and smart materials. Therefore, the organizational capabilities of structural DNA nanotechnology are just beginning to be explored, and the field is ultimately expected to be able to organize a variety of species in the material world.

Another fascinating example is the use of crystalline bacterial cell surface layer (S-layers) proteins as tools in nanofabrication and nanopatterning. The