

Preface

The sequencing of the first genome in 1977 by Sanger and colleagues opened the way to a whole new field of biology: genomics, *i.e.* the study of genes and their function. This new field has boomed since then with the development of high-throughput techniques, such as DNA microarrays, which aim to increase information while driving costs and time per analysis down. In less than 20 years, tremendous progress has been made: whereas the first microarrays, spotted on nylon membranes, allowed profiling of a few tens of genes at the same time, current microarrays allow the detection of a whole transcriptome with more than 2 million probes per array. In the same way, the cost of sequencing the human genome dropped in less than 10 years from over hundreds of millions to a few thousands of dollars. In terms of resolution, current techniques often require a few nanograms of starting material; that is, a few thousands cells.

The cell constitutes the basic unit of all known living organisms. In this context and given the high cellular heterogeneity of some tissues such as the brain, it is quite striking that despite all the technological advances of these last decades, high-throughput data at the single cell level has been reported only in a handful of genomic studies. Indeed, single cell assays remain extremely difficult to carry out and prior amplification of the genetic content is required. Because standard laboratory techniques are not adapted to single cell manipulation, single cell transcriptome and genome analysis currently imply a more than a million-fold dilution of the cell content in microliter volumes. This dilution may impact the assay's sensitivity as it increases the risk of non-specific reactions and/or contamination and put the sensitivity and reliability of single cell analysis at risk.

To understand genomics at the basic and fundamental level of the cell, micro- and nano-tools could be appropriate. Microfluidics lab-on-a-chip seems particularly promising as they allow reactions to be performed at the scale of the

RSC Nanoscience & Nanotechnology No. 15

Unravelling Single Cell Genomics: Micro and Nanotools

Edited by Nathalie Bontoux, Luce Dauphinot and Marie-Claude Potier

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Published by the Royal Society of Chemistry, www.rsc.org

cell, thus at higher concentrations, and the integration of multiple reactions on a single microchip could reduce the risks of contamination and the consumption of reagents.

This book was developed to help scientists understand the latest developments in microfluidics for genomics. After an introduction to molecular and cell biology (Chapters 1 to 3), the need for single cell analysis (Chapters 4 to 6) and the latest developments in this field (Chapters 7 to 10) are reviewed. In the subsequent chapters, microfluidic devices are introduced (Chapter 11) and their application to genomics and proteomics is discussed (Chapters 12 to 15). The development of a microfluidic device for single cell transcriptome analysis is detailed to illustrate key steps, pitfalls, and advantages of such lab-on-a-chips (Chapter 16). The last chapters cover droplet microfluidics (Chapter 17) and discuss detection techniques (Chapter 18) as these hold great promise for easier cell manipulation and increased sensitivity.

In an effort to provide a comprehensive overview, these chapters have been contributed to by experienced scientists with various backgrounds in biology, physics, and chemistry, all working in reference laboratories in Europe. We would like to acknowledge their contribution and warmly thank them.