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Lab on a Chip

Miniaturisation for chemistry, physics, biology, materials science and bioengineering

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EDITORIAL

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Emerging investigators: new challenges spawn new innovations

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In introducing this themed issue on emerging investigators, we couldn't help but reflect on the past and the challenges we often faced as new investigators. In hindsight, some of these challenges seem like simple problems, such as how do we analyze cells at an individual level, how can we control which biomolecules or cells adhere to surfaces, or how do fluids mix, or particles move, or how are molecules concentrated or separated? There have been many innovative solutions, and some of these problems are now "solved". This new generation is now facing new challenges, which are reflected in the range of topics covered within this issue. For example, how can one use new materials to make environments that mimic physiology, to understand tissues better and improve the way we screen drugs? Problems related to manipulating cells continue to be present, but in many cases, solutions focus more directly on specific clinical needs. We also still see significant work on the next generation of materials and chip designs that moves beyond the successful polydimethylsiloxane (PDMS) of the last decade.

Hydrogels have been widely used in tissue engineering research, with many new opportunities in lab on a chip research to create tissue-like constructs, porous but solid scaffolds for molecular assays, and flow control elements. Several of these areas of active research are innovatively approached by the emerging investigators publishing in this issue.

For example, to solve the problem of creating solid phase bioactive regions with high surface areas, Thiele *et al.* created DNA-functionalized hydrogels that act as "artificial nuclei" which enable *in vitro* translational and transcription within droplets (DOI: 10.1039/C3LC51427G). Chu *et al.* use the thermoresponsive properties of some hydrogels to create a valve that allows self-regulated thermostatic culture of cells (DOI: 10.1039/C4LC00039K). Hydrogels that have different crosslinking modalities were also used to enable fabrication of vascular-like patterns followed by sacrificial release to create hollow structures for cell infiltration (Huang *et al.*, DOI: 10.1039/C4LC00069B). Complex tissues can be created by embedding magnetic materials within hydrogel microtissues and then assembling them under a magnetic field (Du *et al.*, DOI: 10.1039/C4LC00081A). Protein coalescence was also studied using microfluidic droplet approaches (Köster and Dammann, DOI: 10.1039/C3LC51418H). Overall, hydrogels will likely offer many new opportunities to interface with cells and biomolecules in microfluidic platforms moving forward.

Situated between fundamental research and engineering practices, the concept of a "lab-on-a-chip" greatly demonstrates how advances in fabrication technology have continuously driven the development of miniaturization and operation of micro-devices. To perform new protocols and innovative experiments in a microfluidic device, researchers are constantly challenged to develop new materials and micro-device fabrication techniques.

One major research focus is to further reduce the consumption (and cost) of the reagents or precious samples, which may be hard to obtain or require a great effort to enrich (*e.g.* the circulating tumor cells in cancer patients' blood). Another major research goal is to exploit the unique characteristics of micro-scale reactions and employ chip-based devices to carry out experiments that cannot be performed in a conventional fashion.

In this issue, we also see investigators extend the collection of materials for micro-device fabrication with the development of a photocurable 'liquid polystyrene' that is compatible with both soft-lithography (Rapp *et al.*, DOI: 10.1039/C4LC00045E) and direct printing of membranes and 3D structures using photocurable PDMS (Kuehne *et al.*,

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DOI: 10.1039/C4LC00320A). We also see droplet manipulation using salt water electrodes in PDMS devices (Abate and Sciambi, DOI: 10.1039/C4LC00078A), the use of laminar flow to pattern the formation of biofilms (Greener *et al.*, DOI: 10.1039/C4LC00084F), and the combination of microarrays and large-scale microfluidics to measure protein biomarkers of large amounts of human serum samples (Maerkl and Garcia-Cordero, DOI:10.1039/C3LC51153G).

Technical advances such as these increase the compatibility of lab on a chip technology with next generation chemical and biological analysis and inspire innovative experimental solutions in a growing range of disciplines.

"Cells on a chip" is an area that has grown rapidly since early 2000. In the beginning, mainly simple cell manipulations and assays were presented, but to date, very sophisticated cell analysis platforms have been developed. It is clear that working with miniaturized tools enables an expanded scope of biological analyses. One area is single cell analysis, where many details of cells can be analyzed, although it is of great importance to also maintain throughput in some cases, in order to not miss any rare events. The tools and assays have also developed over time to become more focused on clinically relevant issues. In this issue, four exciting reports on cell analysis and manipulations are published. One example is a technique to screen thousands of sperm cells for motility, while retaining single species recovery options (Segerink *et al.* DOI: 10.1039/C4LC00050A). Another contribution to the single cell collection is the work by Schroeder *et al.* (DOI: 10.1039/C4LC00057A), who have developed a system for direct observation of intracellular dynamics in free solution. In terms of manipulation of cells on a chip, a new method of trapping cells based on size and deformability is presented by Ma *et al.* (DOI: 10.1039/C4LC00306C) and a new technique for 3D rotation of cells on a chip is presented by Wang *et al.* (DOI: 10.1039/C4LC00312H). Centrifugal microfluidic systems are common in cell and protein analysis. In this issue we see an immuno-based study for the rapid and sensitive measurement of vascular endothelial growth factor intended for patients suffering from diabetic retinopathy and age-related macular degeneration, presented by Murthy *et al.* (DOI: 10.1039/C4LC00279B).

With continually evolving challenges, we are well served by this current crop of innovative new investigators. We'd like to end by calling the next generation of researchers to battle current and future challenges – we need you!