

Advances in intelligent fiber-optic microfluidic-embedded technologies for empowered sensing performance: a review

Shadab Dabagh, Rukmani Singh, Claudia Borri, Hamed Ghorbanpoor, Golara Ghorban Dordinejad, Mahdi Bahadoran, Ambra Giannetti, Francesco Baldini, Huseyin Avci and Francesco Chiavaioli

Citation: Dabagh S, Singh R, Borri C et al. Advances in intelligent fiber-optic microfluidic-embedded technologies for empowered sensing performance: a review. *Intelligent Opto-Electronics* 2, 250015 (2026).

<https://doi.org/10.67704/ioe.2026.250015>

Received: 29 November 2025; Accepted: 29 January 2026; Published online: 25 March 2026

Related articles

Specialty optical fibers for advanced sensing applications

Huanhuan Liu, Dora Juan Juan Hu, Qizhen Sun, et al

Opto-Electronic Science 2023, 2(2): 220025 doi: [10.29026/oes.2023.220025](https://doi.org/10.29026/oes.2023.220025)

Three-dimensional integrated optical fiber devices: emergence and applications

Tingting Yuan, Xiaotong Zhang, Shitai Yang, et al

Opto-Electronic Technology 2025, 1(2): 250007 doi: [10.29026/oet.2025.250007](https://doi.org/10.29026/oet.2025.250007)

Integrated optical fiber devices

Wei Jin

Opto-Electronic Advances 2026, 9(2): 250323 doi: [10.29026/oea.2026.250323](https://doi.org/10.29026/oea.2026.250323)

Optical scanning endoscope via a single multimode optical fiber

Guangxing Wu, Runze Zhu, Yanqing Lu, et al

Opto-Electronic Science 2024, 3(3): 230041 doi: [10.29026/oes.2024.230041](https://doi.org/10.29026/oes.2024.230041)

More related articles in Opto-Electronic Journals Group website 



Advances in intelligent fiber-optic microfluidic-embedded technologies for empowered sensing performance: a review

Shadab Dabagh¹, Rukmani Singh¹, Claudia Borri¹, Hamed Ghorbanpoor^{2,3}, Golar Ghorban Dordinejad⁴, Mahdi Bahadoran⁵, Ambra Giannetti¹, Francesco Baldini¹, Huseyin Avci^{2,6,7} and Francesco Chiavaioli^{1*}

Abstract: The convergence of Lab-on-Fiber (LoF) technology, microfluidics, and artificial intelligence (AI) is emerging as a new and powerful paradigm for next-generation intelligent sensing systems. Combining AI with LoF-microfluidic devices can cover the residual gap by enhancing precise microfluidic control, data analysis, adaptive calibration, and predictive sensing, thereby opening new pathways for intelligent, miniaturized, reliable, and multifunctional devices for biomedical sensing and environmental monitoring. Microfluidic technologies leverage high-precision and flow rate-controlled sample delivery, reagent optimization, and simple prototyping, which make them excellent for real-time sensing. LoF devices showcase unique light control at the nanoscale level and their integration onto microfluidic chips empowers signal-to-noise ratio and, ultimately, limit of detection in a controlled environment. Advances in materials science and engineering have allowed the realization of different types of nanostructures which are integrated onto fiber sensors whose performance can be optimally tuned to detect a variety of markers and molecules. However, open challenges still exist, such as scalability, reproducibility of results, detection of multiple targets, effective compensation of interfering parameters and fast data processing. Innovative AI-driven solutions and novel functional bio-/materials are being developed to overcome these barriers and possibly meet the future demands. A roadmap toward intelligent LoF-microfluidic platforms is finally envisioned.

Keywords: optical fiber sensors; biophotonics; microfluidics; artificial intelligence

DOI: [10.67704/ioe.2026.250015](https://doi.org/10.67704/ioe.2026.250015)

Citation: Dabagh S, Singh R, Borri C et al. Advances in intelligent fiber-optic microfluidic-embedded technologies for empowered sensing performance: a review. *Intell Opto-Electron* 2, 250015 (2026).

1 Introduction

The development of advanced, portable, reliable and high-performance sensing platforms for the detection of molecules surely represents a cutting-edge scientific field, with involvement in a very broad range of applications like biomedical diagnosis, environmental monitoring and pharmaceuticals above all^{1–5}.

The convergence of microfluidic systems and photonic biosensors has facilitated the realization of multiple laboratory functions within a single chip, thereby fostering the advancement of photonic lab-on-a-chip technology. While

significant strides have been made to incorporate such sensors into compact and user-friendly platforms, several critical applications—such as effective and reliable point-of-care (PoC) diagnostics and in vivo biosensing—continue to necessitate sensor probes capable of conducting measurements in specific, often challenging-to-access locations. Optical fibers, owing to their unique light control at nanoscale and capability to transmit light to remote sites, represent an optimal solution to address these conditions. This has spurred the integration of the superior performance characteristics of photonic biosensors deployed on chips with the distinct advantages offered by optical fibers,

Received: 29 November 2025

Accepted: 29 January 2026

Published online: 25 March 2026

¹Institute of Applied Physics "Nello Carrara", National Research Council of Italy (CNR), 50019 Sesto Fiorentino (FI), Italy;

²Cellular Therapy and Stem Cell Production Application and Research Centre, ESTEM, Eskişehir Osmangazi University, 26040 Eskişehir, Türkiye; ³Department of Biomedical Engineering, Eskişehir Osmangazi University, 26040 Eskişehir, Türkiye;

⁴Department of Electrical and Electronics Engineering, Eskişehir Osmangazi University, 26040 Eskişehir, Türkiye;

⁵Department of Physics, Shiraz University of Technology, 71557-13876 Shiraz, Fars, Iran; ⁶Department of Metallurgical and Materials Engineering, Eskişehir Osmangazi University, 26040 Eskişehir, Türkiye; ⁷Translational Medicine Research and Clinical Center (TATUM), Eskişehir Osmangazi University, 26040 Eskişehir, Türkiye.

*Correspondence: F Chiavaioli, E-mail: f.chiavaioli@ifac.cnr.it

culminating in the development of Lab-on-Fiber (LoF) technology^{6–8}. The synergy of hardware integration with artificial intelligence (AI)-driven data analysis can dramatically advance microfluidic-embedded LoF technologies with empowered sensing performance toward becoming intelligent sensing systems capable of adaptive, autonomous, and predictive operation, thus bringing them to the same level of lab-on-a-chip technology.

The concept of LoF lies in the integration of functionalized materials on micro- and nanoscale dimensions referred to as "labs" with optical fibers, enabling the creation of miniaturized, sophisticated, and fully fiber-based platforms. Such innovations hold significant promise for applications in label-free chemical and biological sensing, among others. LoF technology is categorized into three primary paradigms based on the specific location where functional materials are integrated with optical fibers. These include "lab-on-tip" where functional materials are applied to the tip of the optical fiber; "lab-around-fiber", where functional materials are embedded on the external surface of optical fibers; and "lab-in-fiber", where functional materials are incorporated within the internal holey structure of specialty optical fibers like microstructure optical fibers (MOFs) and photonic crystal fibers (PCFs).

LoF technology integrated with microfluidics has undergone huge advances in recent years for ample sensing applications. The combination of microfluidics into fiber optic platforms dramatically empowers the sensitivity while making them ideal for real-time measurements in both harsh environments and biomedical settings. Moreover, this combination leverages portability along with miniaturization that in turn enhances their practical use in different applications. The detection capability of biochemical signals using optical fiber sensors has already been proved to reach remarkable performance^{9–11}, enabling biomarker tracking in clinically-mimicking scenarios toward the development of advanced non-invasive PoC devices^{12–14}.

LoF technology has seen the crucial step forward when nanomaterials have started to be integrated with optical fibers¹⁵, which created sensitive platforms and also improved manufacturing methods like 3D printing and then made quick prototyping and customization of these devices easy¹⁶. This capability is vital for producing devices that are both effective for real-world deployment and adaptable for various sensing scenarios^{17–19}. The design of microfluidic-embedded optical fiber systems showcased the adaptability of LoF in biochemical sensing by means of the integration of functional coatings and nanostructured surfaces, significantly improving surface sensitivity and then detection capability^{20–22}. These advances have provided an innovative method to realize portable, sensitive diagnostic equipment with real-time analytical capacity, hence paving new paths in patient monitoring and clinical diagnostics²³. A significant development in LoF technology has been the use of cavity-enhanced structures, which enabled stronger light confine-

ment and interaction length, hence promoting improved limit of detection (LoD) and faster detection time^{20,24}. Plasmonic nanoparticles on fiber tips have shown extraordinary biosensing properties by increasing light scattering and greater interaction efficiency^{25,26}. The polymer-assisted transfer techniques further augmented these capabilities, allowing for the precise deposition of plasmonic elements onto the optical fibers which can be customized depending on the sensing requirements^{24,27}. Such methodological innovations are pivotal for creating flexible, multifunctional platforms capable of operating effectively in diverse real-world applications^{8,28}. Techniques such as femtosecond laser-induced polymerization have enabled intricate micro- and nanoscale structures to be formed on the optical fibers, paving the way for multifunctional diagnostic capabilities^{29,30}.

Another important application of LoF technology lies in wearable devices thanks to continuously monitor response behavior. Microfluidic-embedded wearable devices enable capture and real-time analysis to provide instant physiological condition feedbacks. Nyein et al. proposed a microfluidic sensor patch to collect sweat effectively to dynamically analyze the level of glucose and electrolytes, which plays a critical role in managing diabetes^{31,32}. Different studies have also noted the significance of creating environmentally responsive materials for LoF systems. By adjusting the sensing structure and/or sensing principle of fiber sensor or the design of microfluidic channels such degrees of freedom allow the assessment of changes in chemical composition or physical states and open a wide application range from environmental sensing to medical diagnostics^{33,34}.

Overall, the synergistic combination of microfluidics with LoF systems has opened up new visions for sensing technologies^{29,35}. To fully realize this potential and make sure that these integrated systems successfully satisfy the requirements of modern applications, ongoing research and development initiatives are still necessary. Therefore, this review aims at providing a thorough understanding of the fundamental concepts and developments of LoF systems that use microfluidic technologies to dramatically improve sensing capabilities, together with a specific focus on cutting-edge application areas as environmental monitoring, and healthcare diagnostics. Each application presents different challenges that LoF technology aims to address, ranging from specificity and multiplexing capabilities to real-time data acquisition and processing. Furthermore, this review not only analyzes the LoF systems in terms of performance metrics, such as sensitivity, specificity, robustness, reliability, and LoD, but also underlines the advantages and constraints faced during sensor fabrication. To envisage a wider deployment of LoF technology, manufacturing scalability, cost-effectiveness, and integration with current diagnostic systems should be considered.

Understanding these challenges is essential for progressing research and promoting future developments that improve the functionality and capabilities of optical

fiber-based sensors. An additional focus of this review is the emerging role of AI and opto-electronic integration in LoF systems, where AI-driven approaches can remarkably enhance data analysis, adaptive calibration, and predictive sensing, while hybrid opto-electronic platforms improve sensitivity and reliability for intelligent biomedical diagnostics and environmental monitoring. The insights gained from this analysis will enhance comprehension of the foundational technologies and motivate future research efforts to address current issues and unveil new possibilities in this emerging sector^{27,36}. At the end, a strategic roadmap toward the development of intelligent LoF-microfluidic platforms is envisioned.

2 Fundamentals of Lab-on-Fiber technology

LoF technology underscores a notable progression in the integration of optics with micro-nanostructures, facilitating multifunctional applications in diverse domains such as bio/chemical sensing, diagnostics, and environmental monitoring. This novel technology adeptly integrates the distinct characteristics of optical fibers with the functionalities of nanophotonic structures, remarkably boosting the detection performance and downsizing^{35,37}. LoF technology fundamentally relies on the deposition of metallic and dielectric nanostructures of different shapes manufactured on the fiber tip (Fig 1(a)), inside the inherent fiber structure (Fig 1(b)) or around the sensitive region of the optical fiber (Fig 1(c))^{37,38}. These nanostructures enhance the light-matter interactions and hence empower the device-target binding signals³⁹ and the system versatility by employing different types of optical fibers tailored for specific applications, from particle counting to biochemical detection^{40,41}. Advance-

ments in manufacturing methods, such as two-photon polymerization, have enabled researchers to construct intricate micro- and nanoscale structures directly on optical fiber substrates. This adaptability in manufacturing methods not only improves the incorporation of functional materials but also facilitates scaling for industrial applications^{42,43}. Recently, the integration of AI in LoF-based systems is opening up a new avenue by creating novel options for real-time data processing and cluster analysis, with the chance of improving sensitivity and specificity across many sensing domains^{36,44}.

Each of the three LoF sensing configurations has advantages and disadvantages, and different domains of application. "Lab-on-Tip" (Fig. 1(a)), despite the lower sensitivity with respect to "lab-around-fiber" that might prevent its use in applications where it is required to reach a very low LoD, possesses the inherent condition to be used for *in vivo* sensing^{45,46}. In this case, any microfluidics is necessary since the fiber probe is directly in contact with the sample (e.g., liquid solution, culture medium, cell tissue or cell) to be analyzed. This application domain is undoubtedly one of the most promising and innovative approach, with outstanding outcomes in the recent years, especially when applied to local treatments of cancers⁴⁷.

"Lab-in-Fiber" (Fig. 1(b)), despite its remarkable potential to exploit in-fiber microchannels as both the sensing region and embedded microfluidic channels, is still at an early stage of technological maturity. Key challenges remain related to the reliable and repeatable functionalization of the inner microchannels, long-term surface stability, and selective bio-recognition in confined geometries. In addition, the micrometer-scale dimensions of the channels impose constraints on mass transport and surface accessibility, which can affect detection specificity and response time. Moreover, when

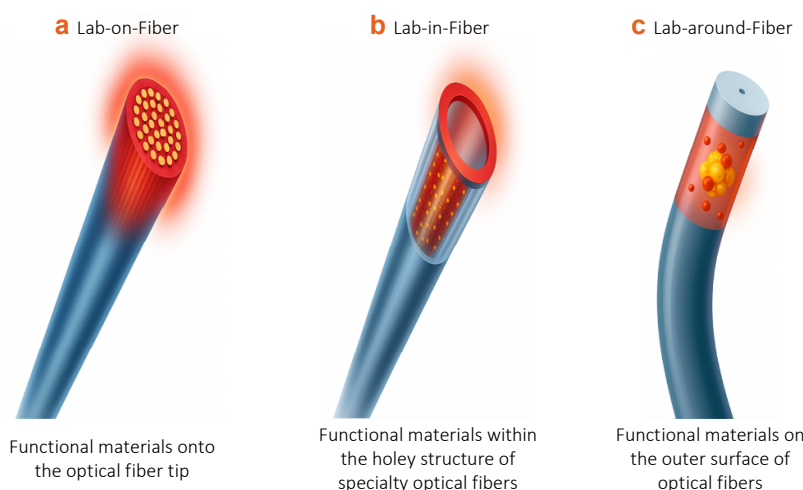


Fig. 1 | Lab-on-Fiber technology is classified into three main paradigms. (a) "Lab-on-Tip", where functional materials are integrated onto the optical fiber tip. (b) "Lab-in-Fiber", where functional materials are integrated within the holey structure of specialty optical fibers and (c) "Lab-around-Fiber", where functional materials are integrated on the outer surface of optical fibers.

dealing with biosensing in complex matrices, clogging can be a further concern. However, these limitations are mainly technological rather than conceptual, and ongoing advances in micro/nano-fabrication, surface chemistry, and nanomaterials science are steadily addressing these issues, making "Lab-in-Fiber" a highly promising platform for future fully-integrated optofluidic devices.

Finally, "Lab-around-Fiber" (Fig. 1(c)) has residual potential to be used for *in vivo*/ex vivo sensing, but combined with nanomaterials to further enhance the light-matter interaction, and with microfluidics to get rid of sensor cross-sensitivities and to reliably control over the sample handling, has gained a huge interest in biochemical sensing in the last decade^{48–56}. In addition to the extraordinary sensitivity that it is possible to attain of about 10^3 – 10^4 nm·RIU^{−1}, this configuration enables to envisage high-performance PoC devices to be used in very diverse applications, also supported by a high versatility and a large degree of customization.

3 The role of nanomaterials in LoF technology

Many materials can be incorporated with optical fibers thanks to the huge step forward in micro/nano-fabrication and technology over the years. This crucial step enables to dramatically improve the interaction strength of the electromagnetic field of the fiber mode with the surrounding environment, thus empowering their sensing capabilities. Graphene and related materials, 2D materials, metal-organic framework or metal-oxides are significant for their excellent morphological, chemical, and electro-optical characteristics, which may match and open up different detection methods. Among all, plasmonic materials, including thin metallic films and metallic nanoparticles (NPs), are often used in hybrid plasmonic fiber sensors to achieve augmented performance^{57,58}. Surface plasmon resonance (SPR) and localized surface plasmon resonance (LSPR), two of the most well-known phenomena in sensing, can be generated by incorporating metallic coatings or NPs with optical fibers. Figure 2(a) showcases the possible applications of LoF technology, while Fig. 2(b) details the types of nanomaterials that can be used to empower optical fiber sensors depending on the different application. Finally, Fig. 2(c) provides a sketch of a LoF-based sensing system and underscores the advantages and open challenges of this technology.

In microfluidic-embedded LoF platforms, the role of nanomaterials extends beyond simple sensitivity enhancement and directly impacts mass transport, selectivity/specificity, and response dynamics. For example, 2D materials, such as carbon-based materials, graphene and transition-metal dichalcogenides, can provide ultra-high surface-to-volume ratios and abundant functional groups, thus enabling efficient biomolecule grafting with fast binding

kinetics under laminar flow conditions^{59–61}. Similarly, metal-organic frameworks can provide the previous advantages owing to their tunable pore size, high porosity, and chemical selectivity. Therefore, when such materials are integrated onto LoF-microfluidic devices, they can tailor analyte-surface interactions, reduce diffusion times, and improve signal stability, so making them particularly advantageous for real-time and multiplexed biosensing⁶².

4 Microfluidics designed for LoF technology

Microfluidic technology has become one of the leading technologies to develop sensing platforms designed for biomedical diagnostics and environmental monitoring⁶³. This technology has particular advantages due to its capacity to precisely handle small fluid amounts and its incorporation with detecting methods and devices. Microfluidics, especially when combined with LoF systems, is leading the integration of diagnostic functions with medicine delivery, leveraging it as a revolutionary technology in contemporary medicine. Its capacity to provide quick, precise, and possibly economical solutions for illness identification, treatment and management continues to stimulate advancements in both laboratory research and clinical practice. The continuous improvement in design, materials, and the integration of various technologies will likely provide greater functions and wider applications for microfluidic systems in the future^{61,64}. However, challenges about optical and fluidic interface optimization and integration are still open⁶⁵.

Microfabrication methods like photolithography and soft lithography are already used in lab-on-a-chip systems. Photolithography has shown superior spatial resolution; however, it is usually expensive and time consuming for complex designs. Conversely, soft lithography, using polydimethylsiloxane (PDMS) pieces, is cost-effective, user-friendly, and efficient, allowing rapid redesigns without the need of a cleanroom environment^{66,67}. 3D printing, a recent and promising technique capable of producing microscale pieces, is garnering attention in microdevice manufacturing for its capacity to realize items quite easily. It has shown the capability to fabricate pieces with elevated aspect ratios; however, this technique cannot still guarantee a spatial resolution of a few or tens nanometer. The technique is surely cost-effective and intuitive, streamlining prototype and production procedures^{68,69}.

A recent study by Zheng et al. highlights the potential of LoF platforms to address difficulties associated with detection efficiency, but also underlines the elevated costs associated to SERS-based LoF systems⁷⁰. Caputo et al. showcase a minimally-invasive platform based on LoF technology integrated in a microfluidic device for light-triggered delivery of drug-loaded particles, precise dosing and targeted transport in order to leverage loco-regional therapy⁷¹. Bazaz et al.

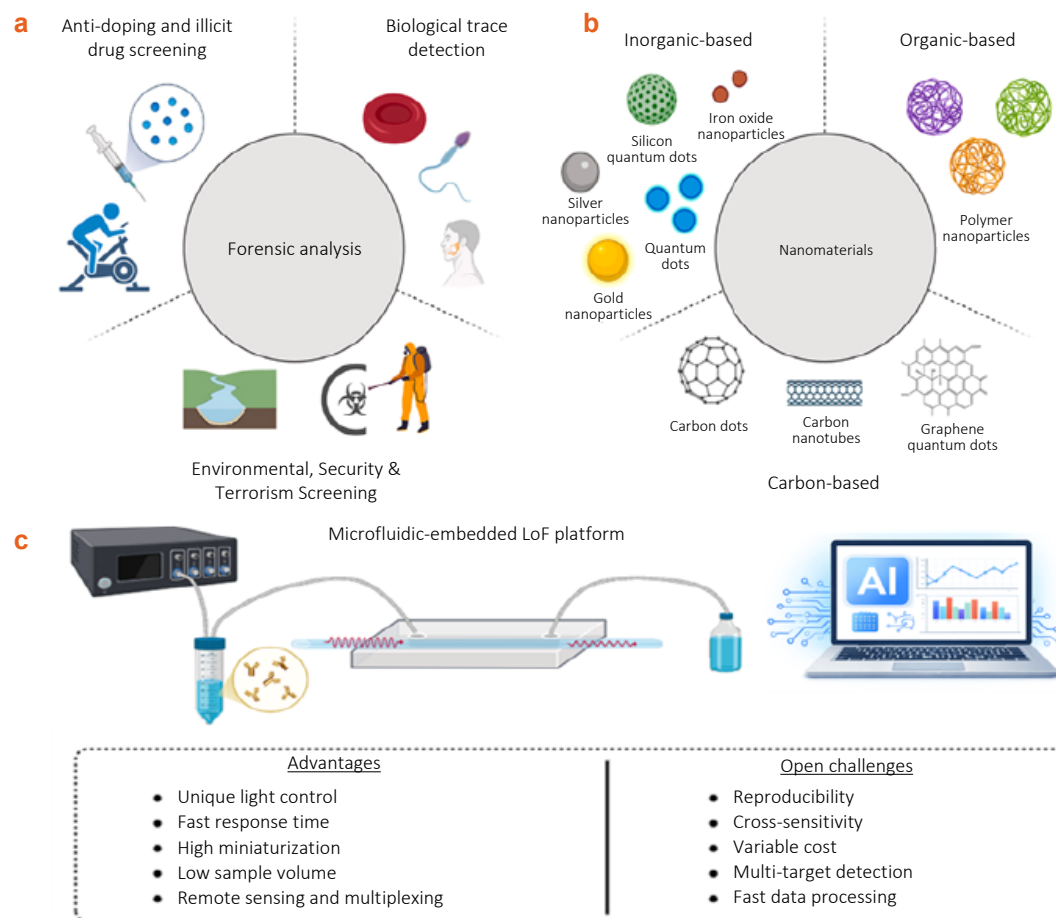


Fig. 2 | Overview of LoF-based sensing technology in terms of (a) applications, (b) nanomaterials that can be used in different applications and are classified into inorganic, organic, and carbon-based types (reproduced with permission under the Creative Commons CC-BY license from ref.⁵⁹, Elsevier B.V.) and (c) inherent advantages and open challenges of a microfluidic-embedded LoF sensing platform empowered by AI (created in <https://bioart.niaid.nih.gov/>).

suggest that 3D printing technology enables researchers to fabricate advanced microfluidic devices without requiring significant microfabrication skills, thereby making access to advanced diagnostic tools⁷². Sanka et al. observed that the creation of libraries for standardized microfluidic equipment might speed up the prototype of devices used in laboratory automation, which is crucial for optimizing processes in research and clinical environments⁷³.

Figure 3(a) shows a fascinating design using a spiral microchannel to optimize interaction between the sample and the sensing area⁷⁴. The sensor employs a long period grating (LPG) structure integrated into the optical fiber (Fig. 3(b)). The inset illustrates the sensing process in which glucose oxidase (GOx) catalyzes the conversion of glucose into gluconic acid, resulting in a decrease in pH and subsequent hydrogel swelling (Fig. 3(c)). This swelling modifies the local RI next to the LPG sensor, enabling optical signal detection associated with analyte concentration. Figure 3(d) illustrates another example of LoF prototype employing a LSPR-based sensor integrated inside a PDMS microfluidic channel⁷⁵. The tip sensor that is connected to the light

source and the detector via an optical fiber coupler (Fig. 3(e)), allows real-time monitoring of biological processes inside the reaction chamber. SEM pictures (Fig. 3(f)) the nanostructure deposited over the LSPR sensor surface, essential for generating the LSPR phenomenon.

Table 1 points out the recent advancements in the integration of optical fibers with microfluidic devices to enhance sensing capabilities and detection performance. These devices implement different sensing schemes, such as LPG, D-shaped fibers, fiber tip, and micro-optics for diverse applications, highlighting the adaptability and increasing capability and functionality of these platforms in biological and analytical fields. In order to thoroughly benchmark against different microfluidic-embedded LoF platforms, Table 1 encompasses quantitative metrics, such as volume sensitivity (S_{vol}), LoD, dynamic range (DR), response time (τ), type of matrix, temperature compensation (T-comp.), and validation in real samples.

It can be observed that the combination of microfluidic systems with LoF technology is an effective and reliable approach for synergistic fluid manipulation and enhanced

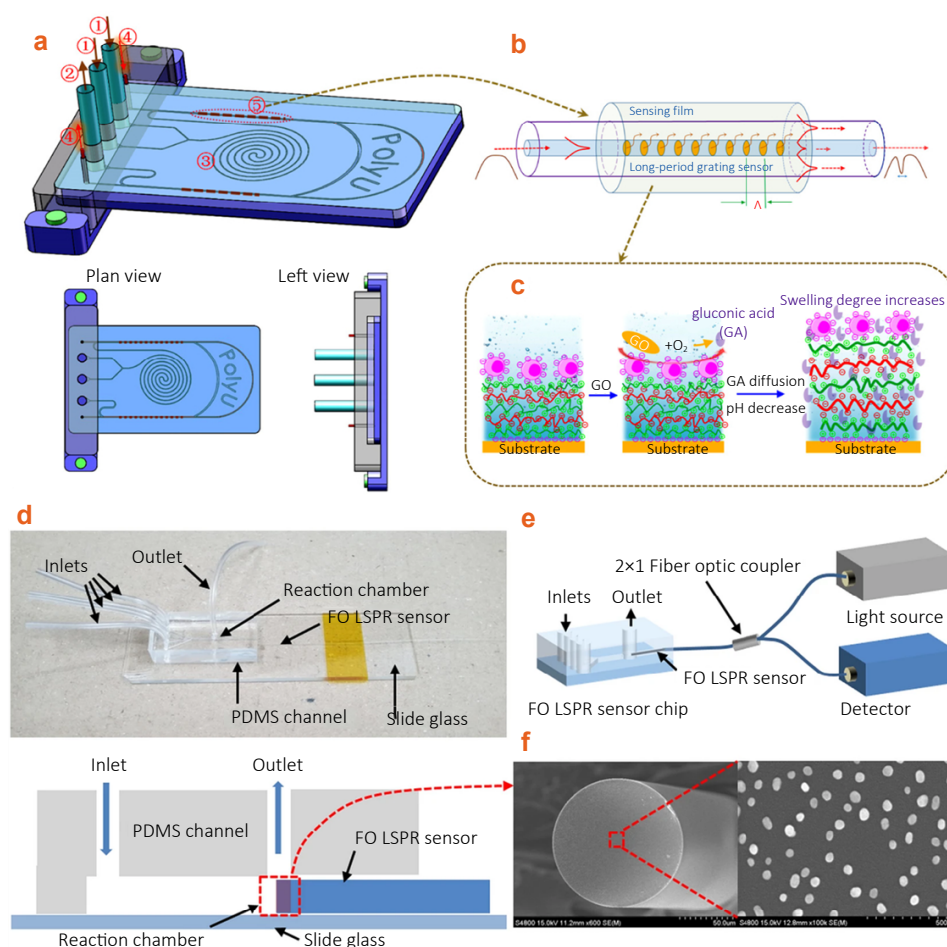


Fig. 3 | (a) Schematic and layout of a microfluidic chip with a spiral microchannel for analyte transport, including plan and left views, together with the optical fiber sensors; (b) Schematic of the used optical fiber LPG sensor coated with an hydrogel film for real-time monitoring of GO processes; (c) Working mechanism of the pH-responsive hydrogel film (previous subfigures reproduced with permission under the Creative Commons CC-BY license from ref.⁷⁴, 2016 Optical Society of America). (d) Photograph and schematic of a PDMS-based microfluidic chip integrated with an optical fiber LSPR sensor placed on a glass slide; (e) Optical setup for detection including a light source, an optical detector and a fiber coupler; (f) SEM images of the sensor tip with zoomed-in nanoparticle distribution confirming uniform nanoparticle decoration essential for LSPR generation (previous subfigures reproduced with permission under Creative Commons Attribution 4.0 International License from ref.⁷⁵, Springer Nature).

sensing across many applications, especially in biomedicine. Material fragility, precise sizing of pieces, alignment of fiber-based components, and accurate control over the flow rates are critical elements that might hinder an easy integration and use of optical fiber-based sensors in demanding environments.

5 Applications of LoF-microfluidics for sensing

5.1 Biomedical-related sensing

The pairing of LoF technology with microfluidics yields substantial progress in chemical and biological sensing applications given the very accurate and precise control of liquid flow in microfluidic environments⁸¹ and benefitting from the distinctive characteristics of optical fibers. The

integration of microfluidics with fiber optic sensors usually provides enhanced sensitivity and stability of the optical signal and hence facilitates continuous monitoring of various properties including temperature, concentration, and refractive index^{82,83}. LoF technology integrated with microfluidics may use several optical detection methods, including spectroscopic approaches (like Raman or UV-visible spectroscopy), labelled methods (like fluorescence or chemi/luminescence), and label-free methods based on the excitation of surface/evanescent waves (like SPR, LSPR, gratings, interferometry, Bloch surface wave, lossy mode resonance (LMR)), which enable *in situ* detection for biological analysis, and environmental monitoring⁸⁴. The size, portability and elevated throughput of these integrated systems make them ideal for clinical diagnosis through PoC devices, where conventional hospital apparatus is impractical. These systems usually need a minimal volume of samples

Table 1 | Microfluidic-integrated LoF platforms for advanced sensing applications: benchmark against different sensing configurations using quantitative metrics.

Sensing scheme	Sensing configuration	Target	S_{vol}	LoD	DR	τ	Matrix	T-comp.	Real-sample validation	Ref
LPG	Small-diameter LPG coated with glucose oxidase layer integrated in PDMS spiral chip	Glucose	205 nm $\cdot$ RIU $^{-1}$	1 nM	2–10 μ M	70 s	Water	—	No	ref. ⁷⁴
TFBG	Au-coated TFBGs integrated into a multi-channel microfluidics	Amyloid Beta 42 (A β ₄₂)	3500 dB $\cdot$ RIU $^{-1}$	30–170 pg $\cdot$ mL $^{-1}$	0.1–1000 ng $\cdot$ mL $^{-1}$	3–7 min	CSF	Yes (inherently via Bragg wavelength)	Yes	ref. ¹³
LMR	LMR D-shaped fiber coated with SnO _{2-x} embedded into a custom microfluidics	IgG	14.5 $\times$ 10 ³ nm $\cdot$ RIU $^{-1}$	1 fM	1 pg mL $^{-1}$ –10 μ g $\cdot$ mL $^{-1}$	~20 min	Serum	Yes (microfluidic system)	No	ref. ⁴⁸
BSW	BSW-based stack-layered D-shaped fiber embedded into a custom microfluidics	IgG	~1500 nm $\cdot$ RIU $^{-1}$	70 aM	10 ⁻⁴ –10 ⁴ ng mL $^{-1}$	~20 min	Serum	Yes (microfluidic system)	No	ref. ¹⁰
Reflectivity	Spherical-tip fiber sensor inserted into a plastic tubing	CD44	120 dB $\cdot$ RIU $^{-1}$	4.68 aM	0.2 aM–100 nM	10 min	Serum	Yes (embedded FBG sensor)	No	ref. ⁵³
Reflectivity + TFBG	TFBG-based ball-resonator fiber sensor inserted into a plastic tubing	HER2	4034 dB $\cdot$ RIU $^{-1}$	151.5 ag $\cdot$ mL $^{-1}$ (PBS) and 3.7 pg $\cdot$ mL $^{-1}$ (Serum)	10 ⁻⁷ –10 ⁻² ng $\cdot$ mL $^{-1}$	—	PBS / Serum	Yes (inherently via Bragg wavelength)	No	ref. ⁷⁶
Michelson interferometry	Vernier effect-assisted Michelson interferometric microstructured fiber sensor embedded into microfluidics	cDNA	8791 nm $\cdot$ RIU $^{-1}$	19.25 nM	1 μ M	—	PBS	—	No	ref. ⁷⁷
Fabry-Pérot interferometry	3D-printed fiber-tip dual-mode (Fabry-Perot interferometry + SPR) sensor inserted into a PDMS microfluidics	cDNA	~1500 nm $\cdot$ RIU $^{-1}$	1.2 nM	5–100 nM	15–20 min	PBS / FBS	Yes (dual-mode sensing)	No	ref. ⁷⁸
LSPR	Fiber-tip decorated with gold NPs and integrated into PDMS microfluidics	Thyroglobulin	—	93.11 fg $\cdot$ mL $^{-1}$ (PBS) 21.18 pg $\cdot$ mL $^{-1}$ (Serum)	0.001–100000 pg $\cdot$ mL $^{-1}$	5 min	PBS / Serum	—	Yes	ref. ⁷⁵
SERS	D-shaped fiber coated with gold NPs and embedded into multi-channel PDMS microfluidics	R6G / MB	—	10 pM	10 ⁻¹¹ –10 ⁻⁶ M	~2 min	Water	—	No	ref. ⁷⁹
SPR	D-shaped fiber SPR sensor coated with MOF-74 and integrated into 3D micro-nano printed microfluidics	Berberine	2640 nm $\cdot$ RIU $^{-1}$	0.38 μ g $\cdot$ mL $^{-1}$	1–100 μ g $\cdot$ mL $^{-1}$	~20 min	PBS	Yes (matrix-based using temperature demodulation)	No	ref. ⁸⁰

* CSF: cerebrospinal fluid; LMR: lossy mode resonance; IgG: immunoglobulin G; BSW: Block surface wave; CD44: transmembrane glycoprotein; HER2: human epidermal growth factor-2; cDNA: complementary DNA; FBS: fetal bovine serum; MOF: metal organic framework.

and provide excellent reliability, making them appropriate for real-time applications in bioanalytic, organ-on-a-chip technologies, and high-resolution chemical analysis^{85,86}.

A representative example of the capabilities of LoF–microfluidic systems in biomedical diagnostics is illustrated in Fig. 4, which showcases a multi-channel plasmonic fiber optic biosensing platform developed for the ultrasensitive detection of Alzheimer’s disease (AD) biomarkers¹³. The system integrates a custom-designed microfluidic module

(Fig. 4(a)) with a gold-coated highly-tilted fiber Bragg grating (TFBG; Fig. 4(b, c)), enabling simultaneous analysis of multiple A β ₄₂ species using sub-microliter sample volumes. As shown in Fig. 4, the TFBG excites a dense comb of narrowband cladding-mode resonances that overlap with the broadband plasmonic absorption of the gold film, providing exceptionally high surface sensitivity to binding interactions. This hybrid TFBG–SPR configuration, operating in the near-infrared, offers long penetration depth and

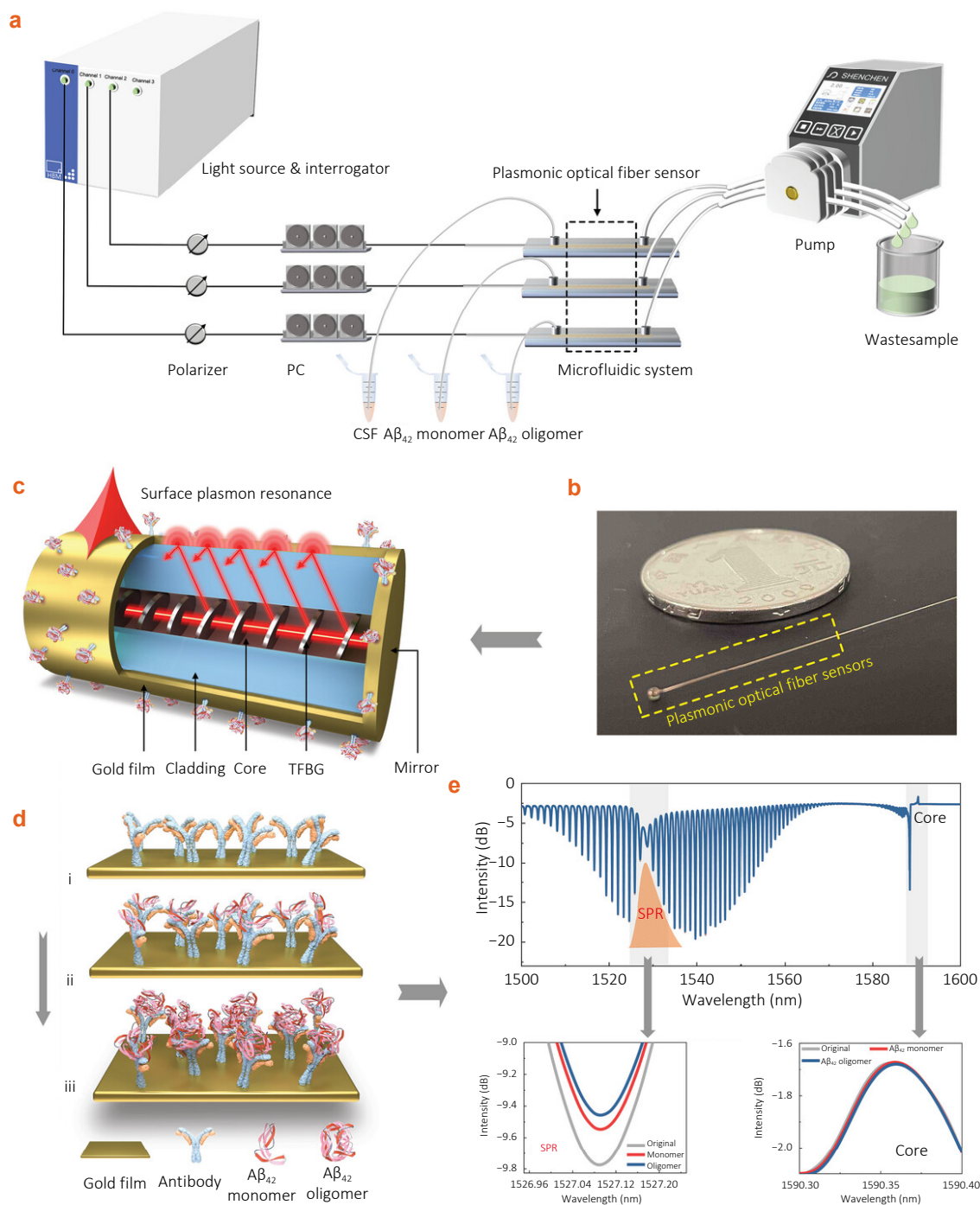


Fig. 4 | (a) Multi-channel microfluidic system integrated with a gold-coated tilted fiber Bragg grating (TFBG) for simultaneous detection of Aβ₄₂ monomers and oligomers for early diagnosis of Alzheimer's disease. (b) Photograph of the compact plasmonic fiber probe. (c) Schematic of the TFBG-assisted SPR mechanism enabling high-sensitivity surface monitoring of binding interactions. (d) Stepwise binding protocol of antibodies, Aβ₄₂ monomers, and Aβ₄₂ oligomers on the gold film. (e) Corresponding spectral responses showing SPR modulation and sensing mechanisms for differentiation between Aβ₄₂ species (previous subfigures reproduced with permission under Creative Commons Attribution 4.0 International License from ref.¹³, 2024 Wiley-VCH GmbH).

strong surface confinement, allowing precise discrimination between Aβ₄₂ monomers and oligomers based on binding kinetics (Fig. 4(d, e)). With LoD in the range of ≈30–170 pg·mL⁻¹ well below the clinical cut-off for the early AD diagnosis, this LoF–microfluidic platform demonstrates how

fiber optic sensors can deliver highly sensitive, multi-parameter, and real-time biomarker detection essential for early-stage disease diagnosis.

Still on AD, another example of LoF system based on LMR sensing phenomenon⁸⁷ is used to detect another

hallmark in AD (i.e., tau protein), with high sensitivity and specificity, enabling rapid and low-volume analysis of cerebrospinal fluid (CSF) samples⁸⁸. Regarding the detection of prostate specific antigen (PSA), microfluidic electrochemical optical fiber sensors using graphene films demonstrate potential applications in clinical diagnosis and personalized medicine⁸⁹. Therefore, it is clear that the fusion of microfluidic systems with LoF technology presents a transformative

path in biomarker and pathogen detection.

Figure 5(a) showcases another illustrative examples of the integration of microfluidic systems with LoF platforms for advanced biomarker and pathogen detection. In particular, it is worth underlining that LoF technology remarkably enables the integration of three components into a single device: laser-based fluorescence detection, photomultiplier tube readout, and vacuum-assisted cell capture⁹⁰. Figure 5(b)

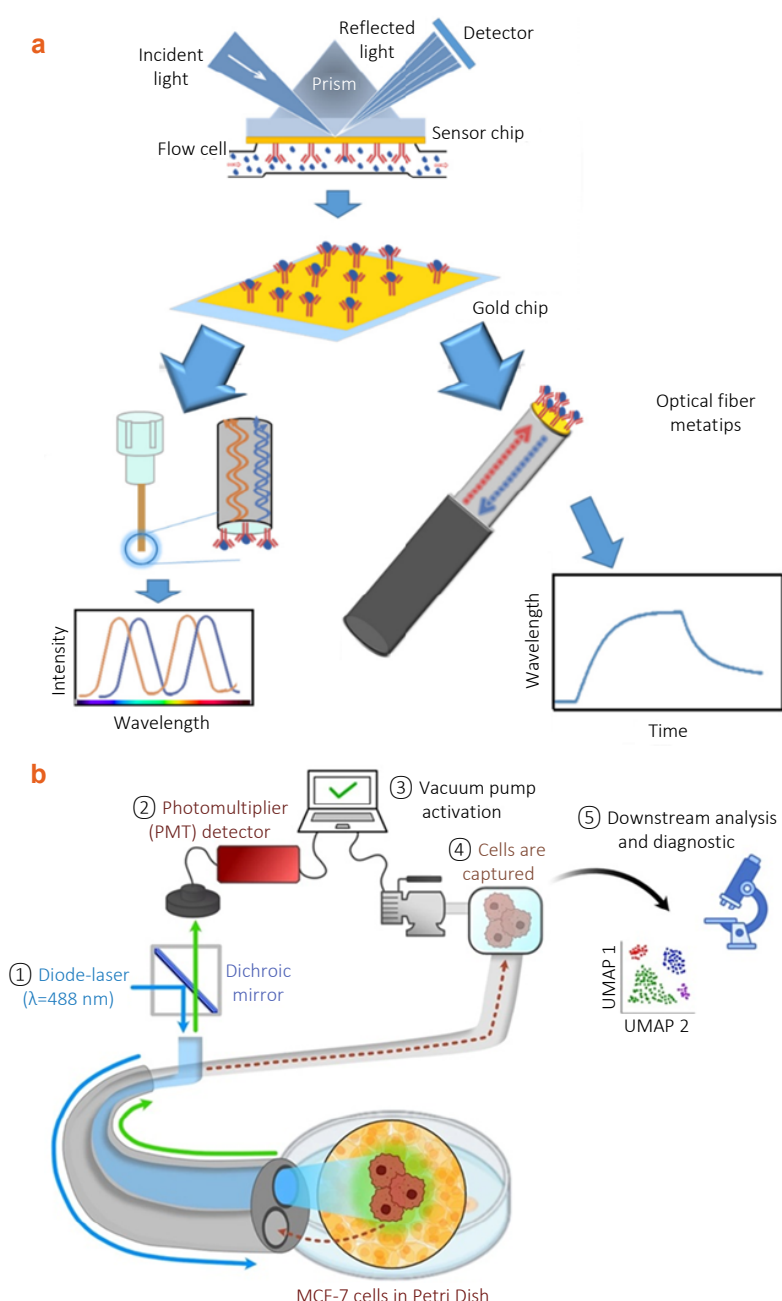


Fig. 5 | (a) A hybrid platform combining microfluidics and SPR for optimized functionalization of fiber surface and detection of target analytes via antibody immobilization (reproduced with permission under Creative Commons Attribution 4.0 International License from ref.⁹⁰, 2022 Licensee MDPI, Basel, Switzerland). (b) LoF platform for live cell capture and diagnostics using a compact laser-based fluorescence tool (reproduced with permission under Creative Commons Attribution 4.0 International License from ref.⁹¹, Springer Nature).

illustrates a fiber-based system that selectively isolates labeled cells (e.g., MCF-7 breast cancer cells) from a culture dish, enabling downstream diagnostic and single-cell analysis while minimizing photobleaching⁹¹.

5.2 Environmental sensing

The integration of microfluidic technology with LoF technology has provided novel opportunities for environmental monitoring and pharmaceutical analysis given the reduced reagent consumption, and hence decreased costs together with high portability⁹².

Recent advancements in microfluidics have facilitated the on-site detection of heavy metals and contaminants, which is essential due to the detrimental impacts of trace heavy metal exposure on human health and ecosystems^{93–95}. Microfluidic devices can be constructed on various substrates, including paper and polymers, have shown adequate sensitivity and selectivity for the detection of metal ions such as lead, cadmium, mercury, and arsenic^{93,96}. These systems provide ongoing real-time monitoring with LoD that may reach sub-nanomolar levels, beyond the limitations of traditional laboratory-based equipment^{94,96}.

However, the design of LoF systems combined with the downsizing of microfluidic channels has dramatically improved the detection capabilities. Through the integration of materials innovation, microfabrication processes, and advanced optical detection technologies, these systems provide a highly integrated, scalable, and reliable solution for the fast and sensitive detection of heavy metal ions, including lead, mercury, and chromium⁹⁷, and other pollutants across diverse environments. These systems use diverse optical detection techniques, such as surface-enhanced Raman scattering (SERS) and SPR for instance^{98,99}.

Mishra et al. develop a cost-effective micro absorbance-based microfluidic system with nanoparticle immobilization for detecting chemical contaminants in drinking water, achieving 0.5 ppb as LoD and higher sensitivity compared to conventional absorbance methods¹⁰⁰. Si et al. propose an electrochemical plasmonic fiber optic sensor that allows ultra-sensitive, real-time heavy metal detection with an LoD as low as 10^{-10} M and a dynamic range spanning five orders of magnitude, ideal for remote environmental monitoring⁹⁷. Dhara et al. present an LSPR fiber optic sensor for detecting lead ions in aqueous solutions, with a sensitivity of 0.28 nm/mM¹⁰¹. Menon et al. report on a metal-organic framework-based fiber optic sensor that detects chromium(VI) ions with an LoD of 1 ppb¹⁰². Hengoju et al. underscore the benefits of using optical fibers in droplet microfluidics, emphasizing their flexibility, low cost, and sensitivity in detecting chemical and biological parameters¹⁰³.

On the other hand, the integration of microfluidic systems and LoF devices presents significant advantages in the detection of pharmacological substances. The ability to analyze small volumes is especially very important in the

issues of global challenge of pharmacological contamination. Vikas and Saccomandi explore the design, development and testing of an indium tin oxide (ITO)-coated fiber optic LMR device specifically for ciprofloxacin detection, demonstrating both effectiveness and practicality in real-world deployment¹⁰⁴. On the same topic, Huang et al. introduce a novel fluorescent optical fiber sensor with very high selectivity¹⁰⁵. Wang et al. spotlight that the microfluidics integration with fiber-optic sensors makes easier the detection of biological and chemical contaminants, as well as pharmaceutical waste¹⁰⁶. These developments aim at reducing the effects of pharmaceutical contamination and facilitate future research in biosensing applications related to environmental safety and public health.

Examples of optofluidic platforms integrating optical fibers with microfluidic channels for environmental sensing are presented in different research. A Fabry–Pérot microcavity formed by two gold-coated optical fiber facets is embedded within a microreactor where chromogenic reagents and phosphate-containing samples are rapidly mixed¹⁰⁷. This configuration enables fast colorimetric reactions and optical readout, dramatically reducing the detection time from minutes to seconds. Another research shows a polymer-based microfluidic platform fabricated using a cyclic olefin copolymer support and PDMS microchannels. Optical fibers are aligned with the measurement chamber to provide continuous monitoring of Hg(II) ions architecture¹⁰⁸. Figure 6 showcases how the combined microfluidics-optical fiber technologies together with engineered bioreceptors can effectively been used for the detection of small molecular weight targets¹⁰⁹. In fact, the accurate detection of per- and polyfluoroalkyl substances (PFAS) in environmental matrices, including drinking water, necessitates the development of highly sensitive and specific sensing methodologies. The proposed label-free biosensing platform enables to address this analytical challenge by incorporating a side-polished optical fiber coated with a nanometer-scale layer of SnO₂ (Fig. 6(a)), which jointly excite the LMR sensing phenomenon, and appropriately engineered bioreceptor, such as delipidated human serum albumin (hSA; Fig. 6(b)). This system that is embedded into a custom-designed thermo-stabilized microfluidic chip (Fig. 6(c)) is employed for the detection of perfluorooctanoic acid (PFOA), a very harmful pollutant. The optical signals corresponding to the conformational changes induced by the binding interaction between hSA and PFOA are monitored through LMR spectral shifts and an LoD around 100 pg mL⁻¹ is attained, so at the same concentrations required in drinking water and groundwater stated by environmental agencies, such as EPA (environmental protection agency, USA) and EEA (european environmental agency, EU).

5.3 AI-Driven sensing

AI has emerged as a transformative force in biochemical

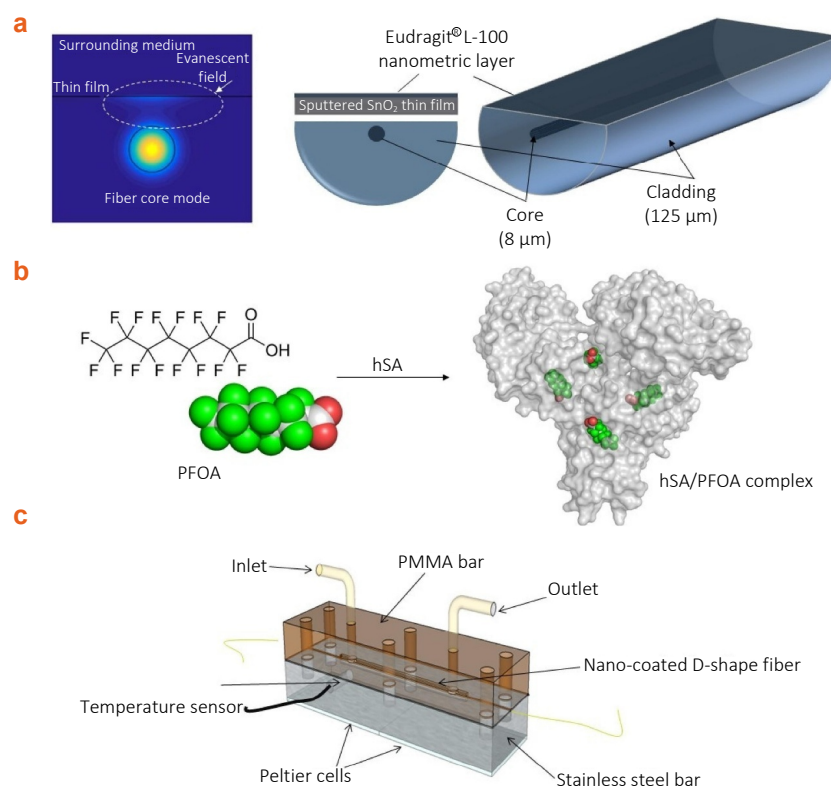


Fig. 6 | (a) Schematic of the side-polished optical fiber sensing region coated with a sputtered SnO₂ thin film and functionalized with an Eudragit® L-100 nanolayer; (b) chemical structure of the perfluorooctanoic acid (PFOA) that has the ability to form a 1:4 complex with delipidated human serum albumin, resulting in the hSA/PFOA complex; (c) advanced microfluidic system consisting of a flow channel for hosting the optical fiber sensor and equipped with a temperature stabilization mechanism based on Peltier cells (previous subfigures reproduced with permission under the Creative Commons CC-BY-NC-ND license from ref.¹⁰⁹, Elsevier B.V.).

sensing, particularly in enhancing real-time signal processing, pattern recognition, and predictive analytics. Concerning microfluidic-based LoF platforms, AI can drive dramatic innovation by leveraging the analysis of complex optical spectral signatures (for instance, resonance wavelength shifts, intensity variations, phase/polarization changes), their de-noising, de-trending for baseline correction, debugging and even the demodulation from multiple overlapped signatures or fingerprints. Machine learning (ML) algorithms, including regression models, neural networks, and convolutional neural networks, can extract subtle patterns from LoF outputs, remarkably improving the LoD, selectivity, reliability and reproducibility even under noisy or variable microfluidic conditions^{110–113}. In addition, AI-driven approaches can envisage to facilitate multiplexed sensing and then quantify multiple targets simultaneously thanks to unmixing and pattern recognition, where multiple nanomaterial-functionalized regions or multi-points sensing along a single optical fiber produce overlapping and intricate spectral signals. This would particularly benefit from PoC diagnostic devices, systems for biomarker quantification in complex biofluids (i.e., sweat, tears, saliva, or plasma), and overall sensing systems devoted to biochemical analysis and

environmental monitoring^{110,111,113}. Despite these advantages, AI integration in LoF systems faces specific challenges. The first lies in limited raw data acquisition for each sensor, necessitating strategies such as transfer learning, physics-informed machine learning, and synthetic data generation to train robust models¹¹⁴. Real-time processing on portable, low-power hardware is also critical for wearable or implantable applications, motivating edge-AI solutions optimized for optical and microfluidic signals. Furthermore, LoF platforms often combine optical, biochemical, and environmental inputs, requiring robust multimodal data-fusion frameworks to maintain accurate predictions and signal interpretability¹¹⁵.

To illustrate practical implementation of AI in LoF-microfluidic platforms, representative example of workflows for both biomedical and environmental applications can be envisaged. In multiplexed biomarker detection systems as a current need in most of diseases, a great amount of spectra is collected from multiple nanomaterial-functionalized regions or from multiple measurands to be recorded along a single optical fiber sensing system, often combined with auxiliary measurements, such as temperature, strain, flow rate, etc., that sometimes are required to get rid of the

cross-sensitivity issues¹¹⁶. Afterwards, AI algorithms can perform spectral de-noising, baseline drift correction (or de-trending), and multi-target signal deconvolution to extract meaningful biomarker concentrations, while detecting unplanned anomalies, such as flow issues or formation of bubbles. Under standardized metrics like LoD, sensitivity among all, models can be validated through cross-batch evaluation using datasets from different sensor fabrication runs, and specific adaptive techniques are applied to account for variations of sample matrices in terms of viscosity and complexity. Lightweight edge-AI models embedded in portable readout units can enable real-time and most-reliable biomarker quantification, while more computationally intensive training occurs on workstation servers¹¹⁴.

For environmental monitoring, LoF-microfluidic platforms generate time-series of optical signals (intensity change and wavelength shift mostly) in terms of the investigated parameter (i.e., ions, heavy metals, chemical compounds, redox signal, concentration of specific element) under continuous flow conditions, with auxiliary inputs, such as pH, temperature, and humidity. AI-related tasks can therefore include noise reduction, drift correction, weak-signal extraction from low-concentration contaminants, and multi-class classification of targets or small molecules^{117,118}. Validation of AI model can involve cross-site data to ensure generalization to different environmental conditions, with metrics including accuracy, selectivity, LoD, and false-positive rates. Practical deployment can rely on edge-computing-driven internet of things (IoT) implementation for continuous monitoring, with periodic uploads to cloud or workstation platforms for retraining of AI model and long-

term trend analysis.

A schematic example of the overall workflow is provided in Fig. 7 and consists of data acquisition, preprocessing of data, definition of AI model and its implementation, and deployment of AI model with final assessment with standardized metrics. The workflow highlights some critical steps, such as drift correction, anomaly detection, and multi-target quantification, providing a practical framework for AI-driven LoF-microfluidic sensing systems.

Although fully operational AI-enhanced microfluidic LoF devices are just at the dawn, ongoing research suggests promising pathways for their development¹¹⁹. These include standardized spectral datasets for different LoF architectures, embedding AI models into portable readout units, and adaptive control loops that dynamically adjust microfluidic flow and sensing conditions in real time. Emerging AI paradigms such as transformer-based time-series analysis and hybrid physics-AI models are expected to further enhance predictive capabilities, reproducibility, multi-functionality and scalability by bringing the knowledge from more mature technologies¹²⁰. Overall, by combining LoF technology, microfluidics, and AI, next-generation sensing platforms can achieve adaptive, autonomous, and predictive operation, providing real-time feedback for healthcare diagnostics, environmental monitoring, and personalized wearable devices. These intelligent platforms can represent a key step toward the integration of AI with smart photonic and microfluidic systems, advancing both analytical performance and operational reliability for an easier translation from laboratories to the market.

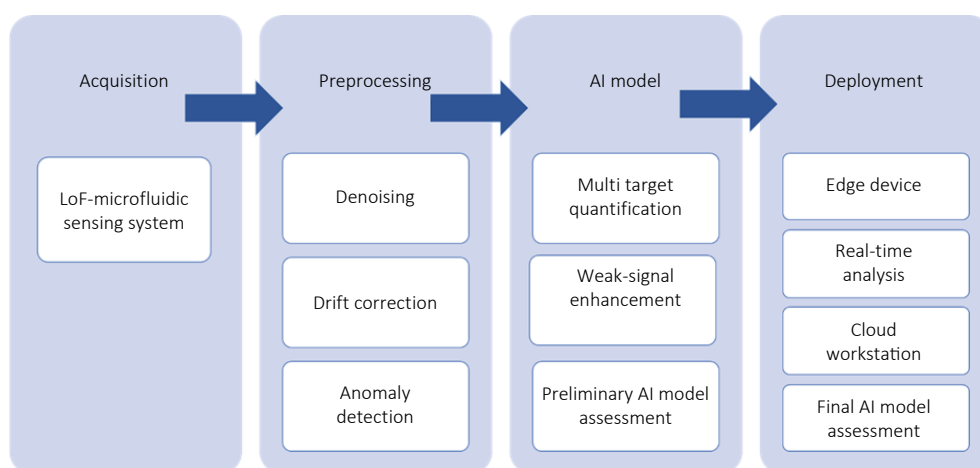


Fig. 7 | A schematic workflow for AI-driven LoF-microfluidic sensing systems consisting of data acquisition (full spectrum, intensity changes and wavelength shifts, multimodal signals such as temperature, flow, or pH), preprocessing of data (spectral denoising, baseline drift correction, anomaly detection, and signal normalization), AI model (multi-target quantification, weak-signal enhancement using neural networks, regression models, or transformer-based algorithms, and preliminary AI model assessment), and deployment by the use of evaluation metrics (accuracy, sensitivity, selectivity, LoD, cross-batch validation, domain adaptation) that can ensure model robustness and generalization. Finally, deployment highlights real-time implementation on edge-computing-driven IoT implementation for portable, wearable, environmental or biochemical monitoring applications, with optional cloud or workstation-based retraining for long-term performance optimization.

5.4 Challenges and future perspectives

Despite the remarkable advances in LoF systems integrated with microfluidics, several engineering challenges remain to bridge the gap toward their reliable, scalable, and real-world deployment. First, fabrication and bonding of microfluidic devices remain critical hurdles. Innovations like the “Click-and-Bond” method provide solvent-free, room-temperature bonding, optimizing polymer-based microfluidic production on a possible large scale¹²¹. Something similar can be envisaged for LoF systems too. Second, when working with real samples, microfluidic systems can be very much susceptible to clogging, channel fouling, and environmental interference, especially at very low flow rates¹²². The use of advanced antifouling coatings can get rid of such issues, also in the case of LoF devices¹²³. Third, the choice of the materials among new polymers and advanced functional nanomaterials can play a crucial role in the device stability, biocompatibility, and then turn into the detection performance^{124,125}. Advances in surface functionalization, hybrid nanostructures, and robust micro/nano-fabrication techniques are therefore essential for reproducible and scalable LoF-microfluidic systems, opening up the possibility for multiplexed sensing capabilities^{11,15}. Fourth, despite the countless and distinct advantages of AI, its integration can introduce additional constraints, such as computational load, data infrastructure, and real-time processing requirements, and related risks as well¹²⁶. Mitigation strategies include embedding edge-compute AI units, implementing adaptive calibration loops, and combining optical, electromechanical, and AI-driven controls to maintain stable and reliable operation. Overall, developing standardized fabrication methods, reporting detailed protocols and well-defined calibration methods, and using uniform definitions for performance metrics would definitely facilitate the comparison across different works and then improve reproducibility of the results dramatically^{122,127}.

Therefore, transforming laboratory LoF prototypes into industrially scalable systems continues to face limitations in terms of sensor packaging, result reproducibility and batch-to-batch variation, particularly arising from nanostructure deposition, surface chemistry, microchannel geometry, and fiber-to-fluidic coupling alignment^{124,125,127}. Looking forward, since operational challenges can be mostly unveiled by means of engineering solutions, an engineering-oriented roadmap for effective and advanced LoF-microfluidic platforms is envisioned:

1) Uniform definition and application of performance metrics: Use the standardized definition of crucial sensing/biosensing metrics (volume and surface sensitivity, LoD, accuracy, stability, etc.) toward a uniform assessment of the device performance¹¹⁹.

2) Standardized fabrication and detailed protocols: Develop guidelines for microchannel geometry, surface roughness, nanostructure deposition, fiber coupling align-

ment, and material selection^{121,124,125}.

3) Robust and reproducible testing: Use testing procedures that enable to assess the performance metrics taking into account the possible reusability, and reproducibility across batches^{122,128}.

4) Integration of AI and real-time control: thanks to IoT, employ edge computing for adaptive calibration, anomaly detection (clogging, flow interruptions), and multi-parameter data fusion¹¹⁴.

5) Packaging and scalability: Optimize bonding techniques, modular design approaches, and low-cost materials (e.g., polyethylene) to enable industrial-scale deployment^{129,130}.

6) Application-specific optimization: Tailor nanomaterial functionalization, flow rates, and sensor configuration for biomedical, environmental, or wearable sensing contexts.

By following this roadmap, LoF-microfluidic platforms might effectively move from the laboratory stage to reliable, reproducible, and commercially viable devices. Multidisciplinary collaboration across experts on optics, photonics, microfluidics, materials science, and AI will be essential to realize the full potential of these compact, versatile, and intelligent sensing systems. With continued innovation and standardized engineering practices, LoF-based optofluidic sensing technologies are poised to become integral tools for next-generation biomedical and environmental monitoring applications.

References

- Gupta BD, Shrivastav AM, Usha SP. *Optical Sensors for Biomedical Diagnostics and Environmental Monitoring* (CRC Press, Boca Raton, 2017).
- Sarabi MR, Jiang N, Ozturk E et al. Biomedical optical fibers. *Lab Chip* **21**, 627–640 (2021).
- Shah RY, Agrawal YK. Introduction to fiber optics: sensors for biomedical applications. *Indian J Pharm Sci* **73**, 17–22 (2011).
- Wolfbeis OS. Fiber-optic chemical sensors and biosensors. *Anal Chem* **78**, 3859–3874 (2006).
- Wang XD, Wolfbeis OS. Fiber-optic chemical sensors and biosensors (2013–2015). *Anal Chem* **88**, 203–227 (2016).
- Vaiano P, Carotenuto B, Pisco M et al. Lab on Fiber Technology for biological sensing applications. *Laser Photonics Rev* **10**, 922–961 (2016).
- Ricciardi A, Crescitelli A, Vaiano P et al. Lab-on-fiber technology: a new vision for chemical and biological sensing. *Analyst* **140**, 8068–8079 (2015).
- Pisco M, Cusano A. Lab-on-fiber technology: a roadmap toward multifunctional plug and play platforms. *Sensors* **20**, 4705 (2020).
- Li WB, Null N, Long YK et al. Wearable photonic smart wristband for cardiorespiratory function assessment and biometric identification. *Opto-Electron Adv* **8**, 240254 (2025).
- Del Villar I, Gonzalez-Valencia E, Kwietniewski N et al. Nano-phonic crystal D-shaped fiber devices for label-free biosensing at the attomolar limit of detection. *Adv Sci* **11**, 2310118 (2024).
- Santano D, Socorro AB, Giannetti A et al. Simultaneous detection of inflammatory process indicators via *operando* dual lossy mode resonance-based biosensor. *Opto-Electron Sci* **4**, 250005 (2025).
- Chen C, Singh K, Huo SY et al. Evanescent wave-based optical biosensors for innovations, medical application and future perspectives.

- tives. *J Adv Res* (2025), <http://doi.org/10.1016/j.jare.2025.07.007>.
13. Zu LJ, Wang XC, Liu P et al. Ultrasensitive and multiple biomarker discrimination for Alzheimer's disease via plasmonic & microfluidic sensing technologies. *Adv Sci* **11**, 2308783 (2024).
 14. Cao SF, Chen RP, Yang QC et al. Point-of-care diagnosis of pre-eclampsia based on microfiber Bragg grating biosensor. *Biosens Bioelectron* **249**, 116014 (2024).
 15. Dabagh S, Singh R, Borri C et al. Functional nanomaterial coatings on optical fibers: toward enhanced biosensing performance. *IEEE Sensors Reviews* **2**, 157–169 (2025).
 16. Rusling JF. Developing microfluidic sensing devices using 3D printing. *ACS Sens* **3**, 522–526 (2018).
 17. Kant K, Abalde-Cela S. Surface-enhanced Raman scattering spectroscopy and microfluidics: towards ultrasensitive label-free sensing. *Biosensors* **8**, 62 (2018).
 18. He XC, Fan C, Luo Y et al. Flexible microfluidic nanoplasmonic sensors for refreshable and portable recognition of sweat biochemical fingerprint. *npj Flex Electron* **6**, 60 (2022).
 19. Bai S, Serien D, Hu AM et al. 3D microfluidic surface-enhanced Raman spectroscopy (SERS) chips fabricated by all-femtosecond-laser-processing for real-time sensing of toxic substances. *Adv Funct Mater* **28**, 1706262 (2018).
 20. Giaquinto M, Aliberti A, Micco A et al. Cavity-enhanced lab-on-fiber technology: toward advanced biosensors and Nano-opto-mechanical active devices. *ACS Photonics* **6**, 3271–3280 (2019).
 21. Yang X, Gong CY, Liu YL et al. Recent progress in fiber optofluidic lasing and sensing. *Photonic Sens* **11**, 262–278 (2021).
 22. Aliberti A, Ricciardi A, Giaquinto M et al. Microgel assisted lab-on-fiber optrode. *Sci Rep* **7**, 14459 (2017).
 23. Consoles M, Quero G, Spaziani S et al. Metasurface-enhanced lab-on-fiber biosensors. *Laser Photonics Rev* **14**, 2000180 (2020).
 24. Wang GR, Chen D, Wang TQ et al. Lab-on-fiber sensing system based on responsive Fabry–Perot optical resonance cavities prepared through *in situ* construction strategy. *Nanotechnology* **32**, 41LT01 (2021).
 25. Zhao QC, Yuan WH, Qu JQ et al. Optical fiber-integrated metasurfaces: an emerging platform for multiple optical applications. *Nanomaterials* **12**, 793 (2022).
 26. Wang GR, Wang L, Cheng Z et al. High-performance plasmonic lab-on-fiber sensing system constructed by universal polymer assisted transfer technique. *Nanotechnology* **33**, 095502 (2022).
 27. Calero V, Suarez MA, Salut R et al. An ultra wideband-high spatial resolution-compact electric field sensor based on lab-on-fiber technology. *Sci Rep* **9**, 8058 (2019).
 28. Zhao HD, Wu DF, Zeng MY et al. A vibration-based vehicle classification system using distributed optical sensing technology. *Transp Res Rec J Transp Res Rec Board* **2672**, 12–23 (2018).
 29. Huang HQ, Liao CR, Zou MQ et al. Four-dimensional printing of a fiber-tip multimaterial microcantilever as a magnetic field sensor. *ACS Photonics* **10**, 1916–1924 (2023).
 30. Zhao QC, Qu JQ, Peng GD et al. Endless single-mode photonics crystal fiber metalens for broadband and efficient focusing in near-infrared range. *Micromachines* **12**, 219 (2021).
 31. Nyein HYY, Bariya M, Kivimäki L et al. Regional and correlative sweat analysis using high-throughput microfluidic sensing patches toward decoding sweat. *Sci Adv* **5**, eaaw9906 (2019).
 32. Nyein HYY, Tai LC, Ngo QP et al. A wearable microfluidic sensing patch for dynamic sweat secretion analysis. *ACS Sens* **3**, 944–952 (2018).
 33. Shih K, Pitchappa P, Manjappa M et al. Microfluidic metamaterial sensor: selective trapping and remote sensing of microparticles. *J Appl Phys* **121**, 023102 (2017).
 34. Omidvar AH, Shahri AA, Serrano ALC et al. A highly sensitive molecularly imprinted polymer (MIP)-coated microwave glucose sensor. *Sensors* **22**, 8648 (2022).
 35. Gupta BD, Pathak A, Shrivastav AM. Optical biomedical diagnostics using lab-on-fiber technology: a review. *Photonics* **9**, 86 (2022).
 36. Kim HT, Yu M. Lab-on-fiber nanoprobe with dual high-Q Rayleigh anomaly-surface Plasmon polariton resonances for multiparameter sensing. *Sci Rep* **9**, 1922 (2019).
 37. Giaquinto M, Ricciardi A, Aliberti A et al. Light-microgel interaction in resonant nanostructures. *Sci Rep* **8**, 9331 (2018).
 38. Scherino L, Giaquinto M, Micco A et al. A time-efficient dip coating technique for the deposition of microgels onto the optical fiber tip. *Fibers* **6**, 72 (2018).
 39. Giaquinto M, Micco A, Aliberti A et al. Optimization strategies for responsivity control of microgel assisted lab-on-fiber optrodes. *Sensors* **18**, 1119 (2018).
 40. Ti CY, Shen Y, Ho Thanh MT et al. Reliable and mobile all-fiber modular optical tweezers. *Sci Rep* **10**, 20099 (2020).
 41. Kumar T, Harish AV, Etcheverry S et al. Lab-in-a-fiber-based integrated particle separation and counting. *Lab Chip* **23**, 2286–2293 (2023).
 42. Liang YZ, Yu ZY, Li LX et al. A self-assembled plasmonic optical fiber nanoprobe for label-free biosensing. *Sci Rep* **9**, 7379 (2019).
 43. Picelli L, van Klinken A, Lindgren G et al. Scalable wafer-to-fiber transfer method for lab-on-fiber sensing. *Appl Phys Lett* **117**, 151101 (2020).
 44. Goda K, Lu H, Fei P et al. Revolutionizing microfluidics with artificial intelligence: a new dawn for lab-on-a-chip technologies. *Lab Chip* **23**, 3737–3740 (2023).
 45. Jin FZ, Xu ZY, Wang W et al. Integrating tumor hypoxic sensing and photothermal therapy using a miniaturized fiber-optic therapeutic probe. *Small Sci* **5**, 2400450 (2025).
 46. Zhang YK, Zheng J, Jin FZ et al. Fiber-optic drug delivery strategy for synergistic cancer photothermal-chemotherapy. *Light Sci Appl* **13**, 228 (2024).
 47. Ran Y, Xu ZY, Chen MF et al. Fiber-optic theranostics (FOT): interstitial fiber-optic needles for cancer sensing and therapy. *Adv Sci* **9**, 2200456 (2022).
 48. Chiavaioli F, Zubiati P, Del Villar I et al. Femtomolar detection by nanocoated fiber label-free biosensors. *ACS Sens* **3**, 936–943 (2018).
 49. Soares MS, Silva LCB, Vidal M et al. Label-free plasmonic immunosensor for cortisol detection in a D-shaped optical fiber. *Biomed Opt Express* **13**, 3259–3274 (2022).
 50. Loyez M, Hassan EM, Lobry M et al. Rapid detection of circulating breast cancer cells using a multiresonant optical fiber aptasensor with plasmonic amplification. *ACS Sens* **5**, 454–463 (2020).
 51. Leal-Junior A, Avellar L, Biazzi V et al. Multifunctional flexible optical waveguide sensor: on the bioinspiration for ultrasensitive sensors development. *Opto-Electron Adv* **5**, 210098 (2022).
 52. Singh R, Wang Z, Marques C et al. Alanine aminotransferase detection using TIT assisted four tapered fiber structure-based LSPR sensor: from healthcare to marine life. *Biosens Bioelectron* **236**, 115424 (2023).
 53. Bekmurzayeva A, Ashikbayeva Z, Assylbekova N et al. Ultra-wide, attomolar-level limit detection of CD44 biomarker with a silanized optical fiber biosensor. *Biosens Bioelectron* **208**, 114217 (2022).
 54. Sypabekova M, Korganbayev S, González-Vila Á et al. Functionalized etched tilted fiber Bragg grating aptasensor for label-free protein detection. *Biosens Bioelectron* **146**, 111765 (2019).
 55. Arcadio F, Zeni L, Montemurro D et al. Biochemical sensing exploiting plasmonic sensors based on gold nanogratings and polymer optical fibers. *Photonics Res* **9**, 1397–1408 (2021).
 56. Zeni L, Perri C, Cennamo N et al. A portable optical-fibre-based surface Plasmon resonance biosensor for the detection of therapeutic antibodies in human serum. *Sci Rep* **10**, 11154 (2020).

57. Hernaez M, Zamarreño CR, Melendi-Espina S et al. Optical fibre sensors using graphene-based materials: a review. *Sensors* **17**, 155 (2017).
58. Qi M, Zhang NMY, Li KW et al. Hybrid plasmonic fiber-optic sensors. *Sensors* **20**, 3266 (2020).
59. Costanzo H, Gooch J, Frascione N. Nanomaterials for optical biosensors in forensic analysis. *Talanta* **253**, 123945 (2023).
60. Lei ZL, Guo B. 2D material-based optical biosensor: status and prospect. *Adv Sci* **9**, 2102924 (2022).
61. Mansor MA, Yang C, Chong KL et al. Label-free and rapid microfluidic design rules for circulating tumor cell enrichment and isolation: a review and simulation analysis. *ACS Omega* **10**, 6306–6322 (2025).
62. Tang H, Niu JQ, Jin H et al. Geometric structure design of passive label-free microfluidic systems for biological micro-object separation. *Microsyst Nanoeng* **8**, 62 (2022).
63. Zhao Y, Hu XG, Hu S et al. Applications of fiber-optic biochemical sensor in microfluidic chips: a review. *Biosens Bioelectron* **166**, 112447 (2020).
64. Xu W, Song D, Liu J, et al. Development of chemiluminescent lab-on-fiber immunosensors for rapid point-of-care testing of anti-SARS-CoV-2 antibodies and evaluation of longitudinal immune response kinetics following three-dose inactivation virus vaccination. *J Med Virol*. **95**, e28190 (2022).
65. Zhang CL, Gong GY, Gong Y et al. Optical fiber microfluidic sensors based on opto-physical effects. In Peng GD. *Handbook of Optical Fibers* 1–35 (Springer, Singapore, 2019).
66. Rogers JA, Nuzzo RG. Recent progress in soft lithography. *Mater Today* **8**, 50–56 (2005).
67. Kim P, Kwon KW, Park MC et al. Soft lithography for microfluidics: a review. *Biochip J* **2**, 1–11 (2008).
68. Waheed S, Cabot JM, Macdonald NP et al. 3D printed microfluidic devices: enablers and barriers. *Lab Chip* **16**, 1993–2013 (2016).
69. Weisgrab G, Ovsianikov A, Costa PF. Functional 3D printing for microfluidic chips. *Adv Mater Technol* **4**, 1900275 (2019).
70. Zheng ZD, Shi M, Xu Y et al. Light-induced dynamic assembly of gold nanoparticles in a lab-on-fiber platform for surface-enhanced Raman scattering detection. *ACS Appl Nano Mater* **5**, 8005–8011 (2022).
71. Caputo TM, Cusano AM, Principe S et al. Sorafenib-loaded PLGA carriers for enhanced drug delivery and cellular uptake in liver cancer cells. *Int J Nanomedicine* **18**, 4121–4142 (2023).
72. Razavi Bazaz S, Rouhi O, Raoufi MA et al. 3D printing of inertial microfluidic devices. *Sci Rep* **10**, 5929 (2020).
73. Sanka R, Lippai J, Samarasekera D et al. 3D μ F - interactive design environment for continuous flow microfluidic devices. *Sci Rep* **9**, 9166 (2019).
74. Yin MJ, Huang BB, Gao SR et al. Optical fiber LPG biosensor integrated microfluidic chip for ultrasensitive glucose detection. *Biomed Opt Express* **7**, 2067–2077 (2016).
75. Kim HM, Jeong DH, Lee HY et al. Design and validation of fiber optic localized surface Plasmon resonance sensor for thyroglobulin immunoassay with high sensitivity and rapid detection. *Sci Rep* **11**, 15985 (2021).
76. Sypabekova M, Amantayeva A, Vangelista L et al. Ultralow limit detection of soluble HER2 biomarker in serum with a fiber-optic ball-tip resonator assisted by a tilted FBG. *ACS Meas Sci Au* **2**, 309–316 (2022).
77. Hu XG, Li ZK, Zhang JW et al. In-situ label-free optofluidic DNA biosensor based on fiber-optic Michelson interferometer with Vernier effect for microfluidic chip. *Measurement* **254**, 117973 (2025).
78. Gong PQ, Li XG, Zhou X et al. Bimodal optical fiber biosensor with high anti-interference based on two-photon polymerization 3D nanofabrication. *Biosens Bioelectron* **290**, 117952 (2025).
79. Bo H, Ke Y, Yong Z et al. Microfluidic integrated D-shaped optical fiber SERS probe with high sensitivity and ability of multi-molecule detection. *Opt Express* **31**, 27304–27311 (2023).
80. Wei Y, Shi C, Zhang YH et al. Temperature-compensated fiber-optic SPR microfluidic sensor based on micro-Nano 3D printing. *Opt Express* **31**, 38179–38190 (2023).
81. Ma J, Wang GY, Jin L et al. Photothermally generated bubble on fiber (BoF) for precise sensing and control of liquid flow along a microfluidic channel. *Opt Express* **27**, 19768–19777 (2019).
82. Qu J, Liu Y, Li Y et al. Microfluidic chip with fiber-tip sensors for synchronously monitoring concentration and temperature of glucose solutions. *Sensors* **23**, 2478 (2023).
83. Li CX, Liu Y, Lang CP et al. Femtosecond laser direct writing of a 3D microcantilever on the tip of an optical fiber sensor for on-chip optofluidic sensing. *Lab Chip* **22**, 3734–3743 (2022).
84. Wang WB, Xia L, Xiao XH et al. Recent progress on microfluidics integrated with fiber-optic sensors for on-site detection. *Sensors* **24**, 2067 (2024).
85. Ricciardi A., Zimmer M., Witz N. et al. Integrated Optoelectronic Devices Using Lab-On-Fiber Technology. *Adv. Mater. Technol.* **7**, 2101681 (2022).
86. Luka G, Ahmadi A, Najjaran H et al. Microfluidics integrated biosensors: a leading technology towards lab-on-a-chip and sensing applications. *Sensors* **15**, 30011–30031 (2015).
87. Chiavaioli F, Janner D. Fiber optic sensing with lossy mode resonances: applications and perspectives. *J Lightwave Technol* **39**, 3855–3870 (2021).
88. Chiavaioli F, Santano Rivero D, Del Villar I et al. Ultrahigh sensitive detection of tau protein as Alzheimer's biomarker via microfluidics and nanofunctionalized optical fiber sensors. *Adv Photonics Res* **3**, 2200044 (2022).
89. Zhang Q, Ma SS, Zhang KY et al. A facile integrated microfluidic chip based on chitosan-gold nanoparticles-anchored three-dimensional graphene fiber film for monitoring prostate specific antigen. *Microchem J* **184**, 108171 (2023).
90. Ucci S, Spaziani S, Quero G et al. Advanced lab-on-fiber optrodes assisted by oriented antibody immobilization strategy. *Biosensors* **12**, 1040 (2022).
91. Varela JC, Harish AV, Maniewski P et al. Lab-in-a-Fiber detection and capture of cells. *Sci Rep* **15**, 9694 (2025).
92. Alhalaili B, Popescu IN, Rusanescu CO et al. Microfluidic devices and microfluidics-integrated electrochemical and optical (Bio) sensors for pollution analysis: a review. *Sustainability* **14**, 12844 (2022).
93. Ding R, Cheong YH, Ahamed A et al. Heavy Metals Detection with Paper-Based Electrochemical Sensors. *Anal. Chem* **93**, 1880–1888 (2021).
94. Filippidou MK, Chatzandroulis S. Microfluidic devices for heavy metal ions detection: a review. *Micromachines* **14**, 1520 (2023).
95. Yew M, Ren Y, Koh KS et al. A review of state-of-the-art microfluidic technologies for environmental applications: detection and remediation. *Glob Chall* **3**, 1800060 (2019).
96. Lace A, Cleary J. A review of microfluidic detection strategies for heavy metals in water. *Chemosensors* **9**, 60 (2021).
97. Si Y, Lao JJ, Zhang XJ et al. Electrochemical plasmonic fiber-optic sensors for ultra-sensitive heavy metal detection. *J Lightwave Technol* **37**, 3495–3502 (2019).
98. Yuan M, Li C, Zheng YZ et al. A portable multi-channel fluorescent paper-based microfluidic chip based on smartphone imaging for simultaneous detection of four heavy metals. *Talanta* **266**, 125112 (2024).
99. Li M, Gou HL, Al-Ogaidi I et al. Nanostructured sensors for detection of heavy metals: a review. *ACS Sustainable Chem Eng* **1**,

- 713–723 (2013).
100. Mishra N, Dhawaj A, Verma D et al. Cost-effective microabsorbance detection based nanoparticle immobilized microfluidic system for potential investigation of diverse chemical contaminants present in drinking water. *Anal Chim Acta* **1205**, 339734 (2022).
 101. Dhara P, Kumar R, Binetti L et al. Optical fiber-based heavy metal detection using the localized surface Plasmon resonance technique. *IEEE Sens J* **19**, 8720–8726 (2019).
 102. Menon S, Usha SP, Manoharan H et al. Metal-organic framework-based fiber optic sensor for chromium(VI) detection. *ACS Sens* **8**, 684–693 (2023).
 103. Hengoju S, Shvydkiv O, Tovar M et al. Advantages of optical fibers for facile and enhanced detection in droplet microfluidics. *Biosens Bioelectron* **200**, 113910 (2022).
 104. Vikas V, Saccomandi P. Design considerations of an ITO-coated u-shaped fiber optic LMR biosensor for the detection of antibiotic ciprofloxacin. *Biosensors* **13**, 362 (2023).
 105. Huang QD, Lv CH, Yuan XL et al. A novel fluorescent optical fiber sensor for highly selective detection of antibiotic ciprofloxacin based on replaceable molecularly imprinted nanoparticles composite hydrogel detector. *Sens Actuators B: Chem* **328**, 129000 (2021).
 106. Wang WB, Xia L, Xiao XH et al. Recent progress on microfluidics integrated with fiber-optic sensors for on-site detection. *Sensors* **24**, 2067 (2024).
 107. Zhu JM, Shi Y, Zhu XQ et al. Optofluidic marine phosphate detection with enhanced absorption using a Fabry–Pérot resonator. *Lab Chip* **17**, 4025–4030 (2017).
 108. Gómez-de Pedro S, Lopes D, Miltsov S et al. Optical microfluidic system based on ionophore modified gold nanoparticles for the continuous monitoring of mercuric ion. *Sens Actuators B Chem* **194**, 19–26 (2014).
 109. Moro G, Chiavaioli F, Liberi S et al. (INVITED) Nanocoated fiber label-free biosensing for perfluorooctanoic acid detection by lossy mode resonance. *Results Opt* **5**, 100123 (2021).
 110. Brasier N, Domenghino A, Meier CA et al. Implementing clinical needs into the development of wearable health-monitoring technology. *Nat Nanotechnol* **20**, 1350–1353 (2025).
 111. Li CH, Wang HL, Song ZW et al. Wireless, wearable elastography via mechano-acoustic wave sensing for ambulatory monitoring of tissue stiffness. *Sci Adv* **11**, eady0534 (2025).
 112. Li F, Wang SG, Gao Z et al. Harnessing artificial intelligence in sepsis care: advances in early detection, personalized treatment, and real-time monitoring. *Front Med* **11**, 1510792 (2025).
 113. Sadasivuni S, Saha M, Bhatia N et al. Fusion of fully integrated analog machine learning classifier with electronic medical records for real-time prediction of sepsis onset. *Sci Rep* **12**, 5711 (2022).
 114. Krishnamoorthy U. Non-invasive biochemical sensing with AI-driven analytics: a comprehensive review of technologies, applications, and future directions. *Anal Methods* **17**, 9736–9777 (2025).
 115. Goel I, Bhaskar Y, Kumar N et al. Role of AI in empowering and redefining the oncology care landscape: perspective from a developing nation. *Front Digit Health* **7**, 1550407 (2025).
 116. Chiavaioli F, Gouveia C, Jorge P et al. Towards a uniform metrological assessment of grating-based optical fiber sensors: from refractometers to biosensors. *Biosensors* **7**, 23 (2017).
 117. Rode M, Wade AJ, Cohen MJ et al. Sensors in the stream: the high-frequency wave of the present. *Environ Sci Technol* **50**, 10297–10307 (2016).
 118. Sharma S, Sharma K, Grover S. Real-time data analysis with smart sensors. In Gulati S. *Application of Artificial Intelligence in Waste-water Treatment* 127–153 (Springer, Cham, 2024).
 119. Shreya, Rawat S, Chand B et al. The role of artificial intelligence in enhancing optical fiber sensors. In Bhardwaj V, Kumar S, Kishor K. *Optical Fiber Sensors and AI: Exploring the Fusion* 33–55 (Springer, Singapore, 2025).
 120. Miller T, Durlík I, Kostecka E et al. Advancements in artificial intelligence circuits and systems (AICAS). *Electronics* **13**, 102 (2023).
 121. Di Iorio D, Rameshbabu S, Bruijns B et al. Click-and-bond: room-temperature and solvent-free bonding of polymer-based microfluidic devices. *Adv Mater Interfaces* **9**, 2200282 (2022).
 122. Stern L, Bakal A, Tzur M et al. Doppler-based flow rate sensing in microfluidic channels. *Sensors* **14**, 16799–16807 (2014).
 123. Vrabcová M, Spasovová M, Forinová M et al. Optical fibre long-period grating sensors modified with antifouling bio-functional Nano-brushes. *Biomater Sci* **13**, 1199–1208 (2025).
 124. Tsao CW. Polymer microfluidics: simple, low-cost fabrication process bridging academic lab research to commercialized production. *Micromachines* **7**, 225 (2016).
 125. Shen FX, Tan MM, Wang ZX et al. Integrating silicon nanowire field effect transistor, microfluidics and air sampling techniques for real-time monitoring biological aerosols. *Environ Sci Technol* **45**, 7473–7480 (2011).
 126. Tang XR, Jin Q, Zhu KL et al. Risks of AI scientists: prioritizing safeguarding over autonomy. *Nat Commun* **16**, 8317 (2025).
 127. Chen M, Li P, Wang R et al. Multifunctional fiber-enabled intelligent health agents. *Adv Mater* **34**, 2200985 (2022).
 128. Nedoma J, Krizan D, Stipal J et al. Decade of advancements in light–matter interaction-based optical fiber biosensing: innovations, challenges, and future directions. *Adv Photonics* **8**, 014004 (2025).
 129. Kumar R, Nguyen H, Rente B et al. A portable ‘plug-and-play’ fibre optic sensor for in-situ measurements of pH values for microfluidic applications. *Micromachines* **13**, 1224 (2022).
 130. Bissen A, Yunusova N, Myrkhieva Z et al. Unpacking the packaged optical fiber bio-sensors: understanding the obstacle for biomedical application. *Front Bioeng Biotechnol* **12**, 1401613 (2024).

Acknowledgements

F.C. acknowledges financial support under the National Recovery and Resilience Plan (NRRP), Mission 4, Component 2, Investment 1.1, Call for tender No. 1409 published on 14/09/2022 by the Italian Ministry of University and Research (MUR), funded by the European Union – NextGenerationEU – Project Title “Fiber optics sensors as a platform for cancer diagnosis and in vitro model testing (FOCAL)” – CUP B53D23024170001 – Grant Assignment Decree No. 1383 adopted on 01/09/2023 by the Italian MUR, and Project Title “Engineering Functional Metal Nanocluster-Protein Architectures for Bio(sensing and catalytic) applications (ProNano4Bio)” – B53D23013940006 – Grant Assignment Decree No. 958 adopted on 30/06/2023 by the Italian MUR. H.A. acknowledges financial support given by the Turkish Scientific and Technological Council (TÜBİTAK 1004-Regenerative and Restorative Medicine Research and Applications) under the grant numbers of 20AG003 and 20AG031, and by TÜBİTAK 1005-National New Ideas and Products under grant numbers of 123E013 and 225S581.

Author contributions

Shadab Dabagh and Francesco Chiavaioli conceived of the idea and designed the review. Rukmani Singh, Claudia Borri, Hamed Ghorbanpoor, Golar Ghorban Dordinejad, and Mahdi Bahadoran created and edited the figures. Shadab Dabagh led the manuscript writing – original draft. Shadab Dabagh, Ambra Giannetti, Francesco Baldini, Huseyin Avci, and Francesco Chiavaioli led the manuscript writing – review & editing. All authors participated in the review and discussion of the manuscript.

Competing interests

The authors declare no competing financial interests.



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 license, and indicate if changes were made. To view a copy of this license, visit <http://creativecommons.org/licenses/by/4.0/>
©The Author(s) 2026.

