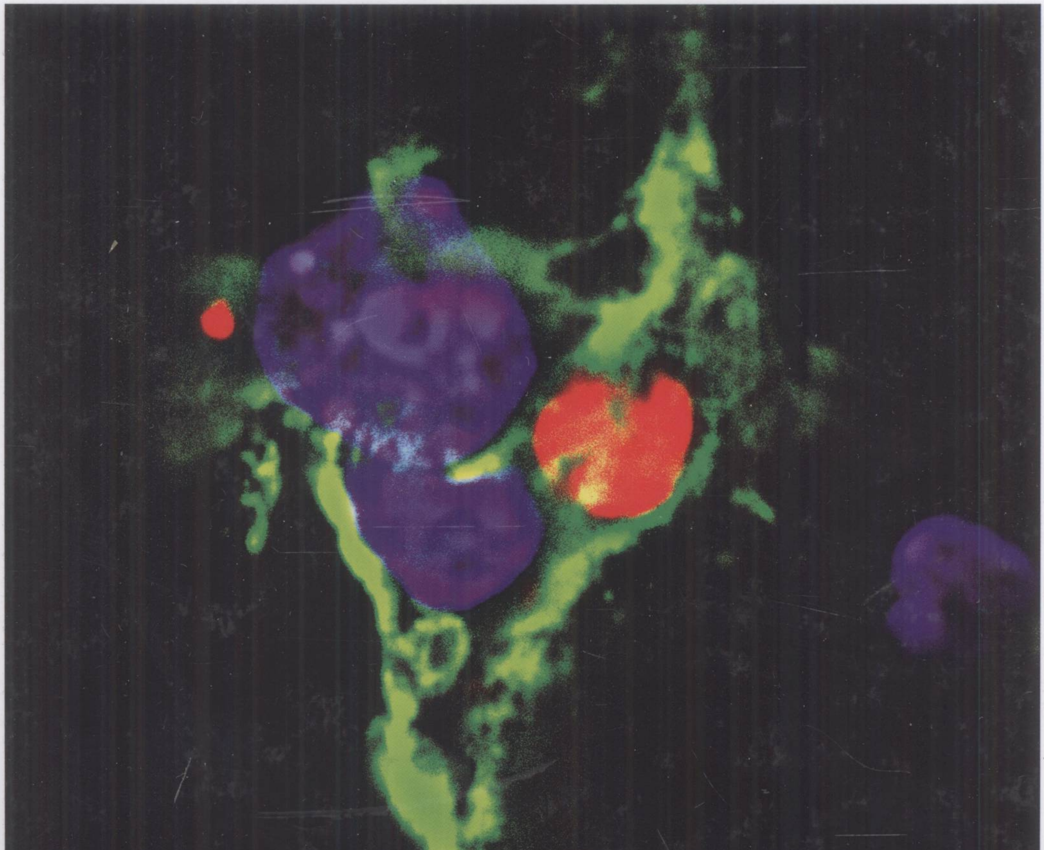
RSC Nanoscience & Nanotechnology

Edited by Pavel Broz

Polymer-Based Nanostructures

Medical Applications



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Preface

Nanotechnology is about small things: medicine usually deals with bigger things – with patients and their diseases. The ultimate goal of all medical sciences is the healing of diseases whenever possible, otherwise the abatement of suffering. The first step of a successful medical treatment is the correct diagnosis of the disease or disease condition, based on clinical knowledge and experience and on diagnostic tools that give insight into macroscopic, microscopic, and biochemical properties of the disease process. Nanomaterials can improve currently available diagnostic applications in medicine and polymer-based nanostructures, especially, have an enormous potential to revolutionize the way clinicians diagnose diseases correctly and efficiently.

The second step when treating patients is a powerful and specific therapy that is low in side effects, which can prolong the survival of the patient or lower the burden of the disease. Again, polymer-based nanostructures are very promising novel tools that might change the way certain diseases are being treated.

The purpose of this book, *Polymer-based Nanostructures: Medical Applications*, is to summarize the knowledge in this field which was gained in the last few years in many different research labs and to present successful applications of polymer-based supramolecular nanometer-sized structures in medicine, both in diagnostic and therapeutic applications for important diseases such as arteriosclerosis, cancer, infections, or autoimmune disorders.

In the first part of this edited book, renowned researchers provide a detailed insight into both chemical and biological/pharmacological basics that have to be managed for successful applications of these nanostructures in human beings. In the second part, invited authors review the main literature in both diagnostic and therapeutic applications with polymer-based nanostructures that have already reached clinical practice or will enter it in the next years. Furthermore, there is subdivision entitled *Polymer-based Nanostructures with*

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an Intelligent Functionality that includes two chapters dedicated to multi-functional, futuristic nanostructures that are based on polymers.

The book starts with the chapter entitled *Polymer Materials for Biomedical Applications*, written by Violeta Malinova and Wolfgang Meier from the University of Basel in Switzerland. This short chapter outlines the primary criteria that must be considered when selecting a polymer for biomedical applications. It gives insight into frequently used polymer formulations and establishes a common basis of knowledge of polymer chemistry for non-expert readers.

The second chapter, *Strategies for Transmembrane Passage of Polymer-based Nanostructures*, present the prerequisites and possibilities for oral delivery of polymer-based nanostructures. The author, Emmanuel Akala from the Howard University in Washington DC, gives an insight into the biological and pharmacological characteristics of natural epithelial barriers in the gastro-intestinal tract and how nanotechnology can be applied to circumvent natural obstacles and barriers for a selective delivery of nanostructures. Many fascinating concepts are being presented that might allow an oral application of polymer-based nanostructures in the future, making unpleasant intravenous or subcutaneous injections unnecessary.

Chapter 3 by Seyed Moghimi from the University of Copenhagen in Denmark, entitled *Nanoparticle Engineering for the Lymphatic System and Lymph Node Targeting*, explores the rationale of lymphatic delivery of polymer-based nanoparticles. The concept of the lymphatic system and lymph node targeting with nanoparticles following subcutaneous injection is being covered, furthermore the chapter highlights on the fate of interstitially injected particles and physicochemical and physiological factors that control their drainage rate and lymphatic distribution.

The fourth chapter, *Strategies for Intracellular Delivery of Polymer-based Nanostructures*, written by Jaspreet Vasir, Chiranjeevi Peetla, and Vinod Labhasetwar from the Cleveland Clinic in Cleveland, USA, covers a critical step of cell-targeted therapeutics. Their efficient delivery across the cell membrane is essential for their efficacy. In order to overcome hurdles such as poor stability in biological environment, insolubility, large molecular size, or interactions with cell membrane-associated efflux pumps, nanomaterials of different composition and properties are being investigated as a carrier system. However, very little is known about the interactions of nanomaterials with cell membrane and their intracellular trafficking pathways. A better understanding of the above aspects of nanoparticles could help in developing efficient nanomaterials for intracellular delivery of therapeutics. The chapter reviews the above aspects of nanomaterials and their implications in drug delivery.

In the fifth chapter, *Strategies for Triggered Release from Polymer-based Nanostructures*, various mechanisms of triggered substance release from polymer constructs are highlighted, an essential condition when trying to develop targeted therapeutics. Authors Violeta Malinova, Lucy Kind, Mariusz Grzelakowski and Wolfgang Meier from the University of Basel in Switzerland are renowned experts in polymer chemistry and have a profound knowledge in designing novel polymer materials. The chapter covers the most important triggering approaches that have been used to stimulate site-specific and/or time-dependent drug delivery from polymeric systems. Major emphasis is being placed on polymers delivering active compounds (e.g. drugs, proteins, genes) in response to certain external (chemical or physical) stimuli. The precise molecular design necessary to develop stimuli-responsive polymers and the basis behind the release mechanism are being commented, furthermore the type of stimulus (e.g. pH, temperature, light, ionic strength) used to provoke release and the main classes of responsive materials developed to date are being presented.

Polymer-based nanostructures have been receiving much attention as materials for diagnostic tools, therefore the next chapters have been dedicated to bring out the information present in the literature on different types of nanostructures in medical diagnosis. The sixth chapter of the book, entitled *Polymer Nanoparticles for Medical Imaging,* was written by Egidijus Uzgiris from the Rensselaer Polytechnic Institute in Troy, USA. It gives a profound insight into the design requirements of polymeric nanoparticles for magnetic resonance imaging, be it linear polymers with different backbones, polymer dendrimers or iron oxide nanoparticles with polymeric coating. The chapter also gives valuable information on future trends in the field, especially targeting agents for novel diagnostic applications.

The seventh chapter, *Polymeric Vesicles/Capsules for Diagnostic Applications in Medicine*, a contribution from Margaret Wheatley from the Drexel University in Philadelphia, USA, reviews a broad range of polymeric nanomaterials that were successfully used as contrast agents for techniques such as X-ray, ultrasound, magnetic resonance imaging, and radionuclide imaging.

The next three chapters concentrate entirely on therapeutic applications, especially drug delivery based on polymeric nanostructures. The eighth chapter, *Polymeric Micelles for Therapeutic Applications in Medicine*, is written by a well-known expert in this field, Vladimir Torchilin from the Northeastern University in Boston, USA. Micelles, self-assembling nanosized colloidal particles with a hydrophobic core and hydrophilic shell are currently successfully used as pharmaceutical carriers for water-insoluble drugs and demonstrate a series of attractive properties as drug carriers. Polymeric micelles possess high stability both *in vitro* and *in vivo* and good biocompatibility, and can solubilize a broad variety of poorly soluble pharmaceuticals. Amongst other applications, polymeric micelles can also be used as targeted drug delivery systems. The targeting can be achieved via the enhanced permeability and retention effect (into the areas with the compromised vasculature), by making micelles of stimuli-responsive amphiphilic block-copolymers, or by attaching specific targeting ligand molecules to the micelle surface. This chapter discusses some recent trends in using micelles as pharmaceutical carriers.

The ninth chapter, *Anti-Cancer Polymersomes*, a contribution from the laboratories of Dennis Discher from the University of Pennsylvania in Philadelphia, USA, focuses on polymer vesicles, also known as polymersomes. Especially their use as cancer therapeutics might reach wide-spread clinical practice in the near future; therefore this chapter concentrates on the design requirements and the science behind drug-loaded polymer vesicles. Polymersomes are polymer-based vesicular shells that form upon hydration of amphiphilic block copolymers. These high molecular weight amphiphiles impart physicochemical properties that allow polymersomes to stably encapsulate or integrate a broad range of active molecules, including both hydrophilic and hydrophobic anticancer drugs. The robustness of polymersomes together with recently described mechanisms for controlled release and escape from endolysosomes suggests that polymersomes might be usefully viewed as having structure/property/function relationships somewhere between lipid vesicles and viral capsids. Here we summarize the assembly, development, and ongoing testing of anti-cancer polymersomes.

The tenth chapter, entitled *Polymer-based Nanoreactors for Medical Applications* and authored by An Ranquin, Caroline De Vocht and Patrick Van Gelder from the Vrije Universiteit Brussel in Belgium, presents concepts that give an intelligent functionality to polymer-based nanostructures. By introducing biotechnological methods into polymer chemistry, it was possible to invent a novel type of polymer vesicles bearing bacterial pore proteins with a defined functionality. These kind of polymeric nanoreactors have been used for specific, enzymatic conversion of pro-drugs to active compounds or for the triggered enzymatic creation of a diagnostic signal within a targeted delivery vehicle. This chapter explains the design requirements of nanoreactors and presents pioneering work that was done in the last years.

Finally, in the last chapter, *Nanoparticles for Cancer Diagnosis and Therapy*, written by Yong-Eun Lee Koo, Daniel A. Orringer and Raoul Kopelman from the University of Michigan in Ann Arbor, USA, emphasis is given to a multifunctional platform based on a polymeric nanoparticle. Nanoparticle-based therapeutic or diagnostic agents for cancer have emerged as candidates that have advantages over molecular drugs or contrast agents. Moreover, multitasking, encompassing tumor-specific detection, treatment, and follow-up monitoring, is possible by single nanoparticle-based agents due to their designable multifunctionality. This chapter describes current problems with cancer diagnosis and therapy and specifically the advantages of nanoparticle-based methods as well as various nanoparticle systems under investigation for the detection and therapy of cancer.

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Contents

1. BASICS

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4. POLYMER-BASED NANOSTRUCTURES WITH AN INTELLIGENT FUNCTIONALITY

1.
BASICS

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