Microfluidics and point-of-care testing

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In many ways, the intrinsic features of microfluidics are a natural fit for a point-of-care (POC) diagnostics device (*i.e.* a diagnostic test performed near the patient without needing a clinical lab): low consumption of reagents and sample, miniaturization of device, and fast turn-around time for analysis. Thus, it comes as no surprise that much research, since the inception of modern microfluidics in the early 1990's, has focused on its application in point-of-care sensors and diagnostics. This special issue of *Lab on a Chip* captures some of the latest areas of interest and technological approaches from leading researchers towards point-of-care microfluidic-based diagnostics.

Point-of-care diagnostic test devices provide rapid results on an ever expanding range of medical tests.[1,2] One rationale for POC testing is that it may streamline healthcare and improve clinical outcomes.[3] Another advantage is that rapid testing will lead in turn to rapid intervention. For example, the finding of a high blood glucose by a diabetic patient can be acted upon immediately by administration of the appropriate therapy.

The earliest POC tests, in fact, detected glucose and were based on tablets containing the test reagents. Subsequent technological innovation led to the development of dip stick devices, and these devices evolved to self-contained lateral flow tests (*e.g.*, for pregnancy, cardiac disease, and HIV-1) that require only the addition of sample. In recent years, POC devices incorporating both disposable microelectronic and microfluidic components have been developed (examples include products from the companies Metrika, Biosite, iSTAT and Unipath). Today, the POC market is estimated to be over $10 billion, with double-digit growth in some areas such as cardiac and infectious diseases.

A consensus is emerging that much of the future growth in POC diagnostics—which will likely require assays of increasing technical complexity—will involve microfluidics, a versatile technology that makes possible the miniaturization of complex fluid handling and integrated detection. As such, research on microfluidics for POC applications has increased markedly in recent years, fueled by an interest in constructing field-deployable analytical instruments.[4] Compared to conventional microfluidics, however, there is one distinguishing requirement of POC diagnostics: extreme simplicity of use, which usually translates to minimal or no ancillary equipment. This feature has proven to be the downfall of many otherwise promising integrated lab-on-a-chip systems, in terms of their ability to be used at the POC.

This special issue features articles covering a range of topics in microfluidics and POC testing:

- Basic science and tools for controlling surface chemistry (Ho), controlling liquid flow (Pamula), integrating optics with microfluidics (a Critical Review by L. Lee), and optimizing assay parameters (Sia)
- Applications in nucleic acid-based molecular diagnostics, including integrated systems involving nucleic acid amplification such as RT-PCR (S. H. Lee) and NABSA (L. Lee), visualization for electrophoresis (Ugaz), and fluorescence *in situ* hybridization (Backhouse)
- Applications in immunoassays (Singh), clinical chemistry (Do) and cell analysis (Toner, Irimia, McDevitt, and a perspective by Kitamori)
- Applications in global health (an area with high clinical impact but laden with special design constraints[5]), including techniques for stable storage of samples (Yager) and centrifugation of samples in the field (Whitesides), paper-based microfluidics (Whitesides, and a Focus article by Zhao and van den Berg), and microfluidics using minimal instruments (a Critical Review by Weigl)

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These studies have the potential to move beyond benchtop-based lab-on-a-chip approaches (typically, a microfluidic chip which may require a manufacturing process that is expensive and non-scaleable, and a microscope and syringe pumps for operation), towards small POC handheld (or even implantable) devices. While some of these features (*e.g.*, expensive manufacturing process) may be appropriate for some settings (*e.g.*, defense applications), it will be important to lower the price point, size, and difficulty of operating the device before an integrated microfluidic test will be attractive for mass use. Current FDA-approved POC devices that incorporate microfluidics with disposable microelectronics illustrate the possibility of building complex devices at low manufacturing cost. Future trends and technologies include:

• New materials, to complement the current focus on planar microfluidics (*e.g.*, paper as substrate, integration of open-channel systems with capillaries, materials that enable autonomous or droplet-based movement of fluids)

• New detection strategies (*e.g.*, impedance measurements, label-free detection)

• New applications (*e.g.*, investment in $1000 whole-genome sequencing may accelerate the development of POC molecular testing)

Is research in microfluidic POC systems becoming too applied? Although much of the remaining technical challenges can be classified as applied science and engineering (and hence best done in industry), the challenges listed above illustrate that there will continue to be a space for basic science. Many promising technologies are still at an early research stage and will need fundamental innovations before clinical use (*e.g.*, cantilever-based detection), and there will always be room for fundamentally new lab-on-a-chip technologies designed for POC use.

We should caution that, in practice, not all clinical diagnostics or analytical applications may be appropriate at the POC. Unless they are aimed to be used by untrained personnel in a short period of time (*i.e.*, equivalent to a CLIA-waived test in the US), performing tests at the POC may place an undue burden on health workers (or patients themselves) and hence prove counterproductive. Even if the test can be engineered for POC use, they may offer little or no clinical benefit; and even if they offer a clinical benefit, the sensitivity of the information (*e.g.*, HIV, and in the future, genetic tests) could raise issues of privacy, theft, and medical counseling that argue against the use of the test at the POC.

The interest in POC microfluidic-based devices has been intense and has cut across all major disciplines in lab-on-a-chip research, including engineering (biomedical, chemical, electrical, and mechanical), chemistry, and physics. This research is just starting to bear fruit in terms of translation into new clinical capabilities.[6] This special issue captures some of the leading directions and themes of today's research, and we expect that the next decade of work will produce more innovative research, but above all, more clinical successes.

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