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From the Literature

Life sciences discovery and technology highlights

Laboratory automation and high-throughput biology

High-throughput platforms for microextraction techniques. The proposal of high-throughput platforms in microextraction-based approaches is important to offer sustainable and efficient tools in analytical chemistry. Particularly, automated configurations exhibit enormous potential because they provide accurate and precise results in addition to less analyst intervention. Recently, significant achievements have been obtained in proposing affordable platforms for microextraction techniques capable of being integrated with different analytical instrumentations. Considering the evolution of these approaches, this article describes innovative high-throughput platforms that have recently been proposed for the analysis of varied matrices, with special attention to laboratory-made devices. Additionally, some challenges, opportunities, and trends regarding these experimental workflows are pointed out (Merib, J. Anal Bioanal Chem, 2023, doi: 10.1007/s00216-022-04504-7).

Advances in high-throughput mass spectrometry in drug discovery. High-throughput (HT) screening drug discovery, during which thousands or millions of compounds are screened, remains the key methodology for identifying active chemical matter in early drug discovery pipelines. Recent technological developments in mass spectrometry (MS) and automation have revolutionized the application of MS for use in HT screens. These methods allow the targeting of unlabelled biomolecules in HT assays, thereby expanding the breadth of targets for which HT assays can be developed compared to traditional approaches. Moreover, these label-free MS assays are often cheaper, faster, and more physiologically relevant than competing assay technologies. In this review, Duenas et al describe current MS techniques used in drug discovery and explain their advantages and disadvantages. The authors highlight the power of mass spectrometry in label-free in vitro assays, and its application for setting up multiplexed cellular phenotypic assays, providing an exciting new tool for screening compounds in cell lines, and even primary cells. Finally, the authors give an outlook on how technological advances will increase the future use and the capabilities of mass spectrometry in drug discovery (Duenas, M.E et al, EMBO Mol Med, 2023, 15(1), e14850).

Automation of hematopoietic cell transplant outcomes reporting leads to dramatic reduction of errors reported to real-world data registry

Background: Institutions that perform hematopoietic cell transplant (HCT) are required by law to report standardized, structured data on transplant outcomes. A key post-transplant outcome is engraftment, the length of time between HCT infusion and reemergence of circulating neutrophils and platelets. At their center, Anderson et al found manual chart abstraction for engraftment data was highly error-prone.

Objectives: The authors developed a custom R/Shiny application that automatically calculates engraftment dates and displays them in an intuitive format to augment the manual chart review. The authors' hypothesis was that use of the application to assist with calculating and reporting engraftment dates would be associated with a decreased error rate.

Study design: The study was conducted at a single tertiary care institution. The application was developed in a collaborative, multidisciplinary fashion by members of an embedded cellular therapy informatics team. Retrospective validation of the application's accuracy was conducted on all malignant HCTs from 2/2016 to 12/2020 (n=198). Real-world use of the application was evaluated prospectively from 4/2021 through 4/2022 (n=53). Welch's two-sample t-tests were performed to compare error rates pre- and post-implementation. Data were visualized using p charts and standard special cause variation rules were applied.

Results: Accuracy of reported data post-deployment increased dramatically: engraftment error rate decreased from 15% to 3.8% (p=0.003) for neutrophils and from 28% to 1.9% (p<0.001) for platelets.

Conclusion: This study demonstrated the effective deployment of a custom R/Shiny application that was associated with significantly reduced error rates in HCT engraftment reporting for operational, research, and regulatory purposes. Users reported subjective satisfaction with the application and that it addressed difficulties with the legacy manual process. Identifying and correcting erroneous data in engraftment reporting could lead to a more efficient and accurate nationwide assessment of transplant success. Furthermore, the authors show that it is possible and practical for academic medical centers to stand up embedded informatics teams that can quickly build applications for clinical operations in a manner compliant with regulatory requirements (Anderson, D. S. et al, Transplant Cell Ther, 2023, 29(3), 207.e1-207.e5).

MicroFPGA: An affordable FPGA platform for microscope control. Modern microscopy relies increasingly on microscope automation to improve throughput, ensure reproducibility or observe rare events. Automation requires computer control of the important elements of the microscope. Furthermore, optical elements that are usually fixed or manually movable can be placed on electronically-controllable elements. In most cases, a central electronics board is necessary to generate the control signals they require and to communicate with the computer. For such tasks, Arduino microcontrollers are widely used due to their low cost and programming entry barrier. However, they are limiting in their performance for applications that require high-speed or multiple paral-

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lel processes. Field programmable gate arrays (FPGA) are the perfect technology for high-speed microscope control, as they are capable of processing signals in parallel and with high temporal precision. While plummeting prices made the technology available to consumers, a major hurdle remaining is the complex languages used to configure them. In this work, Deschamps et al used an affordable FPGA, delivered with an open-source and friendly-to-use programming language, to create a versatile microscope control platform called MicroFPGA. It is capable of synchronously triggering cameras and multiple lasers following complex patterns, as well as generating various signals used to control microscope elements such as filter wheels, servomotor stages, flip-mirrors, laser power or acousto-optic modulators. MicroFPGA is open-source and the authors provide online Micro-Manager, Java, Python and LabVIEW libraries, together with blueprints and tutorials (Deschamps, J. et al, HardwareX, 2023, doi: 10.1016/j.ohx.2023.e00407).

Microfluidics

Modular microfluidics for life sciences. The advancement of microfluidics has enabled numerous discoveries and technologies in life sciences. However, due to the lack of industry standards and configurability, the design and fabrication of microfluidic devices require highly skilled technicians. The diversity of microfluidic devices discourages biologists and chemists from applying this technique in their laboratories. Modular microfluidics, which integrates the standardized microfluidic modules into a whole, complex platform, brings the capability of configurability to conventional microfluidics. The exciting features, including portability, on-site deployability, and high customization motivate us to review the state-of-the-art modular microfluidics and discuss future perspectives. In this review, Wu et al first introduce the working mechanisms of the basic microfluidic modules and evaluate their feasibility as modular microfluidic components. Next, the authors explain the connection approaches among these microfluidic modules, and summarize the advantages of modular microfluidics over integrated microfluidics in biological applications. Finally, the authors discuss the challenge and future perspectives of modular microfluidics (Wu, J. et al, J. Nanobiotechnology, 2023, 21(1), 85).

Digital microfluidics for biological analysis and applications. Digital microfluidics (DMF) is an emerging liquid-handling technology based on arrays of microelectrodes for the precise manipulation of discrete droplets. DMF offers the benefits of automation, addressability, integration and dynamic configuration ability, and provides enclosed picoliter-to-microliter reaction space, making it suitable for lab-on-a-chip biological analysis and applications that require high integration and intricate processes. A review of DMF bioassays with a special emphasis on those actuated by electrowetting on dielectric (EWOD) force is presented here. Firstly, a brief introduction is presented on both the theory of EWOD actuation and the types of droplet motion. Subsequently, a comprehensive overview of DMF-based biological analysis and applications, including nucleic acid, protein, immunoreaction and cell assays, is provided. Finally, a discussion on the strengths, challenges, and potential applications and perspectives in this field is presented (Xu, X. et al, Lab Chip, 2023, 23(5), 1169-1191).

Microfluidic-based blood immunoassays. Microfluidics enables the integration of whole protocols performed in a laboratory, including sample loading, reaction, extraction, and measurement steps on a single system, which offers significant advantages thanks to small-scale operation combined with precise fluid control. These include providing efficient transportation mechanisms and immobilization, reduced sample and reagent volumes, fast analysis and response times, lower power requirements, lower cost and disposability, improved portability and sensitivity, and greater integration and automation capability. Immunoassay is a specific bioanalytical method based on the interaction of antigens and antibodies, which is utilized to detect bacteria, viruses, proteins, and small molecules in several areas such as biopharmaceutical analysis, environmental analysis, food safety, and clinical diagnostics. Because of the advantages of both techniques, the combination of immunoassays and microfluidic technology is considered one of the most potential biosensor systems for blood samples. This review presents the current progress and important developments in microfluidic-based blood immunoassays. After providing several basic information about blood analysis, immunoassays, and microfluidics, the review points out in-depth information about microfluidic platforms, detection techniques, and commercial microfluidic blood immunoassay platforms. In conclusion, some thoughts and future perspectives are provided (Torul, H. et al, 2023, J Pharm Biomed Anal, 228, 115313).

Advances in gene editing

Microfluidics: the propellant of CRISPR-based nucleic acid detection. Since the discovery of collateral cleavage activity, clustered regularly interspaced short palindromic repeats (CRISPR)/Cas systems have become the new generation of nucleic acid detection tools. However, their widespread application remains limited. A pre-amplification step is required to improve the sensitivity of CRISPR systems, complicating the operating procedure and limiting quantitative precision. In addition, nonspecific collateral cleavage activity makes it difficult to realize multiplex detection in a one-pot CRISPR reaction with a single Cas protein. Microfluidics, which can transfer nucleic acid analysis process to a chip, has the advantages of miniaturization, integration, and automation. Microfluidics coupled with CRISPR systems improves the detection ability of CRISPR, enabling fast, high-throughput, integrated, multiplex, and digital detection, which results in the further popularization of CRISPR for a range of scenarios (Chen, Y, et al, 2023, Trends Biotechnol, 41(4), 557-574).

CRISPR technology: A decade of genome editing is only the beginning. The advent of clustered regularly interspaced short palindromic repeat (CRISPR) genome editing, coupled with advances in computing and imaging capabilities, has initiated a new era in which genetic diseases and individual disease susceptibilities are both predictable and actionable. Likewise, genes responsible for plant traits can be identified and altered quickly, transforming the pace of agricultural research and plant breeding. In this Review, Wang and Dounda discuss the current state of CRISPR-mediated genetic manipulation in human cells, animals, and plants along with relevant successes and challenges and present a roadmap for the future of this technology (Wang, J. Y and Dounda, J. A. 2023, Science, 379(6629), eadd8643).

CRISPR-Based Diagnostics: Challenges and Potential Solutions toward Point-of-Care Applications. The COVID-19 pandemic has challenged the conventional diagnostic field and revealed the need for decentralized Point of Care (POC) solutions. Although nucleic acid testing is considered to be the most sensitive and specific disease detection method, conventional testing platforms are expensive, confined to central laboratories, and are not deployable in low-resource settings. CRISPR-based diagnostics have emerged as promising tools capable of revolutionizing the field of molecular diagnostics. These platforms are inexpensive, simple, and do not require the use of special instrumentation, suggesting they could democratize access to disease diagnostics. However, there are several obstacles to the use of the current platforms for POC applications, including difficulties in sample processing and stability. In this review, Ghouneimy et al discuss key advancements in the field, with an emphasis on the challenges of sample processing, stability, multiplexing, amplification-free detection, signal interpretation, and process automation. The authors also discuss potential solutions for revolutionizing CRISPR-based diagnostics toward sample-to-answer diagnostic solutions for POC and home use (Ghouneimy, A. et al, 2023, ACS Synth Biol, 12(1), 1-16).

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Literature Highlights Column: From the Literature

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