Microfluidic Methods for Molecular Biology

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Editors

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Preface

From the optical instruments that first provided a window into the microscopic world, to molecular analysis tools that have helped clarify the genetic underpinnings of life, the most significant advancements in the biological sciences over the past century have largely been driven by the availability of powerful new quantitative tools. A more recent theme in biotechnology has been the miniaturization of analytical tools, enabled in large part by adapting and developing the methods of the microelectronics industry. Microfluidics as a field has experienced a period of rapid development and evolution since the 1980s. Most of the early microfluidics work focused on miniaturization of tools used in analytical chemistry (e.g., chromatography and electrophoresis). Microfluidics provided unparalleled flexibility for miniaturization, integration, and automation. This permitted the creation of devices that were substantially more sophisticated than tools used in conventional analytical chemistry, and at a substantially lower cost of production and operation. Seminal early efforts of the field led to major innovations in both material science (e.g., the wide use of polydimethylsiloxane) and technology (e.g., two-layered pneumatic valves). These important developments greatly expanded the applications of microfluidics and have underpinned a more recent renaissance in microfluidics for biological applications.

With the explosion of genomics in the 1980s (and later of additional "omics" fields), molecular biology has always been an important area of application for miniaturized devices, given these devices' unique access to the size scales relevant to the function of cells. Protein/nucleic acid separation and PCR-based analysis are widely practiced on microfluidic devices. Single-cell analysis has been an intensively explored direction in recent years, due to the unique size advantage associated with microfluidics for single-cell manipulation. With the decreasing cost of next-generation sequencing, recent years have witnessed substantial efforts directed towards genome-wide studies (as opposed to investigations focused on specific loci).

In parallel to new opportunities in basic science, there has been an increasing demand for well-established and robust microfluidic technologies that may have a

direct impact on clinical practice and therapies. Personalized Medicine (PM), more recently re-branded as Precision Medicine, provides just such a unique opportunity. PM is based on the premise that every patient is unique at the tissue, cellular, and molecular level. Thus conducting molecular biology tests on patient samples is essential for providing clinicians with genomics, transcriptomics, epigenomics, and proteomics information that will ultimately improve their ability to optimize decision making for individual patients. Microfluidics offers the ideal platforms for handling and analyzing low quantities of cell/molecular samples to enable this exciting personalized approach; however there remains much work to be done before this paradigm is routine practice.

This book volume highlights recent progress on the topic of microfluidics for molecular biology studies. We cover various aspects of current microfluidics research in this growing field, which now spans the disciplines of biology, physics, chemistry, forensics, engineering, earth and atmospheric sciences, and beyond. Chapters are presented on various types of molecular analysis (genetic, epigenetic, proteomic, and next-generation sequencing), use of model organisms and patient materials, analysis at bulk and single-cell levels, techniques on cell culture and isolation, and a variety of different platforms at the technological cutting edge of these respective fields (flow, droplet, and paper-based microfluidics). We are hopeful that new microfluidic tools will continue to enable new insights into basic science as well as technology and biomedicine. To analyze molecular populations at the resolution of single cells or even single molecules will undoubtedly provide new ways of understanding complex biological processes, for example the dynamics of the adaptive immune system, or the role of tumor heterogeneity in cancer. High-resolution tools translated to the clinic could enable entirely new ways to treat a patient's own disease, as opposed to treating a hypothetical average patient as is the current pharmaceutical paradigm. We hope to provide a succinct but comprehensive picture of the state of the art for microfluidic molecular assays, and we look forward to the advancements yet to come in this exciting and rapidly progressing field.

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