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# Ensuring food safety: Microfluidic-based approaches for the detection of food contaminants

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## Abstract

Detecting foodborne contamination is a critical challenge in ensuring food safety and preventing human suffering and economic losses. Contaminated food, comprising biological agents (e.g. bacteria, viruses and fungi) and chemicals (e.g. toxins, allergens, antibiotics and heavy metals), poses significant risks to public health. Microfluidic technology has emerged as a transformative solution, revolutionizing the detection of contaminants with precise and efficient methodologies. By manipulating minute volumes of fluid on miniaturized systems, microfluidics enables the creation of portable chips for biosensing applications. Advancements from early glass and silicon devices to modern polymers and cellulose-based chips have significantly enhanced microfluidic technology, offering adaptability, flexibility, cost-effectiveness and biocompatibility. Microfluidic systems integrate seamlessly with various biosensing reactions, facilitating nucleic acid amplification, target analyte recognition and accurate signal readouts. As research progresses, microfluidic technology is poised to play a pivotal role in addressing evolving challenges in the detection of foodborne contaminants. In this short review, we delve into various manufacturing materials for state-of-the-art microfluidic devices, including inorganics, elastomers, thermoplastics and paper. Additionally, we examine several applications where microfluidic technology offers unique advantages in the detection of food contaminants, including bacteria, viruses, fungi, allergens and more. This review underscores the significant advancement of microfluidic technology and its pivotal role in advancing the detection and mitigation of foodborne contaminants.

KEYWORDS
agriculture, biosensors, contaminants, food safety, lab on a chip, microfluidics

**Abbreviations:** μPAD, microfluidic paper-based analytical device; AMR, antimicrobial resistance; ARG, antimicrobial resistance gene; AST, antimicrobial susceptibility test; AuNP, gold nanoparticle; CL, chemiluminescent; COC, cyclic olefin copolymer; DON, deoxynivalenol; ELISA, enzyme-linked immunosorbent assay; GC, gas chromatography; GC-MS, gas chromatography-mass spectrometry; HPLC, high-performance liquid chromatography; HRP, horseradish peroxidase; MS, mass spectrometry; NoV, norovirus; PCR, polymerase chain reaction; PDMS, polydimethylsiloxane; PMMA, polymethyl methacrylate; PR, photoresist; RT-RAA, reverse-transcription recombinase-aided amplification; UV, ultraviolet.

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## 1 | INTRODUCTION

The safety and quality of the food that we consume are paramount to human health worldwide. A wide array of contaminants wreaks constant havoc on our food supply, including biological agents (e.g. bacteria, viruses and fungi) and chemicals (e.g. toxins, antibiotics, heavy metals and allergens). The challenge of ensuring food safety for an ample food supply is exacerbated by the escalating global population, which has surpassed 8 billion and is projected to exceed 9.7 billion by 2050.[1] As the demand for safe and abundant food grows, it is essential to prevent harmful contaminants from entering our food supply. Beyond food supply, contaminated food poses significant risks to human health, leading to chemical indigestion, poisoning, allergic reactions, and, most notably, foodborne illnesses.[2] These illnesses affect one in ten individuals annually, with symptoms ranging from mild discomforts, such as nausea, vomiting and diarrhoea, to severe cases resulting in death.[3] Alarmingly, foodborne illnesses claim at least 420 thousand lives each year, accounting for 7.5% of all deaths globally.[4] In addition to the human toll, foodborne illnesses exact a substantial economic burden, with estimates exceeding $100 billion in the United States alone, including $15 billion in medical expenses.[5,6] Given these staggering implications, detecting foodborne contamination is critical for maintaining food safety standards and mitigating both human suffering and economic losses.

There are a wide variety of methods used to evaluate contamination in food sectors. This includes high-performance liquid chromatography (HPLC), gas chromatography (GC), mass spectrometry (MS), enzyme-linked immunosorbent assay (ELISA), and polymerase chain reaction (PCR).[7–12] While these methods are generally highly sensitive, they are also extremely time-consuming and expensive.[13,14] Laboratory personnel and highly complex laboratory equipment are required for all of these processes, which is tremendously inefficient. The ability to send samples to a well-equipped lab for analysis is not universally available and remains highly expensive and time-consuming when performed.[15] This is especially troublesome for resource-limited areas, where contamination is most common.[16] Therefore, there is an urgent need for the development of low-cost and user-friendly rapid detection of food contaminants at all stages of the food supply chain.

Microfluidic technology has emerged as a transformative tool in the realm of food safety, offering unprecedented precision and efficiency in the detection of various analytes.[17,18] Microfluidics involves the controlled manipulation of minute volumes of fluids within the microscale or smaller, enabling the integration of diverse analytical processes on a single, miniaturized platform.[19–21] The fundamental principles governing microfluidics leverage the inherent properties of fluids at the microscale governed by capillary forces and laminar flow.[22] This technology excels in biosensing applications by facilitating rapid and highly sensitive analyses through reduced sample volumes and improved reaction kinetics, acting as a small "lab on a chip".[23] These devices are typically extremely portable and user-friendly, acting as ideal in-field sensors for the reliable identification of contaminants in food safety applications.[24–26] Furthermore, the miniaturization that microfluidics offers is ideal for compartmentalizing a single DNA/RNA copy into a small volume for sample digitization.[27] Microfluidics can manipulate nano-liter samples into wells or droplets, allowing them to serve as independent reactors, thus providing a high-throughput platform for analysis.[28] In fact, compared to bulk micro-litre assays, a nano-litre reactor has demonstrated the ability to generate a high-density environment to concentrate diffusible signals, resulting in a 1000-fold increase in throughput while managing a 50% reduction in detection time.[29,30] The intricate design and versatility of microfluidic devices allow for the seamless integration of sample preparation, nucleic acid amplification, and sample readout, minimizing human intervention and reducing the risk of cross-contamination.[31]

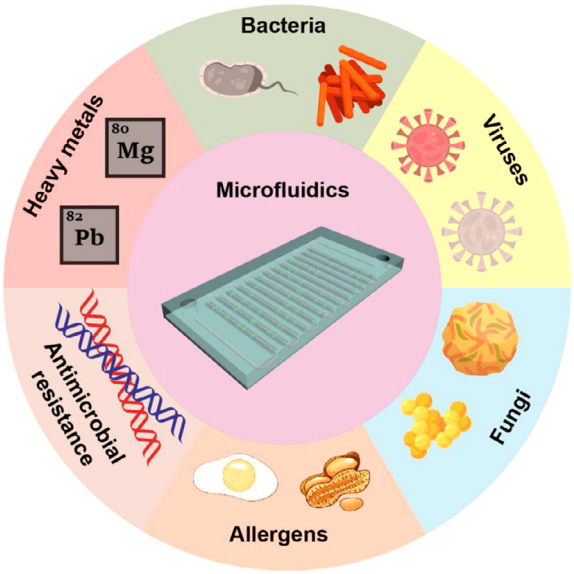


**FIGURE 1** Schematic Illustration of the scope of microfluidic technologies' influence in ensuring food safety.

In this review, we summarize and discuss various microfluidic technologies and their applications for the detection of food contaminants (Figure 1). Firstly, we will highlight the variety of devices currently available and their methods of manufacturing, focusing on the benefits and drawbacks of the current state of each classification of microfluidic device. This will include glass, silicone, polymer and cellulose microfluidic devices, among others. Secondly, we will discuss the wide range of applications that microfluidic technologies employ. Specifically, we will focus on bacteria, viruses, fungi, toxins, antimicrobial resistance (AMR), heavy metals and allergens. We aim to provide a comprehensive summary of the current state of microfluidic technologies in food safety while providing an outlook into the future for such a vital and promising technology.

## 2 | MICROFLUIDIC CHIP MATERIALS AND MANUFACTURING

Microfluidic technology comes in diverse materials each offering unique advantages. Some of the earliest microfluidic-based biosensors

were composed of inorganics, such as glass, due to their exceptional transparency and chemical inertness for precise manipulation and observation of fluids at the microscale.[32] As the field of microfluidics has grown, polymeric microfluidic devices have emerged as the dominant transparent microfluidic device due to their degree of permeability, low cost and extreme flexibility in design and usage.[33] Recently, paper-based microfluidics have leveraged the simplicity and affordability of cellulose substrates, often boasted as the most affordable and simple options for point-of-care diagnostics.[34] As microfluidic devices continue to evolve, their diverse material compositions underline their adaptability and wide-ranging utility in food safety. In this section, we review the most common materials for manufacturing present-day microfluidic devices.

## 2.1 | Inorganics

Inorganic materials such as silicon, glass and quartz played a pivotal role in the fabrication of early microfluidic devices. This was commonly in conjunction with various electrical techniques such as thin-film deposition, lithography and etching.[35] Silicon and glass are distinguished by their robust surface stability, compatibility with solvents, biocompatibility, chemical inertness and hydrophilic attributes. Silicon quickly became a cornerstone of microfluidic chip construction due to its exceptional surface chemical properties conducive to ligand immobilization. Silicon devices are typically employed by anisotropic wet etching by potassium hydroxide and tetramethylammonium hydroxide for wet etching, or reactive ion etching for dry etching.[36] While silicon offers distinct advantages in metal depositing, thermal conductivity and biocompatibility for manufacturing, the use of silicon in newer generations of microfluidic devices is rare due to high costs, long processing times and limited profiling.[37]

Glass, in comparison to silicon, offers advantages in terms of transparency, electroosmotic flow, and ease of processing. Glass chips are commonly manufactured through techniques like photolithography and wet etching.[38] In early microfluidic generations, glass found unique applications in digital microfluidics, allowing accurate control of droplets.[39] Despite these advantages, the trend of utilizing solely glass-based microfluidics has fallen out of favour for similar reasons to silicon devices, including expensive manufacturing and difficult design processes. However, unlike silicon, glass remains relevant and routinely used for microfluidic devices in conjunction with other materials due to its superior transparency, durability and unique thermal resistance.[40]

## 2.2 | Elastomers

Elastomers, particularly polydimethylsiloxane (PDMS), have emerged as the dominant material for present-day microfluidic chip fabrication. First proposed for microfluidic applications in 1998,[41] PDMS has gained widespread acceptance and use owing to its low cost, optical transparency, favourable biocompatibility and permeability. Unlike the first generation of glass and silicon microfluidic chips, PDMS allows for the rapid and versatile design of channels, chambers, wells and more for cost-effective and flexible fabrication. PDMS is commonly moulded with nanometer-level precision for intricate and customizable microfluidic designs specific to their desired applications.[42]

The advantages of PDMS extend beyond its uniquely adaptable manufacturing capabilities. Its elasticity allows for easy deformation under weak stress, followed by rapid return to its original state after stress relaxation, making it an ideal elastomer for microfluidic applications.[43] PDMS is commonly used for applications requiring optimal transparency, such as real-time observation of biological components for food safety via fluorescence or chemiluminescence. This may be with or without the combination of glass for viewing. The material's strong elastic deformation ability makes PDMS chips soft and flexible, allowing for their use in food safety applications such as separation and detection of pathogens and biochemical analysis.[10] The ability to integrate functional units such as micropumps and microvalves on PDMS microfluidic chips further enhances their utility, enabling sophisticated and automated processes.[44] Additionally, PDMS can penetrate gas, which is essential for gas exchange in cell culture and offers advantages in sample digitization.

Elastomer-based microfluidic devices are typically mass-produced from SU-8 moulds, and fabricated using lithography techniques. The process for PDMS microfluidic chip fabrication is shown in Figure 2.[21] Briefly, the SU-8 photoresists (PRs) are spin-coated onto silicon moulds and soft-baked. Brief ultraviolet (UV) exposure then imprints a computer-aided personalized design onto the mould before postexposure baking and alcohol treatment for the creation of a reusable master mould. PDMS chips are then produced in bulk through the mixing of PDMS elastomer base and curing agent at a ratio of 10:1 (w/w). The PDMS mixture is poured onto the mould and degassed. Upon brief thermal curing, the chips are peeled off the mould and can then be altered in various methods. Possible modifications include nanoimprint lithography, inkjet printed electrodes and binding to glass slides via oxygen plasma or corona treatment. Despite the numerous advantages and versatility of PDMS, drawbacks include hydrophobicity and a lack of durability in nanochannels. However, surface modification techniques can improve these issues.[45]

## 2.3 | Thermoplastics

Thermoplastics, while also polymeric, offer markedly different advantages to elastomers for microfluidic fabrication, while also offering cost-effectiveness and versatility. While elastomers undergo significant deformation under weak stress and return to their original state after stress relaxation, thermoplastics can be softened and shaped at certain temperatures for designing hardened microfluidic channels and chambers.[46] Thermoplastics such as polymethyl methacrylate (PMMA), polystyrene, cyclic olefin copolymer (COC), polycarbonate and polyethylene terephthalate offer unique advantages for manufacturing microfluidic devices. The most common thermoplastic used for microfluidic devices is PMMA, which offers thermal processing capabilities and optical clarity for food safety applications.[47] COC is growing

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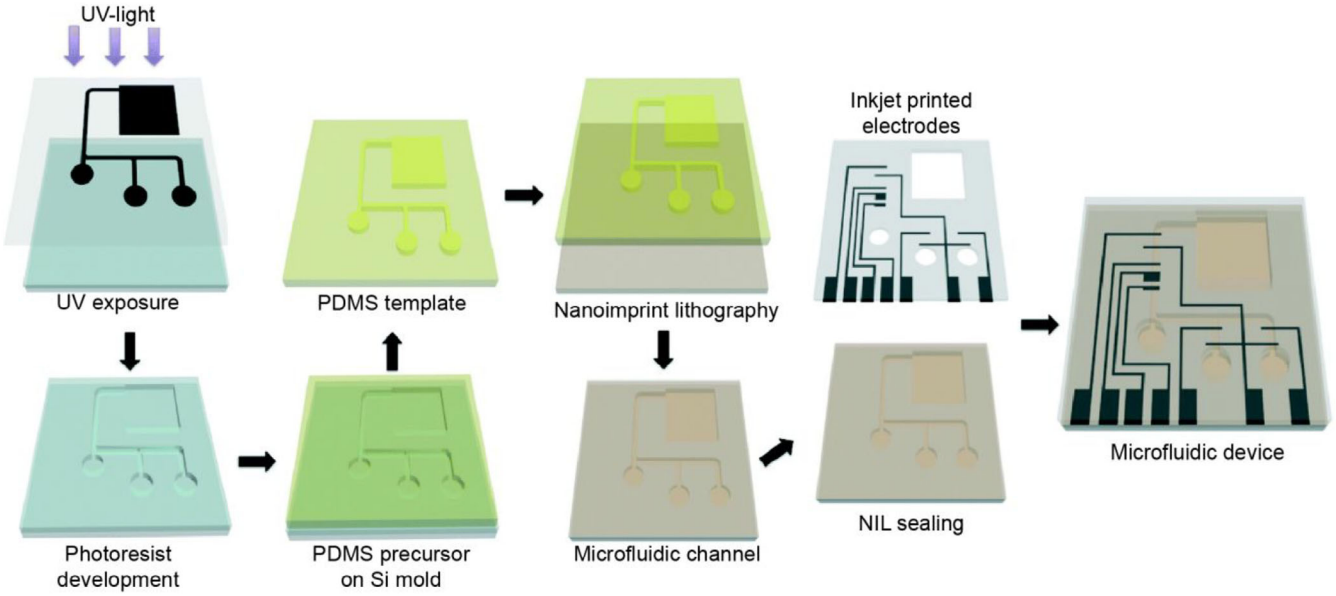


**FIGURE 2** Manufacturing methods to create PDMS microfluidic devices, shown with inkjet printed electrodes. (Reproduced,[21] Copyright 2015, The Royal Society of Chemistry).

in usage and demonstrates enhanced transmission performance and improved thermal stability, making it a promising alternative, particularly in scenarios where heating of the sample is necessary.[48]

Distinct from elastomers, thermoplastics offer the ability to be remoulded at high temperatures, which offers a different route for achieving flexible design and fabrication. Their transition from a solid state to a malleable form at the glass phase transition temperature facilitates easy processing. This process often involves moulding with nanometer-level precision. This adaptability enables the creation of complex miniature structures, making thermoplastics suitable for a broad spectrum of microfluidic applications for improved food safety. Key advantages of thermoplastics include their extremely low cost, optic transparency similar to glass, and ease of mass manufacturing.[47,49]

Manufacturing methods for thermoplastics vary depending on the material and intended usage. In Figure 3A, we highlight a PMMA microfluidic chip designed utilizing several common manufacturing techniques.[50] First, a glass slide was coated with a PR layer for the creation of the intended microfluidic pattern. The slide was etched into a buffered oxide etchant solution, and the PR layer was then stripped. Then, holes were drilled on the glad substrate and aligned and bound to the pre-patterned glass substrate via thermal fusion bonding at extremely high temperatures. A PMMA microfluidic channel is created for the analyte detection layer, where the PMMA substrate is fabricated using hot embossing and attached to the glass via a solvent bonding technique and UV glue. While PMMA chips may be manufactured using simpler methods, complex processes such as hot embossing are typically required, hindering complex designs. Issues such as rigidity after moulding and higher costs compared to elastomers present obstacles to widespread adoption. Additionally, they lack the tolerance to organic solvents and air permeability offered by elastomers, limiting their application in extended cell culture analyses. Despite these challenges, many state-of-the-art microfluidic devices utilize thermoplastics, and the field offers much to be discovered and improved upon as microfluidics continues to grow.[35]

## 2.4 | Paper

Microfluidic paper-based analytical devices (μPADs) are the newest frontier in microfluidic devices, having first been introduced within the past two decades.[51] Even compared to polymer-based devices, μPADs offer increased affordability, ease of miniaturization, biocompatibility and environmentally friendliness. Additionally, they are typically pump-free and facilitate passive flow due to the paper's capillary effect. Typically, μPADs are fabricated by incorporating hydrophobic materials into hydrophilic cellulose fibres through various methods for precise control of fluid flow, with the hydrophobic layers as walls to direct flow.[52] Multi-layered μPAD structures can enable filtration and concentration, meanwhile, microchannels can facilitate many applications for food safety such as the detection of food pathogens, additives or pesticides.[53] In addition to their ease of fabrication and functional structure, μPADs demonstrate excellent biocompatibility. The cellulose-rich composition of filter paper supports the immobilization of biomolecules, making it conducive for applications in food quality control and antibody-based sensing.[54] Colorimetric detection can be carried out through enzymatic or chemical reactions, providing direct observation of results.[55] Alternatively, μPADs can be used for electrochemical detection with fluorescent and chemiluminescent (CL) signal transductions. The porous structure and large surface area of paper contribute to multi-functional capabilities, which can encompass filtration, transportation, and separation.[56]

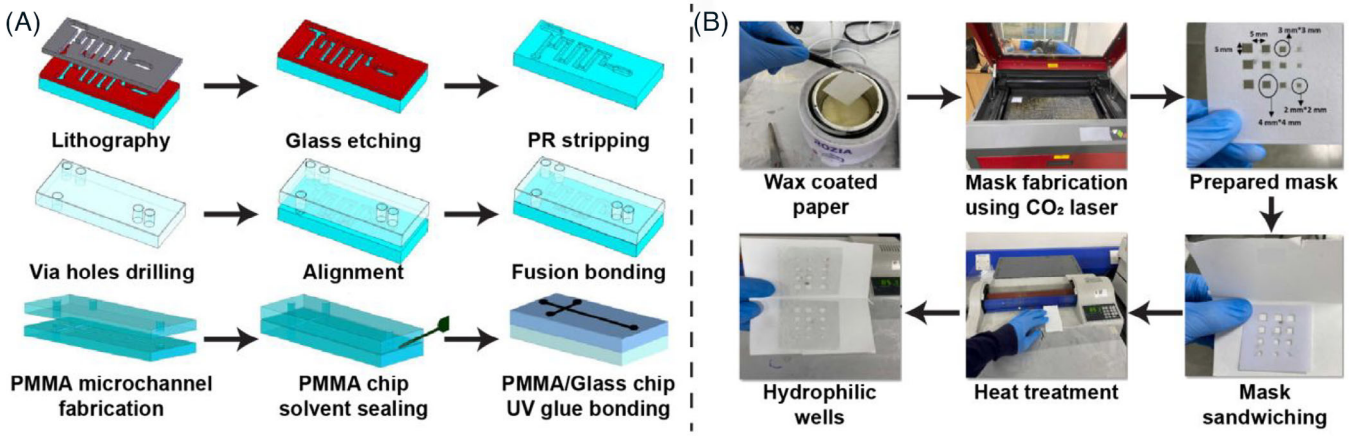


**FIGURE 3** Manufacturing of polymethyl methacrylate (PMMA) and wax-printed microfluidic devices. (A) Manufacturing processes for engineering a PMMA/glass microfluidic device. (Reproduced with permission,[50] Copyright 2012, AIP Publishing). (B) Steps for manufacturing a wax-printed microfluidic μPAD. (Reproduced with permission,[59] Copyright 2023, Elsevier B.V.).

Paper microfluidic devices can be made via simple techniques such as wax printing, inkjet printing, 3D printing, and even drawing.[57,58] Among these, wax printing is the most ubiquitous. Wax printing is a simple technique, as shown in the example in Figure 3B.[59] For this μPAD, Whatman filter paper was first cut into the desired dimensions and then dipped into a wax solution. Various wax laminated paper moulds were then generated from $CO_2$ lasering to create prepared masks. The mould was then fit between more Whatman filter paper and laminated at an increased temperature to form the desired microfluidic channels with hydrophilic wells and hydrophobic wax barriers.

The main limitations of μPADs include transparency and flow control. Typically, μPADs are open-channel, meaning the fluid moves inside the paper fibres itself. The most common material for μPAD fabrication is Whatman series papers. While these are commonly even more cost-efficient than polymeric methods, precision in fluid control and consistent visual transparency are lacking compared to polymer-based methods.[60] Additionally, they lack the ability to perform complex mixing or sample digitization processes offered by polymer-based methods. However, μPADs are still largely in the development stage with few commercial products available as research and understanding of the technology continue to grow.[35] While challenges persist, μPADs stand at the forefront of microfluidic innovation in 2023, especially for point-of-care applications, due to their extreme affordability, biocompatibility and ease of manufacturing.

## 3 | APPLICATIONS FOR FOOD SAFETY

The applications of microfluidics within the realm of food safety are both broad and versatile, encompassing a myriad of critical aspects in the detection and monitoring of food contaminants. In this section, we review the comprehensive landscape of microfluidic applications for food safety, covering the detection of a diverse array of relevant and problematic contaminants. This includes bacteria, viruses, fungi, toxins, allergens, AMR and heavy metals.

### 3.1 | Bacteria

Pathogenic bacteria in food vehicles are among the most prevalent and dangerous threats to food safety, causing food poisoning, various illnesses, and deaths. A wide range of 31 different pathogens have been studied and identified as causing food-borne diseases.[61] The most common of these include *Escherichia coli*, *Listeria monocytogenes*, *Salmonella* species and *Staphylococcus aureus*.[62] For most bacteria, the conventional detection methods require culturing and enrichment of bacteria from food samples, which is expensive, complicated, and time-consuming.[63] To combat this issue, various types of microfluidic devices have been deployed for the timely and sensitive detection of disparate pathogenic bacteria in food systems.

*E. coli* O157:H7 is a highly morbid pathogen that produces the Shiga toxin, causing severe stomach pain, diarrhoea, and often hemorrhagic colitis.[64] While PCR-based methods are much quicker than the culture-based method, these have been hindered by complex sample preparation, pre-processing, and expensive machinery. Therefore, several novel microfluidic approaches have been utilized for the portable and sensitive detection of *E. coli* O157:H7. For example, a recent study developed a microfluidic chip made from a combination of glass and PDMS for the CL detection of *E. coli* O157:H7.[65] The chip utilized micropillars functionalized with streptavidin and hairpin oligonucleotides with biotin. Upon addition of the sample reagents, which included aptamers and a hairpin oligonucleotide with gold nanoparticles (AuNPs) and horseradish peroxidase (HRP), a combination of pumping luminol and hydrogen peroxidase produces a CL readout from the microfluidic chip (Figure 4A). The catalytic hairpin assembly method utilized a sample volume of only 10 μL, producing a visual readout specific to *E. coli* O157:H7 within 1.5 h with a sensitivity as low as 130 CFU/mL (Figure 4B,C). In addition to *E. coli*, *Salmonella*

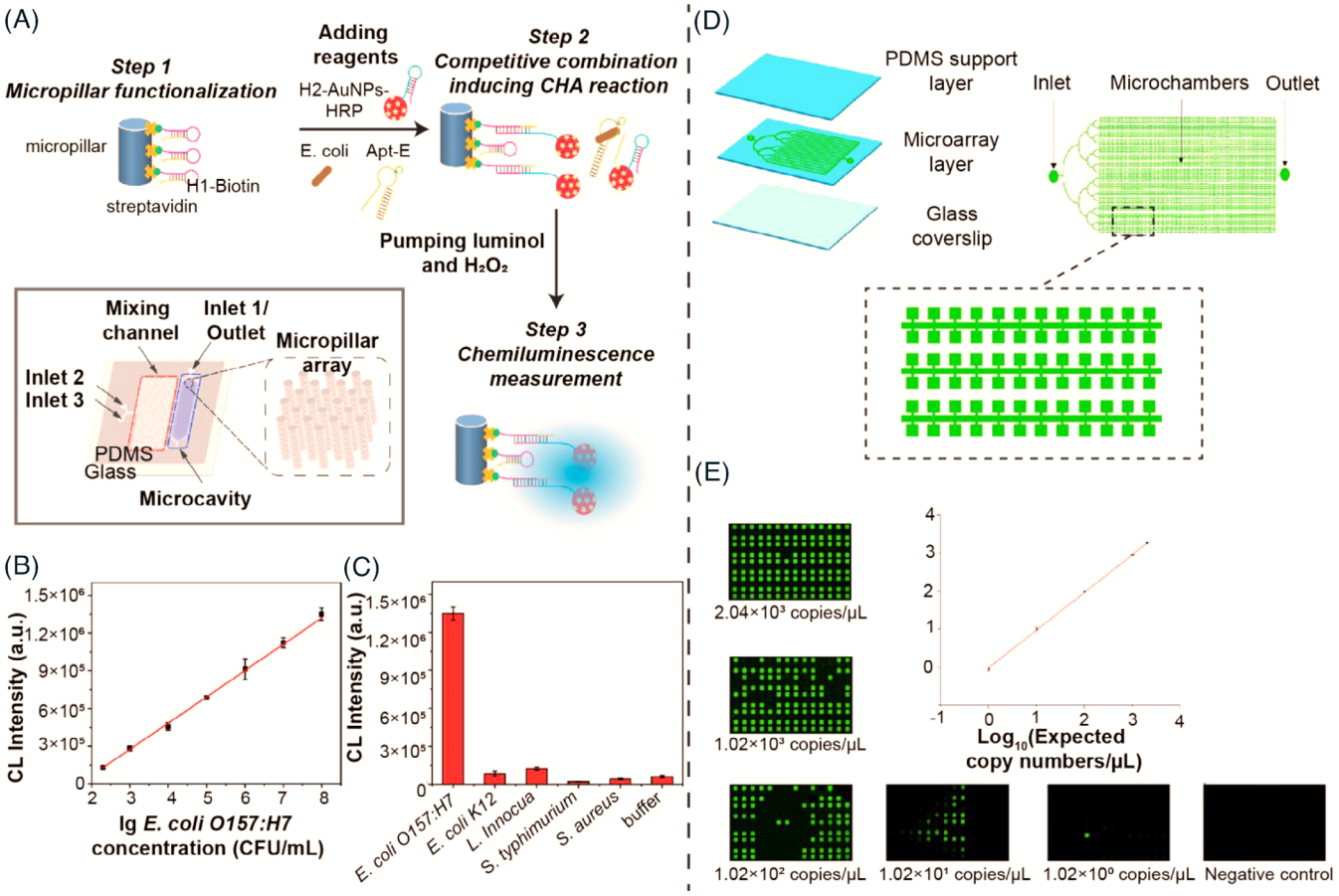


**FIGURE 4** Recent advances in microfluidic-based detection of bacteria and viruses. (A) Schematic illustration of the microfluidic chemiluminescence biosensor based on a multiple signal amplification strategy in a polydimethylsiloxane (PDMS) microfluidic chip. (B) Chemiluminescent spectra of the microfluidic biosensor for different concentrations of *Escherichia coli O157:H7*. Specificity of the microfluidic biosensor for *E. coli* O157:H7 detection with concentrations of all bacteria set to $1 \times 10^8$ CFU/mL. (Reproduced with permission[65] Copyright 2022, Biosensors and Bioelectronics). (D) Schematic illustration of the principle of digital norovirus (NoV) detection with the microfluidic chip (NoV-DID chip). (E) Image of NoV-DID chip with different concentrations of NoV crRNA. And the linear relationship between the measured value (copies/μL) and the expected copy number per reaction. (Reproduced with permission[72] Copyright 2021, Microchemical Journal).

represents the most ubiquitous foodborne pathogen. In another novel study, a PDMS microfluidic chip was adhered to a glass substrate and implanted with a versatile valve for liquid mixing.[66] This chip displayed the detection of *Salmonella* typhimurium as low as 1.0 × 102 copies/μL within 30 min, offering significantly simplified and quicker on-site detection of *Salmonella* compared to PCR-based methods. Furthermore, paper microfluidic devices developed within the past few years have demonstrated the detection of *L. monocytogenes*, *Campylobacter jejuni*, *S. aureus* and *Vibrio parahaemolyticus*.[67–69]

## 3.2 | Viruses

Foodborne viruses, commonly disseminated through water and livestock, present substantial health hazards. The potential for viral contamination during all stages of animal product processing, including slaughtering, processing and storage, underscores the need for comprehensive screening of foodborne viruses.[34] Among these, norovirus (NoV) emerges as the predominant pathogen of concern, causing gastroenteritis with symptoms ranging from diarrhoea to severe cases potentially leading to fatalities.[70] Nucleic acid-based detection and immunoassay methods are the most popular methods for virus detection. However, these standards are often complex, costly, and time-consuming.[71] Given the ubiquity of NoV and additional foodborne viruses such as herpesvirus and rotavirus, accessible screening for foodborne viruses is imperative for effective disease prevention.

Recent advances have highlighted the exceptional ability of microfluidics to provide rapid, portable viral detection. Most commonly, microfluidics provides a platform for isothermal amplification of nucleic acids. A digital isothermal detection chip comprised of three layers of PDMS has been developed for isolating individual nucleotides into nanoliter wells, followed by reverse-transcription recombinase-aided amplification (RT-RAA).[72] Following sequence collection, alignment, and analysis, the researchers designed RAA primers and probes specific to NoV and then confirmed the RAA reaction outside of the chip. The RAA was then performed in the microfluidic device

for quantification, an advantage only uniquely offered by microarrays (Figure 4D). This microfluidic assay achieved a detection limit as low as 1.02 copies/μL in approximately 20 min (Figure 4E). Beyond human viruses, animal viruses are highly important to food systems and can often wreak havoc through livestock, drastically affecting the supply chain. A new microfluidic chip manufactured from photolithography and bound to glass substrates provides on-site PCR detection of multiple swine viruses, including porcine epidemic diarrhoea virus and pseudorabies virus.[73] The chip demonstrated a sensitivity as low as 1 copy/μL within 1 h. Across the spectrum of food safety, the ability to digitize samples into nano and microliter volumes for nucleic acid amplification offered by microfluidics has the potential to drastically improve viral testing.

## 3.3 | Fungi

Fungi are pervasive threats to food safety through sporulation and the production of dangerous mycotoxins. Some of the world's most important food crops are highly susceptible to fungal diseases caused by the dispersion of fungal spores. Spore analysis and the detection of fungal diseases in crops are notoriously difficult and typically rely on PCR or image recognition.[74,75] Rice, one of the most vital crops for feeding the world population, is commonly ailed by airborne fungi spores causing crop diseases. The most common of these include *Magnaporthe grisea* and *Ustilaginoidea virens*. In stark contrast to bacteria, fungi diseases can often be identified by their unique morphological differences. A recent study developed a microfluidic chip to be combined with microscopic hyperspectral detection of rice fungal disease spores.[76] The chip can separate *Magnaporthe grisea* and *Ustilaginoidea virens* spores using a series of separation channels and enrichment areas in a PDMS chip that creates a sparse two-phase flow with a low Reynolds number.

Beyond crop hazards, some fungi produce mycotoxins, which are toxic secondary metabolites that pose severe risks to humans upon ingestion. The current standards for mycotoxin detection rely on chromatographical methods such as HPLC and GC-MS which are unable to be carried out in the absence of skilled technicians and elusive equipment.[77,78] Microfluidics can play a pivotal role in providing more accessible detection of mycotoxins and solving key issues in fungal spore detection. A recent paper-based microfluidic device demonstrated the on-site detection of deoxynivalenol (DON).[79] The nitrocellulose paper μPAD contained a conjugate pad with antibody-labelled AuNPs and utilized capillary action to multiple testing sites with secondary antibodies in a method similar to numerous lateral flow assays (Figure 5A). This method utilizes two signal areas, where the signals in T1 and T2 are negatively correlated, as shown in the images and calibration curves in Figures 5B–-D. The μPAD detected representative mycotoxins with a sensitivity as low as 0.01 ppm in spiked corn, feed, and wheat samples. The entire assay takes under 12 min to run to completion, and costs under $2 per test, providing extremely accessible mycotoxin screening. Additionally, most fungi are capable of producing several mycotoxins at the same time. Therefore, another research group has created a dual-channel microfluidic electrochemical immuno-sensor for the simultaneous detection of two mycotoxins.[80] The electrochemical microfluidic sensor was created using photolithography and contained a PDMS microfluidic channel in conjunction with three electrodes. The sensor simultaneously detected 35 pg/mL DON and 97 pg/mL fumonisin with greater than 90% recovery in spiked corn samples.

## 3.4 | Allergens

Food allergies occur when the immune system elicits an abnormal response to specific dietary foods or components. Predominant allergens include peanuts, tree nuts, milk, eggs, wheat, soy, fish and shellfish.[81] Even a minute amount of these allergens can trigger severe allergic reactions in at-risk individuals. Food allergies cannot presently be cured, leaving allergen avoidance as the only form of resistance for susceptible individuals. Therefore, food must be closely monitored and regularly checked for common allergens to avoid improper labelling or contamination of allergens. The existing standards for food allergen detection rely on immunochemical assays, bulk PCR methods or MS.[82] However, as the percentage of the population with food allergies has risen above 10%, more accessible allergen tests have recently become urgently necessary.[83] Microfluidic technologies have emerged as useful tools to fill the need for rapid, accurate, and readily deployable allergen tests.

Microfluidic immunoassays are common tools for improving the detection of food allergens. For example, a recently developed novel single-piece μPAD lateral flow immunoassay was able to sensitivity detect egg white protein in food samples.[84] The single-unit cellulose device achieved a far simpler design compared to other lateral flow immunoassays with more complex components. The layout of the μPAD is analogous to standard lateral flow devices. It contains a sample pad, conjugate pad for storage of the labelled antibody, nitrocellulose membrane for immobilization of the capture antibodies, absorbent pad for forward liquid flow, and a backing card for physical support. The entire process takes under 15 min from sample collection to signal readout and can be carried out as a free-standing device, in a tube or a well (Figure 5E). This device was able to detect as low as 0.01% egg white spiked in cake mix, highlighting the potential that wax printed μPADs offer for providing simple and reproducible immunoassays for rapid allergen detection (Figure 5F). Other recent microfluidic devices have demonstrated the detection of peanut and wheat allergens in food samples.[85–87]

## 3.5 | Antimicrobial resistance

The scope of food safety spans beyond just actively harmful pathogens. AMR looms as a constantly escalating global threat, characterized by microorganisms evolving to withstand the effects of antimicrobial agents. This phenomenon, accelerated by the overuse of antimicrobial drugs, jeopardizes the future efficacy of antibiotics, rendering once-treatable infections much more challenging.[88] Detection of AMR

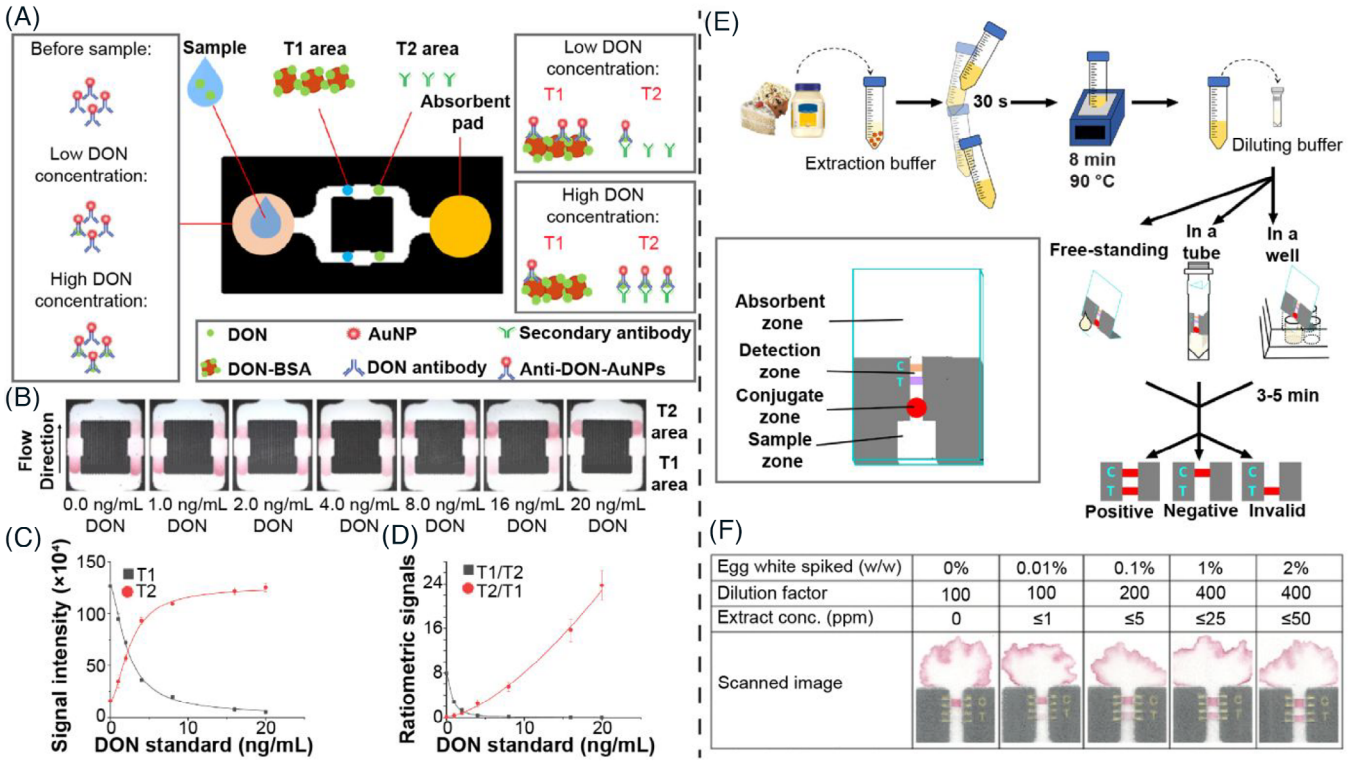


**FIGURE 5** Recent advances in microfluidic-based detection of fungi and allergens. (A) Schematic illustration of the microfluidic paper-based analytical device (μPAD) for the detection of DON (DON-Chip). DON: deoxynivalenol; AuNPs: gold nanoparticles; DON-BSA: DON-conjugated bovine serum albumin; anti-DON-AuNPs: anti-DON antibody conjugated AuNPs. (B) Representative images of T1 and T2 areas in the DON-Chips using different concentrations of DON standard, demonstrating the colourimetric change. (C) Calibration curve using T1 and T2 signals of the DON-chip. (D) Calibration curves using the ratios of T1/T2 and T2/TR1 in the DON-Chip. (Reproduced with permission,[79] Copyright 2019, American Chemical Society). (E) Schematic illustration of the μPAD for on-site food allergen detection including food sample preparation steps and the testing of the extract with three options. (F) Detection of egg white (0%–2%) spiked in a commercial cake mix product. (Reproduced with permission,[84] Copyright 2020, American Chemical Society).

bacteria and AR genes (ARGs) relies on conventional techniques such as bacterial cultivation or molecular methods such as PCR.[89] However, due to the expansive nature of AMR in our environments, sensors designed for AR bacteria and ARG screening should be accessible, portable, and reproducible. Microfluidic technologies offer sensitive and innovative solutions that fill this requirement. For example, microfluidic technologies have demonstrated sensitive detection of cloxacillin, a *β*-lactam antibiotic, in poultry.[90] The microfluidic immunoassay consisted of two layers of microchannels and timed loading steps with an HRP-labeled secondary antibody for a CL readout. The chip provided a sensitive limit of detection of around 96.5 ng/mL in under 2 h.

In addition, antimicrobial susceptibility tests (ASTs) play a pivotal role in gauging the effectiveness of antimicrobial agents against specific pathogens, aiding clinicians in tailoring treatment regimens. Current AST methodologies, however, often entail time-consuming processes, hindering timely intervention. Therefore, microfluidics can provide streamlined and high-throughput ASTs. For example, a recent innovative PDMS microfluidic chip was designed with an antibiotic concentration gradient for determining the antibiotic resistance of *Salmonella* to ofloxacin and ampicillin.[91] The chip utilized a gradient generator and culturing chamber to provide sensitive detection of *Salmonella* at low pH to mimic acidic food conditions in 5 h.

## 3.6 | Heavy metals

Heavy metals are pervasive and troubling contaminants commonly found in both food and water, posing significant threat to human health. Metals such as lead, mercury, cadmium, and arsenic find their way into agricultural systems and water supply through natural sources, industrial processes, and pollution. Once consumed, these metals accumulate in the body, leading to a spectrum of adverse health effects. Lead ($Pb^{2+}$), for instance, is associated with neurological impairments, while mercury ($Hg^{2+}$) exposure is linked to developmental issues and damage to the nervous system.[92] Conventional methods for detecting heavy metals often involve complex laboratory analyses, such as atomic absorption spectroscopy or capillary electrophoresis.[93] However, this presents an obvious challenge in terms of time and accessibility. Microfluidics offers more rapid and cost-effective detection platforms by providing low-volume mixing and simplified signal transduction for the indication of metal ions. A novel microfluidic-based device

developed within the past year combines passive microfluidic mixing with an array of gold-interdigitated electrodes.[94] The sensor utilized immobilized DNAzymes between platinum nanoparticles for selective detection of $Pb^{2+}$ ions with a linear range of 10 nM–1 μM with no cross-reactivity from other metal ions.

### 3.7 | Commercialization in food applications

The commercialization of microfluidic devices is still in its nascent stages, with the current market value estimated at approximately $30 billion. However, the compound annual growth rate for this market is expected to be 12.9%, propelling the market value of microfluidic devices to surpass $100 billion by 2032.[95] This projection encompasses both biomedical and agricultural applications. While current commercial efforts predominantly focus on clinical diagnostics and medicine, major industry players are also beginning to commercialize pivotal products tailored for agricultural applications, including the detection of foodborne contaminants and the authentication of honey purity.[96] Furthermore, numerous start-up ventures originating from academic research laboratories are emerging to address various market demands within the agricultural sector, leveraging technologies such as μPADs and PDMS microfluidic chips. These market demands within agriculture span various detections of foodborne pathogens, such as livestock viruses, crop pathogens, AMR and more related challenges.[97]

Numerous patents have been filed for a diverse array of microfluidic and lab-on-a-chip devices, numbering in the hundreds of thousands. Recent patent analyses have identified key players in passive system microfluidic patents for commercialization including prominent companies such as Fluidigm, Theranos, Semiconductor Energy Laboratory and Abbott Point of Care. Remarkably, the bulk of patents for these systems have been filed during the 21st century, indicating a discernible upward trajectory in patent filings for microfluidic devices.[98] Notably, the United States Department of Agriculture and Food and Drug Administration (FDA) advocate for the development and commercialization of microfluidic devices. The FDA's Center for Devices and Radiological Health has established a dedicated Microfluidics Program aimed at fostering the advancement of microfluidic technology and facilitating the translation of research innovations into commercially viable products.[99] Unfortunately, there is a lack of specific FDA standards tailored for microfluidics, necessitating manufacturers to either adapt existing standards or devise novel methodologies to demonstrate performance and secure patentability. As commercialization continues to grow, governmental organizations should develop more standards and quality assurance for innovators seeking to develop marketable microfluidic products.[100]

## 4 | SUMMARY AND OUTLOOK

Microfluidic technology has emerged as a transformative force in the realm of food safety, offering unparalleled precision and efficiency in the detection of various contaminants. The controlled manipulation of minute fluid volumes within micro and nano-scale devices enables the integration of diverse analytical processes on a single, miniaturized platform. This technology excels in biosensing applications by facilitating rapid and highly sensitive analyses with reduced sample volumes and improved reaction kinetics. Microfluidic devices consisting of a various selection of materials now offer adaptable and wide-ranging utility in food safety applications.

The key advantages of microfluidics are evident in portability, user-friendliness and the ability to seamlessly integrate sample preparation, nucleic acid amplification, and readout processes. The diversity of material composition offers distinct benefits. For example, elastomers such as PDMS provide flexible and complex design, as well as ideal air permeability. Thermoplastics, such as PMMA, offer cost-effective structures that provide durability and full transparency. Lastly, paper-based microfluidic devices provide the utmost affordability and ease of manufacturing while offering a high level of biocompatibility.

Despite the current advantages, microfluidic technologies face many challenges before they can be widely commercially adapted and implemented to reach their full potential. For some devices, such as PDMS, reproducibility for mass manufacturing is a concern. Meanwhile, reproducibility and risk of cross-contamination of results is a key issue in paper-based microfluidic devices. Additionally, while microfluidic devices provide extremely convenient tools for facilitating biosensing reactions, lack of sensitivity and over-complicated designs still hinder the implementation of numerous novel microfluidic devices. However, microfluidic technology has shown continuous growth and improvement over the past decades.

Looking ahead, the future of microfluidics holds great promise for assuring food safety. Continued innovation in materials, manufacturing and integration with state-of-the-art sensing elements will contribute to enhancing simplicity and sensitivity issues. The ability to digitize or mix samples at the nano or micro-level offers significant potential for improving detection across various food contaminants, including bacteria, viruses, fungi, toxins, allergens and heavy metals. As research and understanding of microfluidic technology continue to grow, it is poised to play a pivotal role in addressing the evolving challenges of evaluating food contamination.

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### CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

### DATA AVAILABILITY STATEMENT

Data sharing does not apply to this article, no new data was created.

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