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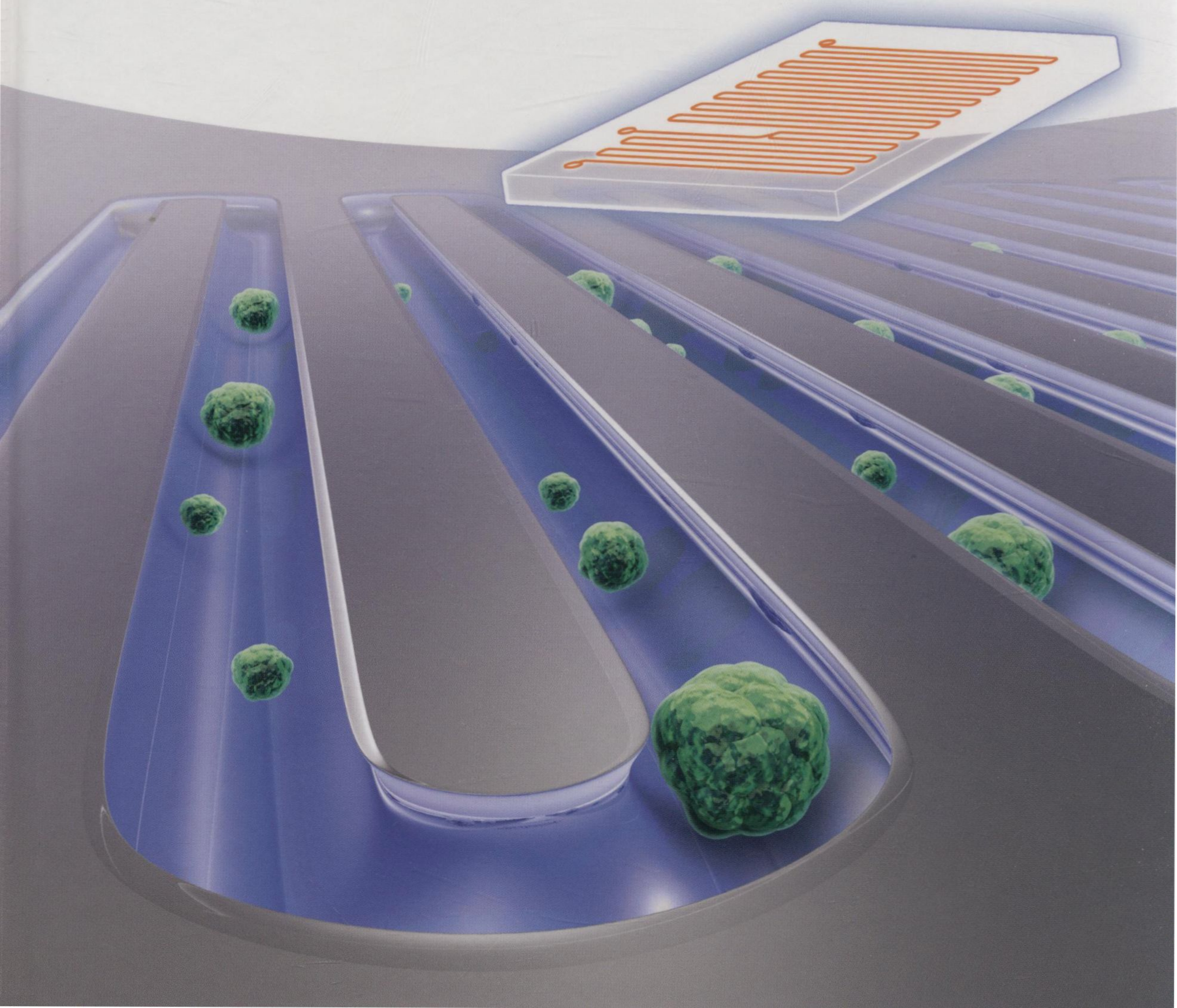
Edited by Emmanuel Delamarche
and Govind V. Kaigala

Open-Space Microfluidics

Concepts, Implementations, Applications



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Summarizing the latest trends and the current state of this research field, this up-to-date book discusses in detail techniques to perform localized alterations on surfaces with great flexibility, including microfluidic probes, multifunctional nanopipettes and various surface patterning techniques, such as dip pen nanolithography. These techniques are also put in perspective in terms of applications and how they can be transformative of numerous (bio)chemical processes involving surfaces.
The editors are from IBM Research – Zurich, the pioneers and pacesetters in this new and rapidly expanding area.

__Emmanuel Delamarche__ studied chemistry in Toulouse, France, and joined IBM Research in Zurich, Switzerland, in 1992 for his PhD in biochemistry with an academic affiliation to the University of Zurich. He then worked on surface patterning techniques involving scanning probe methods, self-assembled monolayers, soft lithography, and microfluidics.
Currently, he leads a research group at IBM Research on "precision diagnostics" with the goal of solving medical problems using microfluidics, micro- and nanotechnology and collaborations with biological and medical experts. Dr. Delamarche has authored more than 120 scientific publications and has received numerous awards, including the Werner Prize from the Swiss Chemical Society in 2006.

__Govind Kaigala__ obtained his PhD from the University of Alberta, Canada, in 2008. After a postdoctoral fellowship at Stanford University, USA, he moved to IBM Research in Zurich, Switzerland, in 2010. His research interests include micro/nano-biosystems and miniaturized assays for microchip-based chemical and biomolecular analysis. He is currently leading activities on liquid-based non-contact scanning technologies – microfluidic probe – and is championing concepts on "microfluidics in the open space" and "tissue microprocessing". These research activities are driven by specific needs in the fields of pathology and personalized medicine. Dr. Kaigala has authored more than 45 scientific publications and received several awards, including IBM Research Division Accomplishments Awards on micro-immunohistochemistry (2014) and high-efficiency biopatterning (2017), and the 2014 Horizon Alumni Award from the University of Alberta.

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The Editors

Dr. Emmanuel Delamarche
IBM Research – Zurich
Säumerstrasse 4
8803 Rüschlikon
Switzerland

Dr. Govind V. Kaigala
IBM Research – Zurich
Säumerstrasse 4
8803 Rüschlikon
Switzerland

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Open-Space Microfluidics

Foreword

Microfluidics is the engineering discipline that deals with devices and phenomena related to minute amounts of fluids – typically with dimensions on the order of less than a millimeter and volumes of less than a milliliter. Nature, as always, did it first: surface tension coalesces water into rain droplets and capillary forces pump fluids through small plant vessels since the dawn of time. Manipulating such small quantities is not easy, and engineers have learned to build very small containers, valves, and pumps to handle fluids at a submillimeter scale. The problem is, once the liquids are inside the channels, they are not very accessible. For example, Beebe *et al.* (Science, 2001) demonstrated that liquid flows inside microchannels could be confined by two physical walls (instead of four, as usual) – leaving "air walls" on the side for gas exchange. However, most biochemical reactions occur in the fluid phase. Starting in 2005, surely inspired by the plethora of legendary, Nobel Prize-winning scanning probes developed by IBM Research (such as the scanning tunneling microscope and the atomic force microscope), the authors at IBM Zürich developed a clever scanning microfluidic probe that allowed for exchanges of fluids on "open" (i.e., pipette-accessible) surfaces and continue to create a range of such probes for use with biological substrates. The editors of this book are thus ideally placed on a privileged vantage point to compile work on open space microfluidics and have been inclusive of numerous scanning liquid localization methods.

21 May 2017

Albert Folch
Professor of Bioengineering
University of Washington
Seattle

Preface

Microfluidics is an extremely active research field, now having many subdisciplines and involving diverse research communities, such as physicists, microtechnologists, electrical engineers, chemists, biologists, and medical researchers. In 2016, nearly 5000 articles on the topic of microfluidics were published, bringing the total number of papers on this area close to 50,000. However, the field of microfluidics did not just expand but also matured in terms of applications. The complexity of samples and applications expanded from chemical analysis and miniaturized biological assays to studying living cells, bacteria, tissues, and even tumorlike cellular ensembles.

The goal of this book is to consolidate the views and latest developments on an emerging topic of open space microfluidics that enables chemical processes on or near surfaces. The vast majority of microfluidic devices currently use networks of sealed microchannels (with four walls) and chambers that are linked to various inputs/outputs to provide a "chip-to-world" interface. In such devices, samples need to be either passed through, for example, a biological sample potentially containing circulating tumor cells or seeded in the device before sealing, for example, by depositing adherent cells in microchambers. Open space microfluidics provide new opportunities for handling, analyzing, and interacting with biological samples and also give a lot of freedom to end users for new class of experiments by removing the need for full containment of chemicals and liquids. This means reducing the number of walls in a microchannel that function to confine a liquid. This is done by creating well-defined chemical environments, typically around a specific area of a surface, using specific strategies for confining liquids. Certain open space embodiments enable chemical reactions to be performed on immersed surfaces while completely eliminating gas–liquid interfaces. Alternatively, electrical forces can be used to direct charged species where desired on a surface.

Concepts for open space microfluidics and localized chemistry are covered in 18 chapters, contributed by experts in their fields. The book is divided into two parts. The first 11 chapters focus on the theory and implementation of a concept called hydrodynamic flow confinement (HFC). Specifically, two chapters show how to create HFC using various platforms and microfluidic devices and how to nest liquids inside each other over a surface. In these chapters, numerous examples of patterning surfaces with biomolecules are provided. Then, three chapters show how to model HFC and design probes for confining liquids using two or more microapertures. These chapters provide insight into the role of flow rates and the probe–surface distance on the envelope of liquid that is confined on the surface as well as the shear stress of objects on surfaces. Then the "microfluidic quadrupole" is described, where four microapertures are elegantly used for creating concentration gradients over live cells. Analyzing and probing more complex biological interfaces such as tissue sections, adherent cells, and organotypic tissue slices using microfluidic probes is then detailed in the next three chapters. These chapters provide a clear account of how a scanning, noncontact microfluidic technology is able to extract valuable information from fragile samples. Next two chapters follow on implementing HFC using a pen-like form factor. In this case, at least three side-by-side channels localize liquids on a surface with a high degree of symmetry. This technique can be applied to numerous single-cell studies where even additional stimulus (e.g., heat, current, etc.) can be applied to a cell. An obvious strength of HFC for studying cells is the possibility to avoid averaging signals and samples from populations of cells but rather probe single cells directly for proteomic analysis.

The second part of the book on "localized chemistry" opens up options for probing immersed surfaces without the requirement of pairing coplanar injection and aspiration channels. This part starts with a striking example in which a two-phase system localizes a liquid inside another one without solid walls. Probes with extremely well-defined channels, having critical dimensions below a few micrometers down to 100 nm, are then described in the next three chapters, where precision in fabrication, positioning, and sampling liquids are the key for local delivery of chemicals to surfaces and cells and for "pick-and-place" of single living cells. These approaches are compatible with analytical techniques ranging from mass spectrometry and optical microscopy to atomic force microscopy (AFM). Using AFM cantilevers having microchannels enables additive lithographic processes and shows that localized chemistry is not constrained to interrogating and interacting with biological interfaces. Soft probes that include microelectrodes are then detailed in two chapters in relation to an impressive number of applications, which range from mapping surfaces at high speed and over large areas, localizing redox reactions for surface modification or analysis, to cell analysis and staining. This part of the book ends with a demonstration of a probe that can be placed in transient contact with a surface for bringing trains of droplets for "interrogating" surfaces with high spatial and temporal resolution.

This book brings to focus a powerful set of methods for local chemistry and analysis on surfaces. And it is an excellent starting point for numerous research communities because all methods presented here can be enhanced and combined with technologies involving optics, electrochemistry, and analytical instruments, for example. In particular, students may very likely benefit from this book by seeing examples of interesting research problems, technologies, and applications, which may inspire them with their own projects. Furthermore, numerous functional elements and microelectromechanical systems (MEMS) can be integrated into probes for open space microfluidics. For this particular reason, we invited Prof. Albert Folch, who has spent a tremendous amount of time on developing bioMEMS and has written a comprehensive textbook on this topic, to provide his views on open space microfluidics in the form of a foreword. Finally, the potential range of applications for the technologies covered here is endless, given the importance of surfaces in technology and life science disciplines, and we hope that this book will inspire researchers and technologists who are interested in moving beyond "classical," closed microfluidics.

10 October 2017
Rueshlikon, Switzerland

Emmanuel Delamarche
Govind V. Kaigala

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