

Abstract

Title of dissertation: Droplet microfluidics in biochemistry and in microbiology.

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Microfluidics is a new field of science focused on i) studying the hydrodynamics and the properties of fluids at the microscale and ii) designing, manufacturing and assembling devices for practical applications in chemistry, biology and material sciences. First demonstration of continuous-flow microfluidic devices dates back to the beginning of the 1990s. The microdroplet technology was first introduced 10 years later, in 2001. Since then, droplet microfluidics has been rapidly evolving with outstanding academic demonstrations of highly efficient technologies. A number of them has already been turned into commercial products for biomedical research, molecular diagnostics and cosmetic industry.

Despite substantial progress of the technology in the last 15 years, there are still technical barriers hindering further implementation of microdroplet technology to experimental biology – especially to biochemistry and microbiology. One of the most important challenges is in acquiring an independent and flexible control over the chemical composition, volume and location of multiple droplets over time. A second important goal that still requires substantial research is to provide methods of passive handling of droplets in autonomous microfluidic systems that might be used for point-of-care diagnostics, i.e. in settings that do not offer neither specialized infrastructure, nor trained personnel.

Research projects presented in this thesis required formation of droplets with arbitrarily set composition through i) liquid handling techniques based on automation and use of external electromagnetic valves, ii) improved hydrodynamic modules that precisely meters and stores a small portion of liquid, and iii) automated generation of libraries of nanoliter droplets. For the purpose of this dissertation, some methods were created from the scratch (droplet libraries), while others (passive traps, automation) are based on previous research carried out in the Group of Microfluidics and Complex Fluids. The main part of the dissertation comprises demonstrations of the utility of these droplet microfluidic methods for selected applications in biochemistry and in microbiology.

Thesis comprises five chapters. Chapter 1 provides an introduction to continuous-flow and biphasic microfluidics and describes the current state of the art applications of microdroplet technologies in biomedical sciences. Chapters 2 and 3 comprise brief description of materials and methods used in the experimental studies. Chapter 4 contains experimental results. Finally, general conclusions and propositions of future research are presented in chapter 5.

The results of experimental studies are arranged into four sections:

1. Technique for passive fluid handling with hydrodynamic traps was used in an autonomous system for determination of microbial susceptibility to antibiotics.
2. Method of controlled droplet splitting with automated microfluidics was used for demonstration of a long-term cultivation of bacteria in microdroplet chemostats.
3. Synergistic combination of automated and passive geometries enables for efficient formation of lipid bilayers at the interface between a pair of nanoliter-sized aqueous droplets and measurements of the activity of single membrane proteins.
4. Automation was used for rapid generation of libraries of nanoliter droplets with predefined chemical compositions. Droplet libraries method, along with techniques for passive and active liquid handling enable for quantification of very high DNA concentrations using droplet digital PCR.