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Editorial

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Intelligent biosensing and point-of-care testing: from molecular recognition to decentralized precision care

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Point-of-care testing (POCT) is changing the way diagnostic information is generated, interpreted, and used. Its value extends well beyond shortening turnaround time. A meaningful POCT result should support a defined clinical or public-health action, such as early triage, treatment selection, disease surveillance, referral, or longitudinal follow-up. In this sense, POCT is best understood as a distributed extension of laboratory medicine rather than a simplified replacement for the central laboratory (Banfi et al., 2024; Plebani et al., 2025).

The need for decentralized testing is becoming increasingly apparent. Diagnostic demand continues to rise everywhere, while specialized instruments, laboratory expertise, and confirmatory capacity remain concentrated in major hospitals. Patients in community settings may face delayed diagnosis, repeated travel, or empirical treatment. Similar gaps exist in food safety, environmental monitoring, and outbreak control, where decisions must often be made before samples can reach a centralized laboratory. However, moving a test closer to the user introduces its own set of challenges related to sampling, reagent storage, operator variation, data transfer, quality assurance, and clinical interpretation. The development of POCT therefore requires a balance between analytical innovation and real-world reliability.

This special issue on "Intelligent Biosensing and Point-of-Care Testing (POCT)" brings together eight articles that cover material-enhanced lateral flow assays, one-pot nucleic acid testing, bacterial pathogen detection, functional genetic diagnostics, biomarker-based disease stratification, microphysiological models, molecular imaging, programmable DNAzyme systems, and precision neurology. These articles address different stages of the translational pathway, from molecular recognition and signal generation to algorithmic interpretation and clinical application. Together, they show that the future of POCT will be shaped not by a single device format, but by deep integration of chemistry, materials science, molecular biology, engineering, artificial intelligence (AI), and laboratory medicine.

Materials-enabled rapid tests

Lateral flow assays remain the most widely used POCT format, owing to their low cost and speed, self-contained nature, and ease of use. Yet the apparent simplicity of a test strip often conceals important limitations, including low analytical sensitivity interference from sample matrices and limited multiplexing capacity. Improvements in recognition probes, nanoparticle labels, membranes, optical readers, and signal-processing strategies have therefore become central to the evolution of lateral flow biosensors (Yetisen et al., 2013; Quesada-González and Merkoçi, 2015).

In this issue, Ding et al. (2026) illustrated the movement from open-tube molecular testing toward integrated workflows. Their one-pot TLAMP-PfAgo assay (OTPA) combines turn-back loop primer-accelerated loop-mediated isothermal amplification (LAMP) (TLAMP) with the sequence-specific cleavage

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capability of *Pyrococcus furiosus* Argonaute (PfAgo). A microcrystalline wax barrier temporally separates amplification and detection within a closed tube, reducing post-amplification manipulation and the associated risk of aerosol contamination. The platform achieved sensitive duplex identification of pork and beef DNA within 30 min and showed complete concordance with polymerase chain reaction (PCR)-based testing of commercial meat products. Its direct blue-light readout, use of short DNA guides, and compatibility with portable heating and fluorescence devices make it particularly relevant to field-based food surveillance. More broadly, this work provides an elegant example of how reaction incompatibility can be addressed through simple physical compartmentalization rather than more complex instrumentation.

Rapid pathogen detection remains another central application of decentralized testing. Zhang et al. (2026) review emerging POCT strategies for bacterial pathogens by organizing current methods around phenotypic characteristics, surface antigens, and nucleic acids. This structure is particularly useful because it links the biological target to the practical purpose of the assay. Phenotype- and antigen-based approaches can support rapid screening, whereas nucleic acid platforms are more suitable for high-specificity identification, genotyping, and resistance-related testing. The review integrates microscopy-based visualization, immunoassays, isothermal amplification, clustered regularly interspaced short palindromic repeats (CRISPR)/CRISPR-associated protein (Cas) systems, and microfluidic biosensors. It also places recent molecular approaches within the broader development of programmable biosensing (Gootenberg et al., 2017; Chen et al., 2018). Its major strength is the clear recognition that the true bottleneck in bacterial POCT is often not molecular recognition itself, but sample pretreatment, enrichment, contamination control, or workflow simplification. The review therefore provides a comprehensive and clinically relevant framework for the development of integrated bacterial testing systems.

Functional diagnostics and data-guided risk stratification

The next generation of POCT will require more than measurement of a static analyte concentration. Functional diagnostics can reveal whether a genetic variant, transporter, enzyme, or signaling pathway is biologically active, thereby providing information that is more reflective of the disease mechanism. Such approaches are especially valuable in rare-disease and precision medicine, where sequence information alone may be insufficient for clinical interpretation.

He et al. (2026) described a nonradioactive selenocystine-based fluorescence assay for functional assessment of cystine transporter variants in cystinuria. By combining a cell-based uptake assay with AlphaFold3-guided structural prediction, the study links measurable transporter function with molecular interpretation. The assay classified eight clinically characterized *SLC3A1* and *SLC7A9* variants according to residual transport activity, producing results consistent with previous radioisotope-based studies. The use of standard microplate-reader infrastructure is a notable advantage because it replaces radioactive assays with a more accessible and scalable workflow. Although not yet a bedside test, it represents a meaningful step toward diagnostic decentralization—enabling high-throughput variant interpretation, genotype-guided decisions, and the future design of simplified functional assays.

Li J et al. (2026) extend the concept of intelligent diagnostics to hepatocellular carcinoma. Their study evaluates plasma protein kinase D3 (PRKD3) as an adjunctive biomarker and integrates it with α-fetoprotein (AFP), prothrombin induced by vitamin K absence-II (PIVKA-II), routine biochemical indicators, demographic variables, and machine-learning algorithms. PRKD3 alone was insufficient for diagnosis, but its value rose substantially when combined with established markers and clinical variables. The integrated model achieved an accuracy of 0.861, sensitivity of 0.863, specificity of 0.925, and precision of 0.862 in 392 plasma samples. This work is valuable because it does not overstate the utility of a single biomarker. Instead, it demonstrates how biologically relevant markers may strengthen a multianalyte diagnostic panel. The study provides a realistic route toward future near-patient screening for high-risk liver-disease populations, while appropriately identifying the need for multicenter validation, AFP-negative subgroup analysis, and practical rapid assays for PRKD3.

Microphysiological models and multimodal precision assessment

POCT development also depends on reliable systems for validating biomarkers, probes, and therapeutic targets before they reach clinical settings. In this regard, microfluidic models and advanced imaging platforms provide an important bridge between analytical design and biological relevance.

In their review, Wang et al. (2026) cover advances in blood–brain barrier (BBB) permeability assessment, from static transwell models to dynamic microfluidic chips, organoid systems, and multimodal in vivo imaging. The review explains how fluid shear stress, cell–cell interactions, and the neurovascular microenvironment shape the physiological relevance of in vitro models. It also compares dynamic contrast-enhanced magnetic resonance imaging, positron emission tomography, near-infrared II fluorescence imaging, and two-photon microscopy for noninvasive permeability assessment. Although these approaches are not conventional POCT technologies, they provide the upstream validation framework needed for future neurological diagnostics. Their integration with AI, high-throughput barrier monitoring, and patient-specific organ-on-a-chip systems may help identify clinically meaningful biomarkers and improve the design of minimally invasive tests.

The review by Li X et al. (2026) on Parkinson's disease biomarkers complements this perspective by showing how molecular pathology, peripheral samples, digital phenotyping, and AI can converge in precision neurology. The article highlights the transition from static protein measurement toward functional detection of pathological α-synuclein seeding activity. It also discusses neurofilament light chain, genetic biomarkers, extracellular vesicles, metabolomics, neuroimaging, and digital biomarkers. Particularly valuable is the proposed deployment framework: low-cost digital or clinical indicators can be used for initial risk stratification, while peripheral or cerebrospinal-fluid molecular tests provide confirmation and longitudinal monitoring. This layered strategy is highly relevant to the future of POCT because it recognizes that decentralized screening should be connected to confirmatory testing and clinical follow-up rather than used in isolation (Parnetti et al., 2019).

Programmable nucleic-acid systems for responsive biosensing

Functional nucleic acids provide a powerful route toward intelligent biosensing because they can be programmed to recognize molecular targets and generate catalytic or fluorescent outputs. DNAzymes are particularly attractive in this context because their activity can be controlled through sequence design, metal-ion cofactors, target accessibility, and microenvironment-responsive nanocarriers (Wang et al., 2019; McConnell et al., 2021).

Luo et al. (2026) review programmable DNAzyme nanocatalysts for tumor immunometabolic modulation. The article presents DNAzymes as not only gene-silencing agents, but also responsive nanoscale biosensing modules that can detect pH, redox gradients, metal ions, and microRNA signatures. By coupling RNA cleavage with the modulation of glycolysis, oxidative stress, mitochondrial activity, and immune signaling, these systems offer a conceptual route toward biosensing-guided therapeutic intervention. The review is notable for its depth in connecting catalytic DNA chemistry with tumor immunometabolism and for its balanced discussion of unresolved translational issues such as in vivo stability, biodistribution, cofactor control, biosafety, and standardized evaluation.

Huang et al. (2026) provide an experimental example of this responsive design through a dual-functional zeolitic imidazolate framework-8 (ZIF-8) nanoplatform for the degradation of circular RNA (circRNA) cerebellar degeneration-related protein 1 antisense (*CDR1as*) and real-time monitoring of microRNA-7 (miR-7) in living cells. The acidic lysosomal environment triggers disassembly of the carrier, releases Zn^{2+} cofactors, activates DNAzyme-mediated cleavage of *CDR1as*, and produces a fluorescence signal through a miR-7-responsive molecular beacon. The major strength of this work is the direct coupling of molecular intervention with real-time signal output. Rather than relying on a separate endpoint assay, the system reports the biological consequence of its own activity. This closed-loop principle is highly relevant to the future of intelligent biosensing, even though substantial simplification, safety validation, and clinically compatible readout formats will need to be in place before translation beyond live-cell research.

Clinical integration, quality assurance, and scalable implementation

The articles in this special issue collectively demonstrate that POCT should be regarded as a continuum extending from molecular recognition to clinical decision-making. Smartphone-linked readers, wearable sensors, portable fluorescence devices, and AI can improve the consistency, accessibility, and interpretability of decentralized tests (Mudanyali et al., 2012; Gao et al., 2016; Ates et al., 2022; Wang et al., 2022). AI has the potential to further assist with image quality assessment, quantitative signal extraction, result classification, and longitudinal risk prediction, provided that algorithms are validated in the populations and workflows for which they are intended (Topol, 2019; Wiens et al., 2019).

Quality assurance must therefore be incorporated at the design stage. Traceability, internal controls, lot-to-lot verification, user training, connectivity, and procedures for discordant results are all essential when testing moves beyond the central laboratory (Venner et al., 2021; Stavelin and Sandberg, 2024). Cost should also be evaluated across the full lifecycle of a device, including consumables, quality-control materials, maintenance, data systems, waste management, and confirmatory testing. Sustainable design is increasingly important because many decentralized platforms rely on single-use plastics and multilayer cartridges (Ongaro et al., 2022).

Summary and outlook

This special issue presents a coherent view of intelligent biosensing and POCT as a field moving from isolated analytical devices toward connected diagnostic ecosystems. The contributions range from one-pot molecular testing to functional genetic diagnostics, multimodal biomarker assessment, responsive nucleic-acid systems, and algorithmic disease stratification. What they have in common is the effort to transform molecular signals into information that is timely, interpretable, and actionable.

Future progress should focus on four priorities. First, every POCT platform should be developed around a specific clinical or public-health decision. Second, laboratory-grade analytical performance must be accompanied by simple sample handling, stable reagents, quality assurance, and clear referral pathways. Third, AI and connected readers should improve result interpretation without obscuring uncertainty or weakening clinical oversight. Finally, precision must be matched by affordability, manufacturability, and sustainability.

The future of POCT will depend on collaboration among analytical scientists, materials engineers, laboratory professionals, clinicians, public-health practitioners, manufacturers, and data scientists. The goal is not simply to create smaller tests, but to establish dependable diagnostic systems that can function well across hospitals, primary-care settings, homes, and field environments.

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Author contributions

Yi ZHANG conceived and edited the draft of the manuscript. Jixi ZHANG performed the literature review and co-wrote the draft. Both authors have reviewed and approved the final manuscript.

Compliance with ethics guidelines

Jixi ZHANG and Yi ZHANG declare that they have no conflicts of interest.

This editorial does not contain any studies with human or animal subjects performed by either of the authors.

Declaration on the use of generative AI tools

During the preparation of this editorial, the authors used DeepSeek-V4 solely for language editing and improvement of clarity and readability. The AI-generated outputs were critically reviewed, verified, and revised by the authors. Generative AI was not used to develop the academic viewpoints, evaluate evidence, or formulate conclusions. The authors take full responsibility for the accuracy, originality, integrity, and final content of the manuscript as submitted.

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Introducing Guest Editors-in-Chief

Yi ZHANG, Ph.D.
Distinguished Research Fellow, Zhejiang Provincial People's Hospital, Affiliated People's Hospital, Hangzhou Medical College

Dr. Yi ZHANG has conducted a series of impactful studies centered on intelligent biomolecular recognition and detection, based on the design and construction of programmable nanobiomaterials. His primary research areas include: rapid and precise detection of acute pathogenic target molecules, early diagnosis and molecular warning of major and malignant diseases, as well as artificial simulation and functional substitution of subcellular structures.

Jixi ZHANG, Ph.D.
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Dr. ZHANG's research focuses on activatable imaging and molecular diagnostic techniques for pathological samples in the perioperative period of tumors through assembly of biosensing molecules and opto-electrically active materials, responsive designs of cascade reaction and constraint coupling toward biomarker sensing systems, as well as signal amplification and anti-interference modulation methods in complex biological media.