Nanotechnologies for the Life Sciences

Edited by Challa Kumar

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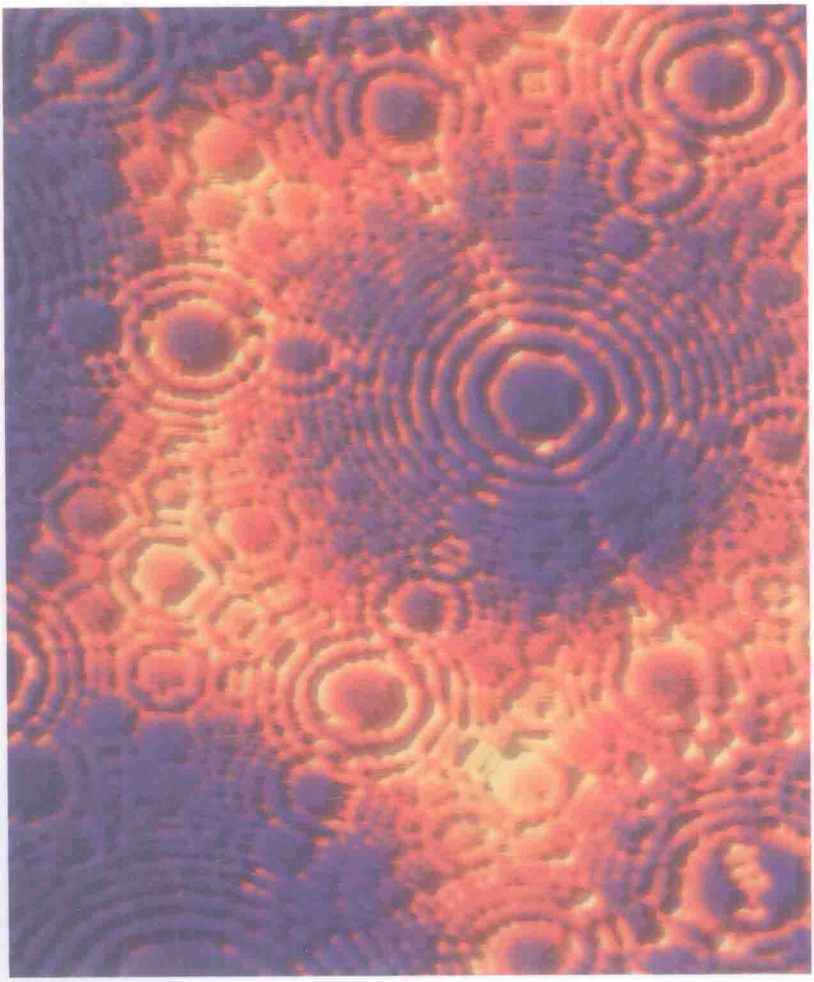
Nanosystem Characterization Tools in the Life Sciences



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Nanotechnologies for the Life Sciences
Volume 3

Nanosystem Characterization Tools in the Life Sciences

Edited by
Challa S. S. R. Kumar

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Preface

The third volume in this series, *Nanosystem Characterization Tools for the Life Sciences*, is being presented to you sooner than expected thanks to the dedication of all the contributing authors. In a very timely manner, they present here their in-depth reviews on several important characterization tools that are currently being utilized and are in the process of development and refinement for nanotechnological applications in the life sciences.

While the book is certainly not an exhaustive source for all the characterization tools, it is for sure first of its kind to provide, under one umbrella, several of the very important tools. My gratitude goes to all those who have been part of this project, most importantly the authors, my employer, family, friends and Wiley-VCH publishers. I do hope that the information provided will help the readers in their scientific pursuits. I do realize that there is always a scope for improvement and therefore, your comments and suggestions are very valuable.

Traditional fluorescence imaging tools have so far helped life scientists in unraveling several mysteries. However, the advent of quantum dots is poised to take fluorescence imaging to a different level altogether. In the first chapter, *Fluorescence Imaging In Biology using Nanoprobes*, author Daniele Gerion from Lawrence Livermore National Laboratory in California, USA, provides a unique perspective to how various nanoprobes are changing the limits of fluorescence imaging, and shares her views on what future holds in this exciting field.

The second chapter in the book is a journey into imaging of biological samples using scanning probe microscopy techniques (SPM). The authors, Anthony W. Coleman and colleagues from CNRS-UCBL, France, critically analyse the utility of SPM in imaging hitherto unseen biological systems, understanding their mechanical properties and how they are useful in developing sensor systems. The chapter is aptly entitled *Characterization of Nanoscale Systems in Biology using Scanning Probe Microscopy Techniques.*

Continuing on the similar theme of imaging techniques, Rhonda Dzakpasu and Daniel Axelrod from the University of Michigan at Ann Arbor, USA, provide an exceptional account of a novel imaging technique using optical microscopy based on dynamic light scattering in the tenth chapter—*Dynamic Light Scattering Microscopy.* It has an all-embracing account on the theory of DLSM followed by a description of the detection system that uses a slow scan CCD to record the rapid kHz range

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fluctuations of DLS, and finally followed by tests on a model system of small polystyrene beads in suspension and a living cell system of macrophages.

While the imaging techniques described in the first two chapters provide direct tools for understanding biological systems, the third chapter is an insight into use of an indirect tool, quartz crystal microbalance (QCM), which is a widely-used, popular and effective tool for evaluation of the assembly of biological structures. David E. Cliffel's group from Vanderbilt University in Nashville, USA, has done a remarkable job in capturing their experience in utilization of QCM techniques in life sciences. In this chapter, *Quartz Crystal Microbalance Characterization of Nanostructure Assemblies in Biosensing*, the authors cover important biological applications of QCM in addition to providing the principles and operational aspects.

Yet another indirect approach for understanding nanoscaled biologically important systems is the use of traditional spectroscopy tools. Nuclear Magnetic Resonance is playing a key role in the development and design of nanoscaled pharmaceutical carriers by providing comprehensive data on the structure and the function of these systems under a large variety of conditions. Christian Mayer from Gerhard Mercator University in Duisburg, Germany, provides an authoritative account of application of NMR tools for nanoscaled systems in the fourth chapter, entitled *NMR Characterization Techniques—Application to Nanoscaled Pharmaceutical Carriers*. The author's own words succinctly summarize the importance of this growing field: Unlike any other analytical technique, it combines a distinctly non-invasive character with the ability to analyze for a chemical composition as well as for local mobility of individual system components.

In the sixth chapter—*In Situ Characterization of Drug Nanoparticles by FTIR Spectroscopy*—Michael Türk and Ruth Signorell from the University of Göttingen, Germany, focus on the *in situ* characterization of nanoparticles by Fourier-transform infrared (FTIR) spectroscopy. *In situ* characterization tools such as these are a must for life scientists as they allow not only investigation, but also provide control of the properties of nanoparticles, especially drug nanoparticles, during their formation.

Electron Spin Resonance (ESR) or synonymously Electron Paramagnetic Resonance (EPR) can be regarded as a sister method for Nuclear Magnetic Resonance (NMR). This is yet another traditional spectroscopy tool that is being developed further to provide understanding of nanoscale drug delivery systems. The seventh chapter contributed by Karsten Mäder from Martin Luther University of Halle, Germany, discusses how ESR can contribute to shedding more light on nanoscaled drug delivery systems, providing examples that show how useful information can be extracted from the spectra and how this information can be used to characterize drug delivery systems. This chapter—*Characterization of Nanoscaled Drug Delivery Systems by Electron Spin Resonance*—is a must not only for practioners of ESR, but also for life scientists interested in nanoscale drug delivery systems.

Synchrotron radiation based spectroscopies have become an indispensable tool in many areas of biological sciences. Of these, soft x-ray absorption spectroscopy (XAS) and soft x-ray emission spectroscopy (XES) are gaining importance in the field of nanoscience. The eighth chapter, entitled *X-ray Absorption and Emission*

Spectroscopy in Nanoscience and Life Science, by Jinghua Guo from Lawrence Berkeley National Laboratory in California, USA, brings out how XAS and XES techniques are sensitive detection tools for nanostructured and molecular materials using a number of examples.

Each characterization tool provides unique information. However, a combination of several techniques is always required in order to obtain complete information about any nanoscaled biological systems. Two chapters, numbers five and nine, provide a broader perspective to the application of multiple characterization tools in nanosystem's characterization. The fifth chapter, *Characterization of Nanofeatures in Biopolymers using Small-angle X-ray Scattering, Electron Microscopy and Modeling*, was written by Angelika Krebs and co-workers from the European Molecular Biology Laboratory (EMBL) at Heidelberg, Germany. This chapter is an indication of how an appropriate combination of characterization tools will be used in future even though such an approach has not yet been well established.

The ninth chapter, *Some New Advances and Challenges in Biological and Biomedical Materials Characterization*, by F. Braet and co-workers from the Australia Key Centre for Microscopy and Microanalysis at Sydney University, Australia, describe recent advances as well as challenges in the microscopy of selected biological and biomedical materials using three very important tools: atom probe tomography, atomic force microscopy, and cryo-transmission electron microscopy.

In the final chapter of the book, *X-ray Characterization Tools for Nanosystems in Life Science*, Cheng K. Saw from Lawrence Livermore National Laboratory in California, USA, provides the basics of using X-ray diffraction techniques to obtain information on the structure and morphology of nanosystems in general.

I do hope that this book will be a useful source of information both for life scientists interested in nanoscale systems and for characterization specialists interested in applying their tools in biological systems.

October 2005, Baton Rouge *Challa S. S. R. Kumar*

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Contents

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Fluorescence Imaging in Biology using Nanoprobes

Daniele Gerion

1.1
Introduction and Outlook

1.1.1
A New Era in Cell Biology

Fluorescence is ubiquitous in biology. Indeed, any biology textbook contains a multitude of colorful images, most of which would not disfigure an art gallery [1]. For decades, biologists have mastered the use of fluorescently labeled molecules to stain cells in cultures or tissues. They developed the tools to target different compartments inside the cells, such as the nucleus and mitochondria, and subcompartment structures, such as chromosomes and the telomeres using light-emitting organic markers. These traditional approaches permitted the unraveling of a wealth of information on organs and tissues and, to a smaller scale, on the cell organization and its functioning. Images of cellular division captured by fluorescence microscopy are breathtaking, particularly the movement of the duplicated chromosomes along the spindle apparatus towards the two poles of the parent cell. Similar examples abound in the scientific literature and in fluorescent dye catalogs to the point that biology may convey a false sense of completeness. Indeed, an engineer or a physicist like myself may have the impression that everything interesting in biology has been already discovered and that only a few blanks remain to be filled.

Yet, in recent years, biology has witnessed an extraordinary revolution. Modern biology looks beyond responses to stimuli or the morphological description of structures. Modern biology does not satisfy itself with the successful sequencing of the human genome because a list of four repeating letters does not reveal a biological function. Modern biology is much more ambitious. It seeks to understand how biological and chemical processes work together to make cells and living organisms [2]. The journey towards this "Holy Grail" of biology depends on our ability to decipher interconnected cellular networks, mainly by observing molecular pathways of proteins and other metabolites in living organisms. The ultimate goal is to know where and when proteins and metabolites are expressed, how and at

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