



Literature Highlights Column: From the Literature

Life sciences discovery and technology highlights

Laboratory automation and high-throughput biology

Automation for Life Science Laboratories. The automation of processes in all areas of the life sciences will continue to increase in the coming years due to an ever increasing number of samples to be processed, an increasing need to protect laboratory personnel from infectious material and increasing cost pressure. Depending on the requirements of the respective application, different concepts for automation systems are available, which have a different degree of automation with regard to data handling, transportation tasks, and the processing of the samples. Robots form a central component of these automation concepts. Classic stationary robots from the industrial sector will increasingly be replaced by new developments in the field of light-weight robots. In addition, mobile robots will also be of particular importance in the automation of life science laboratories in the future, especially for transportation tasks between different manual and (partially) automated stations. With an increasing number of different, highly diverse processes, the need for special devices and system components will also increase. This applies to both, the handling of the labware and the processing of the samples. In contrast to previous automation strategies with a highly parallel approach, future developments will increasingly be characterized by individual sample handling (Thurow, K. *Adv Biochem Eng Biotechnol*, 2022, 182, 3-22).

The next wave of innovation in laboratory automation: systems for auto-verification, quality control and specimen quality assurance. Laboratory automation in clinical laboratories has made enormous differences in patient outcomes, with a wide range of tests now available that are accurate and have a rapid turnaround. Total laboratory automation (TLA) has mechanised tube handling, sample preparation and storage in general chemistry, immunoassay, haematology, and microbiology and removed most of the tedious tasks involved in those processes. However, there are still many tasks that must be performed by humans who monitor the automation lines. The authors are seeing an increase in the complexity of the automated laboratory through further platform consolidation and expansion of the reach of molecular genetics into the core laboratory space. This will likely require rapid implementation of enhanced real time quality control measures and these solutions will generate a significantly greater number of failure flags. To capitalise on the benefits that an improved quality control process can deliver, it will be important to ensure that an automation process is implemented simultaneously with enhanced, real time quality control measures and auto-verification of patient samples in middleware. Therefore, it appears that the best solution may be to automate those critical decisions that still require human intervention and therefore include quality control as an integral part of total laboratory automation (Brown, A. S. and Badrick, T. *Clin. Chem. Lab. Med.*, 2022, doi: 10.1515/cclm-2022-0409).

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High-throughput screening paradigms in ecotoxicity testing: emerging prospects and ongoing challenges. The rapidly increasing number of new production chemicals coupled with stringent implementation of global chemical management programs necessities a paradigm shift towards boarder uses of low-cost and high-throughput ecotoxicity testing strategies as well as deeper understanding of cellular and sub-cellular mechanisms of ecotoxicity that can be used in effective risk assessment. The latter will require automated acquisition of biological data, new capabilities for big data analysis as well as computational simulations capable of translating new data into in vivo relevance. However, very few efforts have been so far devoted into the development of automated bioanalytical systems in ecotoxicology. This is in stark contrast to standardized and high-throughput chemical screening and prioritization routines found in modern drug discovery pipelines. As a result, the high-throughput and high-content data acquisition in ecotoxicology is still in its infancy with limited examples focused on cell-free and cell-based assays. In this work Wlodkowic and Jansen outline recent developments and emerging prospects of high-throughput bioanalytical approaches in ecotoxicology that reach beyond in vitro biotests. The authors discuss future importance of automated quantitative data acquisition for cell-free, cell-based as well as developments in phytotoxicity and in vivo biotests utilizing small aquatic model organisms. The authors also discuss recent innovations such as organs-on-a-chip technologies and existing challenges for emerging high-throughput ecotoxicity testing strategies. Lastly, the authors provide seminal examples of the small number of successful high-throughput implementations that have been employed in prioritization of chemicals and accelerated environmental risk assessment (Wlodkowic, D. and Jansen, M., *Chemosphere*, 2022, 307(Pt 2), 135929).

Microfluidics

Microfluidics for antibiotic susceptibility testing. The rise of antibiotic resistance is a threat to global health. Rapid and comprehensive analysis of infectious strains is critical to reducing the global use of antibiotics, as informed antibiotic use could slow down the emergence of resistant strains worldwide. Multiple platforms for antibiotic susceptibility testing (AST) have been developed with the use of microfluidic solutions. Here Postek et al describe microfluidic systems that have been proposed to aid AST. The authors identify the key contributions in overcoming outstanding challenges associated with the required degree of multiplexing, reduction of detection time, scalability, ease of use, and capacity for commercialization. Postek et al introduce the reader to microfluidics in general, and the authors analyze the challenges and opportunities related to the field of microfluidic AST (Postek, W. et al, *Lab Chip*, 2022, 22(19), 3637-3662).

Microfluidics in smart packaging of foods. The increasing trend in ensuring safe and quality foods necessitates the monitoring of food

products throughout the food supply chain. Food packaging is an indispensable process as it provides various functions such as containment, protection, convenience, and communication. The development of innovative packaging systems is required to ensure foods are micro-biologically, chemically, and physically safe for consumption. In recent years, smart food packaging technologies namely intelligent and active packaging methods have become popular in the food packaging industry. However, in many cases, these smart packaging systems have not been adopted for large commercial-scale production. Development of rapid, sensitive, portable, user-friendly, and cost-effective food safety and quality analytical devices are required to meet both consumer and regulatory demands. Microfluidic technology has become a powerful tool as an alternative method to conventional laboratory-based analytical systems. The applications of microfluidic techniques in monitoring the safety and quality of a packaged food product are promising and rapidly advancing. Several studies have exhibited the development of microfluidic devices for smart food packaging such as time-temperature indicators, critical temperature indicators, food microorganism sensors, food quality detectors, and active food packaging. The future of food packaging lies in smart packaging technology which can function more than just protection and containment. This review focuses on the basic concepts of microfluidic technology and its application on intelligent and active packaging of food products and crystal ball gazing the future perspectives of this technology in food industry (Jolvis Pou, K. R. et al, Food Res Int., 2022, 161, 111873).

Microfluidics for neuronal cell and circuit engineering. The widespread adoption of microfluidic devices among the neuroscience and neurobiology communities has enabled addressing a broad range of questions at the molecular, cellular, circuit, and system levels. Here, Habibey et al review biomedical engineering approaches that harness the power of microfluidics for bottom-up generation of neuronal cell types and for the assembly and analysis of neural circuits. Microfluidics-based approaches are instrumental to generate the knowledge necessary for the derivation of diverse neuronal cell types from human pluripotent stem cells, as they enable the isolation and subsequent examination of individual neurons of interest. Moreover, microfluidic devices allow to engineer neural circuits with specific orientations and directionality by providing control over neuronal cell polarity and permitting the isolation of axons in individual microchannels. Similarly, the use of microfluidic chips enables the construction not only of 2D but also of 3D brain, retinal, and peripheral nervous system model circuits. Such brain-on-a-chip and organoid-on-a-chip technologies are promising platforms for studying these organs as they closely recapitulate some aspects of in vivo biological processes. Microfluidic 3D neuronal models, together with 2D in vitro systems, are widely used in many applications ranging from drug development and toxicology studies to neurological disease modeling and personalized medicine. Altogether, microfluidics provide researchers with powerful systems that complement and partially replace animal models (Habibey, R, et al, Chem. Rev, 2022, 122(18), 14842-14880).

Surface behaviors of droplet manipulation in microfluidics devices. In recent years, the rapid development of microfluidic technology has caused a revolutionary impact in the fields of chemistry, medicine, and life sciences. Also, droplet control is one of the most important technologies in the field of microfluidics. In order to achieve different degrees of droplet transport, the dynamic balance of the competing processes of droplet driving force and fluid resistance should be controlled to achieve good selectivity of droplet transport. Here, the authors focus on the principles of droplet transport in microfluidic devices, including the driving forces for droplet transport in fluids and the effects of transport properties on droplet transport. After that, the effects of external fields on the directional transport of droplets and the advantages and disadvantages of each external field in droplet transport are discussed in detail. Finally, the applications and challenges of droplet microfluidics in chemical, biomedical, and mechanical systems are comprehensively introduced (Wu, L. et al. Adv Colloid Interface Sci, 2022, 308, 102770).

Advances in single cell biology

Single-cell RNA sequencing technologies and applications: a brief overview. Single-cell RNA sequencing (scRNA-seq) technology has become the state-of-the-art approach for unravelling the heterogeneity and complexity of RNA transcripts within individual cells, as well as revealing the composition of different cell types and functions within highly organized tissues/organs/organisms. Since its first discovery in 2009, studies based on scRNA-seq provide massive information across different fields making exciting new discoveries in better understanding the composition and interaction of cells within humans, model animals and plants. In this review, Jovic et al provide a concise overview about the scRNA-seq technology, experimental and computational procedures for transforming the biological and molecular processes into computational and statistical data. The authors also provide an explanation of the key technological steps in implementing the technology. The authors highlight a few examples on how scRNA-seq can provide unique information for better understanding health and diseases. One important application of the scRNA-seq technology is to build a better and high-resolution catalogue of cells in all living organism, commonly known as atlas, which is key resource to better understand and provide a solution in treating diseases. While great promises have been demonstrated with the technology in all areas, the authors further highlight a few remaining challenges to be overcome and its great potentials in transforming current protocols in disease diagnosis and treatment (Jovic, D. et al, Clin Transl Med, 2022, 12(3):e694).

Single-cell sequencing technologies in precision oncology. Single-cell sequencing technologies are revolutionizing cancer research and are poised to become the standard for translational cancer studies. Rapidly decreasing costs and increasing throughput and resolution are paving the way for the adoption of single-cell technologies in clinical settings for personalized medicine applications. In this chapter, Melnekoff and Lagana review the state of the art of single-cell DNA and RNA sequencing technologies, the computational tools to analyze the data, and their potential application to precision oncology. The authors also discuss the advantages of single-cell over bulk sequencing for the dissection of intra-tumor heterogeneity and the characterization of subclonal cell populations, the implementation of targeted drug repurposing approaches, and describe advanced methodologies for multi-omics data integration and to assess cell signaling at single-cell resolution (Melnekoff, D. T. and Lagana, A. Adv. Exp. Med. Biol., 2022, 1361, 269-282).

Advancement of single-cell sequencing in medulloblastoma. Single-cell sequencing is a promising attempt to investigate the genomic, transcriptomic, and multiomic level of individual cell in the larger population of cells. The outward evolution of the technique from a manual method to the automation of single-cell sequencing is cogent. Lately, single-cell sequencing is widely used in various fields of science and has applications in neurobiology, immunity, cancer, microbiology, reproduction, and digestion. This chapter introduces the reader to the details of single-cell sequencing, currently used in several small-scale and commercial platforms. The advancement of single-cell sequencing in brain cancer sheds light on questions unanswered so far in the field of oncology (Verma, D. et al, Methods Mol Biol, 2022, 2423, 65-83).

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