From the bench to the hand: Point of need/point of care technologies and analytical assays for field testing and medical diagnostics

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Two decades ago, a problem echoed by many individuals and authorities was the complexity of chemical and biochemical analysis that typically necessitated well-equipped laboratories and trained personnel able to undertake complex sample pre-treatment procedures and operate specialized and expensive instrumentation. This problem instigated a trend toward the development of low cost, simple, and expedient analytical tools that are easy to apply even with minimal experience or training, can be performed with minimum resources or limited infrastructure and offer fast, robust, and reliable results. Ideally, these assays should also be portable or easily transported at the point-of-interest without loss of function. Such stand-alone platforms offered a new alternative to the mainstream laboratory-based analytical technologies in providing qualitative and quantitative information even to non-expert users in resource limited areas.

The transition of analytical science from the bench to the field required an interdisciplinary approach through the merging of different principles and technologies. Micro- and nanomaterials have played a crucial role in this endeavor enabling the development of new sensing methods and their integration into micro-devices that are able to operate almost autonomously or with minimum user intervention and perform a series of simple and more complex operations. Nowadays, this transition is more than evident not only in the literature but also in everyday life and a large variety of analytical assays and tools for attesting the presence of analytes of human and industrial interest are continually developed.

In the Topical Collection “From the bench to the hand: Point of need/point of care technologies and analytical assays for field testing and medical diagnostics” we aimed at capturing the latest evolvements in the field by gathering innovative works that illustrate the exciting possibilities of point-of-need and point-of-care analytical technologies. All the articles can be accessed via this link: https://link.springer.com/collections/afghbefiej.

A review article by Zhang and co-workers outlines how functional nucleic acid (FNA) technology can achieve effective COVID-19 diagnosis by using in vitro selection of FNA to overcome receptor design barriers, combining FNA with multiple DNA signal amplification strategies to improve sensitivity, and interfacing FNA with portable analyzers to overcome signal readout barriers. The discussion highlights the major scientific barriers for the point-of-care diagnosis of COVID-19 and provides fundamental insights into FNAs and technical features for molecular engineering of FNAs, comprising aptamers and NAES, in order to overcome these barriers combined with diverse signaling tactics (electrochemistry, fluorescence, SERS, thermal conductivity, etc).

The versatility of point-of-care systems was well demonstrated in two studies focusing on SARS-CoV-2 detection. The first work by Hang Tng et al. reported a saliva antigen rapid test (AP-ART) that was based on multimodal viral capture using both S-specific polyclonal antibodies and recombinant human ACE2 at the test line and signal enhancement using linker-free, signal amplification gold nanoparticles introduced via a parallel flow channel. Mobile phone photography and an image processing algorithm was applied to obtain semi-quantitative measurements rather than subjective interpretation of test signal by the naked-eye. Through clinical testing, the proposed AP-ART demonstrated a sensitivity of 97%, approaching that of the gold standard RT-PCR testing in the detection of SARS-CoV-2, and a limit of detection of 0.0064 ng·mL–1, which is one order of magnitude lower than existing dual gold amplification techniques.

A paper-based dot-blot immunofluorescence bioassay for SARS-CoV-2 detection was reported by Celiker et al. The assay employs a novel graft fluorescent
polypyrene-g-poly(ε-caprolactone) (PPy-g-PCL) copolymer conjugated to SARS-CoV-2-specific antibodies using EDC/NHS chemistry. The system is based on a sandwich-type immunoassay with antibodies immobilized over the nitrocellulose membrane followed by the sample for detection and then another addition of an antibody-PPy-g-PCL conjugate for revelation. The membranes were then photographed under UV light to develop the fluorescence related to the presence of the target virus. The proposed sensor showed a limit of detection (LOD) of < 2 LOG viral copy mL−1 and an overall correct response of 93.33% between positive and negative samples. Importantly, the assay demonstrated a high correlation with RT-PCR data.

A colorimetric lateral flow assay (LFA) combined with dye-loaded polymersomes was reported by Moulahoum et al. to detect cannabinoids in saliva. Two LFA’s (sandwich and competitive) using rhodamine B–loaded polymersomes conjugated to antibodies were developed, showing a high level of sensitivity (LODs of 0.53 and 0.31 ng/mL, respectively) and good precision (below 6%). The application of the LFA’s over spiked synthetic saliva or real human saliva demonstrated an overall response of 94% for the sandwich assay and 97% for the competitive LFA.

Damodara et al. demonstrated a low-cost device for the rapid measurement of cell-free DNA (cfDNA) in plasma as a biomarker for sepsis. The device consisted of a silicon tube containing three intertwined polyester fibers and a portable fluorescence imaging setup for measuring the change in fluorescence intensity due to the binding of a fluorescent dye with cfDNA. This configuration enabled not only the storage of the fluorescent dye as a reporter probe but also alleviated the need for sample preparation, external aliquoting and dispensing of reagents, preconcentration, and external mixing while reduced the cost of detection. Importantly, the device offered sufficient resolution to discriminate between survivors (~1 μg/mL cfDNA) and non-survivors (> 4 μg/mL cfDNA) of sepsis, offering a valuable tool to measure cfDNA at the bedside and facilitate its use as a prognostic biomarker for sepsis.

Banga et al. reported a novel electrochemical sensor for the detection of isoprene, using a ZIF-based electrochemical nose. The sensing element incorporated a bifunctional nanocomposite composed of gold nanoparticles encapsulated inside the cavity of ZIF-8 that was used to from a thin film on the surface of the working electrode. Chronoamperometry was then used as the transduction mechanism to monitor the diffusion kinetics of isoprene across the electrode–electrolyte interface. This bifunctional probe, which is referred to as AuNP@ZeNose (ZIF-based electrochemical nose), was used for prototyping a handheld device for non-invasive flu detection by measuring the levels of isoprene in breath. The AuNP@ZeNose could determine isoprene concentrations in breath as low as 10 ppb, which is the threshold level to discriminate flu viral load in healthy and infected individuals.

The versatility and improved fabrication capabilities of 3D printing methods were used to design portable micro-devices for the point-of-care determination of various biomarkers. Costa et al. used 3D printing to fabricate laser-induced graphene (LIG) electrodes from commercial polyimide for portable electrochemical sensing. Using these electrodes, the authors successfully demonstrated the simultaneous voltammetric determination of uric acid and nitrite in biological fluids by differential pulse voltammetry in microvolume sample aliquots. The amperometric determination of the antibiotic ciprofloxacin (CIP) in milk using a single LIG working electrode associated with a 3D-printed portable batch-injection analysis (BIA) cell was also presented. The construction of miniaturized LIG electrodes through a simple, fast (single step), and low-cost approach facilitates the construction of portable electrochemical sensors opening many opportunities for applications in the quality control of complex samples in the field and for the fabrication of wearable biosensing platforms.

Another paradigm of the great capabilities offered by 3D printing technology was given by Esana et al., who developed an automated, pressure-driven injection microfluidic system for microchip electrophoresis (μCE) of preterm birth (PTB)-related peptides and proteins. Using fluorescently labeled PTB biomarkers and laser excitation at 532 nm, the LODs for two PTB biomarkers were 400 pM and 15 nM, which is better than previous methods.

Paper-based analytical devices (PADs) are one of the most popular templates for developing portable micro-analytical devices and toolkits for providing modern analytical testing in resource-limited conditions, remote locations, or occasions of infrastructure shortfalls. A newly developed 3D microfluidic (μ)PAD that utilized for the first-time hydride generation on a paper-based platform was used by Bonacci et al. for the speciation of inorganic arsenic in water samples. The determination was accomplished by using sodium borohydride in the device’s sample zone in order to reduce As(III) or both As(III) and As(V) (i.e., total inorganic As) and generate arsine that then diffused across a hydrophobic porous polytetrafluoroethylene membrane into a detection zone where it reduced Au(III) to Au nanoparticles. This resulted in a colorimetric change that could be related to the concentration of As(III) or total inorganic As concentration. The 3D μPAD is a disposable low-cost and user-friendly device which, under optimal conditions, can accomplish the relatively fast speciation of inorganic As in agricultural waters and waters from the mining industry, where elevated concentrations of As are not uncommon.

An electrochemical paper-based analytical device (ePAD) fabricated in a commercial ink plotter by hydrophobic ink-drawing was reported by Soulis et al. for the determination
of trace Pb(II) and Cd(II) by differential pulse anodic stripping voltammetry, on a bismuth modified electrode. The analysis involved the addition of a drop of sample spiked with Bi(III) onto the test area of the device; as the sample flowed toward the electrodes, bismuth and the target metals deposited simultaneously on the working electrode. Finally, the deposited metals were stripped off the bismuth coated working electrode by applying an anodic potential scan and the response was recorded. The LODs for both metals were in the low μg L⁻¹ level, which is sufficient for detecting the presence of target metals in environmental and food samples.

Overall, the ten articles compiled within this Topical Collection provide an overview of the latest evolvements in analytical technologies that enable the transition from central, large-scale, laboratory facilities to decentralized, user-friendly, portable, instrumentation-free, and low-cost analytical tools.

**Declarations**

**Conflict of interest** The authors declare no competing interests.

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