Preface

Ever since the beginning of the research in the lab on chip (LOC) field, people have been searching for the ''killer app''.[1] Unfortunately, unlike a field such as microelectronics, where Moore's law for memories and processors has driven the development or, rather, set the agenda, over several decades, in the LOC area no such big application has been identified so far. Rather a very diversified field of applications has emerged over time, with areas such as LOC for analytical chemistry,[2] drug development,[3] cell biology,[4] DNA sequencing and analysis,[5] chemical microreactors,[6] and medical applications.[7] Of all these, probably still the highest expectations are found in the latter area. This area is still emerging as indicated by the numerous scientific journals that publish articles relevant to this field, such as *Lab on a Chip*, *Analytical Chemistry*, *Microfluidics and Nanofluidics*, *Biomedical Microdevices*, *Biomicrofluidics* and *Integrative Biology*. Every week a lot of exiting new research is published, aiming to be applied for innovative medical devices, treatments, or diagnostics. While it is impossible to show all work performed in this field, with this volume we try to give an overview and perspective of this research field. Therefore we give an overview of the state-of-the-art given by a collection of world-wide top-level researchers, with contribution in three different, recently emerged subareas of this field: tissue and organs on chip, microfluidic tools for medicine, and point of care diagnostics.

For engineering microtissues on chip, 3D constructs are required, which serve as scaffolds for the different components of the tissue. Fibers are promising structures to make these constructs, which can be adapted in ways suited for the application. In Chapter 1 different types of fiber fabrication using microtechnology are discussed. Besides tissue engineering on chip, organs on chip is another emerging field in microfluidics. An example of this is the kidney on chip, which is discussed in Chapter 2. This chapter

RSC Nanoscience & Nanotechnology No. 36
Microfluidics for Medical Applications
Edited by Albert van den Berg and Loes Segerink

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

was written by Kahp-Yang Suh, who totally unexpectedly and to our deep sadness passed away after finishing the chapter. As a tribute we decided to retain his chapter, to give the reader a nice insight into the brilliant work he did in the organs on a chip field. An overview of the current state-of-the-art is given with respect to this organ. Not only can organs be modelled with microfluidic systems, also the functioning of parts of the body can be modeled using such a system. An example is the functioning of the blood-brain barrier. Although these microfluidic systems are not yet as good as the conventional models, first steps are being made in the development of a reliable model. In Chapter 3 the current status of these microfluidics models is described as well as which parts need to be improved to end up with a model that will be better than the conventional one. An example of how these models can be used to understand a brain-related disease such as Alzheimer's disease is given in Chapter 4. In this chapter some fundamental questions regarding this disease are raised, which can be possibly answered with the help of microfluidics.

Besides the use of microfluidics to model the functioning of organs and as a tool to create constructs for tissue engineering, it can also be used in more general terms for medicine, which is the subject of Chapters 5 to 7. An example of this is the generation of bubbles for both contrast enhancement in ultrasound as well as drugs delivery at a specific spot. For the production of these monodisperse bubbles, also microfluidics can be used, which will be discussed in Chapter 5. The use of other spherical particles, the magnetic particles, is described in Chapter 6. These particles can be actuated with magnets and used for several assay steps in diagnostic devices. Chapter 7 shows the use of lab on a chip systems for assisted reproductive technologies, such as *in-vitro* fertilization and intracytoplasmic sperm injection. These treatments can benefit from miniaturization since it can improve the gamete selection, but also the procedures involved in cryopreservation and embryo development.

The latter section of the book covers some examples of point-of-care diagnostics using lab-on-a-chip systems. This is not solely restricted to traditional microfluidic systems, since the use of paper-based microfluidic tests is especially useful for diagnostics in the developing world. Chapter 8 includes examples of these paper-based devices, but also gives the requirements for testing in low-resource settings. A different example of point-of-care diagnostics is the detection of circulating tumor cells (CTCs). Although it is major challenge to increase the throughput of microfluidics systems to detect these rare cells (a few cells $(10\ mL)^{-1}$), it has potential to improve the detection limit (Chapter 9). A way to perform this detection makes use of electrical impedance measurements, which will be discussed in more detail in Chapter 10. Besides the detection of CTCs, the use of microfluidic impedance cytometry is shown for a full blood count. In addition to the detection of cells in a fluid, microfluidics can also be used to measure analytes in blood. A widespread application of this is the measurement of glucose for diabetics. Chapter 11 covers this example, but also shows other routine clinical laboratory tests that are nowadays used. The last chapter of this book shows the development of a lab on a chip for ion measurements in biological fluids using capillary electrophoresis on chip. Here the steps are described that need to be taken to get a new microfluidic device ready for point-of-care measurements and practical application and market introduction.

We have tried to give you an overview of the diverse applications microfluidic technology can be advantageous in for medical applications. Some topics are still in the research phase, while others are currently incorporated in the hospital or patient's daily life. Furthermore in some cases it will serve as a tool to test drugs; others are used as a tool to detect certain disease markers. Finally we hope that with these examples, you get (more) inspired and enthusiastic to work in this wonderful multidisciplinary field and help to find the killer app!

Loes Segerink and Albert van den Berg

References

1. H. Becker, *Lab on a Chip*, 2009, **9**, 2119–2122.
2. A. Manz, N. Graber and H. M. Widmer, *Sensor. Actuator. B Chem.*, 1990, **1**, 244–248.
3. P. Neuzil, S. Giselbrecht, K. Lange, T. J. Huang and A. Manz, *Nat. Rev. Drug Discov.*, 2012, **11**, 620–632.
4. E. K. Sackmann, A. L. Fulton and D. J. Beebe, *Nature*, 2014, **507**, 181–189.
5. J. Liu, M. Enzelberger and S. Quake, *Electrophoresis*, 2002, **23**, 1531–1536.
6. J. P. McMullen and K. F. Jensen, in *Annual Review of Analytical Chemistry*, Vol. 3, ed. E. S. Yeung and R. N. Zare, 2010, vol. 3, pp. 19–42.
7. A. Floris, S. Staal, S. Lenk, E. Staijen, D. Kohlheyer, J. Eijkel and A. van den Berg, *Lab on a Chip*, 2010, **10**, 1799–1806.