

Review

Innovative Microfluidic Technologies for Rapid Heavy Metal Ion Detection

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Abstract: Heavy metal ion (HMI) contamination poses significant threats to public health and environmental safety, necessitating advanced detection technologies that are rapid, sensitive, and field-deployable. While conventional methods like atomic absorption spectroscopy (AAS) and inductively coupled plasma mass spectrometry (ICP-MS) remain prevalent, their limitations—including high costs, complex workflows, and lack of portability—underscore the urgent need for innovative alternatives. This review consolidates advancements in the last five years in microfluidic technologies for HMI detection, emphasizing their transformative potential through miniaturization, integration, and automation. We critically evaluate the synergy of microfluidics with cutting-edge materials (e.g., graphene and quantum dots) and detection mechanisms (electrochemical, optical, and colorimetric), enabling ultra-trace detection at parts-per-billion (ppb) levels. We highlight novel device architectures, such as polydimethylsiloxane (PDMS)-based labs-on-chip (LOCs), paper-based microfluidics, 3D-printed systems, and digital microfluidics (DMF), which offer unparalleled portability, cost-effectiveness, and multiplexing capabilities. Additionally, we address persistent challenges (e.g., selectivity and scalability) and propose future directions, including AI integration and sustainable fabrication. By bridging gaps between laboratory research and practical deployment, this review provides a roadmap for next-generation microfluidic solutions, positioning them as indispensable tools for global HMI monitoring.

Keywords: heavy metal ions; microfluid; detection technologies; lab on chip; sensing mechanism; environmental analysis; water safety; analytical chemistry



Received: 25 February 2025

Revised: 2 April 2025

Accepted: 8 April 2025

Published: 18 April 2025

Citation: Rauf, M.F.; Lin, Z.; Rauf, M.K.; Lin, J.-M. Innovative Microfluidic Technologies for Rapid Heavy Metal Ion Detection. *Chemosensors* **2025**, *13*, 149. <https://doi.org/10.3390/chemosensors13040149>

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1. Introduction

Heavy metal ions (HMIs) refer to environmental pollutants in water, air, or soil, although their definition is still inconsistent. Some characterize them as elements with densities ranging from 3 to 7 g/cm³, while others insist on atomic weights between 63.5 and 200 g/mol with densities higher than 5 g/cm³ [1,2]. They are broadly classified as essential and non-essential elements. Among them, the essential ones, which include iron (Fe), manganese (Mn), zinc (Zn), and copper (Cu), become toxic above the threshold values, while non-essentials, like arsenic (As), cadmium (Cd), Chromium (Cr), lead (Pb), and mercury (Hg), have a toxic effect even at trace amounts [3,4]. Rapid industrialization and untreated waste are the main sources of HMIs in developing countries which pose substantial threats to the environment and public health. Tenacious contaminants like Pb²⁺,

Hg^{2+} , Cd^{2+} , As^{3+} , Cr^{3+} , and Cr^{6+} are non-degradable and bioaccumulate, exacerbating exposure across populations. This leads to severe health outcomes, including impaired neurological development in children and increased incidences of cardiovascular, renal, and carcinogenic diseases in adults [4–6]. They pose a significant danger to the environment due to their accumulation in water and soil, disrupting biodiversity upon entering food chains. HMIs such as Cd^{2+} and Pb^{2+} interfere with essential soil microbes involved in nutrient cycling, adversely affecting plant growth and agricultural yields [7,8]. Hg^{2+} , a potent neurotoxin present in industrial waste and mining runoff, is linked to cognitive deficits and neurological impairments, particularly in developing fetuses [9–11]. Cd^{2+} exposure, mainly through industrial waste and contaminated food, is associated with kidney damage, bone demineralization, and an elevated risk of cancer [12–14]. As^{3+} , usually present in groundwater, is classified as a carcinogen and is linked to skin, lung, and bladder cancers, as well as cardiovascular diseases [15,16]. As depicted in Figure 1, prolonged exposure to these metal ions, even at low concentrations, leads to severe health outcomes, highlighting the need for accurate and rapid detection in ecological tasters.

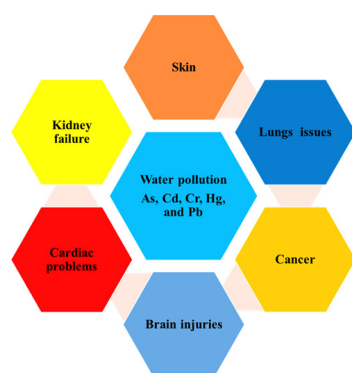


Figure 1. The hazardous effects of HMI pollution on public health.

The permissible limit of detection of hazardous HMs in drinking water, set by different international supervisory authorities, including the United States Environmental Protection Agency (USEPA), European Union directives (EU), National Standard of the Peoples Republic of China (CH), and World Health Organization (WHO), is shown in Table 1 [17–20].

Table 1. Permissible limits of hazardous heavy metals in drinking water as recommended by the USEPA, EU, China, and WHO references for the recommended limits ($\mu\text{g/L}$).

Metals	EPA $\mu\text{g/L}$	EU $\mu\text{g/L}$	China $\mu\text{g/L}$	WHO $\mu\text{g/L}$	Refs.
Arsenic (As)	10	10	10	10	[17–20]
Cadmium (Cd)	5	5	5	3	
Chromium (Cr)	100	50	50	50	
Lead (Pb)	15	10	10	10	
Mercury (Hg)	2	1	1	1	

The tenacity and extensive distribution of these contaminants, along with their profound ecological and public health effects, underscore the urgent need for rapid and reliable detection methods. Developing and optimizing efficient detection techniques is crucial for safeguarding human health and strengthening global environmental monitoring and security frameworks. The challenges of water pollution have driven the scientific community to develop innovative techniques for detecting and quantifying HMI toxins. In analytical chemistry, significant advances have been made in developing robust methods for identifying and monitoring HMIs in environmental matrices. These detection methodologies

are generally classified into three main groups: spectroscopic, electrochemical, and optical techniques [21–24]. Generally employed spectroscopic methods for HMs recognition include atomic absorption spectroscopy (AAS), flame atomic absorption spectroscopy (FAAS), graphite furnace atomic absorption spectroscopy (GF-AAS), X-ray fluorescence (XRF), inductively coupled plasma optical emission spectroscopy (ICP-OES), inductively coupled plasma mass spectrometry (ICP-MS), and atomic force microscopy (AFM) [25–32], these techniques bid elevated sensitivity, precision, and improved detection limits. However, these methods face limitations due to complex sample digestion, which risks contamination and trace element loss. Extended analysis times, reliance on skilled operators, and high operational costs further constrain their routine applicability. Additionally, their inability to conduct multi-element analysis in a single run reduces efficiency, rendering them impractical for real-time monitoring or frequent field use [33]. Electrochemical sensors combined with nanocomposites are widely used for detecting HMIs. Yet, they have notable limitations, including the need for specialized equipment, susceptibility to interference from other substances, and reliance on skilled operators. Furthermore, their fabrication and operation are often complex and costly [22,34–37]. Optical detection methods, including absorption, reflection, and luminescence spectrometry, commonly use chromogenic reagents and indicator dyes for selective metal ion detection. Advances in optical fibers, integrated optics, and capillary systems have improved sensitivity, selectivity, and real-time trace analysis. However, challenges such as matrix interference, high costs, and the need for precise calibration remain [38,39]. These challenges underscore the necessity of optimizing the benefits and constraints in practical real-world solutions, emphasizing the critical need for portable, cost-effective, and rapid yet accurate alternative detection technologies. Microfluidics (MF) has revolutionized HMI detection by enabling precise microscale fluid control, offering reduced reagent consumption; rapid analysis; and the integration of sampling, detection, and data processing in portable platforms. It offers substantial advantages for the detection of HMIs by displaying remarkable efficiency in the on-site, real-time monitoring of environmental water, food safety, and industrial waste management. One key feature of such systems is their multiplexing capability to allow the simultaneous quantification of multiple metal ions in complex matrices. Moreover, the inherent automation of MFs simplifies analytical workflows, considerably reducing operational expenses and processing time without affecting data integrity. Advances in nanomaterials, like graphene and quantum dots (QDs), have enhanced sensitivity and selectivity, achieving ultra-trace detection at ppb levels. These collective attributes spot MFs as a robust, field-deployable alternative to the above-mentioned traditional analytical methods, particularly suited for decentralized testing scenarios and high-throughput applications [40–42].

2. Microfluidic Technologies

2.1. Introduction to Microfluidics

Microfluidics involves the manipulation of liquids within microscale channels, generally in volumes ranging from microliters to picolitres (10^{-6} to 10^{-12} L). It enables fluid control, mixing, separation, and detection on compact platforms, facilitating cost-effective and precise analyses. The basic principle of microfluidics for HMI detection relies on the distinctive characteristics of the fluid dynamics at the microscale such as laminar flow, enhanced surface-to-volume ratio, and rapid mass transfer which allows the integration of multiple analytical steps including sample preparation, reaction, and detection zone into a single miniaturized to boost chemical and biological sensing, minimize reagent consumption, and optimize molecular dynamics as shown in Figure 2 [43]. These devices integrate

reaction sites, reservoirs, and detection zones into intricate microchannel networks, making them ideal for heavy metal ion detection with enhanced accuracy and reduced costs [44,45].

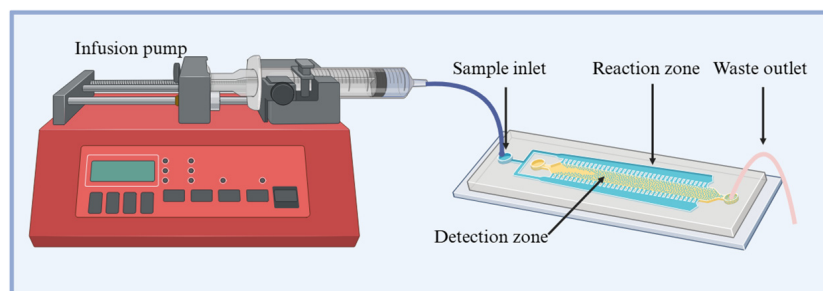


Figure 2. Schematic representation of a microfluidic system for HMI detection, consisting of an infusion pump, sample inlet, reaction zone, detection zone, and waste outlet.

2.2. Materials and Fabrication

The fabrication of microfluidic devices leverages various materials, including glass; silicon; paper; thermoplastic polymers, i.e., poly (methyl methacrylate) (PMMA); cyclic olefin copolymer (COC); polyethylene terephthalate (PET); polyvinyl chloride (PVC); polycarbonate (PC); thermosets, i.e., epoxy resins like nanoscale optical adhesive (NOA) or spin on unipox-8 (SU-8); thermoset polyester (TPE); polyurethane methacrylate (PUMA); thiol-ene epoxy thermoset (OSTEMER); and 3D-printed substrates [46–48]. Glass and silicon, traditional materials, offer biocompatibility, optical transparency, and stability but are costly due to cleanroom fabrication. PDMS is widely used for prototyping due to its affordability, moldability, and compatibility with biological systems [49,50]. LOC devices support diverse applications, including environmental monitoring, point-of-care (POC) diagnostics, and industrial processes like liquid–liquid extraction [51–54]. Integrated microfluidic devices combine multiple laboratory processes into a single platform, effectively meeting the demands of point-of-care (POC) systems as shown in Figure 3 [55].

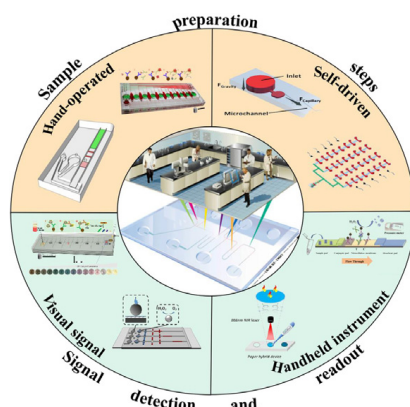


Figure 3. Incorporated microfluidic devices for point-of-care (POC) investigations. Reproduced with permission from Dan Liu, Aggregate; Wiley, 2021 [55].

2.3. Advancements in Materials and Sensors

Material innovations, including nanomaterials like carbon nanotubes, graphene, and metal oxides, have significantly improved the detection and testing of HMIs by enhancing LOC's sensitivity, selectivity, speed, and cost-effectiveness. In contrast to biological molecules, HMIs are readily identifiable due to their unique chemical characteristics and simple detection methods, resulting in enhanced testing capabilities in environmental monitoring, health diagnostics, and industrial applications. Functional materials play a vital role in sensor integration, such as carbon dots (CDs), polymers (e.g., PANI and Nafion),

metal nanoparticles (NPs) (e.g., Au and Ag), and metal oxides (e.g., ZnO and TiO₂) [56–60]. Bioreceptors, including enzymes and DNA, are often combined with these materials to enable biological molecule detection [61–63].

2.4. Detection Methods

Several detection methods, including electrochemical techniques, fluorescence assays, colorimetric analyses, (electro)chemiluminescence, piezo-resistive measurements, surface plasmon resonance (SPR), and surface-enhanced Raman scattering (SERS), have been proposed for integration with microfluidics in portable heavy metal ion detection [64,65]. Detection methods are pivotal for LOC functionality. Electrochemical techniques, including amperometry, potentiometry, and electrochemical impedance spectroscopy (EIS), ensure elevated sensitivity and real-time monitoring for pollutant detection in water [66,67]. Screen-printed electrochemical sensors offer rapid, cost-effective environmental monitoring [68,69]. Optical methods like fluorescence, colorimetry, and SERS are highly sensitive and integrate seamlessly with microfluidic devices for POC applications. Fluorescence methods, while traditionally bulky, now support portable formats [70]. Colorimetric approaches enable simple visual detection, often enhanced by image analysis for quantification [71]. SERS and SPR provide ultra-sensitive detection and detailed spectral signatures, supporting rapid, label-free analyses [72,73].

2.5. Sample Preparation and Digestion for Non-Labile Metal Detection

Sample preparation and digestion are critical preliminary steps in the determination of non-labile metals because they are found in the form of complex matrices and require liberation to be detectable. The complexity of the samples, ranging from environmental samples to biological tissues, demands tailored preparation methods to ensure complete metal recovery and minimize interference. Commonly used traditional methods are acid digestion, microwave-assisted digestion, and enzymatic digestion [74]. However, they are time-consuming, require large amounts of reagents, risk sample contamination or loss, need expensive equipment, and produce hazardous byproducts. Microfluidic techniques have emerged as powerful tools offering high sensitivity, miniaturization, and automation of these processes, having advantages such as the minimal consumption of reagents, faster processing times, and improved control over reaction conditions, making them ideal for detecting non-labile metals in the environment and biological and industrial samples [75]. They integrate sample preparation, digestion, and detection of the metals within LOCs. There are three crucial steps involved in the process. Firstly, LOCs equipped with microwave-assisted acid digestion or enzymatic digestion efficiently prepare and digest samples. Secondly, separation and preconcentration are performed using LOCs to isolate metals from the sample using LPME or SPME. Finally, metal quantification is performed using ICP-MS, the most sensitive technology, frequently combined with microfluidics. Electrochemical sensors in MFDs employ screen-printed electrodes to detect metal ions, while fluorescence and colorimetric tests use optical sensors that react with metal ions [76].

2.6. Applications and Future Directions

Integrated microfluidic devices, combining multiple laboratory processes, are transforming analytical chemistry and biology. By advancing fabrication and material selection, these systems enable portable, efficient, and user-friendly solutions for detecting heavy metals and other analytes, fulfilling the demands of modern scientific investigations [62]. Figure 4 shows a summary of Sections 2.1–2.5 for material selection, fabrication techniques, and detection technologies in advancing microfluidic technologies for analytical applications, particularly in environmental monitoring and HMI detection.

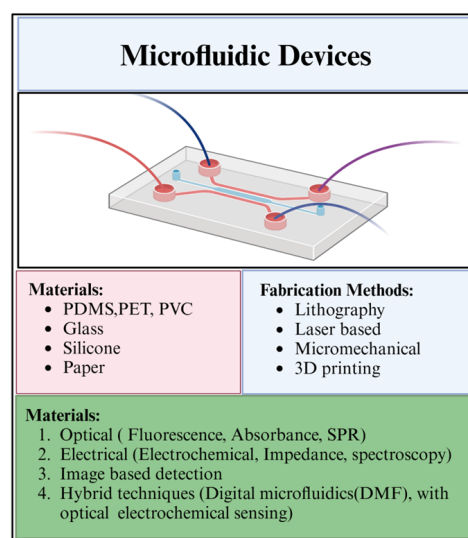


Figure 4. The materials, fabrication, and detection methods used to construct microfluidic devices.

3. Innovation in Microfluidics Devices for HMI Detection

3.1. PDMS-Based LOCs for the Detection of HMIs

Polydimethylsiloxane (PDMS) is a flexible, biocompatible polymer that is widely used for the fabrication of microfluidic devices owing to its transparency, low cost, and ease of manufacturing via soft lithography. For instance, W. H. Huang et al. [77] developed a microfluidic device (MFD) based on PDMS, integrated with graphene oxide (GO)-aptamer sensors for detecting Hg^{2+} and Pb^{2+} concurrently. The detection limits achieved were 0.70 ppb for Hg^{2+} and 0.53 ppb for Pb^{2+} , both of which are below the thresholds established by the World Health Organization (WHO) (Figure 5A). An MFD analog of the Wheatstone bridge (SMAW) utilizing a microgel is an alternative method for detecting Pb^{2+} ions. The PDMS/glass-based SMAW microchip facilitates the real-time, continuous detection of Pb^{2+} via signal conversion and amplification, employing an optical microscope that attained an ultra-low limit of detection (LOD) 10^{-14} M (Figure 5B) [78]. Similarly, Peng et al. [79] constructed a portable, cost-effective microfluidic device for sensing Hg^{2+} with a detection limit of 0.031 μM . The device, bonded via oxygen plasma-treated PDMS and glass, combines online complexation and laser-induced fluorescence (LIF) using a rhodamine derivative (RD) chemosensor. Its high selectivity, rapid response, and minimal reagent use make it ideal for on-site investigation, (Figure 5C). Motalebizadeh et al. [80] designed a smartphone portable POC PDMS device for the simultaneous detection of arsenic (As^{3+}) and Hg^{2+} surface plasmon resonance (SPR). This colorimetric device detects As^{3+} and Hg^{2+} ions via nanoparticle aggregation resulting from the reaction of AuNPs, dithiothreitol, and 10,12-pentacosadiynoic acid, with lysine. The determined LOD for As^{3+} and Hg^{2+} in water samples were 710–1278 $\mu\text{g L}^{-1}$ and 10.77–53.86 $\mu\text{g L}^{-1}$, respectively, as shown in Figure 5D.

Using glass and PDMS, Mishra et al. [81] developed a microfluidic device for the detection of Pb^{2+} , Cr^{3+} , and Hg^{2+} . He accomplished detection by immobilizing NPs within the system utilizing the micro absorbance detection method. The device enables the detection of at least 0.5 ppb for all earlier stated HMIs without labeling. A different method employs a rhodamine derivative, R1, for the highly sensitive and selective detection of Cr(III). Detection occurs via the online derivatization of the Cr(III) ion within a PDMS-based microfluidic device. The use of staggered herringbone grooves ensures the swift and effective blending of metal ions with the reagent and is complemented by a portable LIF detection system. This reduces fluid usage and waste production, achieving an LOD of 0.094 nM [82]. Additionally, W. Zhang et al. [83] developed a localized surface plasmon

resonance (LSPR)-based nanosensor integrated with a PDMS microfluidic chip, bonded with cover glass, and containing nanorod structures. This device detects Hg^{2+} in real water samples with a high sensitivity, reaching an LOD of 2.7 pM. A microfluidic device incorporating unmodified indium tin oxide (ITO) electrodes, fabricated using CO_2 laser ablation, was developed for the detection of Hg^{2+} [84]. The PDMS-based microchannels bonded to a glass substrate with the ITO electrodes via plasma treatment; an integrated pump is installed in the chip to introduce analytes. A smartphone-linked potentiostat enables the identification of several metals, including Hg^{2+} . The microchannel is constructed from PDMS and bonded to a glass substrate with ITO electrodes through plasma treatment; the chip has an integrated pump to introduce the analyte. A moveable potentiostat linked to a smartphone facilitates the detection of various metals, including mercury. The reported LOD for Hg^{2+} was 3.19 μM , with the device also capable of the simultaneous detection of metals like copper (Cu^{2+}) and Hg^{2+} .

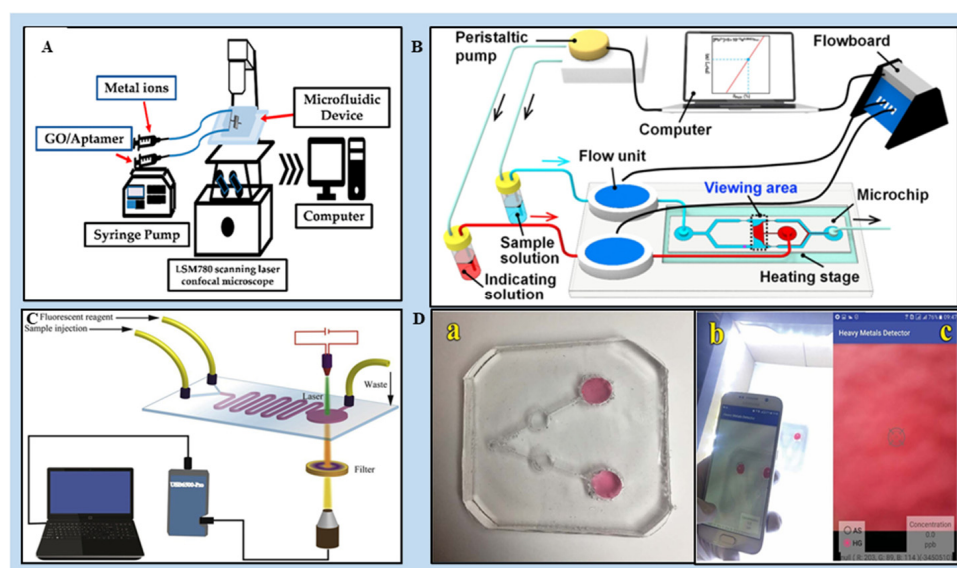


Figure 5. Schematic representation of the MFDs: (A) illustrates the PDMS MFD for detecting Hg^{2+} and Pb^{2+} monitoring systems. Figure reproduced with permission from Ruey-Jen Yang, *Micromachines*; MDPI, 2021 [77]. (B) SMAW microchip-based Pb^{2+} -detecting platform setup. Figure reproduced with permission from Wei Wang, *Chemical Engineering Journal*; ELSEVIER, 2021 [78]. (C) shows flow injection microfluidic device with LIF-coupled online fluorescence detection. Figure reproduced with permission from Jin-Ming Lin, *Spectrochimica Acta Part A*; ELSEVIER, 2018 [79]. (D) shows the fabricated microfluidic kit, smartphone imaging platform, and HMD mobile app. (a) Fabricated microfluidic kit, (b) imaging platform using a smartphone and (c) HMD mobile application. Figure reproduced with permission from Hasan Bagheri, *RSC Advances*, 2018, respectively [80].

3.2. Paper-Based Microfluidics for the Detection of HMIs

Recent innovations have presented microfluidic paper-based analytical devices (μPADs) due to their biodegradable, cost-effective, and disposable nature. These devices are particularly advantageous for developing countries and applications where cost and disposability are key factors. For instance, Fakhri et al. [85] designed a paper-based microfluidic system integrating aptamers with AuNPs for the colorimetric detection of Pb^{2+} . By employing Whatman No. 1 and nylon filter papers, an LOD of 1.2 nM and 0.7 nM, respectively, were achieved, as shown in Figure 6A. Wisang et al. [86] proposed a paper-based microfluidic device (μPAD) for Pb^{2+} detection using two methods: the visual estimation of color change and image-based color intensity analysis. The first method measures Pb^{2+} concentration by the distance of a color change using sodium rhodizonate (NaR), achieving a detection limit of 0.756 mg L^{-1} . The second method utilizes the ImageJ software to analyze

the RGB values. Both approaches are effective, but the visual estimation method is simpler, faster, and cost-efficient, relying solely on direct observation as shown in Figure 6B. Zhou et al. [87] developed a portable paper-based device for the rapid detection of HMIs using ZnSeQDs coupled with ion imprinted polymers (IIPs) for Cd^{2+} and Pb^{2+} sensing, with limits of $0.245 \mu\text{g L}^{-1}$ and $0.335 \mu\text{g L}^{-1}$, respectively. Figure 6C shows that with (A) three layers of paper-based chip, (B) chip assembly, (C) sample addition, (D) top layer rotation for detecting windows, (E) Fluoromax-4 spectrofluorometer testing, (F) photo of the paper-based chip. A prominent advancement is a three-dimensional(3D) microfluidic paper-based device for detecting multiple metals, including Cd^{2+} , Pb^{2+} , and Hg^{2+} , in coastal waters. This device design enhances fluid permeation, enabling a 25-fold metal enhancement and attaining an LOD of $0.007\text{--}0.015 \mu\text{g L}^{-1}$ for all the tested metals. Details of the device are given in Figure 6D as follows: (a) Inlet port overview photo. (b) Inlet tube section exhibiting capillary pressure (P_c , from surface tension) and static pressure (P_s , from water column height). Three samples with (c) 1.2 mm, (d) 1.6 mm, and (e) 2 mm inner diameters of the inlet tube are introduced, and their time-dependent photos are numbered 1, 2, and 3 [88]. Wang et al. [89] designed a rotating hybrid cloth–paper microfluidic device (μCPAD) for Hg^{2+} and Pb^{2+} detection with impressive LODs of $0.18 \mu\text{g L}^{-1}$ and $0.07 \mu\text{g L}^{-1}$, respectively. The construction of the fluorescent sensing component involves the grafting of QDs onto a cotton cloth, followed by modification with ion-imprinted polymers (IIPs), and integrating them into a rotary μPAD substrate, which enhances both sensitivity and portability.

Recognizing the critical need for Hg^{2+} detection, G. Dindorkar et al. [90] developed a microfluidic paper-based analytical device (μPAD) integrated with an Android-based colorimetric application for quantifying Hg^{2+} concentrations ranging from 0.1 g L^{-1} to 0.001 mg L^{-1} in an aqueous medium. Their recognition method employs AuNPs fabricated with Papain and 2,6-pyridine dicarboxylic acid. Additionally, an innovative μPAD integrated with a colorimetric detector is suggested for detecting Hg^{2+} in water [91]. To detect contaminants like Hg^{2+} and Pb^{2+} in water bodies, a paper disk device integrated with a smartphone-based fluorescence reader was proposed by Jin et al. with detection limits down to 20 nM and 4 nM, respectively [92]. Sun et al. [93] designed a paper-based microfluidic device featuring a rotary valve to manage connections between the detection area and fluid channels, emphasizing cost-effectiveness and portability for field detection. The device detected multiple metal ions, particularly Cr^{6+} , using 1,5-diphenylcarbazide as a colorimetric indicator, detecting concentrations as low as 0.18 mg L^{-1} . Shang et al. [94] constructed an environmentally friendly paper-based system comprising six parallel channels designed for the detection of Cr^{3+} , incorporating injection, reaction, and waste zones. This gravity- and capillary-driven chemiluminescence platform is inexpensive, portable, and fast, detecting concentrations as low as 0.0245 mg L^{-1} within 30 s. Li et al. [95] developed a three-dimensional micro-paper analytical device (3D μPAD) for Cr^{6+} detection, featuring an upper layer for sample pretreatment and a lower layer for detection. An L-shaped serpentine flow channel ensures controlled sample delivery, preventing chromogenic reagent diffusion and enhancing color uniformity and precision. Colorimetric smartphone imaging analysis achieved a detection limit of 0.1 mg L^{-1} . A μPAD using diphenylcarbazide (DPC) and a desktop scanner with the ImageJ software detected Cr^{6+} in water at $3 \mu\text{g L}^{-1}$ [96]. Abdellah Muhammed et al. [97] developed a mobile μPAD for Cr^{6+} and Cr^{3+} detection, and Cr^{6+} and total Cr levels were measured in left and right channels, respectively, using 1,5-diphenylcarbazide. The device achieved an LOD of 0.008 mg L^{-1} for Cr^{6+} and 0.07 mg L^{-1} for Cr^{3+} or total Cr.

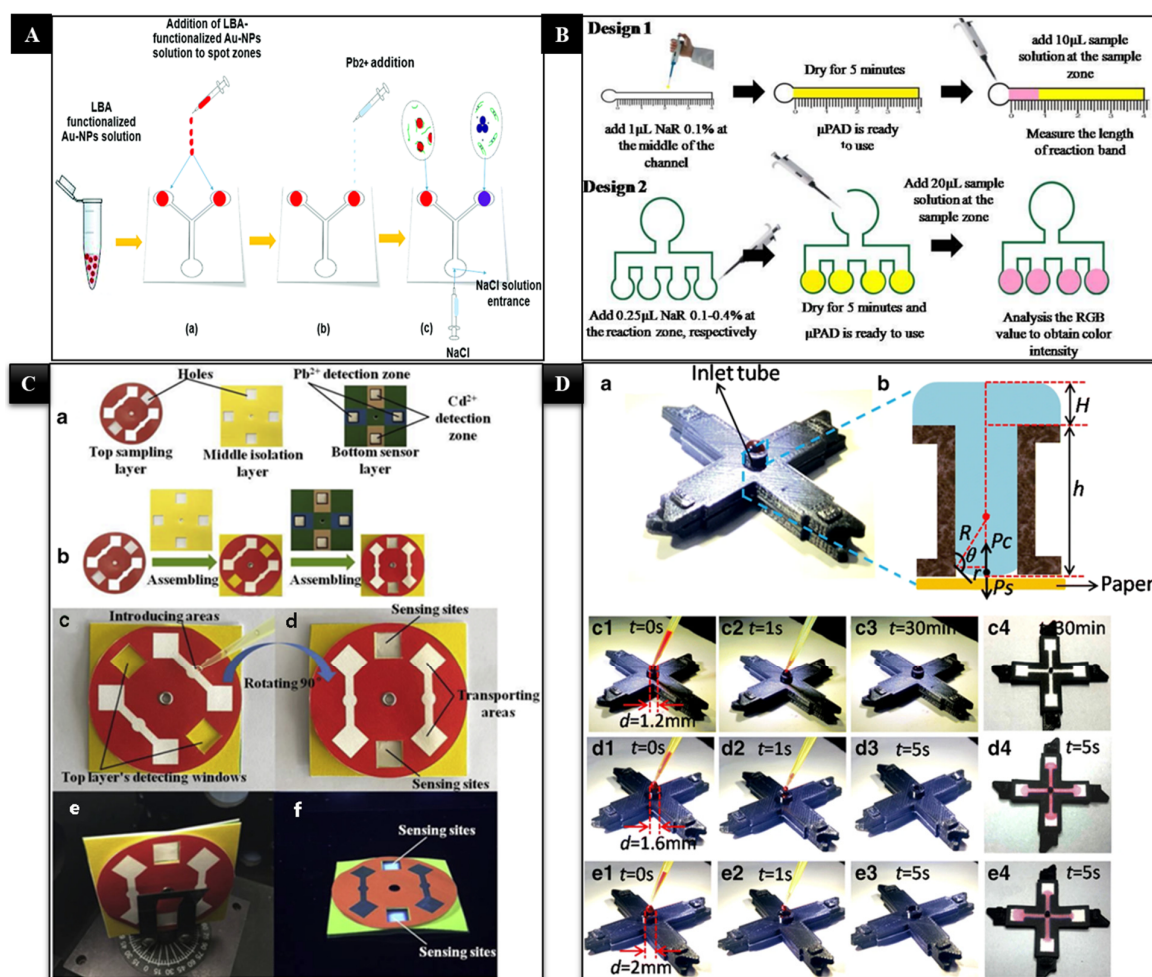


Figure 6. Schematic representation of design, fabrication, and detection mechanism of microfluidic paper-based biosensors for Cd^{2+} , Hg^{2+} , and Pb^{2+} analysis: (A) Schematic for microfluidic paper-based biosensor for Pb^{2+} detection. Figure reproduced with permission from Morteza Hosseini, *Analytical Methods*; RSC, 2018 [85]. (B) The waste sample Pb^{2+} detection method. Figure reproduced with permission from Akhmad Sabarudin, *IOP Conference Series: Materials Science and Engineering*; IOP Publishing, 2019 [86]. (C) Complete ion imprinting paper-based chip assembly and detection. Figure reproduced with permission from Bowie Li, *Sensors and Actuators B: Chemical*; ELSEVIER, 2020 [87]. (D) The 3D microfluidic paper-based device for detecting multiple metals, including Cd^{2+} , Pb^{2+} , and Hg^{2+} , in coastal waters. Figures reproduced with permission from Yunhua Wang, *Anal Bioanal Chem*; Springer Nature 2021, [88].

3.3. 3D Printed Microfluidics for the Detection of HMIs

Additive manufacturing techniques like 3D printing have revolutionized microfluidic device fabrication by enabling rapid prototyping and customizable designs. This technique makes it possible to design intricate, multi-layered devices that may be customized to meet certain detection requirements. For instance, a study reported the detection of Pb^{2+} with a detection limit of 0.0330 mg L^{-1} , a 3D-printed flow reactor with porous carbon electrodes fabricated by direct laser sintering on polymer films, as shown in Figure 7A [98]. Another study reported the electrochemical detection of Pb^{2+} based on epitaxial graphene (EG) on a 3D-printed microfluidic platform, attaining a minimum detection level of 95 nM attributed to the sensor material's higher sensitivity, as shown in Figure 7B [99]. G. Zhao et al. [100] developed a 3D-printed polymer flow cell incorporating electrochemical sensors to detect multiple HMIs in water, including As^{3+} , Pb^{2+} , and Cd^{2+} . A flexible substrate is employed in sensor fabrication, consisting of screen-printed conventional graphite ink for the working

and counter electrodes and Ag/AgCl ink for the reference electrode. This approach enables the development of screen-printed electrodes on a polyimide substrate to detect HMIs (As^{3+} , Cd^{2+} , and Pb^{2+}). Modifying two distinct working electrodes using a $(\text{BiO})_2\text{CO}_3$ reduced GO–Nafion nanocomposite facilitates the identification of $0.8 \mu\text{g L}^{-1} \text{Cd}^{2+}$ and $1.2 \mu\text{g L}^{-1} \text{Pb}^{2+}$. A nanocomposite composed of Fe_3O_4 magnetic nanoparticles, AuNPs, and ionic liquid facilitates the detection of $2.4 \mu\text{g L}^{-1}$ of As^{3+} , as shown in Figure 7C. Another mobile resistive gadget for detecting Pb^{2+} in water was reported, attaining 0.81 nM LOD and 45 days of shelf life. This device integrates miniaturized electronics with a microfluidic well, utilizing $\alpha\text{-MnO}_2/\text{GQD}$ as a sensor, as shown in Figure 7D [101].

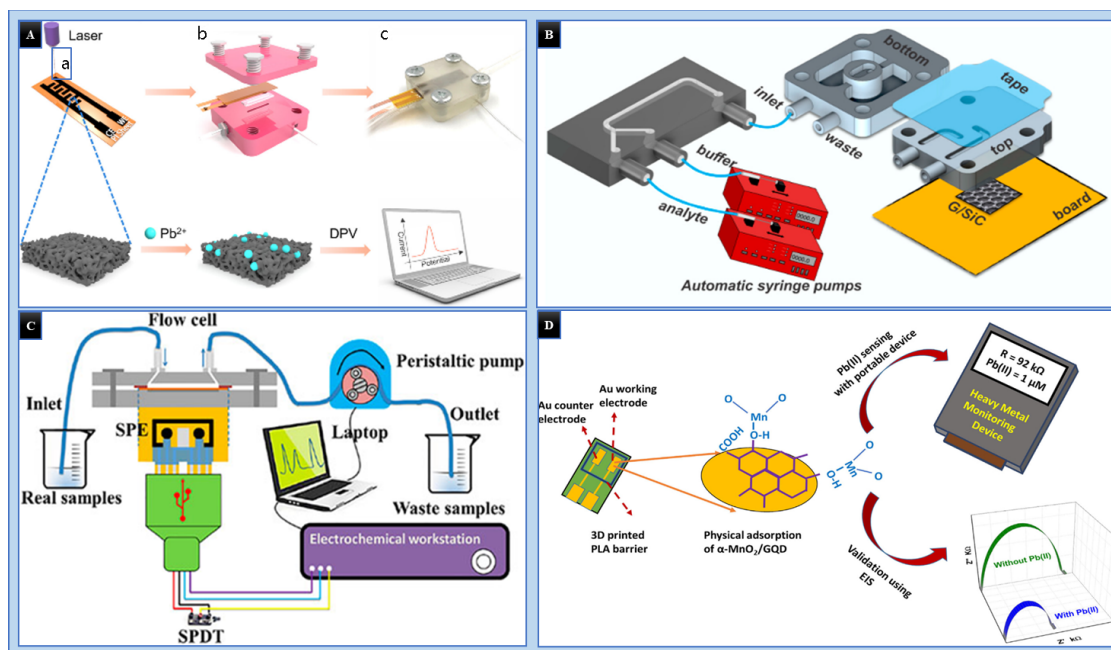


Figure 7. Schematic diagrams of the electrochemical analysis and sensor platforms: (A) Electrochemical analysis procedure—(a) laser sintering; (b,c) electrochemical sensor schematic and digital photos. Figure reproduced with permission from Shengyang Tao, ACS Omega; ACS, 2021 [98]. (B) Sensor platform schematic. Figure reproduced with permission from Jens Eriksson, Sensors (Basel); MDPI, 2019 [99]. (C) HMI analysis flow injection system schematic. Figure reproduced with permission from Ashok Mulchandani, Front Chem; Frontiers in Chemistry, 2022 [100]. (D) Scheme nanosensor manufacture and Pb^{2+} detection approach employing a portable resistive device and impedance analyzer. Figures reproduced with permission from, and Ashish Mathur, IET Nanobiotechnol; Wiley, 2021, [101].

Vassiliki et al. [102] introduced a fully 3D-printed device for detecting low-level Hg^{2+} using anodic stripping voltammetry (ASV). The machine is produced in one step utilizing a dual-extruder 3D printer, comprising a polylactic acid (PLA) vessel and thermoplastic electrodes that are integrated and composed of carbon-loaded PLA. The working electrode is modified with an in situ electroplated gold film, which is optimized for the detection of Hg^{2+} using linear sweep voltammetry and microscopy techniques. The device attains an LOD of $0.52 \mu\text{g L}^{-1}$, exhibiting 3.9% repeatability and 8.9% reproducibility. The method has been effectively utilized for the detection of Hg^{2+} in bottled water and fish oil samples. Christos et al. [103] present a 3D-printed lab-in-a-syringe device that integrates Ca-MOF ($[\text{Ca}(\text{H}_4\text{L})(\text{DMA})_2] \cdot 2\text{DMA}$) for the detection of Hg^{2+} using anodic stripping voltammetry. The Ca-MOF exhibits significant Hg^{2+} sorption, as confirmed by spectroscopic and X-ray analyses. The device is fabricated with a dual-extruder 3D printer, incorporating thermoplastic electrodes and a syringe-based graphite paste/Ca-MOF working electrode.

The detection limit is $0.6 \mu\text{g L}^{-1}$, making it low-cost, portable, and appropriate for on-site applications, with a sensitivity that is comparable to or exceeds that of the current sensors. Additionally, Ma et al. [104] have developed a microfluidic device with an electrochemical sensor in which a 3D Ag-rGO-f-Ni(OH)₂/NF composite is incorporated to amplify electrochemical signals through thermocapillary convection, significantly accelerating pre-concentration and reducing detection time by 300 s. Controlled by a smartphone, this portable device achieves an LOD of $0.00498 \mu\text{g L}^{-1}$ for Pb²⁺ in river water.

3.4. Digital Microfluidics (DMF) for the Detection of HMIs

DMF is a revolutionary concept in microfluidics, which involves the manipulation of discrete droplets within a two-dimensional array of electrodes. Unlike conventional microfluidics, which rely on continuous flow within microchannels, DMF controls the position and motion of droplets electrostatically on an open surface. This section reviews DMF technology, basic principles, applications, and the latest developments. For example, Zhang et al. [105] presented an electrochemical sensor chip and DMF platform for Pb²⁺ detection in water. This handy, energy-efficient appliance features relay control modules that enable automated sample preparation, detection, data acquisition, and runoff collection, with a sensor node that can run for years on a standard energy source, as shown in Figure 8A. Gu et al. [106] investigated the electrowetting properties of gold nanoparticle (AuNP) droplets on a digital microfluidic (DMF) chip. The results show that AuNPs require a higher voltage for manipulation than water droplets, as described by a modified Young-Lippmann equation. The stability of AuNPs remains intact during electrowetting, and solvent evaporation has minimal impact on the sensing process. Hg²⁺ detection with a detection limit of $0.01 \mu\text{M}$ demonstrates the potential for label-free, low-cost, and automated applications in point-of-care testing, as shown in Figure 8B.

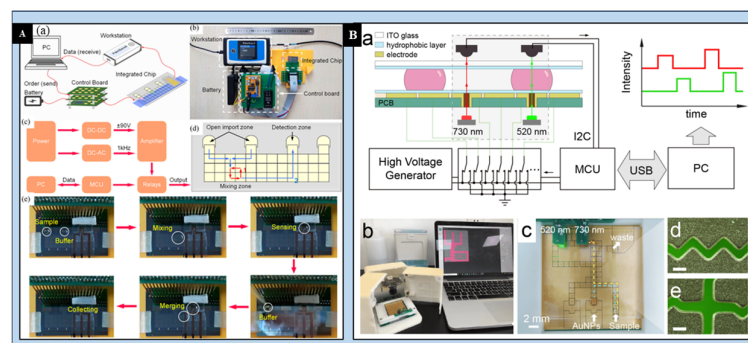


Figure 8. Schematic and functional overview of the DMF system for colorimetric analysis: (A)—(a) Graphic representation and (b) photo of the detection system. (c) Control board block diagram. (d) Pretreatment DMF electrode pattern and droplet transport pathway sketch. Drop mixing is shown by red arrows. (e) Images extracted from a movie showing the progress of the sample as it moves in, undergoes detection, and moves out. Figure reproduced with permission from Pengfei Niu, Nanotechnology and Precision Engineering; AIP Publishing, 2021 [105]. (B)—(a) Design of the DMF system for colorimetric detection at 730 and 520 nm. (b) snapshot of the DMF. (c) DMF with optical sensors. (d,e) are microscope images of electrode crossed-fingers and gaps. Figures reproduced with permission from Hui-Feng Wang, Micromachines (Basel); MDPI, 2021. [106].

Nguyen et al. [107] developed a novel azine-based fluorescent probe, PSSA-4-propoxysulfonate salicylaldehyde azine for the selective detection of Al³⁺ in an aqueous medium. Aluminum binding induced an aggregation-induced emission enhancement process, as identified by different spectroscopic techniques. They verified the aggregate formation using DLS, SEM, and FLIM. The attained detection limit was 153 nM, which is far below the maximum permissible limit according to the WHO guidelines. The probe ex-

hibited very high selectivity in the presence of competing ions. The PSSA probe was further incorporated into a water-in-oil digital microfluidic chip, exhibiting robust and portable Al^{3+} detection in natural and drinking water, ideal for field applications. Han et al. [108] presented a digital microfluidics-based method of mercury detection in coastal seawater. The miniaturization effect of DMF considerably enhances the sensitivity of fluorescence probes, while the commonly encountered issues related to seawater salinity are tackled by incorporating a feedback-driven control loop into the developed assay. It achieves parts-per-billion sensitivity, high selectivity, and stability within 20 s. This low-cost, automated system is suitable for periodic monitoring, and rapid and emergency detection of mercury and other metals in coastal environments.

Table 2 presents a summary of various microfluidic or lab-on-a-chip approaches for the detection of HMIs in the last five years. In numerous instances, the reported LOD aligns with or surpasses the WHO standards. Nonetheless, to our understanding, the majority of these initiatives have not been converted into diagnostic products. The slow adoption of these devices in the industry can be attributed to several factors: (a) the complexity of fabrication, which complicates chip manufacturing and necessitates more intricate external components for sensor control and readout, thereby restricting both autonomous and user-friendly operation; (b) the prevalence of less complex devices, such as paper-based options, which, despite being user-friendly, typically employ colorimetric detection methods that fail to meet legislative limits of detection without integration with camera devices and analysis software, thus confining their application to screening purposes; and (c) the generally low technological maturity and limited reproducibility of device performance. Numerous reported efforts remain unevaluated with complex real water samples and in pertinent industrial settings. Additionally, the industry typically exhibits reluctance to adopt new technologies due to the time and investment necessary for development and implementation of these approaches. To overcome these limitations, it is necessary to develop new fabrication methods, enhance detection schemes and devices for result output, and implement comprehensive evaluation protocols utilizing real samples.

Table 2. Summary of comparative analytical performance of microfluidic platforms for heavy metal ion (HMI) detection, highlighting LOD, device material, and detection methods.

HMI	LOD	Device Material	Detection Method	Ref.
Hg^{2+} , Pb^{2+}	0.70 ppb, 0.53 ppb	PDMS-GO	Fluorescence	[77]
Pb^{2+}	10^{-14} M	PDMS	Electrochemical	[78]
Hg^{2+}	0.031 μM	PDMS-Glass	Fluorescence	[79]
As^{3+} , Hg^{2+}	710–1278 $\mu\text{g L}^{-1}$, 10.77–53.86 $\mu\text{g L}^{-1}$	PDMS	Colorimetry	[80]
Pb^{2+} , Cr^{3+} , Hg^{2+}	0.5 ppb	PDMS-Glass	Absorbance	[81]
Cr^{3+}	0.094 nM	PDMS	Fluorescence (LIF)	[82]
Hg^{2+}	2.7 pM	PDMS	Absorption (LSPR)	[83]
Hg^{2+}	3.19 μM	PDMS-ITO	Electrochemical	[84]
Pb^{2+}	1.2 nM	Paper	Colorimetry	[85]
Pb^{2+}	0.756 mg L^{-1}	Paper	Colorimetry	[86]
Cd^{2+} , Pb^{2+}	0.245 $\mu\text{g L}^{-1}$, 0.335 $\mu\text{g L}^{-1}$	Paper	Fluorescence	[87]
Cd^{2+} , Pb^{2+} , Hg^{2+}	0.007–0.015 $\mu\text{g L}^{-1}$	Paper	Fluorescence	[88]
Hg^{2+} , Pb^{2+}	0.18 $\mu\text{g L}^{-1}$, 0.07 $\mu\text{g L}^{-1}$	Paper	Fluorescence	[89]
Hg^{2+}	0.1 g L^{-1} –0.001 mg L^{-1}	Paper	Colorimetry	[90]
Hg^{2+}	0.001 ppm	Paper	Colorimetry	[91]
Hg^{2+} , Pb^{2+}	20 nM, 4 nM	Paper	Fluorescence	[92]
Cr^{6+}	0.18 mg L^{-1}	Paper	Fluorescence	[93]

Table 2. Cont.

HMI	LOD	Device Material	Detection Method	Ref.
Cr ³⁺	0.0245 mg L ⁻¹	Paper	Chemiluminescence	[94]
Cr ⁶⁺	0.1 mg L ⁻¹	Paper	Colorimetry	[95]
Cr ⁶⁺	3 µg L ⁻¹	Paper	Colorimetry	[96]
Cr ³⁺ , Cr ⁶⁺	0.008 mg L ⁻¹ , 0.07 mg L ⁻¹	Paper	Colorimetry	[97]
Pb ²⁺	0.0330 mg L ⁻¹	3D Material	Electrochemical	[98]
Pb ²⁺	95 nM	3D Material	Electrochemical	[99]
As ³⁺ , Pb ²⁺ , Cd ²⁺	2.4 µg L ⁻¹ , 1.2 µg L ⁻¹ , 0.8 µg L ⁻¹	3D Material	Electrochemical	[100]
Pb ²⁺	0.81 nM	3D Material	Electrochemical	[101]
Hg ²⁺	0.52 µg L ⁻¹	3D Material	Electrochemical	[102]
Hg ²⁺	0.6 µg L ⁻¹	3D Material	Electrochemical	[103]
Pb ²⁺	0.00498 µg L ⁻¹	3D Material	Electrochemical	[104]
Pb ²⁺	1 ppb	DMF	Electrochemical	[105]
Hg ²⁺	2 ppb	DMF	Colorimetry	[106]
Al ³⁺	4.1 ppb	DMF	Fluorescence	[107]
Hg ²⁺	0.5 ppb	DMF	Fluorescence	[108]

4. Discussion on Challenges, Limitations, and Future Perspectives

4.1. Challenges and Limitations

Microfluidic technology offers significant advantages in chemical sensing but faces persistent challenges in real-world applications. Sensitivity and selectivity remain critical concerns, as ultra-trace detection is often compromised by interfering organic matter, competing ions, and environmental factors. While functionalized surfaces and nanomaterial-based enhancements improve performance, stability issues require further research into adaptive calibration and antifouling strategies.

Fabrication scalability also poses a barrier, despite advances in 3D printing and soft lithography. Reproducibility and stability remain problematic, particularly in paper-based microfluidic designs, necessitating standardized manufacturing protocols and durable materials. Additionally, the performance gap between laboratory and field applications highlights the need for self-cleaning surfaces, automated data correction, and AI-driven analysis to enhance reliability.

Commercialization remains the biggest challenge due to high R&D costs and reliance on expensive nanomaterials, limiting accessibility, especially in resource-limited regions. Cost-effective fabrication methods, simplified designs, and scalable production techniques are essential for widespread adoption. Addressing these limitations through AI integration, real-time calibration, and low-cost materials will be key to transitioning microfluidic chemosensors from research to practical deployment.

To address the above-mentioned challenges and drive innovation, we are highlighting several key areas of development:

4.2. Future Perspectives

Future directions in microfluidic technology for heavy metal detection present exciting opportunities, with advancements in materials science, hybrid systems, artificial intelligence (AI) integration, sustainability, and commercialization.

4.2.1. AI Integration for Enhanced Data Analysis and Decision Making

i. Machine Learning Algorithms (MLAs):

Advanced MLAs will be employed to analyze complex datasets generated by MFDs. These algorithms will be capable of normalizing data, reducing noise, and extracting relevant features, leading to more accurate and reliable detection results.

ii. Real-Time Sensor Calibration:

AI-driven adaptive algorithms will dynamically calibrate and optimize sensors in response to changing environmental conditions and sample matrices. This will ensure consistent performance and minimize the impact of interferences, leading to improved detection accuracy and selectivity.

iii. Predictive Modeling and Early Warning Systems:

AI-powered predictive models will analyze historical and real-time data to identify patterns and trends in heavy metal contamination. This will enable the development of early warning systems that can alert authorities and communities to potential risks, facilitating timely intervention and mitigation strategies.

4.2.2. Advancing Field Testability for Robust and User-Friendly Devices

i. Enhanced Robustness and Durability:

Research and development efforts will focus on improving the durability of microfluidic devices to withstand harsh environmental conditions like temperature fluctuations, humidity, and vibration. This could involve the exploration of novel materials and device design modifications to ensure reliable performance in the field.

ii. Integrated Sample Handling and Preprocessing:

Microfluidic devices will incorporate automated sample handling and preprocessing steps, minimizing the need for user intervention and reducing potential sources of error. This could involve microfluidic pumps, valves, and separation techniques for efficient sample preparation and analysis.

iii. Portable Power Solutions:

The development of portable and energy-efficient microfluidic devices will be prioritized to enable independent operation in remote locations. This could involve advancements in battery miniaturization, energy harvesting technologies, and low-power sensor designs.

4.2.3. Other Promising Directions

i. 3D Printing Advancements:

The continued development of 3D-printing techniques will enable the fabrication of increasingly complex microfluidic structures with multiple layers and integrated sensors. This will open up new possibilities for creating versatile and customizable devices tailored to specific detection needs.

ii. Paper-Based Microfluidics:

The potential of paper-based microfluidics will be further explored for developing low-cost and disposable devices. These environmentally friendly platforms offer a promising solution for accessible and affordable heavy metal detection, particularly in resource-limited settings.

4.2.4. Commercialization Strategies

Collaboration with industry partners and government agencies will be crucial for scaling up microfluidic device production and bringing them to market. Exploring innovative business models and identifying market opportunities will be essential for the successful commercialization and widespread adoption of these technologies.

By focusing on these key areas, the future of microfluidic technologies in HMI detection will offer a powerful tool for safeguarding human health and the environment. The integration of AI, advancements in field testability, and exploration of new materials and fabrication techniques will pave the way for a new generation of devices that are more accurate, reliable, accessible, and environmentally friendly.

5. Conclusions

Microfluidic technologies have emerged as a transformative solution for detecting HMIs, overcoming many of the limitations associated with conventional analytical methods, i.e., AAS and ICP-MS. These technologies offer several advantages, including miniaturization, portability, rapid analysis, and reduced reagent consumption, making them ideal for the field-based and real-time monitoring of environmental contaminants. Innovations like LOCs, paper-based microfluidics, and 3D-printed devices have expanded the versatility and accessibility of microfluidic platforms, allowing for low-cost and scalable solutions that can be deployed in both industrial and public health contexts. Moreover, the integration of advanced materials like nanomaterials and quantum dots has significantly enhanced the sensitivity and specificity of these devices, enabling the detection of heavy metals at ultra-trace levels. However, challenges remain, particularly in achieving the high sensitivity and selectivity required for detecting heavy metals in complex environmental matrices, as well as in scaling up the production of microfluidic devices for commercial applications. Ongoing research is focused on overcoming these barriers, with particular attention to improving the stability of sensors, enhancing device reproducibility, and integrating artificial intelligence (AI) and machine learning (ML) for advanced data processing. Looking ahead, the future of microfluidic technologies for heavy metal detection is promising. Continued advancements in materials science, AI integration, and the development of blended systems that integrate microfluidics with other analytical techniques are expected to further enhance the capabilities of these devices. Additionally, the growing emphasis on sustainability and the development of eco-friendly, disposable platforms will ensure that microfluidic systems remain at the forefront of environmental monitoring technologies. In conclusion, microfluidic technologies hold significant potential for revolutionizing the field of heavy metal detection, offering rapid, accurate, and cost-effective solutions that can be applied in diverse settings. With continued innovation, these systems are poised to become an integral part of global efforts to monitor and mitigate the environmental and public health impacts of heavy metal contamination.

Funding: This work was financially supported by the National Key R&D Program of China (No. 2021YFF0600700).

Conflicts of Interest: The authors declare no conflicts of interest.

References

1. Ali, H.; Khan, E. What are heavy metals? Long-standing controversy over the scientific use of the term ‘heavy metals’—proposal of a comprehensive Definition. *Toxicol. Environ. Chem.* **2018**, *100*, 6–19. [[CrossRef](#)]
2. Rajoria, S.; Vashishtha, M.; Sangal, V.K. Treatment of electroplating industry wastewater: A review on the various techniques. *Environ. Sci. Pollut. Res. Int.* **2022**, *29*, 72196–72246. [[CrossRef](#)] [[PubMed](#)]

3. Sharma, B.M.; Komprdova, K.; Lorinczova, K.; Kuta, J.; Pribylova, P.; Scheringer, M.; Sebejova, L.; Piler, P.; Zvonar, M.; Klanova, J. Human biomonitoring of essential and toxic trace elements (heavy metals and metalloids) in urine of children, teenagers, and young adults from a Central European Cohort in the Czech Republic. *J. Expo. Sci. Environ. Epidemiol.* **2024**, 1–16. [\[CrossRef\]](#) [\[PubMed\]](#)
4. Zamora-Ledezma, C.; Negrete-Bolagay, D.; Figueroa, F.; Zamora-Ledezma, E.; Ni, M.; Alexis, F.; Guerrero, V.H. Heavy metal water pollution: A fresh look about hazards, novel and conventional remediation methods. *Environ. Technol. Innov.* **2021**, 22, 101504. [\[CrossRef\]](#)
5. Hama Aziz, K.H.; Mustafa, F.S.; Omer, K.M.; Hama, S.; Hamarawf, R.F.; Rahman, K.O. Heavy metal pollution in the aquatic environment: Efficient and low-cost removal approaches to eliminate their toxicity: A review. *RSC Adv.* **2023**, 13, 17595–17610. [\[CrossRef\]](#)
6. Sarker, A.; Masud, M.A.A.; Deepo, D.M.; Das, K.; Nandi, R.; Ansary, M.W.R.; Islam, A.; Islam, T. Biological and green remediation of heavy metal contaminated water and soils: A state-of-the-art review. *Chemosphere* **2023**, 332, 138861. [\[CrossRef\]](#)
7. Abd Elnabi, M.K.; Elkaliny, N.E.; Elyazied, M.M.; Azab, S.H.; Elkhaila, S.A.; Elmasry, S.; Mouhamed, M.S.; Shalamesh, E.M.; Alhorieny, N.A.; Abd Elaty, A.E.; et al. Toxicity of Heavy Metals and Recent Advances in Their Removal: A Review. *Toxics* **2023**, 11, 580. [\[CrossRef\]](#)
8. Harpprecht, C.; Miranda Xicotencatl, B.; van Nielen, S.; van der Meide, M.; Li, C.; Li, Z.; Tukker, A.; Steubing, B. Future environmental impacts of metals: A systematic review of impact trends, modelling approaches, and challenges. *Resour. Conserv. Recycl.* **2024**, 205, 107572. [\[CrossRef\]](#)
9. Collin, M.S.; Venkatraman, S.K.; Vijayakumar, N.; Kanimozhi, V.; Arbaaz, S.M.; Stacey, R.G.S.; Anusha, J.; Choudhary, R.; Lvov, V.; Tovar, G.I.; et al. Bioaccumulation of lead (Pb) and its effects on human: A review. *J. Hazard. Mater. Adv.* **2022**, 7, 100094. [\[CrossRef\]](#)
10. Chen, B.; Dong, S. Mercury Contamination in Fish and Its Effects on the Health of Pregnant Women and Their Fetuses, and Guidance for Fish Consumption-A Narrative Review. *Int. J. Environ. Res. Public Health* **2022**, 19, 15929. [\[CrossRef\]](#)
11. Kothapalli, C.R. Differential impact of heavy metals on neurotoxicity during development and in aging central nervous system. *Curr. Opin. Toxicol.* **2021**, 26, 33–38. [\[CrossRef\]](#)
12. Wu, B.; Hou, S.; Peng, D.; Wang, Y.; Wang, C.; Xu, F.; Xu, H. Response of soil micro-ecology to different levels of cadmium in alkaline soil. *Ecotoxicol. Environ. Saf.* **2018**, 166, 116–122. [\[CrossRef\]](#) [\[PubMed\]](#)
13. Verzelloni, P.; Urbano, T.; Wise, L.A.; Vinceti, M.; Filippini, T. Cadmium exposure and cardiovascular disease risk: A systematic review and dose-response meta-analysis. *Environ. Pollut.* **2024**, 345, 123462. [\[CrossRef\]](#) [\[PubMed\]](#)
14. Qu, F.; Zheng, W. Cadmium Exposure: Mechanisms and Pathways of Toxicity and Implications for Human Health. *Toxics* **2024**, 12, 388. [\[CrossRef\]](#)
15. Monteiro De Oliveira, E.C.; Caixeta, E.S.; Santos, V.S.V.; Pereira, B.B. Arsenic exposure from groundwater: Environmental contamination, human health effects, and sustainable solutions. *J. Toxicol. Environ. Health B Crit. Rev.* **2021**, 24, 119–135. [\[CrossRef\]](#)
16. Wadgaonkar, P.; Wang, Z.; Chen, F. Endoplasmic reticulum stress responses and epigenetic alterations in arsenic carcinogenesis. *Environ. Pollut.* **2024**, 347, 123565. [\[CrossRef\]](#)
17. EU 20202184; European Union Standards for Drinking Water Quality Are Outlined in Directive EU 20202184. European Union: Brussels, Belgium, 2020.
18. GB-5749-2006; National Standard of the People's Republic of China, GB-5749-2006-Standards-for-Drinking-Water-Quality. National Health Commission of the People's Republic of China: Beijing, China, 2006.
19. EPA-822-R-02-047; National Recommended Water Quality Criteria. Office of Water, Office of Science and Technology, US EPA: Washington, DC, USA, 2002.
20. WHO. *Guidelines for Drinking Water Quality*, 4th ed.; WHO Press: Geneva, Switzerland, 2011.
21. Arjomandi, M.; Shirkhanloo, H. A review: Analytical methods for heavy metals determination in environment and human samples. *Anal. Methods Environ. Chem. J.* **2019**, 2, 97–126. [\[CrossRef\]](#)
22. Sulthana, S.F.; Iqbal, U.M.; Suseela, S.B.; Anbazhagan, R.; Chinthajinjala, R.; Chitathuru, D.; Ahmad, I.; Kim, T.H. Electrochemical Sensors for Heavy Metal Ion Detection in Aqueous Medium: A Systematic Review. *ACS Omega* **2024**, 9, 25493–25512. [\[CrossRef\]](#)
23. William, T.; Jerry Winberry, J. *Compendium of Methods for Determination of Inorganic Compounds in Ambient Air*; Center for Environmental Research Information Office of Research and Development U.S. Environmental Protection Agency Cincinnati: Cincinnati, OH, USA, 1999; pp. 3–31.
24. Malik, L.A.; Bashir, A.; Qureashi, A.; Pandith, A.H. Detection and removal of heavy metal ions: A review. *Environ. Chem. Lett.* **2019**, 17, 1495–1521. [\[CrossRef\]](#)
25. Gong, T.; Liu, J.; Liu, X.; Liu, J.; Xiang, J.; Wu, Y. A sensitive and selective sensing platform based on CdTe QDs in the presence of l-cysteine for detection of silver, mercury and copper ions in water and various drinks. *Food Chem.* **2016**, 213, 306–312. [\[CrossRef\]](#)
26. Lebedev, A.; Sinikova, N.; Nikolaeva, S.; Poliakova, O.; Khrushcheva, M.; Pozdnyakov, S. Metals and organic pollutants in snow surrounding an iron factory. *Environ. Chem. Lett.* **2003**, 1, 107–112. [\[CrossRef\]](#)

27. Xia, L.; Zhu, D.; Wei, Y. Affirmation of the Method that Determination of Water Heavy Metals by Flame Atomic Absorption Spectrophotometry. *IOP Conf. Ser. Mater. Sci. Eng.* **2018**, *394*, 052086. [\[CrossRef\]](#)
28. Wang, M.; Lai, J.; Ni, Y.; Zhou, W. A microwave digestion method for determination of heavy metals in shallow lake sediments by graphite furnace atomic absorption spectrometry. *Chin. J. Anal. Lab.* **2012**, *31*, 51–54.
29. Sitko, R.; Janik, P.; Zawisza, B.; Talik, E.; Margui, E.; Queral, I. Green approach for ultratrace determination of divalent metal ions and arsenic species using total-reflection X-ray fluorescence spectrometry and mercapto-modified graphene oxide nanosheets as a novel adsorbent. *Anal. Chem.* **2015**, *87*, 3535–3542. [\[CrossRef\]](#)
30. Yang, Y.-C.; Sun, Y.-Z.; Zhang, C.; Yan, J.; Zhao, H.-L.-B. Simultaneous determination of arsenic, lead and cadmium in cosmetics by ICP-OES. *China Surfactant Deterg. Cosmet.* **2017**, *47*, 598–602. [\[CrossRef\]](#)
31. Wang, H.; Wu, Z.; Chen, B.; He, M.; Hu, B. Chip-based array magnetic solid phase microextraction on-line coupled with inductively coupled plasma mass spectrometry for the determination of trace heavy metals in cells. *Analyst* **2015**, *140*, 5619–5626. [\[CrossRef\]](#)
32. Kim, Y.; Kang, S.K.; Choi, I.; Lee, J.; Yi, J. Molecular Level Detection of Heavy Metal Ions Using Atomic Force Microscope. *Clean. Technol.* **2005**, *11*, 69–74.
33. Evans, E.H.; Pisonero, J.; Smith, C.M.M.; Taylor, R.N. Atomic spectrometry update: Review of advances in atomic spectrometry and related techniques. *J. Anal. At. Spectrom.* **2021**, *36*, 868–891. [\[CrossRef\]](#)
34. Fakayode, S.O.; Walgama, C.; Fernand Narcisse, V.E.; Grant, C. Electrochemical and Colorimetric Nanosensors for Detection of Heavy Metal Ions: A Review. *Sensors* **2023**, *23*, 9080. [\[CrossRef\]](#)
35. Hutton, L.A.; O'Neil, G.D.; Read, T.L.; Ayres, Z.J.; Newton, M.E.; Macpherson, J.V. Electrochemical X-ray fluorescence spectroscopy for trace heavy metal analysis: Enhancing X-ray fluorescence detection capabilities by four orders of magnitude. *Anal. Chem.* **2014**, *86*, 4566–4572. [\[CrossRef\]](#)
36. Shirsat, M.D.; Hianik, T. Electrochemical Detection of Heavy Metal Ions Based on Nanocomposite Materials. *J. Compos. Sci.* **2023**, *7*, 473. [\[CrossRef\]](#)
37. Amali, R.K.A.; Lim, H.N.; Ibrahim, I.; Huang, N.M.; Zainal, Z.; Ahmad, S.A.A. Significance of nanomaterials in electrochemical sensors for nitrate detection: A review. *Trends Environ. Anal. Chem.* **2021**, *31*, e00135. [\[CrossRef\]](#)
38. Li, Y.; Zhong, H.; Huang, Y.; Zhao, R. Recent Advances in AIEgens for Metal Ion Biosensing and Bioimaging. *Molecules* **2019**, *24*, 4593. [\[CrossRef\]](#) [\[PubMed\]](#)
39. Taha, A.; Farooq, N.; Singh, N.; Hashmi, A.A. Recent developments in Schiff base centered optical and chemical sensors for metal ion recognition. *J. Mol. Liq.* **2024**, *401*, 124678. [\[CrossRef\]](#)
40. Li, L.; Xu, S.; Li, X.; Gao, H.; Yang, L.; Jiang, C. Design of microfluidic fluorescent sensor arrays for real-time and synchronously visualized detection of multi-component heavy metal ions. *Chem. Eng. J.* **2024**, *493*, 152636. [\[CrossRef\]](#)
41. Wang, G.; Chu, L.T.; Hartanto, H.; Utomo, W.B.; Pravasta, R.A.; Chen, T.H. Microfluidic Particle Dam for Visual and Quantitative Detection of Lead Ions. *ACS Sens.* **2020**, *5*, 19–23. [\[CrossRef\]](#)
42. Zeng, S.; Zhu, H.; Sohan, A.; Liu, J.; Wan, X.; Lin, X.; Yin, B. A remote-controlled portable workstation for highly sensitive and real-time chemiluminescent detection of cadmium. *Food Chem.* **2024**, *452*, 139549. [\[CrossRef\]](#)
43. Whitesides, G.M. The origins and the future of microfluidics. *Nature* **2006**, *442*, 368–373. [\[CrossRef\]](#)
44. Cui, W.; Ren, Z.; Song, Y.; Ren, C.L. Development and potential for point-of-care heavy metal sensing using microfluidic systems: A brief review. *Sens. Actuators A Phys.* **2022**, *344*, 113733. [\[CrossRef\]](#)
45. Sekhwama, M.; Mpofu, K.; Sudesh, S.; Mthunzi-Kufa, P. Integration of microfluidic chips with biosensors. *Discov. Appl. Sci.* **2024**, *6*, 458. [\[CrossRef\]](#)
46. Cheng, Z.; Gu, Y.; Li, S.; Wang, Y.; Chen, H.; Cheng, J.; Liu, P. Enclosed casting of epoxy resin for rapid fabrication of rigid microfluidic chips. *Sens. Actuators B Chem.* **2017**, *252*, 785–793. [\[CrossRef\]](#)
47. Mitrogiannopoulou, A.M.; Tselepi, V.; Ellinas, K. Polymeric and Paper-Based Lab-on-a-Chip Devices in Food Safety: A Review. *Micromachines* **2023**, *14*, 986. [\[CrossRef\]](#) [\[PubMed\]](#)
48. Raffy, S.; Palleau, E.; Calvignac, B.; Brotons, G.; Lefebvre, G.; Rolley, N.; Teychene, S.; Viguier, B.; Cerezo, S.C.; Truan, G.; et al. “All in One” Epoxy-Based Microfluidic Chips at Your Fingertips. *ACS Appl. Polym. Mater.* **2021**, *3*, 801–810. [\[CrossRef\]](#)
49. Nielsen, J.B.; Hanson, R.L.; Almughamsi, H.M.; Pang, C.; Fish, T.R.; Woolley, A.T. Microfluidics: Innovations in Materials and Their Fabrication and Functionalization. *Anal. Chem.* **2020**, *92*, 150–168. [\[CrossRef\]](#)
50. Filippidou, M.K.; Chatzandroulis, S. Microfluidic Devices for Heavy Metal Ions Detection: A Review. *Micromachines* **2023**, *14*, 1520. [\[CrossRef\]](#)
51. Amini, Y.; Hassanvand, A.; Ghazanfari, V.; Shadman, M.M.; Heydari, M.; Alborzi, Z.S. Optimization of liquid-liquid extraction of calcium with a serpentine microfluidic device. *Int. Commun. Heat. Mass. Transf.* **2023**, *140*, 106551. [\[CrossRef\]](#)
52. Marsousi, S.; Karimi-Sabet, J.; Moosavian, M.A.; Amini, Y. Liquid-liquid extraction of calcium using ionic liquids in spiral microfluidics. *Chem. Eng. J.* **2019**, *356*, 492–505. [\[CrossRef\]](#)

53. Ding, R.; Cheong, Y.H.; Ahamed, A.; Lisak, G. Heavy Metals Detection with Paper-Based Electrochemical Sensors. *Anal. Chem.* **2021**, *93*, 1880–1888. [\[CrossRef\]](#)
54. Xing, G.; Lin, J.M. Microfluidics for foodborne bacteria analysis: Moving toward multiple technologies integration. *Biomicrofluidics* **2024**, *18*, 061301. [\[CrossRef\]](#)
55. Liu, D.; Wang, Y.; Li, X.; Li, M.; Wu, Q.; Song, Y.; Zhu, Z.; Yang, C. Integrated microfluidic devices for in vitro diagnostics at point of care. *Aggregate* **2022**, *3*, e184. [\[CrossRef\]](#)
56. Nigam, A.; Sharma, N.; Tripathy, S.; Kumar, M. Development of semiconductor based heavy metal ion sensors for water analysis: A review. *Sens. Actuators A Phys.* **2021**, *330*, 112879. [\[CrossRef\]](#)
57. Buledi, J.A.; Amin, S.; Haider, S.I.; Bhanger, M.I.; Solangi, A.R. A review on detection of heavy metals from aqueous media using nanomaterial-based sensors. *Environ. Sci. Pollut. Res. Int.* **2021**, *28*, 58994–59002. [\[CrossRef\]](#) [\[PubMed\]](#)
58. Hou, H.; Zeinu, K.M.; Gao, S.; Liu, B.; Yang, J.; Hu, J. Recent Advances and Perspective on Design and Synthesis of Electrode Materials for Electrochemical Sensing of Heavy Metals. *Energy Environ. Mater.* **2018**, *1*, 113–131. [\[CrossRef\]](#)
59. Lu, Y.; Liang, X.; Niyungeko, C.; Zhou, J.; Xu, J.; Tian, G. A review of the identification and detection of heavy metal ions in the environment by voltammetry. *Talanta* **2018**, *178*, 324–338. [\[CrossRef\]](#)
60. Numan, A.; Gill, A.A.S.; Rafique, S.; Guduri, M.; Zhan, Y.; Maddiboyina, B.; Li, L.; Singh, S.; Nguyen Dang, N. Rationally engineered nanosensors: A novel strategy for the detection of heavy metal ions in the environment. *J. Hazard. Mater.* **2021**, *409*, 124493. [\[CrossRef\]](#)
61. Chauhan, S.; Dahiya, D.; Sharma, V.; Khan, N.; Chaurasia, D.; Nadda, A.K.; Varjani, S.; Pandey, A.; Bhargava, P.C. Advances from conventional to real time detection of heavy metal(loid)s for water monitoring: An overview of biosensing applications. *Chemosphere* **2022**, *307*, 136124. [\[CrossRef\]](#)
62. Tseng, H.Y.; Lizama, J.H.; Alvarado, N.A.S.; Hou, H.H. Lab-on-PCB: One step away from the accomplishment of muTAS? *Biomicrofluidics* **2022**, *16*, 031302. [\[CrossRef\]](#)
63. Lace, A.; Cleary, J. A Review of Microfluidic Detection Strategies for Heavy Metals in Water. *Chemosensors* **2021**, *9*, 60. [\[CrossRef\]](#)
64. Rai, P.K.; Islam, M.; Gupta, A. Microfluidic devices for the detection of contamination in water samples: A review. *Sens. Actuators A Phys.* **2022**, *347*, 113926. [\[CrossRef\]](#)
65. Alhalaili, B.; Popescu, I.N.; Rusanescu, C.O.; Vidu, R. Microfluidic Devices and Microfluidics-Integrated Electrochemical and Optical (Bio)Sensors for Pollution Analysis: A Review. *Sustainability* **2022**, *14*, 12844. [\[CrossRef\]](#)
66. Eddaif, L.; Shaban, A.; Telegdi, J. Sensitive detection of heavy metals ions based on the calixarene derivatives-modified piezoelectric resonators: A review. *Int. J. Environ. Anal. Chem.* **2019**, *99*, 824–853. [\[CrossRef\]](#)
67. Li, S.; Zhang, C.; Wang, S.; Liu, Q.; Feng, H.; Ma, X.; Guo, J. Electrochemical microfluidics techniques for heavy metal ion detection. *Analyst* **2018**, *143*, 4230–4246. [\[CrossRef\]](#) [\[PubMed\]](#)
68. Zhang, C.; Li, C.; Han, X. Screen printed electrode containing bismuth for the detection of cadmium ion. *J. Electroanal. Chem.* **2023**, *933*, 117291. [\[CrossRef\]](#)
69. Choudhari, U.; Jagtap, S.; Ramgir, N.; Debnath, A.K.; Muthe, K.P. Screen-printed electrochemical sensors for environmental monitoring of heavy metal ion detection. *Rev. Chem. Eng.* **2023**, *39*, 1227–1268. [\[CrossRef\]](#)
70. Shin, Y.-H.; Teresa Gutierrez-Wing, M.; Choi, J.-W. Review—Recent Progress in Portable Fluorescence Sensors. *J. Electrochem. Soc.* **2021**, *168*, 017502. [\[CrossRef\]](#)
71. Lin, Y.; Gritsenko, D.; Feng, S.; Teh, Y.C.; Lu, X.; Xu, J. Detection of heavy metal by paper-based microfluidics. *Biosens. Bioelectron.* **2016**, *83*, 256–266. [\[CrossRef\]](#)
72. Xu, G.; Song, P.; Xia, L. Examples in the detection of heavy metal ions based on surface-enhanced Raman scattering spectroscopy. *Nanophotonics* **2021**, *10*, 4419–4445. [\[CrossRef\]](#)
73. Liu, T.; Li, S.; Deng, J.; Wang, G.; Liu, Y. Design and study of microfluidic differential phase surface plasmon resonance sensor. *J. Phys. Conf. Ser.* **2022**, *2206*, 012026. [\[CrossRef\]](#)
74. Zhong, Y.; Ji, M.; Hu, Y.; Li, G.; Xiao, X. Progress of environmental sample preparation for elemental analysis. *J. Chromatogr. A* **2022**, *1681*, 463458. [\[CrossRef\]](#)
75. Nadumane, S.S.; Biswas, R.; Mazumder, N. Integrated microfluidic platforms for heavy metal sensing: A comprehensive review. *Anal. Methods* **2024**, *16*, 2810–2823. [\[CrossRef\]](#)
76. Kwon, S.-Y.; Kim, Y.-I.; Kim, Y.-K.; Lee, Y.-B.; Mok, J.H. Microwave-assisted sample preparation for screening of heavy metal elements in food additives by ICP-MS. *Lwt* **2024**, *208*, 116708. [\[CrossRef\]](#)
77. Huang, W.H.; Mai, V.P.; Wu, R.Y.; Yeh, K.L.; Yang, R.J. A Microfluidic Aptamer-Based Sensor for Detection of Mercury(II) and Lead(II) Ions in Water. *Micromachines* **2021**, *12*, 1283. [\[CrossRef\]](#) [\[PubMed\]](#)
78. Peng, J.; Zhao, N.; Lin, S.; Wang, W.; Zhang, M.-J.; Su, Y.-Y.; Xie, R.; Ju, X.-J.; Liu, Z.; Chu, L.-Y. Smart microfluidic analogue of Wheatstone-bridge for real-time continuous detection with ultrasensitivity and wide dynamic range. *Chem. Eng. J.* **2021**, *407*, 127138. [\[CrossRef\]](#)

79. Peng, G.; Chen, Y.; Deng, R.; He, Q.; Liu, D.; Lu, Y.; Lin, J.M. Highly sensitive and selective determination of Hg(II) based on microfluidic chip with on-line fluorescent derivatization. *Spectrochim. Acta A Mol. Biomol. Spectrosc.* **2018**, *204*, 1–6. [\[CrossRef\]](#)
80. Motalebizadeh, A.; Bagheri, H.; Asiaei, S.; Fekrat, N.; Afkhami, A. New portable smartphone-based PDMS microfluidic kit for the simultaneous colorimetric detection of arsenic and mercury. *RSC Adv.* **2018**, *8*, 27091–27100. [\[CrossRef\]](#)
81. Mishra, N.; Dhawaj, A.; Verma, D.; Prabhakar, A. Cost-effective microabsorbance detection based nanoparticle immobilized microfluidic system for potential investigation of diverse chemical contaminants present in drinking water. *Anal. Chim. Acta* **2022**, *1205*, 339734. [\[CrossRef\]](#)
82. Peng, G.; He, Q.; Lu, Y.; Huang, J.; Lin, J.-M. Flow injection microfluidic device with on-line fluorescent derivatization for the determination of Cr(III) and Cr(VI) in water samples after solid phase extraction. *Anal. Chim. Acta* **2017**, *955*, 58–66. [\[CrossRef\]](#)
83. Zhang, W.; Liu, G.; Bi, J.; Bao, K.; Wang, P. In-situ and ultrasensitive detection of mercury (II) ions (Hg^{2+}) using the localized surface plasmon resonance (LSPR) nanosensor and the microfluidic chip. *Sens. Actuators A Phys.* **2023**, *349*, 114074. [\[CrossRef\]](#)
84. Mohan, J.M.; Dudala, S.; Amreen, K.; Javed, A.; Dubey, S.K.; Goel, S. Microfluidic Device Integrated With PDMS Microchannel and Unmodified ITO Glass Electrodes for Highly Sensitive, Specific, and Point-of-Care Detection of Copper and Mercury. *IEEE Trans. Nanobiosci.* **2023**, *22*, 881–888. [\[CrossRef\]](#)
85. Fakhri, N.; Hosseini, M.; Tavakoli, O. Aptamer-based colorimetric determination of Pb^{2+} using a paper-based microfluidic platform. *Anal. Methods* **2018**, *10*, 4438–4444. [\[CrossRef\]](#)
86. Wisang, Y.F. Microfluidic Paper-based Analytical Devices (μ PADs) For Analysis Lead using Naked Eye and Colorimetric Detections. *IOP Conf. Ser. Mater. Sci. Eng.* **2019**, *546*, 032033. [\[CrossRef\]](#)
87. Zhou, J.; Li, B.; Qi, A.; Shi, Y.; Qi, J.; Xu, H.; Chen, L. ZnSe quantum dot based ion imprinting technology for fluorescence detecting cadmium and lead ions on a three-dimensional rotary paper-based microfluidic chip. *Sens. Actuators B Chem.* **2020**, *305*, 127462. [\[CrossRef\]](#)
88. Wang, M.; Song, Z.; Jiang, Y.; Zhang, X.; Wang, L.; Zhao, H.; Cui, Y.; Gu, F.; Wang, Y.; Zheng, G. A three-dimensional pinwheel-shaped paper-based microfluidic analytical device for fluorescence detection of multiple heavy metals in coastal waters by rational device design. *Anal. Bioanal. Chem.* **2021**, *413*, 3299–3313. [\[CrossRef\]](#) [\[PubMed\]](#)
89. Wang, L.; Li, B.; Wang, J.; Qi, J.; Li, J.; Ma, J.; Chen, L. A rotary multi-positioned cloth/paper hybrid microfluidic device for simultaneous fluorescence sensing of mercury and lead ions by using ion imprinted technologies. *J. Hazard. Mater.* **2022**, *428*, 128165. [\[CrossRef\]](#)
90. Dindorkar, G.; Rathee, V.; Balpande, S.; Kalambe, J. Detection of Mercury in Water using Filter Paper Based Channel and Colorimetric-Android Readout. *Int. J. Eng. Adv. Technol.* **2019**, *9*, 434–438. [\[CrossRef\]](#)
91. Abdollahiyan, P.; Hasanzadeh, M.; Pashazadeh-Panahi, P.; Seidi, F. Application of Cys A@AuNPs supported amino acids towards rapid and selective identification of Hg(II) and Cu(II) ions in aqueous solution: An innovative microfluidic paper-based (μ PADs) colorimetric sensing platform. *J. Mol. Liq.* **2021**, *338*, 117020. [\[CrossRef\]](#)
92. Jin, B.; Li, Z.; Zhao, G.; Ji, J.; Chen, J.; Yang, Y.; Xu, R. Upconversion fluorescence-based paper disc for multiplex point-of-care testing in water quality monitoring. *Anal. Chim. Acta* **2022**, *1192*, 339388. [\[CrossRef\]](#)
93. Sun, X.; Li, B.; Qi, A.; Tian, C.; Han, J.; Shi, Y.; Lin, B.; Chen, L. Improved assessment of accuracy and performance using a rotational paper-based device for multiplexed detection of heavy metals. *Talanta* **2018**, *178*, 426–431. [\[CrossRef\]](#)
94. Shang, Q.; Zhang, P.; Li, H.; Liu, R.; Zhang, C. A flow chemiluminescence paper-based microfluidic device for detection of chromium (III) in water. *J. Innov. Opt. Health Sci.* **2019**, *12*, 1950016. [\[CrossRef\]](#)
95. Li, F.; Hu, Y.; Li, Z.; Liu, J.; Guo, L.; He, J. Three-dimensional microfluidic paper-based device for multiplexed colorimetric detection of six metal ions combined with use of a smartphone. *Anal. Bioanal. Chem.* **2019**, *411*, 6497–6508. [\[CrossRef\]](#)
96. Alahmad, W.; Tungkijanansin, N.; Kaneta, T.; Varanusupakul, P. A colorimetric paper-based analytical device coupled with hollow fiber membrane liquid phase microextraction (HF-LPME) for highly sensitive detection of hexavalent chromium in water samples. *Talanta* **2018**, *190*, 78–84. [\[CrossRef\]](#) [\[PubMed\]](#)
97. Muhammed, A.; Hussien, A.; Kaneta, T. Speciation of chromium in water samples using microfluidic paper-based analytical devices with online oxidation of trivalent chromium. *Anal. Bioanal. Chem.* **2021**, *413*, 3339–3347. [\[CrossRef\]](#) [\[PubMed\]](#)
98. Ding, B.; Zhang, Q.; Yang, C.; Yang, W.; Liu, J.; Li, C.; Tao, S. Laser-Induced Carbon Electrodes in a Three-Dimensionally Printed Flow Reactor for Detecting Lead Ions. *ACS Omega* **2021**, *6*, 12470–12479. [\[CrossRef\]](#) [\[PubMed\]](#)
99. Santangelo, M.F.; Shteplyuk, I.; Filippini, D.; Puglisi, D.; Vagin, M.; Yakimova, R.; Eriksson, J. Epitaxial Graphene Sensors Combined with 3D-Printed Microfluidic Chip for Heavy Metals Detection. *Sensors* **2019**, *19*, 2393. [\[CrossRef\]](#)
100. Zhao, G.; Tran, T.T.; Modha, S.; Sedki, M.; Myung, N.V.; Jassby, D.; Mulchandani, A. Multiplexed Anodic Stripping Voltammetry Detection of Heavy Metals in Water Using Nanocomposites Modified Screen-Printed Electrodes Integrated with a 3D-Printed Flow Cell. *Front. Chem.* **2022**, *10*, 815805. [\[CrossRef\]](#)
101. Gupta, A.K.; Khanna, M.; Roy, S.; Pankaj; Nagabooshanam, S.; Kumar, R.; Wadhwa, S.; Mathur, A. Design and development of a portable resistive sensor based on $\alpha\text{-MnO}_2$ /GQD nanocomposites for trace quantification of Pb(II) in water. *IET Nanobiotechnol.* **2021**, *15*, 505–511. [\[CrossRef\]](#)

102. Katseli, V.; Thomaidis, N.; Economou, A.; Kokkinos, C. Miniature 3D-printed integrated electrochemical cell for trace voltammetric Hg^{2+} determination. *Sens. Actuators B. Chem.* **2020**, *308*, 127715. [[CrossRef](#)]
103. Kokkinos, C.; Economou, A.; Pournara, A.; Manos, M.; Spanopoulos, I.; Kanatzidis, M.; Tziotzi, T.; Petkov, V.; Margariti, A.; Oikonomopoulos, P.; et al. 3D-printed lab-in-a-syringe voltammetric cell based on a working electrode modified with a highly efficient Ca-MOF sorbent for the determination of $\text{Hg}(\text{II})$. *Sens. Actuators B Chem.* **2020**, *321*, 128508. [[CrossRef](#)]
104. Ma, S.; Zhao, W.; Zhang, Q.; Zhang, K.; Liang, C.; Wang, D.; Liu, X.; Zhan, X. A portable microfluidic electrochemical sensing platform for rapid detection of hazardous metal Pb^{2+} based on thermocapillary convection using 3D Ag-rGO-f-Ni(OH)₂/NF as a signal amplifying element. *J. Hazard. Mater.* **2023**, *448*, 130923. [[CrossRef](#)]
105. Zhang, M.; Zhang, X.; Niu, P.; Shen, T.; Yuan, Y.; Bai, Y.; Wang, Z. On-site low-power sensing nodes for distributed monitoring of heavy metal ions in water. *Nanotechnol. Precis. Eng.* **2021**, *4*, 013005. [[CrossRef](#)]
106. Gu, Z.; Luo, J.J.; Ding, L.W.; Yan, B.Y.; Zhou, J.L.; Wang, J.G.; Wang, H.F.; Kong, C. Colorimetric Sensing with Gold Nanoparticles on Electrowetting-Based Digital Microfluidics. *Micromachines* **2021**, *12*, 1423. [[CrossRef](#)] [[PubMed](#)]
107. Nguyen, H.L.; Kumar, N.; Audibert, J.-F.; Ghasemi, R.; Lefevre, J.-P.; Ha-Thi, M.-H.; Mongin, C.; Leray, I. Water-soluble aluminium fluorescent sensor based on aggregation-induced emission enhancement. *N. J. Chem.* **2019**, *43*, 15302–15310. [[CrossRef](#)]
108. Han, S.; Liu, X.; Wang, L.; Wang, Y.; Zheng, G. An efficient protocol to use feedback-controlling digital microfluidic fluorimetric sensor for detection of mercury (II) in coastal seawaters. *MethodsX* **2019**, *6*, 1443–1453. [[CrossRef](#)] [[PubMed](#)]

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