Preface

This book provides current information on the development of microfluidics, nanotechnologies, and physical science techniques for the separation, detection, manipulation, and analysis of biomolecules, and should be useful to a wide audience, including molecular and cell biologists, biochemists, microbiologists, geneticists, and medical researchers. Chapters cover a variety of topics and techniques ranging from lab-on-chip technologies and microfluidics-coupled mass spectrometry for separation and detection of biomolecules, including proteins and nucleic acids, to manipulating and probing biomolecules with nanopores, nanochannels, optical, and other physical means, with the possibility of isolation and analysis of individual biomolecules from a single cell, and to structural and functional analysis of biomolecules with liquid nuclear magnetic resonance, X-ray and neutron scattering techniques. The book presents emerging nanotechnologies including quantum dots and molecular fluorescence for imaging and tracking of biomolecules and nanotechnologies for biomolecular delivery, gene therapy, and gene-expression control. Each chapter describes a specific technology with its fundamental mechanism and practical applications for a particular subject area, so that a competent scientist who is unfamiliar with the technology can understand its capabilities and basic procedures. In many cases, a reader should be able to carry out the techniques successfully at the first attempt by simply following the detailed practical procedures (protocols) and/or information (including useful notes) provided in the book. For sophisticated technologies such as neutron scattering, the book describes their physical concepts and discusses the new opportunities that these new technologies may bring for both basic and applied research in the fields of molecular biology and biotechnology. This book consists of 41 chapters that are organized into four parts. The chapters were contributed by nearly 100 authors worldwide, who are among the world's prominent scientists in their fields.

The first half of the volume covers microfluidic and physical methods of bioanalysis. It consists of Part I on applications of microfluidics and nanopores in separation, manipulation, detection, and analysis of biomolecules, and Part II on technologies of physical science in detection and analysis of biomolecules. It contains valuable protocols on microfluidics and physical science-related technologies that may benefit the field of molecular biology. Chapter topics are briefly described below.

Part I consists of Chaps. 1–10: Chap. 1 describes a commercially available nanoflow analytical technology conducted on a microfabricated chip that allows for highly efficient HPLC separation and superior sensitivity for MS detection of complex proteomic mixtures; Chaps. 2–4 describe fabrication of nanofluidic channels for manipulation of DNA molecules, a single-molecule barcoding system using nanoslits for DNA analysis, and microfluidic devices with photodefinable pseudovalves for protein separation, respectively; Chap. 5 introduces specific antibody detection by using a microbead-based assay with quantum dot (QD) fluorescence on a microfluidic chip; Chap. 6 describes a biomolecular sample-focusing method based on a device design incorporating arrays of addressable on-chip microfabricated electrodes that can locally increase the concentration of DNA in solution by electrophoretically sweeping it along the length of a microchannel; Chap. 7 describes a solid-state nanopore technique for detecting individual biopolymers, and Chap. 8 reports a method of inserting and manipulating DNA in a nanopore with optical tweezers; Chaps. 9 and 10 describe techniques of forming an α-hemolysin nanopore for single-molecule analysis and for nanopore force spectroscopy of DNA duplexes.

Part II consists of Chaps. 11–22: Chap. 11 describes an electrochemical method for quantitative chemical analysis of neurotransmitter release from single cells; Chaps. 12–14 introduce techniques for trapping and detection of single molecules in water, ZnO nanorods as an intracellular sensor for pH measurements, and analysis of biomolecules using surface plasmons; Chap. 15 reports use of residual dipolar couplings in structural analysis of protein–ligand complexes by solution NMR spectroscopy; Chaps. 16 and 17 report Raman-assisted X-ray crystallography for the analysis of biomolecules and methods and software for diffuse X-ray scattering from protein crystals, and Chaps. 18–20 describe deuterium labeling for neutron structure–function–dynamics analysis, the basics and instrumentation of small-angle neutron scattering for molecular biology, and small-angle scattering and neutron contrast variation for studying biomolecular complexes, respectively; Chap. 21 describes the application of tandem mass spectrometry to identification of protein biomarkers of disease, and Chap. 22 describes the use of hyphenated MS techniques for comprehensive metabolome analysis.

The second half of the volume covers nanotechnologies for biosystems, and consists of Part III on applications of quantum dots and molecular fluorescence in detection, tracking, and imaging of biomolecules, and Part IV on nanotechnologies for biomolecular delivery, gene therapy, and expression control. It contains valuable information on nanoscience-empowered molecular biotechnologies.

Part III consists of Chaps. 23–32: Chaps. 23–25 describe multicolor detection of combed DNA molecules using quantum dots, quantum dot molecular beacons for DNA detection, and a gel electrophoretic blotting technique for identifying quantum dot–protein/protein–protein interactions; Chaps. 26 and 27 present techniques for in vivo imaging of quantum dots and efficient biolabels in cancer diagnostics, respectively; Chap. 28 describes monitoring and affinity purification of proteins using dual tags with tetracysteine motifs, and Chap. 29 reports use of genomic DNA as a reference in DNA microarray analyses; Chap. 30 describes single-molecule imaging of fluorescent proteins expressed in living cells; Chap. 31 describes micropositron emission tomography (PET), single-photon emission computed tomography (SPECT), and near-infrared (NIR) fluorescence imaging of biomolecules in vivo, which could lead to a number of exciting possibilities for biomedical applications, including early detection, treatment monitoring, and drug development; Chap. 32 reports a revolutionary photo-based imaging technology: the ultrahigh resolution imaging of biomolecules by fluorescence photoactivation localization microscopy (FPALM) that can now image molecular distributions in fixed and living cells with measured resolution better than 30 nm, which likely represents a breakthrough technology that has now shattered the classic limit of light microscopy resolution associated with the wavelength-dependent light diffraction barrier, thought to be unbreakable for more than 100 years.

In Part IV, Chaps. 33–41 describe nanotechnologies with potential biomedical applications. Specifically, Chap. 33 describes real-time imaging of gene delivery and expression with DNA nanoparticle technologies and Chap. 34 reports nanoparticle-mediated gene delivery. Chapters 35 and 36 describe magnetic nanoparticles for local drug delivery using magnetic implants and functionalized magnetic nanoparticles as an in vivo delivery system, and Chap. 37 reports formulation/preparation of functionalized nanoparticles for in vivo targeted drug delivery; Chap. 38 reports detection of mRNA in single living cells using atomic force microscopy nanoprobes; Chap. 39 describes a gene transfer technique through reverse transfection using gold nanoparticles; Chap. 40 presents custom-designed molecular scissors for site-specific manipulation of the plant and mammalian genomes, and Chap. 41 describes a technique for determining DNA sequence specificity of natural and artificial transcription factors by cognate site identifier analysis, both of which could lead to modern applications in molecular biology and biomedicine.

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Springer

http://www.springer.com/978-1-934115-40-4

Micro and Nano Technologies in Bioanalysis
Methods and Protocols
Lee, J.W.; Foote, R.S. (Eds.)
2009, XX, 668 p. 143 illus., 36 illus. in color., Hardcover
ISBN: 978-1-934115-40-4
A product of Humana Press