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Integrated Approaches in Microfluidic Design for Enhanced Droplet Manipulation and Biological Insights

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Abstract. The Institute of Fundamental Technological Research's Microfluidic Laboratory is focused on enhancing the accuracy and practical use of microfluidic methods for chemical and biological studies, as well as creating tailored microfluidic instruments to address specific biological research needs. In this document, we present a few of our latest projects.

Keywords: Micro-, Nano- and Bio-flows, Multi-phase Flows, Droplets

1. Introduction

Microfluidics has rapidly evolved from its inception, becoming a vital interdisciplinary field that spans fluid mechanics at microscales and has myriad uses in biology, chemistry, and diagnostics [1]. Its allure lies in the ability to precisely control and manipulate fluid flows, achieved through the tiny dimensions of microchannels, the smooth, laminar flow characteristics [2], and the significant influence of surface tension in flows involving different phases [3]. Our research focuses on both single and multiphase flows.

2. Droplet microfluidics

Using more than one immiscible phase allows for the controlled formation [4] and manipulation of droplets in microfluidic channels. Each droplet can be a miniature reactor containing samples, reagents, or biological components.

Our research delves into the basic principles of two-phase flows within microchannels [4,5]. Utilizing the insights gained, we craft innovative microfluidic designs, such as for the passive handling of droplets [6,7] and sequential logic devices for meticulous droplet management [7,8]. These advancements allow for the execution of complex procedures intricately encoded within the layout of our microfluidic systems.

Additionally, we employ digital algorithms to precisely adjust concentrations by selectively merging and equally dividing droplets, enhancing our processes' accuracy, repeatability, and adaptability [9].

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3. Applications in biomedical research

Confined geometry of microfluidic chambers and superior flow control renders this technology suitable for mimicking physiological conditions for culturing cells [10]. One of our lab's primary objectives is to tailor microfluidic devices to meet specific biological research needs. A notable achievement is developing a microfluidic system that precisely controls the generation of tension gradients through the deformation of epithelial layers, enabling a detailed study of tissue mechanics, including strain and curvature effects on epithelial responses.

In collaboration with the University Grenoble Alpes in France, this system's application has provided insights into how curvature influences the propagation of calcium waves caused by folding on short timescales and affects gene expression spatially over more extended periods [11]. Our findings reveal that gradients in cell shape and the mechanical stresses they induce lead to distinct biochemical responses across the tissue layer, offering new perspectives on cell differentiation mechanisms during tissue development.

Another example is a device developed in collaboration with the University of Oxford, designed to study erythrocytes' oxygen release rate [12]. Our microfluidic system with the medium exchange chamber was applied for an experimental method to monitor the oxygen flow in individual red blood cells, combining ultrarapid solution switching to manipulate gas tension with single-cell O2 saturation fluorescence microscopy.

Recently, this approach has been used to investigate human kidneys perfused with stored blood during transplantation; the respiratory rate of the organ was measured [13]. The study challenges the conventional definition of oxygen delivery based on blood flow and oxygen content, highlighting its inadequate representation of blood efficiency in tissue oxygenation. However, the research uncovered a robust correlation between monitored kidney respiration and erythrocytes' oxygen release rate.

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