Preface

This volume is dedicated to a new and rapidly expanding field of nanopore technology for single-molecule sensing, detection, and characterization. The main aim in this area of science is to develop a nanopore-based technology that can be used for the manipulation and analysis of biological molecules. A major application of nanopores exists in sensing, leading toward the promise of ultrafast sequencing of DNA molecules with the ultimate goal of building a nanoscale device that will make rapid and cheap DNA sequencing a reality. In such a device, an external electrical field would drive molecules electrophoretically through the nanoscale pore in a membrane that acts as a molecular sensor identifying single molecules passing through it. This book is primarily oriented for biophysicists, biochemists, molecular biologists, and bioengineers who are interested in modern biomolecule characterization technologies.

In living cells, tiny holes in cellular membranes—nanometer diameter pores—are used for recognition and transport of ions and molecules between compartments within the cell, as well as between the extracellular environment and the cell itself. In the recent years, there has been great interest in utilizing the power of artificial nanopores for single-molecule manipulation and characterization, the two practical applications inspired by Nature. While proteinacious pores offer biological compatibility with studied molecules, nanopores in artificial materials are more stable and, in some instances, allow for greater control over the nanopore environment.

The book is divided into four parts. In Part I, single-molecule characterization techniques utilizing biological pores, such as a bacterial ion channel alpha-hemolysin (αHL) pores, are presented. Alpha-hemolysin was the first pore used for DNA detection and characterization in the pioneering work of Kasianowicz, Brandin, Branton, and Deamer [1]. Robustness of this protein pore under varying physiological conditions combined with the dimensions comparable with the effective diameter of the DNA molecule made it a perfect candidate for the DNA sensing application. This pore along with the Mspa nuclear pore still remains the best candidate for fast DNA sequencing in the nearest future. Chapter 1 describes some of the methods and approaches used to interrogate the interactions between an αHL pore and different types of analytes. Chapter 2 presents a detailed protocol for the preparation of engineered αHL pores that can used for the detection, characterization, and analysis of various polypeptides. Chapter 3 discusses a procedure for the immobilization of DNA in the αHL protein nanopore. This method enables for low-noise, high-precision measurements of the ionic current blockages which could be associated with differences in the sequence and structure of the DNA. In Chap. 4, αHL pore is utilized to study DNA unzipping and protein unfolding.

In Part II, a variety of methods for biomolecule characterization with nanoporous artificial membranes are described. Different solid-state materials are used for making nanoporous membranes, with silicon nitrate and silicon dioxide being the most popular. In Chap. 5, ion beam sculpted silicon nitride nanopores are applied for DNA characterization. This work in particular discusses how to determine the quality of nanopores necessary

for DNA detection. Chapter 6 introduces a novel method for DNA sequencing using induced photon emission—optical detection of molecular beacons which are stripped off the biomolecule during translocation through a silicon nitride nanopore thus revealing DNA sequence. Chapter 7 describes an experimental technique for single biopolymer manipulation in a single nanopore involving an "optical tweezer" for application of mechanical force to the biomolecule. In Chap. 8, nanometer diameter glass capillaries are used to analyze single DNA molecules.

Part III is devoted to the computational studies of the biomolecule confined within the nanopore environment. Chapter 9 describes a method of DNA molecule characterization by transverse electrical current (current flows perpendicular to the direction of the polymer translocation). In Chap. 10, molecular dynamics techniques for atomic resolution modeling of DNA translocating through biological nanopores are developed and optimized. Chapter 11 introduces a new method for multiscale simulation of a semiconductor nanopore device with Brownian dynamics modeling of a chain polymer such as a DNA molecule.

Part IV presents techniques that use novel materials in conjunction with nanopore sensing. In Chap. 12, a nanopore device based on a graphene membrane of 1–5 nm thickness is realized and used for biomolecular characterization. Graphene is a material which is made of a single atomic layer of carbon atoms arranged in a hexagonal lattice. Recently, this novel material has captured a few headlines due to its remarkable properties that led to the 2010 Nobel Prize in Physics. Chapter 13 is devoted to characterization of single-walled carbon nanotubes with solid-state nanopores. In addition, translocation of DNA-wrapped nanotubes is also discussed. Finally, Chap. 14 describes procedures for integrating electrodes into the nanopore membrane which can be used for modulation of a nanopore's ionic conductance as well as charged biomolecule translocation.

To conclude, the nanopore-based single-molecule characterization techniques (described in this book and others) are emerging to become the next generation of technologies for fast and cheap DNA sequencing with practically no limitations on the read lengths. The field is rapidly evolving, and new ideas and novel materials are constantly being generated and tried out. The collection of methods described in this volume provides a good representation of the present-day available techniques for biomolecule characterization with nanoporous membranes.

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Reference

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