Preface

The broad field of nanotechnology has undergone explosive growth and development over the past five years. In fact, no field in the history of science has experienced more interest or larger government investment. Indeed, by the end of 2006, the worldwide government and private sector investment in nanotechnology is projected to be approximately $9 billion. The enthusiasm researchers have for this field is fueled by: 1) the desire to determine the unusual chemical and physical properties of nanostructures, which are often quite different from the bulk materials from which they derive, and 2) the potential to use such properties in the development of novel and useful devices and materials that can impact and, perhaps even transform, many aspects of modern life.

The subfield known as Nanobiotechnology holds some of the greatest promise. This highly interdisciplinary field, which draws upon contributions from chemistry, physics, biology, materials science, medicine and many forms of engineering, focuses on several important areas of research. Some of these include: 1) the development of methods for building nanostructures and nanostructured materials out of biological or biologically inspired components such as oligonucleotides, proteins, viruses, and cells; these structures are intended for both biological and abiological uses, 2) the utilization of synthetic nanomaterials to regulate and monitor important biological processes, and 3) the development of synthetic and soft matter compatible surface analytical tools for building nanostructures important in both biology and medicine. Advances in this field offer novel and potentially useful approaches to building functional structures including computational tools, energy generation, conversion and storage materials, powerful optical devices, and new detection and therapeutic modalities. Indeed, advances in Nanobiotechnology have the potential to revolutionize the way the medical community approaches modern disease management.

Although the field is still embryonic, major strides have been made. Powerful new forms of signal amplification have been realized for both DNA and protein based detection systems. Indeed, the first commercial molecular diagnostic systems that rely upon nanoparticle probes are expected to be available in 2007. Biological labels based upon nanocrystals are commercially available and used routinely for research purposes in laboratories worldwide. Many new nanomaterials have boosted the efficacy and viability of several powerful pharmaceutical agents.

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Nanofabrication tools that allow one to routinely build oligonucleotide, protein, and other biorelevant nanostructures on surfaces with extraordinary precision have evolved to the point of commercialization and widespread use. These examples represent only a small part of this expansive field but are realized potential and serve as motivators for future developments within it.

In 2004, we edited the book *Nanobiotechnology: Concepts, Applications and Perspectives* which was intended to provide a systematic and comprehensive framework of specific research topics in Nanobiotechnology. Due to the great success of this first volume, *Nanobiotechnology II – More Concepts and Applications* now follows the notion of its precursor by combining contributions from bioorganic and bioinorganic chemistry, molecular and cell biology, materials science and bioanalytics to cover the entire scope of current and future developments in Nanobiotechnology. The collection of articles in this volume again emphasizes the high degree of interdisciplinarity necessarily implemented in the joint-venture of biotechnology and nano-sciences. During the selection of potential chapters for this volume we took into account, on the one hand, the progress by which particular areas had developed in the past three years. Because this occurred primarily in two areas, namely the development of nanoparticle science and applications as well as in the refinement of scanning probe microscopy related methods, the majority of the chapters are concerned with these issues. On the other hand, additional topics not yet covered in the first volume were identified, thus leading to contributions from the area of small molecule- and peptide-based self-assembly (chapters 1 and 2), the use of nanomaterials for medicinal applications (section 3), and the utilization of biomolecular machinery to create hybrid devices with mechanical functionalities (section 4).

The current volume is divided into four main sections. Section I (Chapters 1–6) concerns novel principles in self-assembly and nanoparticle-based systems. In Chapter 1, Mary S. Gin, Emily G. Schmidt, and Pinaki Talukdar provide an overview of artificial transmembrane channels, attainable by organic synthesis and the assembly of small molecule building blocks. This synthetic approach to ion channels, initially aimed at elucidating the minimal structural requirements for ion flow across a membrane, nowadays is focusing on the development of synthetic channels that are gated, thus providing a means to control whether the channels are open or closed. Such artificial signal transduction could lead to novel sensing and therapeutic applications. The self-assembly of small molecules also represents the underlying theme of Chapter 2, written by Maxim G. Ryadnov and Derek N. Woolfson. They summarize current efforts to build nanoscopic and mesoscopic supramolecular structures from short oligopeptides comprising the α-helical coiled-coil folding motif. Examples of nanostructures and materials made from such coiled-coil building blocks include programmable nanoscale linkers, molecular switches, and fibrous and gel-forming materials which may be useful for the production of peptide-polymer hybrids combining the advantages of both natural and synthetic polymers. These structures also could lead to the design of peptide-based switches that may render hybrid networks more controllable and increase sensitivity and responses to local environments.

The notion of the first two chapters is connected with the area of nanoparticle research in chapter 3, where Erik Dujardin and Stephen Mann illustrate how unraveling the specific interactions between bio-derived templates and inorganic materials not only yields a better understanding of natural hybrid materials but also inspires new methods for developing the potential of biological molecules, superstructures and organisms as self-assembling agents for materials fabrication. In particular, the chapter describes the use of various types of bio-related molecules, ranging from biopolymers, peptides, oligonucleotides to the complex biological architecture of proteins, viruses and even living organisms, for the synthesis and assembly of organized nanoparticle-based structures and materials. Two additional chapters deal with the conversed approach, that is, the modification of nanoparticles with biomolecules to add functionality to the inorganic components. In Chapter 4, Rochelle R. Arvizo, Mrinmoy De, and Vincent M. Rotello describe recent developments involving protein functionalized nanoparticles. These conjugates, which are produced either by covalent or non-covalent coupling strategies, hold potential for the creation of novel materials and devices in the biosensing and catalysis fields. The combination of proteins and nanoparticles also opens up novel approaches to the synthesis of nanoparticles, as summarized in Chapter 6, written by Ronan Baron, Bilha Willner, and Itamar Willner. They describe the application of biocatalysts, enzymes, such as oxidases and hydrolases, as active components for the synthesis and enlargement of nanoparticles and for biocatalytic growth of nanoparticles, mediated by specific enzyme reactions. This concept has strong implications in biosensor design, and the nanoparticle-enzyme hybrid systems also can be used as biocatalytic inks for the generation of metallic nanowires, and thus, bioelectronic devices.

The self-assembly behavior of another class of biomolecular recognition elements is described in Chapter 5. There, Thomas H. LaBean, Kurt V. Gothelf, and John H. Reif summarize the current state-of-the-art of self-assembling DNA nanostructures for patterned assembly of (macro)molecules and nanoparticles. This field of research, which was initially covered in the previous volume of Nanobiotechnology, has evolved significantly within the past three years. A large number of groups are actively conducting research on such DNA-based nanoarchitectures. Although it is not yet clear whether commercially relevant applications of DNA scaffolds will ever be realized, the basic exploration of design principles based on the predictable Watson-Crick interaction of oligonucleotides opens up long term perspectives in studying novel nanoelectronic structures, sensing mechanisms, and materials research.

The increasing importance of nanostructures in analytical applications is reflected in the seven chapters of section II (Chapters 7–13). Developments of nanoparticle-based technologies are described in the first three chapters. As shown by Joseph Wang, the large number of inorganic ions incorporated within nanoparticles can be employed for signal amplification by electrochemical means. This approach offers unique opportunities for electronic transduction of biomolecular interactions, and thus, for measuring protein and nucleic acid analytes (Chapter 7). The peculiar optical properties of semiconductor nanoparticles are also used for bioanalytical purposes. Hedi Mattoussi and colleagues describe in their contribution the latest developments in this area (Chapter 8). This quantum dot biolabeling is rapidly moving towards sophisticated applications in cell and tissue imaging as well as in FRET-based immuno-assays, thereby posing great demands on the chemical and structural integrity of the hybrid probes. A more fundamental approach combining nanoparticle technologies and spectroscopy is described in Chapter 9 by Richard P. Van Duyne and colleagues. The localized surface plasmon resonance, occurring in optically coupled nanoparticles, coupled with the size, shape, material and local dielectric environment dependence of the nanostructures, forms the basis for a novel class of biosensors.

While the above mentioned chapters have the ''bottom-up'' assembly of functional nanostructures in common, the following four chapters of section 2 take advantage of micro- and nanosized probe structures fabricated by conventional ''top-down'' methodologies. The developments of micromechanical cantilever array sensors for bioanalytical assays are described by Hans Peter Lang, Martin Hegner, and Christoph Gerber in Chapter 10. The cantilever arrays respond mechanically to changes in external parameters, like temperature or molecule adsorption, and thus, can be used to monitor binding events and chemical reactions occurring at the sensors' surfaces. In Chapter 12, James R. Heath reviews work on nanotube-based sensors, which enable the label-free detection of biomarkers for cancer and other diseases. It is pointed out here that the establishment of viable carbon nanotube or semiconductor nanowire devices for routine diagnostics will require a high-throughput fabrication method with an extraordinary high level of integration of nanoelectronics, microfluidics, chemistry, and biology.

Chapter 11, written by Harald Fuchs and colleagues, reports on uses for shear force-controlled scanning ion conductance microscopy. By using a local probe that is sensitive to ion conductance in an electrolyte solution, gentle scanning of delicate biological surfaces, allows one to obtain well resolved images of fine surface structures, such as of membrane proteins on living cells. In Chapter 13, Chad Mirkin and colleagues report on the preparation of arrays of nanoscale features of biomolecular compounds by using dip-pen nanolithography. Arrays with features on the nanometer length scale not only open up the opportunity to study many biological structures at the single particle level, but they also allow one to contemplate the creation of a combinatorial library, for instance, a complex protein array, underneath a single cell. This would open new possibilities for studying important fundamental biological processes, such as cell-surface recognition, adhesion, differentiation, growth, proliferation, and apoptosis.

Section III (Chapters 14–19) of this volume concerns the use of nanostructures in medicinal applications. The six chapters focus on three major topics: the development of nanoparticle-based drug delivery systems, the use of nanoparticles for imaging, and the design of scaffolds for tissue engineering. Chapter 14, written by Rudy Juliano, gives an introductory overview on biological barriers to nanocarrier-mediated delivery of therapeutic and imaging agents. This chapter also provides a brief assessment of the toxicology of nanomaterials, a subject which has currently initiated widespread discussion because it is anticipated that nano(bio)-

technology will be a key aspect of the future economy. With respect to the development of suitable carrier systems, Larken E. Euliss, Julie A. DuPont, and Joseph M. DeSimone in Chapter 15 summarize work on the development of biocompatible organic nanoparticles, in particular, by means of top-down fabrication techniques, so called lithographic imprinting, adapted from the electronics industry. This method enables the inexpensive fabrication of monodisperse particles of various size and shape from a large variety of matrix materials, which have great potential as functionalized carriers for applications in nanomedicine. An alternative class of particles is described in Chapter 16, where Thommey P. Thomas and colleagues report on poly(amidoamine) dendrimer-based multifunctional nanoparticles as a tumor targeting platform. The biocompatible dendrimer macromolecules act as carriers of molecules for delivery into tumor cells and can achieve increased drug effectiveness at significantly lower toxicity as compared to the free drug.

With respect to clinical imaging techniques, Young-wook Jun, Jae-Hyun Lee, and Jinwoo Cheon review current work on the development of magnetic nanoparticle-based contrast agents for molecular magnetic resonance imaging in Chapter 17. This research is aimed towards advances in cancer diagnosis because nanoparticle contrast agents promise *in vivo* diagnosis of early staged cancer with sub-millimeter dimension, and might help to unravel fundamental biological processes, such as *in vivo* pathways of cell evolution, cell differentiations, and cell-to-cell interactions. A different class of nanoparticles is described in Chapter 19 by Samuel A. Wickline and colleagues. They have developed nanoparticles comprised of perfluorocarbon materials which are biologically and metabolically inert, chemically stable, and non-toxic. These nanoparticles have been employed for molecular imaging with MRI and targeted drug delivery.

Chapter 18 of this section, written by Robert L. Langer and colleagues reviews methodologies for generating two- and three-dimensional scaffold architectures for tissue engineering. The authors analyze the use of micro- and nanoscale engineering techniques for controlling and studying cell-cell, cell-substrate and cell-soluble factor interactions as well as for fabricating organs with controlled architecture and resolution.

Section IV of this volume is devoted to one of the most innovative topics of Nanobiotechnology which concerns the fabrication of hybrid devices using organic and inorganic structures equipped with parts of Nature's biomolecular machinery. To facilitate an introduction to natural molecular nanomotors, Manfred Schliwa describes in Chapter 20 how these fascinating molecular machines are built from amino acids and how they convert chemical energy into mechanical motion. In Chapter 21, Carlo D. Montemagno and colleagues summarize current approaches to fabricate biologically inspired hybrid nanodevices. In particular, two lines of work are shown, protein-based mechanical devices and cellular power generation devices, which both have in common the theme of combining biological molecules with synthetic host structures.

Similar to the first volume, the purpose of *Nanobiotechnology II – More Concepts and Applications* is to provide both a broad survey of the field as well as instruction and inspiration to scientists at all levels from novices to those intimately engaged in this new and exciting field of research. To this end, the current state-of-the-art of the above described topics has been accumulated by international renowned experts in their fields. Each of the chapters consists of three sections, (i) an overview which gives a comprehensive but still condensed survey on the specific topic, (ii) a methods section which points the reader to the most important techniques relevant for the specific topic discussed, and (iii) an outlook discussing academic and commercial applications as well as experimental challenges to be solved.

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Chad A. Mirkin
Christof M. Niemeyer