Analytical and Bioanalytical Chemistry
https://doi.org/10.1007/s00216-022-03987-8

EDITORIAL

Point-of-care testing—new horizons for cross-sectional technologies and decentralized application strategies

Oliver Hayden[1] · Peter B. Luppa[2] · Junhong Min[3]

Accepted: 22 February 2022
© The Author(s) 2022

Near-patient biochemical testing, also called point-of-care testing (POCT), enables healthcare professionals and caregivers to perform rapid clinical laboratory testing in close proximity to the patient or directly at the patient's side. POCT also allows patients to perform self-monitoring in chronic disease states. In both cases, predictive biomarkers for clinical decision-making or self-management of for instance diabetes or antithrombotic therapies are of pivotal importance. Because delays are no longer caused by clinical sample preparation, transport, or central laboratory analysis, innumerable clinical applications are possible that shorten the clinical decision-making time with implications for additional testing or therapy. Even though the field of omics increases our understanding of cellular mechanisms exponentially, only a few new diagnostic biomarkers were identified in the last two decades with clinical impact usually due to a lack of therapy options. On the other hand, new biomarkers can be important drivers for therapeutic research and preventive medicine.

Published in the topical collection *Point-of-Care Testing* with guest editors Oliver Hayden, Peter B. Luppa, and Junhong Min.

✉ Oliver Hayden
oliver.hayden@tum.de

Peter B. Luppa
p.luppa@tum.de

Junhong Min
junmin@cau.ac.kr

[1] Heinz-Nixdorf-Chair of Biomedical Electronics, Department of Electrical and Computer Engineering, TranslaTUM, Campus Klinikum rechts der Isar, Bau 522, Einsteinstraße 25, 81675 München, Germany

[2] Institute of Clinical Chemistry and Pathobiochemistry, Klinikum Rechts Der Isar, TU München, Ismaninger Str. 22, 81675 München, Germany

[3] Department of Biomedical Engineering, School of Integrative Engineering, Chung-Ang University, 84 Heukseok-ro Dongak-gu, 06974 Seoul, South Korea

POCT has been seen as a disruptive technology already for several years. Novel transducer technologies, miniaturization, multiplexing, and smartphone-derived IT tools nowadays enable test results to be viewed within minutes. Thus, clinical chemistry analysis moves away from centralized laboratories to near-patient diagnostics, whenever there is an advantage for clinical decision-making. In particular, for patients suffering from chronic disease or at the intensive-care unit, POCT is an opportunity for personalization of treatments. Here, continuous monitoring modality is the noble clinical goal for the near future! Already today, continuous glucose monitoring (CGM) is widespread and beneficial in the millionfold use.

The analytical approaches, described in three papers of this topical collection (O´Connell, Tombelli and Lefter) and linked to this topic, go far beyond the one-dimensional measurements of interstitial glucose concentrations that today's CGM devices are able to perform. An easy-to-install permanent intravascular microdialysis catheter is the key to a continuous measuring mode! O'Connell and Krejci describe the theoretical background and capabilities of microdialysis techniques in biochemical analytics. In vivo measurements, performed by the use of microdialysis catheters, are subject to dynamic changes due to mass transfer and provide valuable information about the patient's physiological state. Tombelli et al. offer a fascinating view of a future continuous monitoring of therapeutic drug (TDM) blood levels. TDM–related immunoassays are performed at the surface of a sophisticated disposable plastic chip in conjunction with bioconjugated submicrometric fluorescent magnetic particles. And finally, Lefter et al. presents a novel, tunable electrochemical sensor for wearable continuous, multi-metabolite monitoring. The multi-analyte sensing platform utilizes gold and platinum surfaces allowing fully reversible and stable sensing of different redox species in solution with superior analyte selectivity.

In addition to continuous measurements, POCT has the potential to support acute care diagnostics. Electrochemical

Published online: 10 March 2022

sensing was employed by Yagati et al. to detect thrombin in clinical samples directly. The indium tin oxide (ITO) electrode with polypyrrole and palladium was synthesized, and liposomes encapsulating $K_4[Fe(CN)_6]$ as labeling agent were introduced to maximize the signal corresponding to thrombin from a human serum sample. This aptamer-based electrochemical biosensor showed quantitative measurement for the linear segment (dynamic range, 0.1–1000 nM) of thrombin in serum with an LOQ of 1.1 pM and an LOD of 0.3 pM.

Less acute but of relevance for newborn development are the oligosaccharide diagnostics of breast milk discussed by Chung et al. Using impedimetric biosensing, a handheld device is reported, which allows determining the content of 2′-fucosyllactose with implications for infant health and development. The authors correlated impressively the lectin sensor accuracy for 2′-fucosyllactose with HPLC using banked milk samples for validation in a blinded study. Increased analytical sensitivity and new materials for reagents are not only necessary for electrochemical sensing tools but also important topics for novel lateral flow assay (LFA)–type platforms. Rink et al. discussed the commercially available fine-tuned liposomes (350 nm) containing sulforhodamine B (SRB) to detect interleukin 6 (IL-6) from human serum using the photometric LFA format. The newly designed liposomes with a high encapsulating load (150 mmol L^{-1} SRB) easily outperformed normal gold nanoparticles in photometric LFAs (LOD 7 pg mL^{-1}) with an extraordinary shelf life of over 1 year at ambient temperature and up to 8 years under a liquid-phase storage condition.

The analytical sensitivity could be also dramatically increased by combining LFA with nucleic acid amplification methods. Agarwal et al. focused loop mediated isothermal amplification (LAMP) combined with LFA–formatted POCT for SARS-CoV-2 N-gene detection in clinical swab–extracted RNA samples. The LAMP protocol was newly designed with the biotinylated dUTP and FITC–labeled primer to incorporate in a lateral flow strip sensor (control line with anti-IgG and test line with streptavidin) with an anti-FITC antibody–coated gold nanoparticle. The authors validated this isothermal nucleic acid amplification–combined POC LFA with 82 SARS-CoV-2–positive RNA samples and showed impressive accuracy of 81.66% with an LOD as low as C_t of 33 in RT-PCR. With cerium oxide nanoparticles which possess outstanding oxidation activities for organic molecules, Kong et al. achieved a simple yet elegant colorimetic C-reactive protein LFA without requiring an oxidizing agent or a reader with an LOD ~ 100 ng mL^{-1} in human serum. This platform idea with a robust reagent solution could increase the shelf life of LFA as it does not depend on H_2O_2 storage and a turnaround-time of 3 min was reported, which outperformed conventional LFA with an Au-NP readout.

Instead, advanced Au nanostructures used by Kim et al. show improved surface-enhanced Raman spectroscopy (SERS) conditions to detect C-reactive protein (CRP). SERS probes were synthesized with target-specific DNA complex conjugated with porous gold nanoplates (pAuNPs) consisting of methylene blue (as labeling probe) and target-specific aptamer-coated Au-Te nanostructures (as capture probe) on ITO substrates. With this nanomaterial-supported biosensing approach, a CRP LOD of 3.11 pM is reported in diluted clinical serum samples. By advancing the LFA format to the third dimension, a microfluidic-based biosensing approach was developed for a pump-free workflow integration and still accurate biomarker measurements.

Lee et al. proposed a three-dimensional paper-based microfluidic analytical device (3D-μPAD) capable of sophisticated multi-step reactions required for ELISA. The 3D-μPAD sensor was used to detect the breast cancer biomarker thioredoxin-1 in clinical human serum samples, and the precision of the device was validated with conventional ELISA. Despite integration, any progress for POCT also depends on the standardization of already-established measurements. There is a lot of catching up to do here. Consequently, DuBois et al. thankfully focus on their international study on the standardization of one of the oldest and still indispensable clinical chemistry parameter: creatinine in serum. This analyte allows the early identification of chronic kidney disease, a major global public health problem. Lastly, field testing of the POCT is required for clinical acceptance and a future innovation step, which was performed by clinicians around Wechselberger. With an optical immunoassay based on a smart microfluidic solution in close proximity to the photodetector, fast binding kinetics and high quantum yields are achieved, which allowed anti-SARS-CoV-2 IgG testing in the population of Austria and demonstrating POC opportunities for pandemic monitoring.

In the not-too-distant future, we expect to be able to check our individual health status with a simple act, such as checking the time. The perfect storm COVID-19 already demonstrates the impact of POCT to manage the countermeasures of societies. For hospital POCT, the notion of conventional and POCT laboratory services residing within the same health facility seems contradictory, but these two are, in fact, complementary. Together, POCT and the central laboratory are pivotal in covering the demands of diagnostic processes. This topical collection of ABC bears witness to the creative solutions this field offers.

Funding Open Access funding enabled and organized by Projekt DEAL.

Open Access This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long

as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by/4.0/.

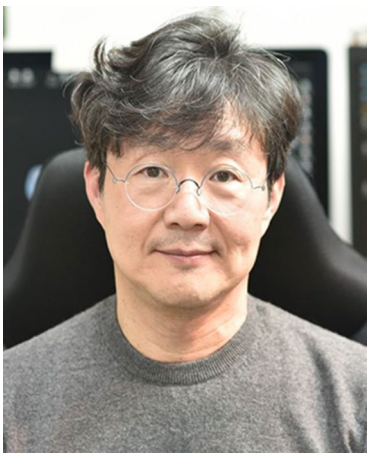
Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.



Oliver Hayden conducts research aimed at the development of innovative ways of using in vitro and in vivo diagnostic techniques to improve clinical and decentralized healthcare workflows. His interdisciplinary research activities draw on the fields of electronics, optics, microfluidics, and materials sciences. He studied biochemistry at the University of Vienna and completed his doctorate there in 1999. After holding a postdoctoral position at Harvard University and completing his postdoctoral teaching qualification in analytical chemistry at the University of Vienna, he joined the IBM Research Laboratory in Zürich in 2005. Since 2007, he has been researching organic electronic techniques for medical imaging and diagnostics at Siemens Corporate Technology and Siemens Healthineers. In 2017, he was appointed to the Heinz-Nixdorf-Chair of Biomedical Electronics located at the TranslaTUM of TU Munich, where he is working on POCT applications with clinicians at the campus of Klinikum München Rechts der Isar.



Peter B. Luppa MD, is a clinical pathologist currently heading the core clinical chemistry laboratory of the Institute of Clinical Chemistry and Pathobiochemistry at the University Hospital Rechts der Isar, Munich, Germany. He also runs a research laboratory for optical biosensor developments. He specialized in clinical pathology as Senior Fellow at the Institute of Clinical Chemistry and Pathobiochemistry, before becoming Associate Professor at the Technical University of Munich. His research interests span steroid biochemistry, surface plasmon resonance sensorics in autoantibody detection, and point-of-care testing (POCT) technologies. He is editor of the first German textbook on POCT (3rd German and 1st English edition 2018) and founder of the biannually organized international "Munich POCT Symposium." As chair of the POCT division within the German Society for Clinical Chemistry, he is particularly interested in the implementation of POCT procedures in extended clinical application areas.



Junhong Min conducts research in advanced biotechnology and biochemical engineering with a focus on microfluidic biosensing devices for in situ detection of biomarkers and pathogens in clinical and environmental samples through novel sample preparation, electrochemical biosensor design, and nanomaterial application. In 1998, he received his PhD from Sogang University in Seoul and was a postdoctoral fellow at Cornell University in 2000. He worked for a start-up company in the USA before becoming a project leader in Samsung Group (South Korea, 2003–2007). He is currently working as Professor in the Department of Biomedical Engineering at Chung-Ang University in Seoul, South Korea.