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EDITED BY
Jonathan Cooper,
University of Glasgow, United Kingdom

REVIEWED BY
Pedro Estrela,
University of Bath, United Kingdom

*CORRESPONDENCE
Michael G. Mauk,
mmauk@seas.upenn.edu

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Editorial: Celebrating 1 year of Frontiers in lab on a chip technologies

Michael G. Mauk*

MEAM Department, School of Engineering and Applied Science, University of Pennsylvania, Philadelphia, PA, United States

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Editorial on the Research Topic
Celebrating 1 year of frontiers in lab on a chip technologies

Almost 20 years ago, Nathan Blow published an article in *Nature Biotechnology* entitled "Microfluidics: In Search of the Killer App" (Blow, 2007), surveying efforts to develop integrated, automated microfluidic systems for nucleic acid, protein, and cell-based assays. These systems would facilitate customized platforms for high-throughput analysis and initiate wider adoption of microfluidics technology by life science researchers. At the time, the future appeared to involve foundries providing made-to-order systems that were fabricated by soft lithography in PDMS (polydimethylsiloxane) silicon polymer. The search for a lab-on-a-chip "killer-app" has been a lively topic of discussion. Calcedo and Brady (2016) surmised that the challenge for microfluidics was instead to bridge technical gaps so that the adoption of microfluidics would yield significant operational advantages and/or substantial cost reductions, rather than finding a killer app.

Concurrent to the development of these specialized microfluidic systems as research tools there have been decades-long efforts to develop microfluidic lab-on-a-chip devices for point-of-care (POC) diagnostics. Lateral flow strips for immunoassays, such as home pregnancy tests, COVID-19 antigen tests, and drug-of-abuse tests, are premier examples of widely used, commercialized POC devices. The challenge lies in implementing more complicated "molecular" diagnostics (such as nucleic acid amplification tests) that integrate sample processing, enzymatic amplification, and real-time detection in a low-cost, streamlined, minimally instrumented device.

Some comparisons between microfluidics and microelectronics, the most consequential technology of the last half century are instructive. Microelectronics has largely converged into a consolidated technology base: transistor devices are made of silicon and a handful of other materials, made using well-established, industry-wide methods, to realize implementations of a standard set of functions (e.g., logic, data storage, and signal processing). Microfluidic systems, on the other hand, are still made from a wide variety of materials and diverse fabrication methods, with no standard device-building block component similar to a transistor, and are applied to an expanding scope of functions ranging from immunoassays and sample processing to tissue and cell culture.

Four articles in the Frontiers Research Topic Celebrating 1 Year of Frontiers in Lab-on-a-Chip Technologies underscore the wide range of applications and characteristics of microfluidics technology, in ways and areas perhaps not anticipated in the first decades of the field.

In "Point-of-care testing: a critical analysis of the market and future trends" Khan et al. surveyed wearable sensors (e.g., patches, wristbands, bandages, and contact lenses) in addition to microfluidic technology. The authors offered several avenues for expanding microfluidics in the point-of-care diagnostics realm, including integrating artificial intelligence and machine learning with point-of-care technology (such as microfluidic lab-on-a-chip devices and sensors). With improvements in sensitivity and compliance with more stringent clinical standards, the authors are optimistic about POC technology making significant inroads as an alternative to traditional clinical testing. While POC diagnostics focus on infectious diseases, wider use in non-communicable diseases and continuous patient monitoring offers opportunities for dramatic changes in healthcare delivery.

A second article, "An economical self-coalescing microfluidic device with an observable readout" by Kamat et al., is an example of exploiting the features of fluid flow phenomena at the microscale to implement a minimally-instrumented multiplexed assay. Dried reagents are spotted in the channel of the chip for multiple assays and are reconstituted by the infusion of a liquid. By controlling device geometry, self-coalescence phenomena maintain reagent separation, allowing for multiple simultaneous colorimetric tests. Further, a simple fabrication technology involving laser-cut silicone tape over a coverslip with spotted reagents was used by the authors.

Tissue chips are microfluidic systems used as experimental platforms that simulate physiological conditions. For example, they can be used to study the response of cells immobilized in channels to microgravity, radiation, drug stimulation, toxins, and blood infusions. In a third article, Taylor et al. ("An analysis of trends in the use of animal and non-animal methods in biomedical research and toxicology publications") surveyed the use of Non-Animal Models (NAMs) in biomedical research at the intersection of microfluidics, lab-on-a-chip and *in vitro* studies that replace *in vivo* animal models. The motivation for using NAMs in research is to avoid the use of animals, shorten study times, and lower costs. Typically, NAMs are the first phase of projects, after which findings are confirmed with *in vivo* studies. Research areas include lung disease, heart disease, breast cancer, blood cancer, diabetes, toxicology, and neurodegenerative diseases.

Continuing on the theme of the use of microfluidic platforms for culturing tissues, in the fourth and final article, Jogdand et al. ("Organs in orbit: how tissue chip technology benefits from microgravity, a perspective") reviewed the use of tissue chips (also referred to as "organ-on-a-chip") in space. These systems have the specific objective of predicting health risks to astronauts, and have sparked wider interest because microgravity can simulate accelerated aging and other disease processes. Moreover, low gravity can increase the permeability of the blood-brain barrier, allowing the passage of chemotherapeutics. The authors provided a perspective on microgravity tissue chip technology for the musculoskeletal, cardiovascular and nervous systems. This research area exemplifies how microfluidics enables and facilitates the simulation and probing of model systems to investigate disease mechanisms and assess therapies. The field of microfluidics may well further divide into two sectors: a POC sector focused on minimally instrumented, multiplexed molecular assays made by high-volume manufacturing processes ("lab-on-a-chip"), and a customized analytical systems sector ("chip-in-a-lab") with increasingly sophisticated designs and ambitious performance aims, including organ-on-a-chip and high-throughput, highly-instrumented analysis platforms (Streets and Huang, 2013; Mohammed et al., 2015).

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