Ämne: LifeSciMicro Access request

Datum: 25 juni 2024 18:23:08 CEST

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Project title	Multimodal acoustophoresis control

Aim of project

The project aims to develop a novel microfluidic multiplex acoustic cell and particle manipulation platform. The goal is to apply many different vibration modes, instead of single modes in current state-of-the-art acoustic micromanipulators, to gain additional degrees of freedom for the manipulation. Ideally, complete, and independent control over the paths and positions of many different cells is achieved at single-cell resolution. The project is a breakthrough in single-cell handling. The technology will provide a more flexible, cheaper, biocompatible, label-free, and reliable alternative to optical tweezers. It will ultimately enable pipetting-free single-cell mass spectrometry studies, higher precision cell interaction studies (e.g. The interaction between natural killer cells and tumor cells), novel organ-on-a-chip applications, and cell patterning for tissue engineering.

Scientific background

This project aims to resolve several major challenges in biomedical engineering and cell handling research: A novel technology for single-cell handling will be developed that offers more versatility in microfluidic applications. The result is a novel multiplex standing wave acoustic manipulator that achieves precise and independent positioning of multiple cells, with versatility like acoustic tweezers, while keeping the simplicity of standing wave manipulation chambers. The project will revolutionize lab-on-a-chip applications, single-cell analysis, tissue engineering, drug screening, and allow high-precision control for the differentiation of stem cells.

Motivation for need of microfluidics

The project pushes the current research frontier concerning single-cell handling and aims at offering a highly multiplex alternative to optical trapping. The project requires devices with

chamber dimensions from hundreds of micrometers to small millimeter scale. The chamber dimensions and design requirements as well as the need for cell handling demand a microfluidic approach. Additionally, microfabrication techniques are essential to build devices of a sufficiently high quality. To achieve strong acoustic modes a high acoustic impedance mismatch is needed, which requires the chamber walls to be made of aluminum or harder even harder materials. To achieve reproducible modes, which are essential to be able to use model-based reinforcement learning approaches, the chamber needs to have precise dimensions. Therefore, the use of microfluidics and microfabrication technology is paramount to the success of the project.

Expected outcome

The devices produced by the Life Science Microfluidics platform will be the acoustic resonator chambers used within the project. These novel acoustic manipulators will employ an actively controlled combination of multiple modes for label-free single-cell handling. The main advantage of my technology towards acoustic tweezer technology is that my system is free from any moveable parts, is gentle (no strong focused laser beams), and free from optical requirements regarding the sample. Furthermore, the technology will allow to position of cells in a grid or pattern and subsequently isolate individual cells again. This will revolutionize single-cell analysis as a group of cells can be studied and individual targeted cells can be extracted for further culturing or more detailed analysis.

An additional straightforward application is the ability to hold cells against an external flow. Holding targeted cells against an external flow will allow for on-demand medium exchange a task that needs to be performed many times when culturing cells and can also applied to control the differentiation of stem cells or to perform drug response studies.

The technology will also allow the trapping of particle clusters against an external flow. Acoustic trapping of particle clusters has previously been shown to be an effective tool for the extraction and isolation of nanoparticles and extracellular vesicles (EV). Extracellular vesicles are small lipid containers that are released by cells. They and their contents are the topics of current research. Trapping and enriching them is one of the current challenges of biotechnology. Current acoustic vesicle trapping technology works in capillaries only, with our suggested design, the additional versatility would allow us to move away from glass capillaries and perform the same vesicle extractions in silicon devices.

Having full control over the position of many cells will allow the construction of arbitrary patterns and greatly improve current tissue engineering applications. Combining acoustics with tissue engineering is still in its early stages. Single-mode acoustic manipulation has previously been used to arrange spheroids in a tubular construct by exploiting a single resonance of a cylindrical tube or to form functional cylindroids of cells inside a hydrogel. The patterning performed by our multimodal trap can be used to create artificial muscle, tendon fibers, or vessels. This could also enable neural cells to be patterned and cultured into transplants for regeneration in spinal cord injuries.