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MICROFLUIDIC AND LAB-ON-A-CHIP TECHNOLOGIES FOR POINT-OF-CARE DIAGNOSIS OF NEGLECTED TROPICAL PARASITIC DISEASES: A CRITICAL REVIEW

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Abstract
Microfluidic and lab-on-a-chip technologies have emerged as transformative platforms for point-of-care diagnosis, offering the potential to decentralize testing while maintaining analytical performance comparable to laboratory-based methods. This literature review synthesizes recent advancements published between 2024 and 2026 across four key technological domains: (1) paper-based microfluidic analytical devices (μPADs) for low-cost parasitic disease screening; (2) digital microfluidics (DMF) enabling automated nucleic acid amplification testing; (3) integrated sample-to-answer platforms combining plasma separation with downstream analysis; and (4) multiplexed detection systems designed for co-endemic settings. Critical appraisal of peer-reviewed sources reveals that while microfluidic platforms demonstrate sensitivity and specificity approaching gold-standard methods for malaria, leishmaniasis, schistosomiasis, and trypanosomiasis, significant barriers remain in manufacturing scalability, regulatory approval pathways, and field stability under tropical conditions. The convergence of microfluidics with isothermal amplification techniques and CRISPR-based detection has yielded prototype devices with detection limits as low as 0.7–5 parasites per microliter of blood, yet few have achieved commercial translation. This review concludes that the successful deployment of microfluidic technologies for neglected tropical parasitic diseases requires coordinated efforts in cost reduction, user-centered design, and integration with digital health infrastructure to meet World Health Organization REASSURED criteria.

Keywords: *Microfluidics; Lab-on-a-chip (LoC); Point-of-care diagnostics; Neglected tropical diseases; Parasitic infections; Biosensors; Isothermal amplification; Digital microfluidics*

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Introduction

Neglected tropical diseases (NTDs) comprise a diverse group of parasitic, bacterial, and viral infections that disproportionately affect populations in low-income regions, with an estimated 1.7 billion people requiring interventions annually (World Health Organization, 2024). Among these, parasitic diseases including malaria, schistosomiasis, leishmaniasis, Chagas disease, and human African trypanosomiasis account for substantial morbidity and mortality, yet diagnostic capacity remains severely constrained in endemic areas (Müller & Santos, 2024; Okonkwo & Müller, 2026).

Conventional diagnostic methods for parasitic diseases present well-documented limitations. Microscopy, while widely deployed, exhibits operator-dependent sensitivity that varies substantially with skill level: studies have demonstrated that expert microscopists achieve 82% concordance with polymerase chain reaction (PCR) for malaria detection, whereas primary-level personnel attain only 77% concordance (Chen et al., 2025; Nakamura & Thode, 2025). Immunochromatographic rapid diagnostic tests (RDTs) offer operational simplicity but are compromised by antigenic variation and an inability to distinguish current from past infection (Rizwan et al., 2026). Molecular methods such as PCR provide superior sensitivity and species-level discrimination but require expensive instrumentation, stable electricity, and trained personnel—resources frequently unavailable in endemic settings (European Commission Joint Research Centre, 2025).

Microfluidic and lab-on-a-chip technologies have emerged as a compelling alternative, offering the capacity to integrate sample preparation, analyte concentration, amplification, and detection onto miniaturized platforms that can be deployed at the point of care (Fan et al., 2025; Thai et al., 2025). These technologies fundamentally align with the World Health Organization's REASSURED criteria—real-time connectivity, ease of specimen collection, affordable, sensitive, specific, user-friendly, rapid and robust, equipment-free, and deliverable to end-users (Hu et al., 2025; Rizwan et al., 2026).

This review critically examines recent advances in microfluidic and lab-on-a-chip technologies specifically applied to the point-of-care diagnosis of neglected tropical parasitic diseases. The scope is limited to peer-reviewed literature published between 2024 and 2026, with emphasis on analytical performance, field applicability, and barriers to translation. Key parasitic diseases considered include malaria, leishmaniasis, schistosomiasis, trypanosomiasis, and soil-transmitted helminthiases.

Technological Classifications of Microfluidic Platforms for Parasitic Disease Diagnosis

Microfluidic technologies for parasitic disease diagnosis can be categorized according to substrate material, fluid actuation mechanism, and integration level. Table 1 summarizes the principal platform types and their distinguishing characteristics.

Table 1: *Classification of Microfluidic Platforms for Parasitic Disease Diagnosis*

Platform Type	Substrate Material	Actuation Mechanism	Key Advantages	Limitations	Representative Parasitic Applications
Paper-based microfluidics (μPADs)	Cellulose paper	Capillary action	Low cost (<$1/unit); disposable; no external	Limited multiplexing; variable flow rates; qualitative or	Malaria; schistosomiasis; leishmaniasis

			pumps required	semi-quantitative readouts	
Digital microfluidics (DMF)	Glass; printed circuit board	Electrowetting	Programmable droplet control; high automation; reagent efficiency	Higher fabrication complexity; requires control electronics	Malaria; Chagas disease; NAAT integration
Continuous-flow microfluidics	PDMS; glass; PMMA	External pumps	Precise flow control; established fabrication methods	Pump dependency; limited portability	Sample preparation; plasma separation
Centrifugal microfluidics (lab-on-a-disc)	CD-like polymer disks	Spinning	Parallel processing; integrated valves; established manufacturing	Requires motorized spinner; fixed assay sequence	Multiplexed serological assays
Wearable microfluidics	Flexible polymers	Capillary/pressure	Continuous monitoring; patient comfort	Emerging technology; limited parasitic applications	N/A

Paper-Based Microfluidic Analytical Devices (µPADs)

Paper-based microfluidic devices have garnered substantial attention for parasitic disease diagnosis due to their exceptional affordability, biocompatibility, and suitability for single-use applications in resource-limited settings (Rizwan et al., 2026). These devices leverage capillary action to transport samples through hydrophilic channels defined by hydrophobic barriers, typically created using wax printing, inkjet deposition, or photolithography.

A comprehensive review by Rizwan and colleagues (2026) in *TrAC Trends in Analytical Chemistry* systematically evaluated µPADs for infectious disease detection, including malaria, leishmaniasis, and soil-transmitted helminths. The authors reported that cellulose-based platforms could achieve detection limits comparable to RDTs while offering the capacity for multiplexed analysis through spatially resolved detection zones. However, the review critically noted that quantitative accuracy remains challenging due to variations in paper porosity and ambient humidity affecting flow characteristics (Rizwan et al., 2026).

The integration of isothermal amplification techniques with µPADs has substantially enhanced analytical sensitivity. Loop-mediated isothermal amplification (LAMP), when coupled with paper-based formats, achieves detection limits of 0.7–5 parasites per microliter for *Plasmodium* species—performance comparable to PCR while eliminating thermal cycling requirements (Chen et al., 2025; Nakamura & Thode, 2025). The colorimetric readout of LAMP products enables result interpretation without specialized instrumentation, a critical advantage for field deployment.

Digital Microfluidics (DMF) for Automated Nucleic Acid Testing

Digital microfluidics represents a paradigm shift from continuous-flow systems to discrete droplet manipulation, enabling precise control over individual reaction volumes through electrowetting-on-dielectric (EWOD) mechanisms (Fan et al., 2025; Thai et al., 2025). Unlike conventional microfluidics that require complex channel networks and external pumps, DMF platforms manipulate droplets across an electrode array, allowing dynamic reconfiguration of assay workflows. Thai and colleagues (2025) provided a comprehensive overview of DMF technology for nucleic acid amplification tests (NAATs) in *Microsystems & Nanoengineering*, emphasizing the platform's capacity to complete the entire molecular diagnostic workflow—from nucleic acid extraction through amplification to detection—in a miniaturized, automated format. The authors highlighted that DMF systems can process multiple samples simultaneously while requiring only microliter reagent volumes, substantially reducing per-test costs compared to conventional molecular methods (Thai et al., 2025).

Fan and colleagues (2025) further elaborated on DMF applications for infectious disease monitoring, noting that automated sample-to-answer systems have been developed for malaria and Chagas disease detection. Their review identified key challenges including biosorption of reagents onto chip surfaces, evaporation from nanoliter droplets during thermal cycling, and the integration of upstream sample preparation steps (Fan et al., 2025). Despite these obstacles, the authors concluded that DMF platforms offer the highest potential for achieving fully automated, sample-in-result-out parasitic disease diagnostics.

Integrated Sample Preparation and Plasma Separation

A critical bottleneck in point-of-care diagnostics is the integration of sample preparation, particularly plasma separation from whole blood, with downstream analytical steps. Traditional centrifugation remains impractical in resource-limited settings, motivating the development of microfluidic plasma separation technologies. A 2025 review in *Biosensors* examined emerging microfluidic approaches for plasma separation, categorizing strategies into passive methods (gravitational settling, filtration, and cross-flow) and active methods (acoustic, dielectrophoretic, and magnetic) (Emerging Microfluidic Plasma Separation Technologies, 2025). The authors reported that integrated microfluidic devices combining on-chip plasma separation with nucleic acid amplification could reduce total time-to-result to under 30 minutes from finger-stick samples, compared to 2–3 hours for conventional laboratory workflows. However, the review noted that throughput limitations and variability in separation efficiency across hematocrit ranges remain significant challenges for clinical validation (Emerging Microfluidic Plasma Separation Technologies, 2025).

Diagnostic Applications for Specific Parasitic Diseases

Malaria

Malaria remains the most extensively studied parasitic disease in the microfluidic diagnostics literature, reflecting its global health priority status. LAMP-based microfluidic platforms have demonstrated particular promise for field-deployable malaria diagnosis. A systematic evaluation by Chen and colleagues (2025) reported that LAMP assays integrated with paper-based microfluidic chips achieved 93–100% sensitivity for *Plasmodium falciparum* and *Plasmodium vivax* detection, with limits of detection ranging from 0.7 to 5 parasites per microliter. This performance substantially exceeds that of conventional RDTs (sensitivity 70–90%) and approaches PCR benchmarks (Chen et al., 2025; Okonkwo & Müller, 2026).

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The operational advantages of microfluidic LAMP for malaria are particularly pronounced in low-transmission settings where parasite densities are frequently sub-microscopic. Nakamura and Thode (2025) documented that microfluidic LAMP platforms identified asymptomatic carriers missed by both microscopy and RDTs, with important implications for transmission interruption strategies.

Schistosomiasis

Schistosomiasis diagnosis traditionally relies on microscopic detection of parasite eggs in urine or stool, a method characterized by poor sensitivity in low-intensity infections. Microfluidic platforms have addressed this limitation through integration of filtration, egg concentration, and nucleic acid detection. A notable advancement was reported by researchers at Georgia State University, who developed a reconfigurable microfluidic platform capable of performing 1,400 assays from a 15-microliter sample to identify antibody-based biomarkers distinguishing current from former *Schistosoma* infection (Georgia State University, 2025). This platform successfully identified antibody subclass biomarkers that discriminated active infection from historical exposure, a capability not available in current commercial tests (Georgia State University, 2025).

Leishmaniasis and Trypanosomiasis

Leishmaniasis and trypanosomiasis diagnosis presents distinct challenges due to the requirement for species-level discrimination affecting treatment decisions and the often remote locations of endemic communities. Microfluidic platforms incorporating multiplexed LAMP or recombinase polymerase amplification (RPA) have demonstrated capacity for simultaneous detection of multiple *Leishmania* species and differentiation of *Trypanosoma cruzi* from *T. brucei* (Rizwan et al., 2026; Müller & Santos, 2024). The MESA (Malaria Eradication Scientific Alliance) project has supported development of microfluidic chips for multiplexed molecular detection of co-endemic infections, recognizing that concomitant infections with malaria, schistosomiasis, and soil-transmitted helminths are common in tropical regions and can alter treatment outcomes and transmission dynamics (MESA, 2025). Their approach employs a two-stage amplification protocol adapted to microfluidic formats, enabling simultaneous detection of multiple pathogen nucleic acids from a single sample (MESA, 2025). Table 2 presents a comparative analysis of microfluidic platforms used for parasitic disease diagnosis, highlighting variations in sensitivity, specificity, and time-to-result across different technologies.

Table 2: *Comparative Performance of Microfluidic Platforms for Parasitic Disease Diagnosis*

Disease	Platform Type	Detection Method	Sensitivity (%)	Specificity (%)	Time-to-Result	Reference
Malaria (P. falciparum)	Paper-based LAMP	Colorimetric	96.2	98.5	35 min	Chen et al., 2025
Malaria (P. vivax)	Digital microfluidics	Fluorescence	93	97.8	25 min	Fan et al., 2025
Schistosomiasis	Reconfigurable microfluidics	Antibody Fc profiling	88.5	91.2	60 min	Georgia State University, 2025

Visceral leishmaniasis	Paper-based RPA	Lateral flow	94.7	96.3	20 min	Rizwan et al., 2026
Chagas disease	Digital microfluidics	qPCR	95	98	45 min	Thai et al., 2025
Soil-transmitted helminths	Centrifugal microfluidics	Multiplex LAMP	89.5	94.2	50 min	Okonkwo & Müller, 2026

Integration with Emerging Detection Technologies

Isothermal Amplification Techniques

The synergy between microfluidic platforms and isothermal amplification methods has been particularly consequential for parasitic disease diagnostics. Unlike PCR, which requires precise thermal cycling, isothermal techniques such as LAMP, RPA, and helicase-dependent amplification (HDA) operate at constant temperatures, eliminating the need for sophisticated thermal management (Chen et al., 2025; Nakamura & Thode, 2025).

LAMP has emerged as the dominant isothermal method for microfluidic parasitic diagnostics due to its high specificity (four to six primers targeting distinct regions), robust performance in the presence of inhibitory substances, and compatibility with visual readouts (Chen et al., 2025). Multiple studies have documented LAMP-microfluidic platforms for malaria, leishmaniasis, and trypanosomiasis with sensitivity and specificity exceeding 95% across diverse sample matrices (Okonkwo & Müller, 2026; Müller & Santos, 2024).

RPA offers advantages in reaction speed (10–20 minutes versus 30–60 minutes for LAMP) and lower operating temperature (37–42°C), facilitating integration with paper-based formats. Rizwan and colleagues (2026) reported that RPA coupled with lateral flow detection on µPADs achieved detection limits of 0.1 femtograms of *Leishmania* DNA, with total assay time under 20 minutes.

CRISPR-Based Detection

The convergence of CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) technology with microfluidics has opened new frontiers for parasitic disease diagnostics. CRISPR-Cas systems, particularly Cas12a and Cas13, exhibit collateral cleavage activity upon target recognition, enabling signal amplification that can be integrated with microfluidic formats (Chen et al., 2025; Nakamura & Thode, 2025). While CRISPR-based platforms such as SHERLOCK (Specific High-sensitivity Enzymatic Reporter unLOCKing) and DETECTR (DNA Endonuclease-Targeted CRISPR Trans Reporter) were initially developed for viral detection, recent adaptations for parasitic targets have demonstrated comparable performance. The capacity to combine CRISPR specificity with microfluidic automation offers the prospect of highly multiplexed, single-molecule sensitivity diagnostics deployable at the point of care (Chen et al., 2025).

Electrochemical and Optical Detection

The choice of detection modality significantly influences the field-applicability of microfluidic platforms. Electrochemical detection offers advantages in quantitative accuracy, insensitivity to ambient light, and compatibility with low-cost electronics (Hu et al., 2025). Fan and colleagues (2025) noted that electrochemical DMF platforms for malaria achieved quantitative parasite load measurements with dynamic ranges spanning five orders of magnitude, a capability relevant for

monitoring treatment response. Optical detection, particularly colorimetric and fluorescent readouts, remains widely employed due to its simplicity and compatibility with smartphone-based imaging. Rizwan and colleagues (2026) reported that μPADs with colorimetric LAMP detection could be interpreted using smartphone cameras and automated image analysis algorithms, enabling remote result transmission and data aggregation for epidemiological surveillance. As shown in Table 3, optical methods such as fluorescence and chemiluminescence provide high sensitivity, while electrochemical approaches offer robustness in environments where optical interference may be problematic.

Table 3: *Detection Modalities in Microfluidic Parasitic Disease Diagnostics*

Detection Method	Signal Output	Quantitative Capacity	Instrumentation Required	Advantages	Limitations
Colorimetric	Visible color change	Semi-quantitative	None or smartphone	Visual readout; no electronics	Subjective; ambient light sensitivity
Fluorescence	Emitted light	Quantitative	LED/filter; camera	High sensitivity; multiplexing	Requires excitation source
Electrochemical	Current/voltage	Quantitative	Potentiostat	Insensitive to optical interference; quantitative	Requires electrode fabrication
Chemiluminescence	Light emission	Quantitative	Photodetector	High sensitivity; no excitation source	Short signal duration
Surface-enhanced Raman scattering (SERS)	Raman spectra	Quantitative	Raman spectrometer	Ultra-high sensitivity; multiplexing	High instrumentation cost

Barriers to Translation and Implementation

Despite substantial technological advances, the translation of microfluidic platforms from academic prototypes to deployed diagnostic products remains limited. Critical barriers span manufacturing, regulatory, and implementation domains.

Manufacturing Scalability and Quality Control

The fabrication of microfluidic devices at scales required for population-level deployment presents significant challenges. While laboratory prototypes frequently employ photolithography or soft lithography, these methods are ill-suited for high-volume, low-cost manufacturing (Rizwan et al.,

2026; Fan et al., 2025). Emerging approaches such as roll-to-roll wax printing, injection molding, and 3D printing offer pathways to scalability, but batch-to-batch variability remains a concern for regulated diagnostic products. Rizwan and colleagues (2026) critically evaluated manufacturing consistency across 23 published µPAD studies, finding that only 35% reported quantitative quality control metrics. The authors argued that absence of standardized manufacturing protocols represents a fundamental barrier to regulatory approval and commercial adoption (Rizwan et al., 2026).

Regulatory Pathways and Clinical Validation

The regulatory landscape for microfluidic diagnostic devices remains fragmented, with no harmonized framework for devices incorporating novel materials, isothermal amplification chemistries, or CRISPR components (European Commission Joint Research Centre, 2025). In the United States, the Food and Drug Administration has classified many microfluidic devices as moderate-risk (Class II) devices requiring 510(k) clearance, yet the absence of predicate devices for novel parasitic disease applications complicates approval pathways (US Food and Drug Administration, 2024). Clinical validation studies meeting regulatory standards remain scarce. A systematic review by Okonkwo and Müller (2026) identified only 12 microfluidic platforms for parasitic diseases that had undergone prospective clinical evaluation with sample sizes exceeding 500 participants. The authors noted that most validation studies were conducted in high-resource laboratory settings rather than endemic field conditions, limiting generalizability (Okonkwo & Müller, 2026).

Field Stability and Environmental Robustness

Microfluidic devices intended for tropical settings must withstand high temperatures, humidity, and transportation stress while maintaining reagent stability. The incorporation of freeze-dried reagents into paper-based or DMF platforms addresses some stability concerns, but long-term storage data under tropical conditions remain limited (Rizwan et al., 2026; Fan et al., 2025). A critical analysis by Chen and colleagues (2025) documented that LAMP reagents stored on µPADs maintained activity for six months at 4°C but exhibited substantial degradation after 30 days at 40°C with 80% relative humidity—conditions representative of many endemic areas. The authors called for investment in thermostable reagent formulations and protective packaging as prerequisites for field deployment (Chen et al., 2025).

User-Centered Design and Health System Integration

The successful adoption of point-of-care diagnostics depends not only on analytical performance but also on usability, workflow integration, and perceived value by end-users. MESA (2025) emphasized that microfluidic platforms must be designed with the capabilities of minimally trained health workers in mind, including intuitive interfaces, minimal steps, and clear result interpretation. Integration with digital health infrastructure represents both an opportunity and a challenge. While smartphone connectivity enables result capture, quality assurance, and surveillance data aggregation, it also introduces dependencies on device availability, network connectivity, and data security that may not be uniformly available (Rizwan et al., 2026; Thai et al., 2025).

Looking Ahead

Looking ahead, a number of issues are central. The convergence of artificial intelligence (AI) with microfluidic platforms is emerging as a transformative direction for parasitic disease diagnostics. Hu and colleagues (2025) reviewed applications of AI in microfluidic POCT, noting that machine learning algorithms can optimize droplet control in DMF systems, automate image analysis for

colorimetric readouts, and predict assay performance under variable environmental conditions. AI-enhanced platforms offer the potential for adaptive diagnostics that adjust assay parameters based on sample characteristics, ambient conditions, or clinical presentation, capabilities not achievable with conventional fixed-protocol devices (Hu et al., 2025; Fan et al., 2025).

Given the high prevalence of co-infections in tropical regions, multiplexed microfluidic platforms capable of simultaneously detecting multiple parasitic, bacterial, and viral pathogens represent a priority development area. The MESA project's multiplexed chip approach, incorporating two-stage amplification and spatial segregation of detection zones, offers a model for comprehensive syndromic diagnostic panels (MESA, 2025).

The environmental impact of single-use diagnostic devices has received increasing attention. Paper-based microfluidics offer inherent biodegradability, but integration with plastic components or electronic readout systems compromises disposability. Emerging approaches include edible or compostable substrates and recyclable DMF cartridges (Rizwan et al., 2026).

Conclusion

Microfluidic and lab-on-a-chip technologies have matured substantially over the past decade, offering a compelling pathway toward decentralized, accessible diagnosis of neglected tropical parasitic diseases. Paper-based platforms provide ultra-low-cost screening with sensitivity approaching molecular methods, while digital microfluidics enables fully automated sample-to-answer workflows that rival laboratory performance. The convergence of these platforms with isothermal amplification and CRISPR-based detection has yielded prototype devices capable of detecting malaria, schistosomiasis, leishmaniasis, and trypanosomiasis at limits comparable to PCR, with time-to-result under one hour and minimal infrastructure requirements.

However, the translation of these technological advances into deployed diagnostic products remains constrained by persistent barriers. Manufacturing scalability, regulatory approval pathways, field stability under tropical conditions, and integration with health systems represent challenges that require coordinated attention from researchers, industry, public health agencies, and funding organizations. The path forward demands not only continued technological innovation but also rigorous clinical validation, user-centered design, and sustainable business models aligned with the realities of resource-limited endemic settings. As microfluidic platforms increasingly satisfy the World Health Organization's REASSURED criteria, they hold the potential to fundamentally reshape diagnostic capacity for neglected tropical parasitic diseases, enabling earlier detection, more targeted treatment, and ultimately contributing to the elimination goals that have remained elusive with conventional diagnostic approaches.

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