Lab on a Chip

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Emerging Investigators 2016: discovery science meets technology

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Observing the nascent careers of new scientific investigators is both exhilarating and humbling. Emerging Investigators bring a determined sense of excitement, brashness, and creativity to the pursuit of fundamental and applied science that is certain to spawn new developments across multiple fields of research. For these reasons, we are delighted to introduce the 2016 Emerging Investigators themed issue for *Lab on a Chip*. This issue showcases the work of 18 Emerging Investigators who are pursuing outstanding research in the highly interdisciplinary field of microfluidics and microscale systems. The topics addressed in this issue have acquired a unique flavor based on the work of a tenacious set of young investigators.

Perhaps not surprisingly, research in this issue focuses on some of the most pressing and interesting problems facing the field today. How can we optimize detection of minute amounts of analytes and cells for clinical applications? How can we leverage microfluidic systems to engineer stem cell niches and to optimize protein crystallography? How can we trap, manipulate, and understand the dynamics of colloids and soft materials using microfluidics? Clearly, these topics are highly interdisciplinary and span multiple traditional fields of science and engineering. Despite the diverse nature of the topics, these articles can be loosely classified into three groupings by subject. In the first group, research is focused on sensors and detection, including detecting analytes derived from biological samples and new sorting methods and sequential chemistry in an on-chip format. In the second group, research is focused on lab-chip solutions for biological systems, including hydrogel platforms, stem cell growth, and microdevice development for crystallography. In the third group, research is largely focused on soft materials and rheology, including a new analysis framework for active microrheology, optofluidics for imaging and detection, and drop dynamics in microfluidic devices. In the following, we briefly summarize these contributions and highlight the importance and novelty of the work.

One of the major goals of using lab-on-chip devices is to perform detection and measurement with the highest possible sensitivity and accuracy. In this issue, we see more developments that extend the technological repertoire in this area. In many cases, it is clear that new materials are the key to new functions. Zeng *et al.* developed a novel approach that employs graphene oxide induced polydopamine 3D porous surfaces to isolate exosomes through highly-specific immuno-capture, which greatly enhances the sensitivity of fluorogenic ELISA. This device has been demonstrated to perform ovarian cancer diagnostics from extremely small amounts of plasma without sample processing (DOI: 10.1039/C6LC00279J). Huang and coworkers take advantage of micromachined structures in a PMMA device to perform whole blood processing with improved ease of use and efficiency. Combined with dual CMOS polysilicon nanowire sensors, this device can perform label-free electrical detection of multiple analytes, enabling the hemoglobin-A1 test to serve as a diabetes diagnosis with limited sample volumes and short analysis times (DOI: 10.1039/C6LC00410E). New fabrication methodologies bring new possibilities. Issadore and coworkers report a replication method to fabricate large-format (centimeter scale) magnetic trap devices. Such devices, made by cost-efficient electroplating, offer a significantly increased throughput that enables potential rare cell (*e.g.* circulating tumor cell, or CTC) enrichment and capture with input volumes at the milliliter scale (DOI: 10.1039/C6LC00487C). Kaigala, Bercovici and coworkers developed a phase separation structure to integrate with a vertical microfluidic probe device with open channels to eliminate the oil contact to the reaction surface. This design is elegant and easy to couple with many other formats of

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microfluidic applications, such as the reaction kinetics measurement and microenvironment screening demonstrated in the paper (DOI: 10.1039/C6LC00473C). Integration can also be creative. Zhu and coworkers presented a clever design to seamlessly integrate a series of cascade reactions for highly sensitive, quantitative, and user-friendly point-of-care detection of aflatoxin B1. This exquisite approach uses highly specific aptamer-based recognition to trigger the release of gold nanoparticles and hence catalyzes the decomposition of hydrogen peroxide to generate oxygen, which can be indicated and quantified through a moving segment of ink in a microchannel (DOI: 10.1039/C6LC00474A).

Biological applications have always been an important focus in microfluidics research, both in terms of basic research and with respect to biotechnological applications. This is well reflected in the present issue, where several papers address fundamental biological, biomedical, or biochemical questions, but at the same time provide proof-of-principle for exciting future applications. To this end, Watanabe *et al.* present a biomimetic system to study transport in and through biological membranes (DOI: 10.1039/C6LC00155F). The method exploits the superb controllability of microfluidics and offers a high-throughput way to study both fundamental questions in membrane science as well as applications to drug screening. In their work on high-throughput stem cell screening, Liu and coworkers investigate an utterly important and interesting class of cells (DOI: 10.1039/C6LC00331A). The critical point they address with their experimental technique is the separate control of cell culture conditions in individual microwells. In this way, biochemical, physical, and biological factors can be defined and screened in an efficient and effective way. Perry and coworkers address the problem of high-throughput crystallography (DOI: 10.1039/C6LC00451B). Serial crystallography is based on single pulse exposures of a large number of very small crystals and subsequent computational derivation of a diffraction patterns. A critical point for all X-ray applications is the choice of window materials, and the authors solve this here in a clever way by using ultrathin graphene layers. The authors use their chip at a synchrotron source, opening up additional opportunities at the recently introduced free electron lasers (FELs). Huh and coworkers address an important problem in medicine by mimicking the human placental barrier on chip (DOI: 10.1039/C6LC00259E). The system opens up a plethora of opportunities to study the permeability of the placenta by, for example, drugs, toxins, nutrients or pathogens *in vitro*. The proof-of-principle study is a very important first step towards highly controlled medical studies in the future. Ren and coworkers combine microfluidics and agar-gel-based cell culture in an innovative way and use their novel device for testing antimicrobial susceptibility to drugs (DOI: 10.1039/C6LC00417B). This work addresses an important issue we are facing today, namely the rapid increase of antimicrobial resistance caused by the use of broad-spectrum antibiotics due to the lack of rapid and cost-efficient antimicrobial susceptibility tests. The presented method is low-cost, fast and straightforward to use, enabling broad use of the technique.

This issue also presents several articles that focus on key problems in soft materials and rheology. Zia and coworkers present a new theoretical framework for active microrheology that allows for analysis of arbitrary size probe particles in a bath of colloidal particles (DOI: 10.1039/C6LC00476H). This article presents a detailed and elegant theoretical analysis of the problem, and this work essentially resolves prior discrepancies between theory and experiment in cases where the size of the probe particle used in active microrheology experiments was not matched exactly to the sample or bath particle size. Tan and coworkers present an experimental study of droplet dynamics induced by AC electric fields (DOI: 10.1039/C6LC00448B), which is highly relevant to droplet-based microfluidics for compartmentalized reactions and sorting. This work presents an important step forward in understanding drop dynamics under AC fields, thereby extending beyond prior work in considering DC field dynamics. Microfluidics can be further leveraged to study the dynamics of different complex fluids such as emulsions and concentrated drop suspensions. Tang and coworkers present an intriguing study on the effect of confinement and viscosity ratio on the breakup of a concentrated suspension of droplets in a microfluidic constriction (DOI: 10.1039/C6LC00478D). These experiments are highly useful in informing the development of personal care products and foods. Multiphase fluid flow was also investigated in a paper by Oakey and coworkers, who study the interfacial effects of crude oil–salt solutions (DOI: 10.1039/C6LC00287K). Importantly, these experiments are relevant to understanding and optimizing the process of enhanced oil recovery. In the field of soft materials and complex fluids, the ability to trap and manipulate single particles is essential for understanding microscale interactions. To this end, Xu and coworkers report the use of acoustic bubbles for the trapping and release of small particles in microfluidic devices (DOI: 10.1039/C5LC01420D), including direct measurement of the secondary radiation force for trapping. Finally, a topic of current interest in the field of microfluidics is the combination of light and optics to fluidic devices, otherwise known as optofluidics. In one study, Chung and coworkers develop a new method to generate anisotropic particles using 4-dimensional optofluidics by combining time together with three-dimensional spatial control of particle morphology in a microfluidic flow lithography fabrication scheme (DOI: 10.1039/C6LC00208K). In a different study, Yang and coworkers present an interesting study that combines hydrodynamic focusing with total internal reflection (TIR) microscopy by effectively achieving TIR illumination in a central core stream (low index of refraction) surrounded by immiscible sheath flows (high index of refraction)

(DOI: 10.1039/C6LC00078A), which could prove useful for nanoparticle imaging, counting, and detection.

In closing, we are excited to share these articles with you and to celebrate the success of these young investigators. In recent weeks, we have been truly impressed by the scope and rigor of these articles, and we believe that this enthusiasm will be infectious with the readership of *Lab on a Chip*! To all young investigators – please keep pushing the boundaries and following your heart in pursuing the challenging and difficult work that others say cannot be done. The community needs your creative solutions to the world's pressing problems.