

The Science and Applications of Cell Biology in Microsystems

DOI: 10.1039/b418165b



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From the beginning of MicroElectro Mechanical Systems, biological applications for micro devices have been envisioned. Early micromotors prompted thoughts of micro "roto rooters" that might someday clean plaque from arteries. While this vision has not been fulfilled, several successful commercial applications of MEMS have appeared. With the emergence of microfluidics and soft lithography techniques, the hopes for successful biological applications were again raised. However, only recently has the field matured to where microfluidic systems for biology have gone beyond simply replicating methods and techniques performed using more traditional means. As highlighted in this special issue, the development of Lab on a Chip devices for cell biology is rapidly moving from demonstration to utility. One of the key shifts has been to a more intelligent use of micro scale phenomena and systems to either improve functionality or more importantly, to perform functions in beneficial ways not possible before. There are numerous biomedical applications that benefit from miniaturization. The materials and fabrication methods used are as varied as the application to which they are best suited, but the common theme is one of new or enhanced performance.

While cell culture has become an essential tool in cell and molecular biology and in biotechnology, it is now

falling behind in the pace of progress brought by genome sequencing, imaging probes, and high-throughput testing of biochemicals. For over a century, cell culture technology has essentially consisted of the immersion of a large population of cells in a homogeneous fluid medium. This requires large numbers of cell culture surfaces, bulky incubators, large fluid volumes, and expensive human labor and/or equipment. Moreover, cells respond to local concentrations of a variety of molecules which may be dissolved in the extracellular medium (*e.g.*, enzymes, nutrients, small ions), present on neighboring scaffolds (*e.g.*, extracellular matrix proteins) or on the surface of adjacent cells (*e.g.*, membrane receptors). Microfabrication technology has an inherent potential for providing the next generation of cell culture and cell analysis tools where large numbers of single cells or small cell populations can be probed inexpensively, at high throughput, and in a cellular microenvironment of increased physiological relevance with respect to present cell culture methods.

The 16 papers gathered for this special issue span a wide range of topic areas across "the science and applications of cell biology in microsystems." Papers from Schuler¹ and Williams² describe systems designed to provide insights into very basic biological questions such as the mechanisms responsible for the development of tight intercellular junctions in the blood-brain barrier and thermal control of dorsal root ganglion neurons respectively. Important considerations when designing microsystems for cell culture were recently discussed in LOC.³ Four papers describe systems that address various aspects of culturing cells in Lab on a Chip. Lee⁴ describes a system for high throughput cell culture, while Kennedy⁵ demonstrates the ability to monitor insulin secretion using electrophoretic-based immunoassays on continuously perfused cells. Jeon⁶ and Folch⁷ describe methods and systems



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that allow for patterning cells within microchannels and for their long term study (6 days and > 2 weeks, respectively) and Bhatia describes patterning in a 3D hydrogel matrix.⁸ Systems that allow enhanced separation or sorting functionality are described by Liepmann⁹ and Toner,¹⁰ while Jensen¹¹ and Lee¹² utilize electroporation for cell lysis and for increasing cell membrane permeability. Van den Berg describes a microfluidic chip for cell trapping enabling imaging of cell status after exposure to fluorophores indicating different states of cell death.¹³ One of the earliest examples of microfluidics and cell biology is in the field of embryology. This tradition continues here with three papers that describe advances in this area. Park¹⁴ describes a system to transport, isolate, orient and immobilize embryos. Chemical and mechanical manipulation of embryos is described in two papers by Beebe^{15,16} that demonstrate enhanced functionality over traditional methods. Finally, Laurell¹⁷ describes a method for the efficient separation of lipid particles from red blood cells in a system that should have important clinical applications. In summary, this special issue, while far from exhaustive, presents a selection of the state-of-the-art in the science and application of cell biology in microsystems. As these papers make clear, the field is rapidly moving from exploratory demonstrations to sophisticated and

targeted applications where the unique properties of microsystems can be leveraged to provide new or enhanced functionality.

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