MetamorphChip Report Summary

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Periodic Reporting for period 1 - MetamorphChip (Dynamic Microfluidic Structures for Analysis of Single Cell Systems)

Reporting period: 2016-04-01 to 2017-09-30

Summary of the context and overall objectives of the project

The interaction and communication between individual cells plays a central role in virtually all fields of biology, from the cooperative work of cells in the immune system, through the differentiation of stem cells, and to the proliferation of cancer cells. In recent years it has been shown that these processes are fundamentally coupled to cell-to-cell heterogeneity and variability, which manifests itself in all cell functions, from the level of the genome, transcriptome, and proteome, to the level of proliferation, migration, differentiation and apoptosis. Studying cellular ensembles masks these differences, and may yield observations that are not representative of any individual cell type or subpopulation. Despite this, most current studies consider cell populations, largely due to technological limitations in the ability to dynamically compartmentalize, manipulate, and analyze single cells. Gaining further insight into the role of heterogeneity at the single cell level is an essential step towards developing new therapeutic approaches. Progress in this field requires a significantly improved ability to access and study cellular interaction at the single cell level, and to support quantitative modeling of such processes.

In the past decade, there has been considerable development in high-throughput methods of single-cell analysis. Tools developed include various microfluidic chips for individual or paired cell capture and analysis, droplet microfluidics, digital microfluidics, FACS and microFACS. Particularly notable is the use of on-chip pneumatic valves enabling elaborate multi-step protocols to be performed. These tools have reduced time necessary for hands-on work, and allowed for work at previously unattainable single-cell scales, enabling fundamental discoveries in all aspects of biology. However, despite these advantages, many of the high-throughput single cell analysis technologies are still single-purpose “protocols on chips” rather than true “labs on chips”: they do not allow the flexibility and real-time experimental decision-making essential to scientific work. After carrying out a predetermined protocol, it is rarely possible to perform unplanned follow-up experiments on the same cells or on the same system, based on the obtained results. Rapid progress in research depends on the ability to make real-time experimental decisions, in which the observations from the current step direct subsequent steps in the experiment – a level of flexibility unattainable with current tools.

In this project we aim to develop a new concept for a single-cell-level bioanalytical workspace that is dynamically configurable in real time. By using electrokinetically driven surface deformations, microfluidic structures may be created or destroyed in real-time allowing cells to be introduced, separated, reunited, or removed, and liquids to be selectively introduced to, removed from, or moved between specific cells, either based on a predetermined program or more importantly – on demand (by the researcher, or an image processing algorithm), based on the state of the experiment at any time point. This workspace will be implemented in a microfluidic chip format, which we term the MetamorphChip.
Work performed from the beginning of the project to the end of the period covered by the report and main results achieved so far

“We have essentially completed the theoretical aspect of the project, and have developed complete models for deformations of elastic sheets using electrooostic forces. The models have been generalized to allow introduction of alternative forces, and we have complete analytical and numerical solutions allowing us to design and predict deformation states. The work has been published in 3 peer-reviewed publications in the leading journals of the field, and a 4th publication combining the theory with experimental validation is currently under review.


As planned, we have constructed a first working prototype demonstrating the physical principle of the Metamporph Chip. We are currently working on the next generation which would include a large number of control electrodes allowing higher resolution control. One critical sub-task which took longer than expected is the ability to measure the deformation the structures we’re creating. A long survey of devices and methods revealed that there are no off-the shelf solutions which fit our needs exactly. We therefore combined purchasing of a holographic microscope which suits well measurement over small fields of view, with development of our own method based on scanning beads deposited on the surface, which suits measurements over large field of view.

The work was disseminated though presentation in numerous conferences:

8. M. Bercovici, Lab on a Chip and Microfluidics World Congress, San-Diego, Oct 2-4, 2017. (invited keynote)

Progress beyond the state of the art and expected potential impact (including the socio-economic impact and the wider societal implications of the project so far)

All of our work done to date goes beyond the state of the art, and was published in leading peer-reviewed journals.
By the end of the project, we expect to demonstrate a fully-configurable MetamorphChip, and apply to the manipulation of cells.

Related information

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