RESEARCH PAPER

Multiplexed Lab-On-Chip Biosensors For Viral Detection

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ABSTRACT

Multiplexed lab-on-chip (LOC) biosensors have emerged as a transformative class of analytical devices, enabling the concurrent detection of multiple viral biomarkers within a single, miniaturized platform. This capability is pivotal for differential diagnosis of co-circulating pathogens such as Dengue, Zika, chikungunya, and SARS-CoV-2, where overlapping clinical symptoms can hinder timely and accurate patient management. Integrating microfluidics with electrochemical, optical, and hybrid transduction modalities, multiplex LOC systems reduce assay time, minimize sample volume, and support deployment in resource-limited settings. Recent advances have demonstrated the use of nanomaterial-enhanced surfaces, gold nanoparticles, graphene derivatives, and metal–organic frameworks to increase active surface area, improve electron transfer kinetics, and enable high-density probe immobilization. Aptamer-based recognition elements are increasingly favored over antibodies due to their superior stability, facile chemical modification, and compatibility with multiplexing chemistries such as thiol–gold self-assembly, carbodiimide coupling, and π–π stacking. Representative platforms employ screen-printed electrode arrays, graphene field-effect transistor chips, and paper–microfluidic hybrids, achieving sub-nanogram per milliliter limits of detection with assay times under 30 minutes. This review critically evaluates the design strategies, immobilization approaches, and performance metrics of state-of-the-art multiplex LOC biosensors, identifies key challenges in cross-reactivity and standardization, and outlines future directions toward clinically validated, AI-integrated, and wearable diagnostic systems for rapid viral surveillance and outbreak control

Keywords: Multiplex biosensor; lab-on-chip; aptamer; electrochemical detection; point-of-care; nanomaterials; viral diagnostics

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INTRODUCTION

Infectious diseases such as dengue, Zika, chikungunya, and COVID-19 share overlapping clinical symptoms, making rapid differential diagnosis crucial for patient management and outbreak control (Sufi Aiman Sabrina et al., 2025). Conventional diagnostics like RT-PCR and ELISA offer high sensitivity (Reta et al., 2020) but require centralized laboratories, trained personnel, and extended turnaround times. The co-circulation of multiple viruses with similar clinical presentations further complicates diagnosis, underscoring the need for multiplexed diagnostics that can detect and differentiate multiple pathogens simultaneously. Lab-on-chip (LOC) biosensors, which integrate microfluidics and miniaturized sensing arrays, enable parallel detection in minimal sample volumes, reduce assay time, and allow portability attributes essential for deployment in both well-equipped and resource-limited settings.

Recent advances in multiplexed LOC biosensors leverage electrochemical, optical, and hybrid detection modalities, often enhanced with engineered nanomaterials to improve analytical performance (Ranjan Srivastava et al., 2023). Gold nanoparticles (AuNPs), graphene derivatives, and metal–organic frameworks (MOFs) offer increased surface area, enhanced electron transfer kinetics, and enable high-density immobilization of biorecognition elements (Arivazhagan et al., 2024). Aptamer-based recognition elements are increasingly preferred over antibodies for their superior stability, lower immunogenicity, and ease of chemical modification, facilitating highly specific multiplex assays(Wu et al., 2021). Immobilization chemistries such as thiol–gold self-assembly, carbodiimide coupling, and π–π stacking enable orthogonal functionalization of sensing sites, minimizing cross-reactivity (Chen et al., 2019). Combined with device architectures like screen-printed electrode arrays (SPEAs) (Paimard et al., 2023), graphene field-effect transistor (GFET) chips (Xu et al., 2022), and paper–microfluidic hybrids (Lomae et al., 2024), these systems achieve sub-nanogram per milliliter limits of detection with analysis times under 30 minutes. This convergence of nanomaterial engineering, aptamer chemistry, and POC integration is transforming viral diagnostics.

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Table 1. Common Strategies for Multiplexing in LOC Biosensors

Strategy	Principle	Advantages	Limitations	Reference
Spatial Multiplexing	Separate microchambers/electrodes for each target	Simple fabrication, clear signal separation	Larger device footprint	(Li et al., 2022)
Signal Encoding	Different electrochemical redox labels or optical wavelengths	High-density detection, minimal footprint	Requires advanced signal processing	(Souza et al., 2021)
Microarray Patterning	Immobilizing multiple probes on a single substrate	Compact, scalable	Potential cross-reactivity between probes	(Zhang et al., 2021)
Sequential Fluid Routing	Directing the sample sequentially to multiple sensing zones	Minimal crosstalk, shared reagents	Increases assay time	(Tu et al., 2025)

2.0 Recent Advances in Multiplexed LOC Biosensors

Multiplexing strategies in lab-on-chip (LOC) biosensors have evolved significantly in recent years to address the diagnostic challenges posed by co-circulating viral pathogens (Siavashy et al., 2024). Spatial multiplexing, in which individual microchambers or electrodes are dedicated to separate analytes, remains the most straightforward approach, offering minimal signal interference and straightforward fabrication (Li et al., 2022). Signal encoding strategies, employing unique electrochemical redox labels or optically distinguishable fluorophores, enable high-density detection on a reduced footprint, making them particularly suited for portable devices (Souza et al., 2021). Microarray patterning immobilizing multiple biorecognition elements on a single substrate allows simultaneous monitoring of diverse biomarkers, although optimization is required to mitigate cross-reactivity (Zhang et al., 2021). Sequential fluid routing in microfluidic architectures ensures controlled sample delivery to distinct sensing zones, enabling time-resolved, multi-analyte measurements while conserving reagents (Tu et al., 2025). These design strategies collectively enhance assay throughput, reduce testing time, and improve analytical reliability in point-of-care (POC) settings.

Electrochemical detection platforms dominate the multiplex LOC field due to their inherent sensitivity, cost-effectiveness, and ease of integration with miniaturized electronics. Screen-printed electrode arrays (SPEAs) have gained particular interest as they are compatible with scalable manufacturing, can be functionalized with diverse capture probes, and support independent measurement of multiple analytes on a single chip (Barros Azeredo et al., 2022). Nanomaterial modifications such as gold nanoparticles (AuNPs), graphene, and carbon nanotubes further enhance electron transfer kinetics and surface loading capacity, improving both sensitivity and limit of detection (LOD) (Kaya et al., 2022). Optical modalities, including surface plasmon resonance (SPR) imaging and fluorescence-based detection, provide complementary capabilities, enabling real-time label-free sensing or multiplexed spectral discrimination (Nava et al., 2022). Hybrid electrochemical optical devices integrate the robustness of electrochemical detection with the high-resolution capabilities of optical readouts, achieving improved assay confidence and versatility (Mitchell et al., 2022). These recent studies report sub-nanogram per milliliter LODs and total assay times under 30 minutes using these multiplex LOC designs, positioning them as viable candidates for clinical-grade rapid viral diagnostics.

3.0 Aptamer-Based Multiplex LOC Platforms

Aptamers synthetic single-stranded DNA or RNA oligonucleotides generated through the Systematic Evolution of Ligands by EXponential enrichment (SELEX) have emerged as versatile biorecognition elements for multiplexed lab-on-chip (LOC) biosensors due to their exceptional stability under varying environmental conditions, cost-effective synthesis, and ease of site-specific chemical modification for immobilization (Chung et al., 2025). Compared to antibodies, aptamers exhibit lower batch-to-batch variability and reduced immunogenicity, enabling reproducible performance in complex biological matrices (Chatterjee et al., 2022). Their integration with nanomaterial-modified sensing interfaces such as gold nanoparticles (AuNPs), graphene derivatives, carbon nanotubes (CNTs), and metal–organic frameworks (MOFs) significantly enhances probe density, electron transfer rates, and target capture efficiency (Fritea et al., 2021). Immobilization strategies are critical for ensuring the stability and functionality of aptamer layers in multiplex configurations: thiol–gold bonding facilitates strong and oriented attachment to AuNP-coated electrodes; carbodiimide coupling chemistry (EDC/NHS) enables covalent linkage between amine-modified aptamers and carboxyl-functionalized surfaces; and π–π stacking, mediated by pyrene linkers, allows non-covalent adsorption of aptamers onto graphene or CNT substrates without compromising their three-dimensional structure. These orthogonal immobilization approaches support spatial separation of capture probes on screen-printed electrode arrays (SPEAs) (Barros Azeredo et al., 2022), graphene field-effect transistor (GFET) chips (Hu et al., 2024), and paper–microfluidic hybrid devices (Lin et al., 2022), thereby minimizing cross-reactivity and signal interference in multiplex assays. Recent aptamer-based multiplex LOC platforms have demonstrated sub-nanogram per milliliter

limits of detection for co-circulating viral biomarkers such as dengue NS1, Zika NS1, chikungunya E1, SARS-CoV-2 spike protein, and influenza hemagglutinin, with assay times typically under 30 minutes positioning them as strong candidates for next-generation point-of-care (POC) diagnostics in outbreak-prone settings.

4.0 Challenges and Future Outlook

Multiplexed Despite significant progress, multiplexed lab-on-chip (LOC) biosensors face persistent challenges that hinder clinical translation. One major limitation is cross-reactivity between capture probes, particularly in high-density multiplex formats, which can generate false positives or reduce assay specificity. Signal interference caused by overlapping electrochemical peaks or optical spectra in multi-analyte detection remains another barrier, necessitating optimized probe design, orthogonal detection chemistries, and advanced signal deconvolution algorithms. Reproducibility in fabrication is critical for batch-to-batch consistency, yet micro/nanofabrication of multiplex LOC devices often suffers from variations in electrode dimensions, surface morphology, and functionalization efficiency. Standardized validation protocols for multiplexed biosensors are lacking, with no universally accepted metrics for assessing analytical performance, cross-reactivity, and stability under real-world conditions. Overcoming these issues will require robust antifouling surface chemistries such as zwitterionic polymers and PEGylation to minimize nonspecific adsorption in complex biological matrices, as well as automated, high-throughput manufacturing techniques (e.g., roll-to-roll printing, laser-induced graphene patterning) to enable scalable production. Future directions include integration with AI-driven data analytics for automated pattern recognition and real-time multi-analyte interpretation, wearable LOC systems for continuous pathogen monitoring in high-risk environments, and smartphone-based readouts that combine portability with cloud-connected epidemiological surveillance. With these advancements, multiplex LOC biosensors could become pivotal tools for global-scale, real-time outbreak monitoring, enabling rapid containment strategies and improving public health preparedness.

5.0 Conclusion

Multiplexed lab-on-chip (LOC) biosensors are poised to transform viral diagnostics by enabling rapid, simultaneous detection of multiple pathogens with high sensitivity and portability. Advances in nanomaterial engineering, aptamer-based biorecognition, and microfluidic integration have driven significant improvements in assay speed, specificity, and limit of detection, making these platforms increasingly viable for point-of-care (POC) applications. Nonetheless, challenges in cross-reactivity, fabrication reproducibility, and standardized validation must be addressed to achieve large-scale clinical adoption. Future integration with AI-powered analytics, wearable designs, and smartphone-based readouts will further expand the scope of multiplex LOC biosensors, positioning them as essential tools for real-time outbreak surveillance and global health preparedness.

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7.0 Conflict of Interest

The Authors have no conflicts of interest in this manuscript.

8.0 Data Availability Statement

There is no data for this review.

9.0 Ethics Statement

None.

10.0 Informed Consent

None..

REFERENCE

1. Arivazhagan, M., Pavadai, R., Murugan, N., Jakmunee, J., 2024. Surface engineered metal–organic framework-based electrochemical biosensors for enzyme-mimic ultrasensitive detection of glucose: recent advancements and future perspectives. Anal. Methods 16, 6474–6486. https://doi.org/10.1039/D4AY01429D
2. Barros Azeredo, N.F., Ferreira Santos, M.S., Sempionatto, J.R., Wang, J., Angnes, L., 2022. Screen-Printed Technologies Combined with Flow Analysis Techniques: Moving from Benchtop to Everywhere. Anal. Chem. 94, 250–268. https://doi.org/10.1021/acs.analchem.1c02637
3. Chatterjee, T., Johnson-Buck, A., Walter, N.G., 2022. Highly sensitive protein detection by aptamer-based single-molecule kinetic fingerprinting. Biosensors and Bioelectronics 216, 114639. https://doi.org/10.1016/j.bios.2022.114639
4. Chen, C., Liu, W., Hong, T., 2019. Novel approaches for biomolecule immobilization in microscale systems. Analyst 144, 3912–3924. https://doi.org/10.1039/C9AN00212J
5. Chung, Y.-D., Tsai, Y.-C., Wang, C.-H., Lee, G.-B., 2025. Aptamer selection via versatile microfluidic platforms and their diverse applications. Lab Chip 25, 1047–1080. https://doi.org/10.1039/D4LC00859F
6. Fritea, L., Banica, F., Costea, T., Moldovan, L., Dobjanschi, L., Muresan, M., Cavalu, S., 2021. Metal Nanoparticles and Carbon-Based Nanomaterials for Improved Performances of Electrochemical (Bio)Sensors with Biomedical Applications. Materials 14, 6319. https://doi.org/10.3390/ma14216319

7. Hu, J., Liu, X., Li, F., Qiu, Y., Hu, Y., Zhou, Y., Wang, P., Wan, H., 2024. Ultrasensitive graphene field-effect transistor biosensor for rapidly detecting miRNA-208a. Sensors and Actuators B: Chemical 418, 136262. https://doi.org/10.1016/j.snb.2024.136262

8. Kaya, S.I., Cetinkaya, A., Ozkan, S.A., 2022. Carbon Nanomaterial-Based Drug Sensing Platforms Using State-of-the-Art Electroanalytical Techniques. CAC 18, 79–101. https://doi.org/10.2174/1573411016999200802024629

9. Li, H., Liu, X., Zhu, F., Ma, D., Miao, C., Su, H., Deng, J., Ye, H., Dong, H., Bai, X., Luo, Y., Lin, B., Liu, T., Lu, Y., 2022. Spatial barcoding-enabled highly multiplexed immunoassay with digital microfluidics. Biosensors and Bioelectronics 215, 114557. https://doi.org/10.1016/j.bios.2022.114557

10. Lin, D., Li, B., Fu, L., Qi, J., Xia, C., Zhang, Y., Chen, J., Choo, J., Chen, L., 2022. A novel polymer-based nitrocellulose platform for implementing a multiplexed microfluidic paper-based enzyme-linked immunosorbent assay. Microsystems & Nanoengineering 8, 53.

11. Lomae, A., Teekayupak, K., Preechakasedkit, P., Pasomsub, E., Ozer, T., Henry, C.S., Citterio, D., Vilaivan, T., Chailapakul, O., Ruecha, N., 2024. Peptide nucleic acid probe-assisted paper-based electrochemical biosensor for multiplexed detection of respiratory viruses. Talanta 279, 126613. https://doi.org/10.1016/j.talanta.2024.126613

12. Mitchell, K.R., Esene, J.E., Woolley, A.T., 2022. Advances in multiplex electrical and optical detection of biomarkers using microfluidic devices. Anal Bioanal Chem 414, 167–180. https://doi.org/10.1007/s00216-021-03553-8

13. Nava, G., Zanchetta, G., Giavazzi, F., Buscaglia, M., 2022. Label-free optical biosensors in the pandemic era. Nanophotonics 11, 4159–4181. https://doi.org/10.1515/nanoph-2022-0354

14. Paimard, G., Ghasali, E., Baeza, M., 2023. Screen-Printed Electrodes: Fabrication, Modification, and Biosensing Applications. Chemosensors 11, 113. https://doi.org/10.3390/chemosensors11020113

15. Ranjan Srivastava, V., Kumari, R., Chandra, P., 2023. Miniaturized surface engineered technologies for multiplex biosensing devices. Electroanalysis 35, e202200355. https://doi.org/10.1002/elan.202200355

16. Reta, D.H., Tessema, T.S., Ashenef, A.S., Desta, A.F., Labisso, W.L., Gizaw, S.T., Abay, S.M., Melka, D.S., Reta, F.A., 2020. Molecular and Immunological Diagnostic Techniques of Medical Viruses. International Journal of Microbiology 2020, 1–19. https://doi.org/10.1155/2020/8832728

17. Siavashy, S., Soltani, M., Rahimi, S., Hosseinali, M., Guilandokht, Z., Raahemifar, K., 2024. Recent advancements in microfluidic-based biosensors for detection of genes and proteins: Applications and techniques. Biosensors and Bioelectronics: X 19, 100489. https://doi.org/10.1016/j.biosx.2024.100489

18. Souza, M.I.O., Mota, A.F.D., Pepino, V.M., Carmo, J.P., Borges, B.-H.V., 2021. Multi-Purpose Microwave Biosensor Based on Signal Encoding Technique and Microfluidics for Improved Sensitivity. IEEE Sensors J. 21, 4571–4581. https://doi.org/10.1109/JSEN.2020.3033970

19. Sufi Aiman Sabrina, R., Muhammad Azami, N.A., Yap, W.B., 2025. Dengue and Flavivirus Co-Infections: Challenges in Diagnosis, Treatment, and Disease Management. IJMS 26, 6609. https://doi.org/10.3390/ijms26146609

20. Tu, J., Yeom, J., Ulloa, J.C., Solomon, S.A., Min, J., Heng, W., Kim, G., Dao, J., Vemu, R., Pang, M., Wang, C., Kim, D.-H., Gao, W., 2025. Stressomic: A wearable microfluidic biosensor for dynamic profiling of multiple stress hormones in sweat. Sci. Adv. 11, eadx6491. https://doi.org/10.1126/sciadv.adx6491

21. Wu, L., Wang, Y., Xu, X., Liu, Y., Lin, B., Zhang, M., Zhang, J., Wan, S., Yang, C., Tan, W., 2021. Aptamer-Based Detection of Circulating Targets for Precision Medicine. Chem. Rev. 121, 12035–12105. https://doi.org/10.1021/acs.chemrev.0c01140

22. Xu, L., Ramadan, S., Akingbade, O.E., Zhang, Y., Alodan, S., Graham, N., Zimmerman, K.A., Torres, E., Heslegrave, A., Petrov, P.K., Zetterberg, H., Sharp, D.J., Klein, N., Li, B., 2022. Detection of Glial Fibrillary Acidic Protein in Patient Plasma Using On-Chip Graphene Field-Effect Biosensors, in Comparison with ELISA and Single-Molecule Array. ACS Sens. 7, 253–262. https://doi.org/10.1021/acssensors.1c02232

23. Zhang, H., Klose, A.M., Miller, B.L., 2021. Label-Free, Multiplex Glycan Microarray Biosensor for Influenza Virus Detection. Bioconjugate Chem. 32, 533–540. https://doi.org/10.1021/acs.bioconjchem.0c00718

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