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REVIEW ARTICLE

Advances in aptamer-based biosensors for monitoring foodborne pathogens

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Abstract Biosensors are analytical devices for detecting a wide range of targets, including cells, proteins, DNA, enzymes, and chemical and biological compounds. They mostly rely on using bioprobes with a high binding affinity to the target for specific detection. However, low specificity and effectiveness of the conventional biosensors has led to the search for novel materials, that can specifically detect biomolecules. Aptamers are a group of single-stranded DNA or RNA oligonucleotides, that can bind to their targets with high specificity and serve as effective bioprobes for developing aptamer-based biosensors. Aptamers have a shorter production time, high stability, compared to traditional bioprobes, and possess ability to develop them for specific target molecules for tailored applications. Thus, various aptasensing approaches, including electrochemical, optical, surface plasmon resonance and chip-dependent approaches, have been investigated in recent times for various biological targets, including foodborne pathogens. Hence, this article is an overview of various conventional foodborne pathogen detection methods, their limitations and the ability of aptamer-based biosensors to overcome those limitations and replace them. In addition, the current status and advances in aptamer-based biosensors for the detection of foodborne pathogens to ensure food safety were also discussed.

Keywords Aptamer · Food Safety · Foodborne pathogens · Aptasensor · Biosensor

Introduction

Food is an integral part of human existence, as it is the fuel that energizes the body by supplying nutrients, vitamins, and minerals (Sarojnalini and Hei 2019). Consequently, food safety is of prime importance and has health and general well-being implications (Kwol et al. 2020). A reduction in food quality has been a major challenge in recent years and has been the cause of food waste and foodborne disease outbreaks and deaths (Astill et al. 2019). It was estimated by the World Health Organization (WHO) that about 600 million foodborne disease cases are recorded each year, leading to the loss of about 420,000 lives globally. An estimated 30% of this number are children below the age of 5 years (World Health 2015). Thus, good food hygiene practices and quality assurance should be implemented followed by food testing for the presence of these pathogens and to eliminate them (Huang et al. 2020). It can be noted that in the U.S. alone, about 48 million cases of foodborne diseases yearly, with hospitalization of about 128,000 people and the death of 3000 people, according to the Food and Drugs Administration (FDA) in 2020. These foodborne diseases are caused by consuming food contaminated by pathogens, chemicals, or toxins (Jaklevic 2020). In general, foodborne pathogens are

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bacteria, parasites, or viruses, where presence in food causes foodborne illness (Bintsis 2018). Among the pathogens, bacteria are the most common causative agent for foodborne diseases. Some examples of pathogenic bacteria include *Staphylococcus aureus*, *Escherichia coli*, *Listeria monocytogenes*, *Clostridium botulinum*, *Campylobacter jejuni*, *Salmonella* spp., *Shigella* spp., *Vibrio* spp., and *Yersinia enterocolitica* (Gourama 2020a; Pandhi et al. 2023). Other prominent foodborne parasites are *hepatitis* A, *norovirus*, *Toxoplasma gondii*, *Trichinella spiralis* and *Cyclospora cayetanensis* (Bintsis 2018). In addition to these microbes, environmental factors also increases the chance of contamination and microbial growth in food, if not controlled (Sheng and Wang 2021). Thus, food must be tested for the presence of these pathogens to eliminate them.

The traditional methods available for detecting these foodborne pathogens can be grouped into two, such as culture-based and independent of culture. The culture-based method is the most conventional approach for microbial food analysis and is also the "gold standard" (Foddai and Grant 2020). It is a preferred method because it is cheap, easy to perform, and can be used for various pathogens. This method involves preparing microbial culture by growing the pathogen on a suitable medium (e.g. agar plates) and observing certain physical and biochemical characteristics. The success of this process depends on the culturability or multiplication potential of the pathogen. Growth of the pathogen can take up to several days, making the method particularly slow. There is also the possibility of detecting false results, especially at a low pathogen level in the sample, because the food sample may have some indigenous bacteria that can interfere with the detection process (Foddai and Grant 2020; Law et al. 2015; Velusamy et al. 2010).

Culture-independent methods include immunology-based methods and polymerase chain reaction (PCR). Immunology-based detection methods take advantage of the antibody-antigen binding behaviour to detect the presence of pathogens in a sample. The most common immunology-based detection method is enzyme-linked immunosorbent assay (ELISA), and it has been used over the years to detect pathogens such as *Vibrio parahaemolyticus* (Kumar et al. 2011), *Clostridium perfringens*, *E. coli*, *Botulinum*, and *Staphylococcus* species (Aschfalk and Müller 2002; Zhao et al. 2014). Variations of this method have been developed for commercial use with better detection rates and full or partial automation (Glynn et al. 2006; Gómez-Govea et al. 2012; Meyer et al. 2011). However, the production of antibodies, the requirement of animal hosts, and the long reaction time (several weeks) cause process delays and are the major limitations of this method.

PCR can rapidly detect pathogens in food with high specificity and accuracy by amplifying the target pathogen instead of the signal. This ability reduces false positives, compared to culture-based methods in pathogen detection, and can detect a wide variety of pathogenic strains (Velusamy et al. 2010). However, PCR is expensive, requires skilled personnel, and cannot detect pathogen viability (Foddai and Grant 2020). Hence, researchers are in a quest to develop an efficient, rapid, portable, cheaper, simple, sensitive, and selective method for detecting food pathogenic microbes due to the numerous disadvantages of traditional detection methods (Law et al. 2015). Recently, biosensors have gained significant research focus for detecting foodborne pathogens.

Biosensors are analytical devices used as biological materials for recognising biological compounds (Liu et al. 2023). However, biosensors based on antibody bioaffinity approaches can have certain limitations, such as lack of stability, low selectivity, and sensitivity. Aptamers, which are a group of short-stranded DNA or RNA oligonucleotides, can bind to their targets with great sensitivity and specificity, and are often used as biosensors to overcome the specificity and selectivity limitations (Suliman Maashi 2023). Some of the advantages of aptamer-based biosensors include shorter production time, non-requirement of animal hosts, high stability, and the ability to develop to bind and detect specific targets (Long et al. 2022). Biosensors generally have two major parts, namely bioreceptors and transducers. The bioreceptor is the moiety that receives and interacts directly with the target (e.g., aptamer and antiobody bioreceptors). The transducer is the part of the biosensor that transforms biological recognition into a signal that can be measured and interpreted. The mechanism of transduction eventually determines the type of biosensing technique. Electrochemical, optical, surface plasmon resonance, and chip-based detection of biological targets (Geng and Bhunia 2006; Law et al. 2015; Zhang et al. 2019) are some examples of biosensing methods. This article discusses various aptamer-based biosensors for detecting foodborne pathogens. The molecular methods, considerations for selecting aptamers to detect foodborne pathogens, and their prospects are also discussed.

Global overview of foodborne pathogens and food safety

Food is a primary requirement for assuring health in humans and animals (Sousa 2008) but is also a common potent vehicle for transmitting illnesses. Although the challenges of food safety in developed countries differ substantially from those faced by developing countries, issues such as climate change, coupled with population growth and changing demographics, urbanization, migration, and increasing international travel, are all major contributing factors to changes in the global food system, and this change has implication in food security and safety (Sousa 2008; Velusamy et al.

2010). For instance, ready-to-eat foods are sold on the streets in most developing countries, while in technologically advanced countries, discussions on foodborne contamination may gain attention towards the processing and packaging of food (Sousa 2008).

Foodborne diseases may arise from physical hazards, such as the erosion of metals from cans, glass, or plastics. Other factors, such as food allergens, antibiotic resistance, mycotoxins and their derivatives, endocrine-active contaminants, and foodborne pathogens, threaten food safety (Flynn et al. 2019; Sousa 2008). Particularly, the emergence of new and re-emergence of old foodborne pathogens are changing the epidemiology of foodborne diseases (Flynn et al. 2019) and greatly affecting global food safety. The ability of food pathogens to evolve via gene transfer, coupled with the possibility of acquiring foreign DNA, has led to new phenotypes and genotypes (de Blackburn and McClure 2009). Additionally, the adaptation of microbes to the environment has also led to resistant strains of certain foodborne pathogens, as in the case of *Salmonella typhimurium* DT 104 (Holman et al. 2019).

According to the World Health Organization, about 600 million people globally fall ill from consuming contaminated food, with an associated death of 420000 every year (Mahmoud 2019). An estimated 23 million cases of foodborne illness and about 5000 associated deaths are recorded annually in Europe despite continuous investment (Lee and Yoon 2021). Although studies suggest that most cases are mild, chronic sequelae lead to billions of dollars in medical costs and lost productivity (Mulugeta 2010). This undoubtedly creates an enormous economic burden on any country and its citizens. For instance, an estimated $152 billion is spent each year on foodborne diseases in the United States (Mulugeta 2010). The number of cases is expected to be higher in most developing regions, such as Africa and some parts of South America, where a combination of factors such as lack of technical and financial resources and a general lack of public awareness about food safety among the population exist (Desta 2020; Pires et al. 2021). In cases where the source of food contamination can be traced to an eatery or food company, the establishment may suffer drastic economic losses and closure due to damage to its reputation (Hussain and Dawson 2013). Foodborne pathogens (mostly microbes, including bacteria, fungi, viruses, and parasites) cause illnesses by secreting toxins into the intestinal tract of the person after ingestion of contaminated food or byreleaasing toxins into the food before ingestion (Abdul-Mutalib et al. 2015; Bintsis 2017).

Studies have shown that over 30 foodborne pathogens can lead to major human illness (Adley and Ryan 2016). Most foodborne illnesses and their outbreaks have been attributed to bacteria, of which *Campylobacter spp.*, *Salmonella spp.*, *Escherichia coli*, *Listeria monocytogenes, Vibrio cholera*, and *Staphylococcus aureus* have been identified as the most common causative agents (Abdul-Mutalib et al. 2015; Adley and Ryan 2016; Velusamy et al. 2010). Most pathogenic food bacteria survive in moderate environmental conditions, even though some are capable of surviving in extreme conditions (Bintsis 2017). Further, most foods that acts as carriers for these pathogens are of animal origin, including egg and egg products, broiler meat and cheese, fish and fish products, milk and dairy products, and crustaceans (Bintsis 2017; Coral-Almeida et al. 2015). Recent studies have shown that foodborne bacteria can be transmitted at different stages of food preparation. At the farm, contamination can arise from animals already infected with a pathogenic microorganism or when animal-based food products, such as milk or meat, are contaminated (Heredia and García 2018). Moreover, transporting food products farther from the origin also increases the risk of food contamination (Stein and Chirilã 2017).

Generally, a microbe must be able to survive in the food for a foodborne pathogen to cause disease. The pathogen must also identify niches, multiply, and express virulence factors to cause host cell damage after entering human or animal hosts (Bhunia 2018). Therefore, the incidence of foodborne illnesses depends on interactions among the pathogen, host, food, and environment (Gourama 2020a). It is noteworthy that several groups, including elders, pregnant women, infants, patients with immune system diseases, and people under medication, such as proton pump inhibitors, and the malnourished are vulnerable to foodborne illnesses (Lund and O'Brien 2011). Typical symptoms of foodborne diseases include abdominal pain, diarrhoea, vomiting, nausea, fever, respiratory difficulties, and, in severe cases, death (Gourama 2020a). Further, foodborne diseases can potentially lead to chronic, life-threatening, and or neurological, gynaecological, or immunological disorders, as well as multi-organ failure, some cancers, and death (Grace 2015).

Several approaches, such as enhanced agricultural practices, manufacturing practices, and hazard analysis and critical control points (HACCP), are available to reduce toxigenic microbes in food to make food safe for consumption (Velusamy et al. 2010). However, detection and enumeration of these foodborne pathogens are vital steps to further strategies to contain them (Saravanan et al. 2021). Thus, novel approaches are required for the detection of foodborne pathogens with high selectivity and specificity.

Conventional and molecular methods for foodborne pathogen detection

Methods for detecting pathogens are in high demand in the food industry (Priyanka et al. 2016). These methods can

be classified into conventional and molecular methods, as shown in Fig. 1.

Culture-based methods

Conventional methods can be subclassified into traditional culture methods and isolation of single-species colonies for detecting and identifying foodborne microbes, especially bacteria and further characterization, as shown in Fig. 1. The identification is based on the morphological, physiological, and genetic (phenotype and genotype) characteristics of the microbe. Three main detection approaches, namely, (a) morphological observation, (b) gram staining, and (c) biochemical assays, are used in culture-based methods.

Conventional culturing methods are still considered the gold standard for pathogen detection due to their reliability, sensitivity, efficiency, and range of application. Traditional culture relies on the organism's capacity to metabolise substrates in growth media and form visible colonies following growth and multiplication (Foddai and Grant 2020). These techniques are still the primary option for various food testing laboratories as they are sensitive, affordable, and simple. They provide qualitative or quantitative information on the quantity and type of live microorganisms present in food samples (Doyle et al. 2020). However, traditional approaches are tedious and time-consuming to detect foodborne pathogens (Zhao et al. 2014). Furthermore, aseptic practices must be strictly followed to avoid contamination. In addition, the non-uniform distribution of pathogens in the food, especially if they are present at very low titres, food matrix effects and complexities, and the existence of indigenous microorganisms that interfere with the results from culture-based approaches (Mandal et al. 2011). Therefore, culture-independent methods, such as molecular approaches, have been a recent alternative for detecting viable foodborne pathogens.

Molecular methods

Molecular methods depend on nucleotide hybridization techniques such as amplification (PCR, qPCR, and rt-PCR), DNA microarrays, and whole-genome sequencing (WGS) approaches, which utilizes genomic markers specific to nucleic acid sequences.

Amplification methods

The basic principle of PCR is the gene amplification of various pathogens, where specific and targeted primers are developed per gene. Since its discovery in 1985 (Priyanka et al. 2016), numerous variations of PCR have evolved, each with its nomenclature based on the original PCR's modified

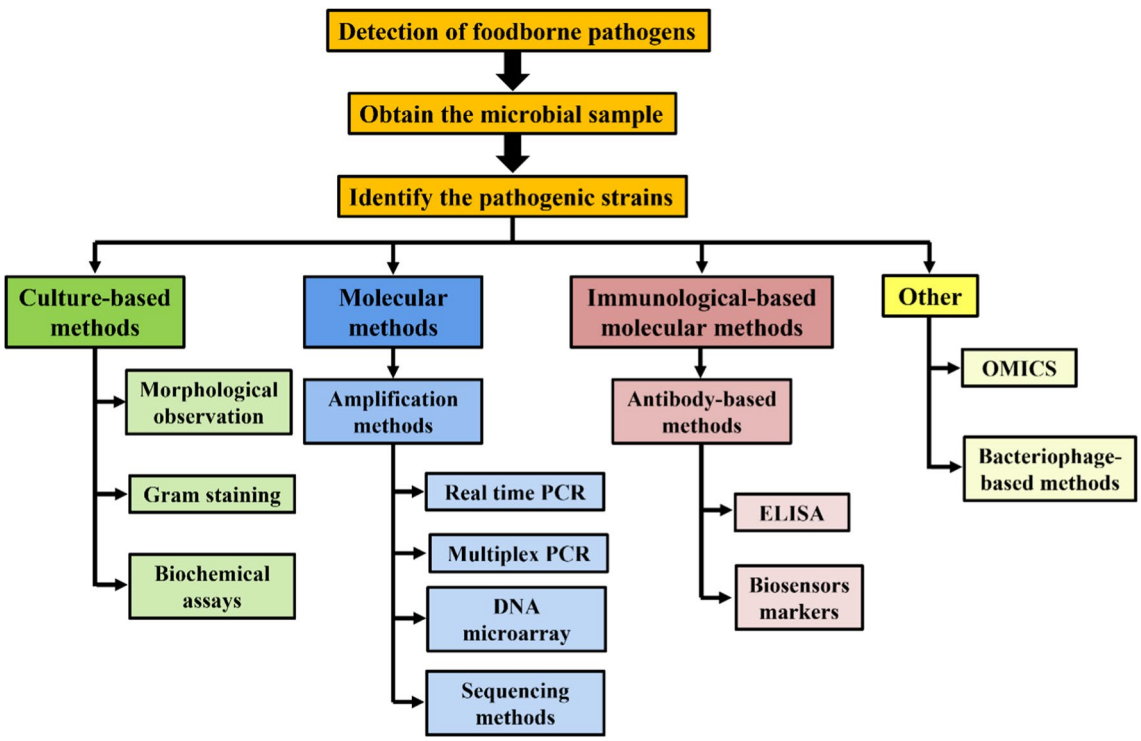

Fig. 1 Schematic representation of the methods for the detection of pathogens. *ELISA* Enzyme-linked immune-sorbent assay, *PCR* Polymerase chain reaction, *RT* Real-time

technique. The technique is rapid and sensitive, which is one of the main advantages of PCR compared to culture-based and immunoassay-based approaches. The amplified product can be obtained in ~ 30 min, and discrimination between strains has become easier due to the employment of several primer pairs. The detection limit for DNA amplicons is in the femtograms (10^{-15} g) range, but this can be improved (Holmqvist et al. 2009). This technique is a more time-saving and less labour-intensive, compared to culture-based methods (Radhika et al. 2014). Real-time and multiplex are the two sub-classes of PCR, that are widely used for foodborne pathogen dection. Real-time PCR enables target quantification and, when used with a rapid cycling platform, can give data after 30 min of the initiation of heat cycles (Zhou et al. 2022). Hence, real-time qPCR is the preferred technology for identifying and quantifying microbes, as they are rapid, highly sensitive, precise, and capable of simultaneously detecting several microbes, especially bacteria and virus, (Postollec et al. 2011). The major advantage of real-time PCR is its ability to provide quantitative data, high sensitivity for the detection of bacteria, and is cheaper, compared to culture-based methods (Priyanka et al. 2016). Similarly, multiplex or multiple primer PCR is a technique that uses at least two primers to amplify various nucleic acid fragments (Boukharouba et al. 2022). Multiplex PCR is superior to the aforementioned PCR-based approaches as it enables the simultaneous identification of several bacteria species by using distinct primers to amplify DNA coding sections for targeting particular genes of each bacterial strain (Touron et al. 2005). In recent years, multiplex PCR methods have gained potential significance, especially in reducing genotyping costs and improving throughput (Chen et al. 2021). This method is also rapid, compared to other PCR methods, which is highly beneficial for the simultaneous detection of most foodborne pathogens such as *Escherichia coli* O157:H7, *Salmonella*, *Staphylococcus aureus*, *Listeria monocytogenes*, and *Vibrio parahaemolyticus* (Kim et al. 2007; Tao et al. 2020).

DNA microarray

DNA microarray is gaining attention among researchers for pathogenic microbial detection due to its speed, accuracy, specificity, and ability to do high-throughput analysis (Nehra et al. 2022). Numerous investigations identified that waterborne infections and pathogens in marine fish possess a significant concern indirectly due to fish consumption (Zeng et al. 2018). This DNA microarray approach was used to construct a nationwide genetic subtyping network for foodborne illness surveillance named Pulse Net, which is beneficial in the identification of each pathogen outbreak (Chao et al. 2007). Pulse Net was useful at laboratories run by municipal, state, and federal health and regulatory agencies in the United States. This surveillance system primarily aids in reducing product recalls, restaurant closures, and other associated procedures while still being useful for detecting a foodborne epidemic outbreak (Chao et al. 2007). However, suboptimal design or probe selection and certain incorrect probe annotations and preparations are the limitations of DNA microarray (Berhanu and Dula 2020).

Sequencing methods

Whole Genome Sequence (WGS) can provide detailed information on bacterial species. This technique eases the identification of pathogens, antibiotic resistance gene, and the detection of bacterial epidemics (Bharadwaj et al. 2019; Hurley et al. 2019). WGS is advantageous due to its non-requirement precise targets; compared to PCR, therefore, there is no need to build new primers depending on the evolution of bacteria. Next-generation sequencing (NGS) is better than WGS as they can sequence millions of fragments concurrently in each run. Currently, numerous reactions can be carried out on a microscale, and simultaneously on a single chip (Ronholm 2018). Further, metagenomics is a useful tool for detecting, analysing and characterising a wide range of pathogens in a single experiment without needing to culture the organisms first (Miller and Chiu 2022). On the other hand, specialised expertise is required for sample handling, sequencing of genome, and bioinformatics data analysis in other not to arrive at false positives (Ferone et al. 2020). Even though these approaches are quite informative, the amount of bioinformatic effort necessary to examine the data acquired from these methods, as well as the general shortage of employees with expertise in this field, are their primary limitations (Billington et al. 2022; Jagadeesan et al. 2019; Voelkerding et al. 2009).

Molecular immunoassays

Antibodies are a distinct natural family of immune system-related glycoproteins known as immunoglobulins created by differentiated B cells in response to an immunogen during an immunological response. The precise contacts and exceptionally high equilibrium association constants (1010/M and larger) were identified to be achieved by antibody and its associated antigen. Further, antibodies are highly sensitive and selective and this makes them useful in immunoassays (Farka et al. 2017). The incorporation of antibodies into biosensors provides a novel analytical technique with a wide area of application, including pathogen identification in food. The major limitation of antibody-based method is the requirement of purified antibodies for the detection of pathogens as a negligible level of impurity can lead to errors in the results (Celik Uzuner 2020).

Enzyme-linked immunosorbent assay (ELISA) is one of the most widely used molecular immunoassay methods as an alternative to antibody-based approach (Santiago-Felipe et al. 2014). Engvall and Perlmann (1972) initially described ELISA in 1972, and it is currently a widely used method for bacterial immunological identification (McMeekin 2003). ELISA technique can detect cell-surface displayed antigens, or toxins produced by a food pathogen (Ferone et al. 2020). In this method, the type of antibody utilized will determine the sensitivity and detection limits for the bacterial pathogens (Byrne et al. 2009). ELISA systems are rapid, easy to use, and are used to gather qualitative and quantitative food safety data. However, antibodies for ELISA are not always commercially available for all microbes of interest, which necessitates their ad hoc production. Further, ELISA technique have successfully screened for pathogens in poultry production materials such as feed, excrement, litter, water, and carcass washings (Ferone et al. 2020). On the other hand, ELISA method are susceptible to contamination by pollutants present in food. This drawback makes them unsuitable for online and real-time detection of microbial contamination in a non-destructive or non-invasive method.

Biosensor markers

Biosensors are among the most recent detection technologies, with certain higher detection limits, thereby reducing or eliminating the limitations of conventional PCR techniques (Zeng et al. 2018). Biosensors are pathogen detection devices that typically have three components, such as a biological capture molecule (i.e. probes and antibodies), a technique for turning the capture molecule, such as target interactions into a signal, and output data (Gould et al. 2013). Further, biosensors can detect pathogens with high specificity, high sensitivity, and low detection limits. However, this approach requires costly devices and suitable computer software, making the technique cost-prohibitive (Zeng et al. 2018).

Nanobiotechnology-based approaches are the most recent technique to enhance biosensor ability for pathogen detection. In this case, aptamers are gaining significant attention as a building block in the design of sensors for detecting a wide range of biomolecules, including proteins, DNA, and small molecules. For instance, a nucleic acid aptamer and polydiacetylene-based detection system picked up 98.5% of *E. coli* O157:H7, compared to the usual culture-based method (Zeng et al. 2018). The high affinity and specificity of aptamers make them suitable for coupling various nanoparticles to enhance their efficiency (Zhang et al. 2015). Recently, gold nanoparticles were employed in colourimetric methods due to their electrical, photonic, and catalytic properties to be utilized in unique applications. These nanobiotechnology-based biosensors are non-toxic and may easily bind to antibodies due to their exclusive characteristics (Zhang et al. 2015). Furthermore, these biosensors can be included along with other methods, such as omics approaches.

Other methods

Foodomics was initially coined in 2009 as a field that uses modern omics techniques to study food and nutrition domains to increase customer well-being, health, and confidence (Cifuentes 2009). Cajka et al. (2014) suggested that foodomics methodologies can be useful in solving certain limitations of modern food safety and quality assessment requirements, such as the detection of food contaminants, food origin and traceability, and food fingerprints and biomarker discovery (Cajka et al. 2014). For instance, researchers can utilize various omic techniques (genomic, transcriptomic, and metabolomics) to investigate the impacts of food ingredient-derived molecules on body system components and the overall impact on human health. Food-omic techniques are also useful in addressing the challenges of microbiological food safety. Metagenomics methods were also identified to be useful for detecting food pathogens in foods and the microbial ecology during fermented food preparation. Moreover, omics technologies can be used to investigate the physiological condition of pathogens present in foods and their microbial response to physical, chemical, and biological food preservation methods. However, this method must be included with other methods to efficiently utilize omics approach for the detection of food contamination by microbes (Ferone et al. 2020). Similarly, phage-based therapies are beneficial in foodborne pathogen detection due to their extreme specificity and inherent affinity of bacteriophages to host cells. The knowledge that bacteriophages can only survive and reproduce when in living cell hosts means that phage-based approaches can be used to determine the viability of microorganisms (Richter et al. 2018). Schmelcher and Loessner (2014) examined the use of bacteriophages in identifying foodborne pathogens (Schmelcher and Loessner 2014). A combination of lytic plaque phase assay with an end-point detection approach (e.g. immunological or molecular tests) was used to identify progeny phages or phage DNA, which eventually allows rapid phage-based detection (Foddai and Grant 2020). Among all the methods, qPCR and biosensors are identified as one of the most potential approaches for foodborne pathogen detection. Their application, when used in conjunction with several phage-based lytic approaches has led to the effective detection of pathogens from various matrices, such as food (Anany et al. 2018) and clinical samples (Sergueev et al. 2010). Biosensors are highly beneficial in the detection of foodborne pathogens rapidly, compared to qPCR. However, the sensitivity of these biosensors are lower than qPCR and

this can be improved by the incorporation of aptamers as bioprobes (Nassarawa et al. 2022), which is discussed in the consecutive sections.

Selection of aptamers against foodborne pathogens

Aptamers are considered as a new-age bioreceptor for biosensing and monitoring pathogens, are short-stranded DNA or RNA oligonucleotides that bind to their targets with excellent sensitivity and specificity. They are developed through a structured, iterative method established in 1990 called the systematic evolution of ligands by exponential enrichment (SELEX) (Ellington and Szostak 1990; Tuerk and Gold 1990). This process is based on the ability of the oligonucleotides to bind with the target. It has been used successfully in the selection of countless aptamers against various targets, ranging from small molecules, such as mycotoxins, bacteria, viruses, cocaine and organic dyes, to proteins, including tumour markers, thrombin and growth factors, in addition to even complex targets, including whole mammalian cells (Kolm et al. 2020). SELEX involves a series of iterative cycles consisting of three general stages, including (1) In vitro incubation of a DNA or RNA library with the target. In this stage, a massive library (up to 1015 sequences) of various nucleic acid molecules, called Initial oligonucleotide pool (IOP) is incubated with the pathogen for the selection of aptamer. This library is a chemically synthesized oligonucleotide group made up of two constant regions at 3' and 5' ends in between random region. (2) The bound sequences are separated from the unbound sequences, where the unbound aptamers are eliminated from the library through different buffer washing steps. (3) The bound sequences are eluted through application of heat or washing with a buffer solution. Later, they can undergo PCR amplification and become the new starting library. This process is repeated until a sequence with desirable binding characteristics is obtained, usually between 5 and 20 rounds, which were later cloned and sequenced (Fang et al. 2014; Hamula et al. 2006; Teng et al. 2016; Xu et al. 2021).

During the SELEX approach, the most significant and time-consuming steps are binding and separating bound from unbound sequences. These steps can significantly reduce the entire SELEX time if performed in real-time. Hence, various techniques, such as affinity chromatography columns, magnetic beads, and microfluidic chips, have been introduced in the SELEX approach for the rapid binding and separation of sequences. Among these methods, magnetic beads have gained attention due to their ability to ease the chemical-based modification of sequences with a rapid and effective separation mechanism (Duan et al. 2016b; Hünniger et al. 2014; Ma et al. 2018). Different modified SELEX methods can be combined in certain cases to achieve better results. Hong et al. (2019) combined magnetic bead-based SELEX with a microfluidic system to select Ebola virus aptamers, which led to selecting an aptamer with a high affinity in three cycles (Hong et al. 2019).

SELEX has been used to select aptamers against both live bacteria and molecules from the surface of bacteria (Hamula et al. 2008; Shamah et al. 2008). The SELEX procedure uses purified bacterial targets to develop aptamers against live bacterial cells attached to a solid surface, such as a column, which ensures that the target molecule is immobilized. The bound sequence is separated from the unbound aptamers with ease via centrifugation. This solid surface is not an accurate representation of the target's indigenous surroundings, which may lead to an alteration in its configuration (Hamula et al. 2008).

A SELEX methodology that utilizes capillary electrophoresis (CE) separation is an upgraded version of the conventional methods used to select aptamers against bacterial cells. In this method, the bacteria and the initial oligonucleotide pool are incubated in solution, as shown in Fig. 2, eliminating the step of immobilizing the bacteria on a solid surface. Capillary electrophoresis is used to separate the bound sequences from the unbound aptamers. This protocol requires purified bacteria cells for every cycle of incubation. The purification process may alter the configuration of the cell from its indigenous form, and this technique may not work for unknown targets, such as the molecules present on a cell's surface (Hamula et al. 2008; Pestourie et al. 2006; Wang et al. 2003).

Live cells in suspension are used as targets for the oligonucleotides to select aptamers against live bacterial cells without purifying the bacterial target before incubation. This approach also can be used to separate the bound cells using simple centrifugation, and the technique has been reported for different bacterial cells, including *Lactobacillus acidophilus* (Hamula et al. 2008), *Campylobacter jejuni* (Dwivedi et al. 2010) and *Staphylococcus aureus* (Cao et al. 2009). Lorenz et al. (2006) developed a SELEX method called Genomic SELEX, where a genomic DNA library is utilized, unlike the chemically synthesized library used in the conventional SELEX. In this method, the IOP is obtained by adding specific primers to genomic DNA isolated from the target organism. A Klenow-fragment extension is performed on the new strand later, followed by the transcription of the IOP into RNA and the process of selection. A counter selection step is performed against immobilization matrix to initiate the process and the incubation of the target with the IOP. The oligonucleotides that are bound to the target undergo reverse transcription to become cDNA and they form the new IOP for the next cycle. After numerous cycles, the resultant sequences are obtained through high throughput sequencing (HTS) and mapping analysis

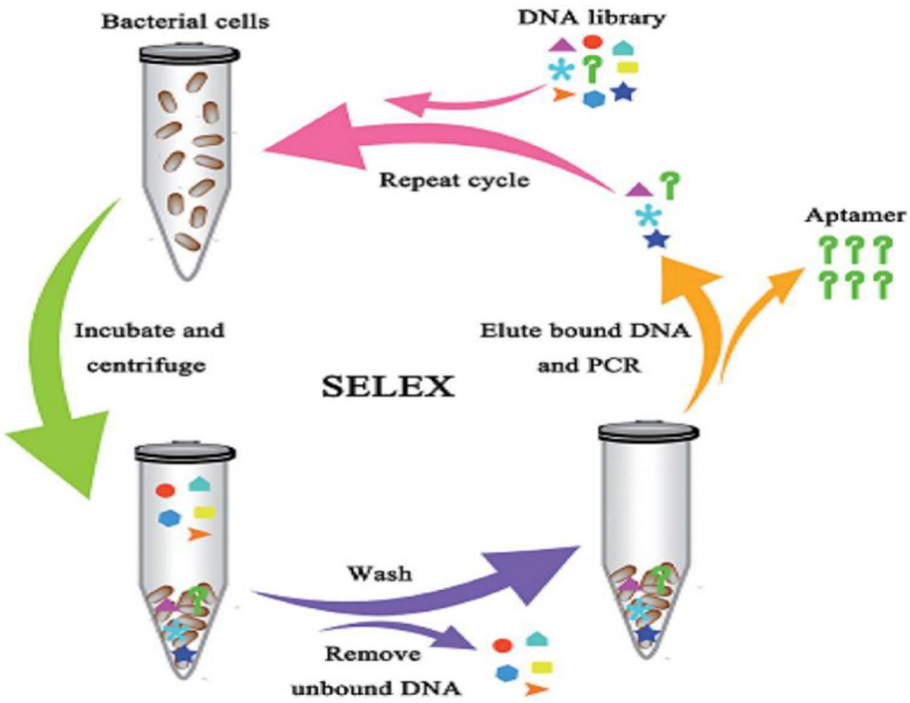

Fig. 2 Aptamer selection against live bacteria using whole-cell SELEX (Teng et al. 2016)

(Lorenz et al. 2010; Lorenz et al. 2006). Other modified SELEX methods were inspired from this SELEX method, such as transcriptomic SELEX (Fujimoto et al. 2012) and primer-free genomic SELEX (Wen and Gray 2004). Table 1 summarizes certain modified SELEX methods that have the potential to be utilized in desired commercial applications.

Applications of aptamers as foodborne pathogen biosensors

Staphylococcus aureus is one of the most resilient (grows at temperatures between 7 and 47.8 °C) pathogens that do not form spores and are present in the blood, skin, mouth, intestine or respiratory tract of infected mammals. They can survive outside living hosts, in the air, food, water and

Table 1 Summary of modified SELEX techniques for aptasensor application (Xu et al. 2021)

Methods	Characteristics	Advantages
In vivo SELEX	This technique uses living animal models as the targets for aptamer selection	Aptamer selection is done in whole organisms, making it suitable for drug delivery
Cell SELEX	The target for selection is a whole cell	No purification is needed prior to selection There is no alteration to the conformation of the target Aptamers can be selected without prior knowledge of the target on the cell surface It is a great method for the selection of aptamers against foodborne pathogens
Capture SELEX	The oligonucleotides are immobilized on a solid substrate to capture the targets	The target maintains its natural configuration Immobilization of the target is not difficult Suitable for small molecular targets like foodborne pathogens
Capillary Electrophoresis SELEX	The separation is based on the electrophoretic mobility difference between bounded and unbounded sequence	It is easy to operate, rapid, cheap and efficient
High-throughput SELEX	This is a combination of conventional SELEX and high throughput sequencing system. Sequencing is done in each round, not only after the last round	It is efficient and applicable to many targets
Magnetic bead-based SELEX	Target immobilization is done on the magnetic bead, and separation is also done by magnetic means	Cheap, shorter rounds, quick and simple

dust, and generally cause weakness, nausea, chills and several other symptoms upon infection. *Staphylococcus aureus* species are usually present in animal-based protein sources, such as sausage, salmon, milk, turkey, oysters and shrimp (Bacon and Sofos 2003; Bintsis 2018). *Escherichia coli* is another mostly harmless bacterial strain, although there are a few pathogenic strains. These strains are spread through the faecal matter of infected humans and animals, which eventually enter into the food chain or water system (García et al. 2010). *E. coli* infection is a critical health issue because a small dose is all that is required for infection, but it can lead to several health consequences (Croxen et al. 2013). This bacterial strain thrives for a long time in the environment and can grow on and be transmitted through fresh products, such as vegetables and other foods (Bintsis 2018). *Listeria monocytogenes* is another bacteria species identified as a major cause of foodborne illnesses-related death for people with compromised immune systems (babies, older people, and pregnant women). It is a pathogen that thrives in soil, water, sewage, and decomposing food matter. It is usually transmitted through cold or undercooked food (meats and vegetables), and can cause gastroenteritis, meningitis, and septicemia (Buchanan et al. 2017). It has a high mortality rate compared to other pathogens and can survive well in cold and wet environments, making it difficult to get rid of it (Gandhi and Chikindas 2007; Jemmi and Stephan 2006). In addition to these bacterial strains, fungi, algae, viruses and other pathogens also contaminates food and causes diseases in humans. In the past decades, numerous technologies have been successfully developed to aid the detection of these foodborne pathogens. However, there has always been a requirement for rapid detection methods, which led to the development of immunosensors (biosensors whose biorecognition elements are antibodies) and aptamer-based biosensors (biosensors, utilizing aptamers as their biorecognition element). This section discusses some applications of various aptamer-based biosensors in pathogen detection and monitoring with emphasis on the food industry.

Optical sensors

Optical aptamer-based sensors are biosensors that use aptamers as their biorecognition elements and can receive and convert signals from various sources into light radiations (visible, ultraviolet (UV) or infrared (IR)) (Majdinasab et al. 2018; Zahra et al. 2021). Optical aptamer-based biosensors can be classified into fluorescence, chemiluminescence, surface-enhanced Raman spectroscopy (SERS), surface plasmon resonance (SPR) and colourimetric aptamer-based biosensors based on parameters such as absorption, dispersion, refraction and reflection (Holban and Grumezescu 2018; Rubab et al. 2018). This type of aptasensor exhibit rapid response with high simplicity, sensitivity and specificity (Zahra et al. 2021). Recently, Liu et al. (2022) reported a novel liquid crystal-based optical aptasensor, which was formed by disorderly arranged nematic 4-cyano-4'-pentylbiphenyl molecules. Aptamers that can specifically bind with the target gram-negativ bacteria model (*E. coli*) were self-assembled on the interface of the liquid crystal to act as an optical sensor. The optical aptasensor exhibited 27 colony forming unit (cfu)/ml of ultralow detection limit of *E. coli* in food products such as soft drink and fruit juice (Liu et al. 2022). The major advantage of optical aptamer-based sensors is their ability to detect food-borne pathogens in a rapid, simple, specific manner at a low-cost (Chen et al. 2022). However, the requirement of bulky optical devices with surface modifications are the major limitations of optical aptamer-based sensors (Divya et al. 2022).

Colourimetry is the most common optical aptamer-based sensor technique widely used for pathogen detection due to its simplicity. Yi et al. (2019) developed an aptamer-based agglomerated gold nanoparticle colourimetry to detect *Salmonella*. The aptamer was immobilized on chitosan and bound to gold nanoparticles via electrostatic interactions. Combining the *Salmonella* with the fixed aptamer led to the 'striping' of aptamers from the nanoparticle and allowed the nanoparticles to agglomerate and give a colour change when a salt solution was added. An ultraviolet spectrophotometer can record this phenomenon as a marker of *Salmonella* detection. The recoveries of *Salmonella* from spiked milk samples was between 92.4 and 97.2%, further reasserting the utility of this method in detecting pathogens in real-life (Yi et al. 2019). Further, Zhu et al. (2021) prepared a novel ultrasensitive and label-free colorimetric aptasensor for the effective detection of *S. aureus* bacteria. In this study, SA31 aptamer was coated on octahedral manganese oxide nanoparticle surface, which binds with the bacteria and changes color from green to yellow. The aptasensor detected 10 to 2×10^5 cfu/ml of *S. aureus* in milk and pork samples with 3 cfu/ml low detecton limit (Zhu et al. 2021). In general, simplicity, high sensitivity and rapid detection are the major advantage of colourimetric aptamer-based sensors (Lerdsri et al. 2020). However, incomplete dissociation of the adsorbed non-target binding segments of the aptamer sequence upon target binding is the major limitation of this method (Alsager et al. 2018).

Surface-enhanced Raman Spectroscopy (SERS) is a less common optical aptasensor technique in foodborne pathogen detection. This method combines Raman spectroscopy and nanotechnology and is often used to detect protein biomarkers (Rubab et al. 2018). SERS works on the principle that nanomaterials and biomolecules bound to them may significantly enhance the Raman scattering of photons, thereby allowing for the detection of molecular signals (Schatz et al. 2006; Smolsky et al. 2017). Zhang et al. (2015) developed a SERS-based aptasensor for quantifying *S. aureus*. As a

signal probe, the authors modified gold nanoparticles with Raman signal molecules and then attached aptamers of *S. aureus*. the capture probe consisted of gold electrodes with immobilized aptamers. Aside from a relatively quick detection time of 3 h, the developed aptasensor was sensitive and selective and showed a 35 cfu/ml detection limit (Zhang et al. 2015). Similarly, Duan et al. (2016a, b) developed an aptasensor-based assay to detect and quantify *S. typhimurium*. The authors reported a limit of detection of 15 cfu/ml and a detection range spanning 15 and 1.5×10^6 cfu/ml. The authors used gold-silver core–shell nanoparticles modified with thiolated aptamer as the capture probe. X-rhodamine (ROX)-coupled aptamer was used for the Raman reporter probe. This system detected *S. typhimurium* spiked into milk samples and provided better results than conventional culturing methods (Duan et al. 2016a). Recently, Tian et al. (2023) utilized rolling cycle amplication to design a novel gold nanoparticle-based SERS aptasensor for the detection of *E. coli* O157:H7 bacterial strain. In this study, double stranded DNA were utilized as aptamer for the recognition, providing a Raman signal after binding with the bacteria. The results showed that the aptasensor possess 0.3 cfu/ml detection limit with 10^2–10^7 cfu/ml of wide detection range (Tian et al. 2023). The major advantage of the SERS aptamer-based sensor was its rapid analysis ability and non requirement of qualified personnel for the detection of the foodborne pathogen (Zavyalova et al. 2021). However, lack of possibility for quantitative determination and the involvement of sophisticated and expensive approaches for the detection of foodborne pathogens are the limitations of SERS-based aptasensors (Gribanyov et al. 2021).

Chemiluminescence is considered as the most sensitive optical aptasensor method, due to its excellent results (Park et al. 2013). Chemiluminescence has become a promising optical aptasensor technique in food safety analysis, as a chemical reaction produces energy, and having an excitation source for sample radiation during a chemical reaction is unnecessary. A cost-effective optical aptasensor was developed by Khang et al. (2016) for the rapid quantification and monitoring of *E. coli* 0157:H7 using graphene oxide (GO)/iron nanocomposites and guanine chemiluminescence detection. The results revealed that the limit of detection (LOD) was 4.5×10^3 cfu/ml, in a sample incubated for 1 h at 37 °C (Khang et al. 2016). Further, Gao et al. (2022) demonstrated the fabrication of a novel potentiometric aptasensor that can detect the presence of *E. coli* in food samples via eletrogenerated chemiluminescence. In this study, the electrode was modified with single-walled carbon nanotubes. The working electrode was made up of gold modified with $Ru(bpy)_3^{2+}$ and an *E. coli* detecting specific aptamer was utilized as the reference electrode. The results showed that the aptasensor possessed 2 cfu/ml detection limit with 5–1000 cfu/ml of linear range for *E. coli* 0157:H7 detection (Gao et al. 2022). The aptamer-based sensor possessed high specificity and sensitivity as their advantage (Han et al. 2019), whereas high cost and the requirement of trained personnel are the limitations of this approach (Yan et al. 2020).

Electrochemical aptamer-based biosensors

Electrochemical aptamer-based biosensors detect current or potential changes that results in redox reactions at the transducer surface (see Fig. 3). They are easy to operate, small in size, highly selective and sensitive, making them suitable for detecting foodborne pathogens (Hayat and Marty 2014). Various electrochemical methods, including voltametric, potentiometric, amperometric, impedimetric and conductometric, have been developed to transform the aptamer-analyte interaction into a measurable signal (Radi 2011).

For the first time, a rapid electrochemical aptasensor was reported in 2010 to detect tetracyclines in milk (Arghya et al. 2012). Tetracyclines are a class of broad-spectrum antibiotics that can be hepatotoxic to pregnant women. The tetracycline aptamer was immobilized on the surface of glassy carbon (GC) electrodes as a specific affinity molecule. A detection limit of 1 ng /ml was achieved with a detection time of 5 min, and the linear relationship between the tetracycline concentration and the current was 0.1–100 ng /ml (Zhang et al. 2010). Likewise, an electrochemical method for detecting *S. aureus* detection was developed by Cai et al. (2021). The authors coupled an aptamer onto the magnetic bead to capture the pathogens and release complementary strand cDNA. The release and shutdown of the signal in the next step controlled the gold electrode that modified the triple-helix structure. This system detected pathogens in water and honey samples with a limit of detection of 8 cfu/ml and a linear range of 30–3×10^8 cfu/ml (Cai et al. 2021).

Mishra et al. (2015) reported an impedimetric aptasensor for the rapid detection and quantification of OTA (Ochratoxin A) in cocoa beans (Mishra et al. 2015). OTA is a toxic mycotoxin towards a wide range of mammalian species and is usually present in agricultural products during storage (Sorrenti et al. 2013). Diazonium-coupling reaction mechanism for the immobilization of anti-OTA-aptamer on screen printed carbon electrodes (SPCEs) was used for the development of this aptasensor. The sensor exhibited a LOD as low as 0.15 ng/ml, and an increase in electron transfer resistance, that are linearly proportional to OTA concentration in the range of 0.15–2.5 ng/ml, as well as, an acceptable recovery percentage between 91 and 95% (Mishra et al. 2015). Further, an impedimetric aptasensor for the detection of *Salmonella* was fabricated using a nanocomposite of reduced graphene oxide (rGO) and multiwalled carbon nanotubes (MWCNTs), coated on the surface of glassy carbon electrode (GCE).

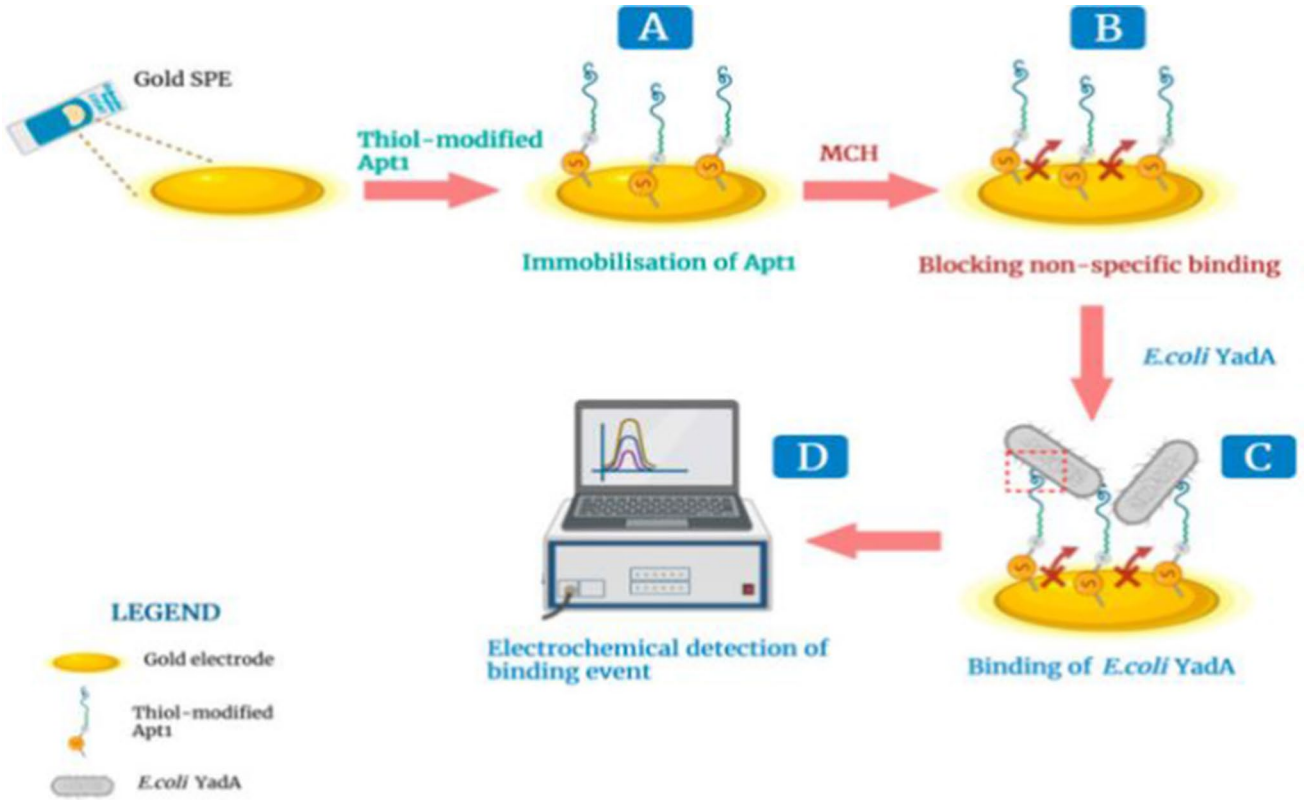

Fig. 3 Schematic representation of aptamer-based optical biosensor for the detection of virulence factor named YadA of *Yersinia enterocolitica*. Reproduced with permission from Sande et al. (2022), ©MDPI, 2022 (Sande et al. 2022)

Functionalisation of GCE was achieved using a mixture of carboxyl-modified MWCNTs and rGO in a one-step electrodeposition process. Following this, amino-modified aptamers selective for *Salmonella* was immobilized onto the surface of the rGO-MWCNTs/GCE. The resultant label-free aptasensor was able to detect *Salmonella* with a limit of detection of 25 cfu/ml and a linear range $75–7.5 \times 10^5$ cfu/ml (Jia et al. 2016). Recently, Nguyen and Gu (2023) utilized an ultrasensitive electrochemical aptasensor for the detection of *S. aureus*. In this study, SA37 aptamer was used to bind with bacterial cell, SA81@HRP aptamer was utilized as a catalytic probe and a tyramide signal amplification system made up of biotinyl-tyramide and streptavidin-HRP was used as electrocatalytic signal tags. The results revealed that the aptasensor possessed 3 cfu/ml dection limit in buffer and 8 cfu/ml detection limit in tap water and beef broth (Nguyen and Gu 2023). Rapid response, high sensitivity, multi-analyte analysis, potential for miniaturization, low cost and high simplicity are the advantages of electrochemical aptamer-based sensor, similar to other aptamer-based sensors (Yuan et al. 2023). However, the limited selectivity of the sensing layer is a core limitations of the electrochemical aptamer-based sensors (Radi and Abd-Ellatief 2021).

Aptasensor-based lateral chromatography test strip

Lateral flow assays are a paper-based platform for detecting targets such as pathogenic bacteria. This method is applicable in diverse fields, such as health care, food safety and environmental health, due to their low cost, ease of use and rapid results. Further, they can also be applied to a wide range of biological samples (saliva, sweat, urine, blood, serum) (Jauset-Rubio et al. 2017). It works on the principle of affinity interaction, where a visible line is observed on a test strip after the detection of an analyte. A lateral flow aptasensor consists of a sample pad (which transports sample to other parts of the test strip), conjugate pad (which contains the labelled aptamer), nitrocellulose membrane (which contains test and control lines which determine the sensitivity of the test strip) and wicking or absorbent pad (which maintains liquid sample flow rate and prevents backflow), that are arranged on a plastic backing pad (Jauset-Rubio et al. 2017; Majdinasab et al. 2018).

Fang et al. (Fang et al. 2014) developed a lateral flow aptamer-based assay based on aptamer-mediated strand displacement signal amplification but without DNA extraction from the microbial cell. This assay detected *Salmonella enteritidis* in spiked milk with a detection limit of 10 cfu/ml (Fang et al. 2014). Similarly, Wu et al. (Wu et al. 2015) quantitatively detected *E. coli* 0157:H7 using two aptamers selective for various *E. coli* cell membrane proteins. A limit of detection of 10 cfu/ml, a linear range of 10–1×10^6 cfu and a recovery range of 86.4–112% was obtained in this assay to detect the pathogen in food samples, such as milk, apple juice and water samples (Wu et al. 2015). Further, a rapid and simple method based on thermophilic helicase-dependent amplification and a lateral flow assay for the detection of *Salmonella* was developed in 2017. A *Salmonella* detection limit of 1.3–1.9 cfu/ml was obtained in chicken products and infant cereal within 2 h. There was no cross-reaction with other types of bacteria, making this approach suitable for use in areas with limited equipment (Du et al. 2017). Song et al. (2023) prepared a single probe by combining gold nanoparticles with aptamer targeting aflatoxin B1 (carcinogenic metabolite secreted by *Aspergillus* species) to utilize them as a colorimetric aptasensor. This aptasensor was combined with a chromatographic strip for rapid dection of aflatoxin B1in corn samples. The study showed that the aptasensor possess 0.5–50 ng/ml of linear detection range with 0.5–500 ng/ml detection range and 51 ng/ml of semi-quantitative detection limit (Song et al. 2023). The technique possesses advantages such as affordability, specificity, sensitivity, rapidity, robustness, and user-friendliness (Jaisankar et al. 2022). However, the narrow linear range in tests can be a major limitations of this sensor type (Zhang et al. 2018).

Fluorescence detection aptamer-based biosensors

This method is used to quantify the target based on the fluorescence (emission of light by an excited molecule when returning to the ground state) intensity of the materials and it is generally used to detect low concentrations of analytes. Generally, fluorescence aptamer-based biosensors are fabricated with the combination of a fluorescent biorecognition element (aptamer) and an optical transducer. These aptamer-based biosensors are divided into labelled and label-free sensors, depending on the type of external fluorescent material, which is required to obtain a measurable signal as not all the aptamers are auto-fluorescent. Hence, a typically labelled fluorescence utilized Förster (Fluorescence) resonance energy transfer (FRET) method for the detection of pathogens. Fluorescence detection aptamer-based biosensors are often preferred due to their high efficiency, high sensitivity, simplicity and rapid analysis (Huang et al. 2021; Majdinasab et al. 2018; Rubab et al. 2018; Wang et al. 2021).

Xu et al. (Xu et al. 2015) developed a magnetic nanobead coupled to quantum dots for the fluorescent-based detection of several food pathogens simultaneously. Their system was rapid, sensitive, and served as a specific aptasensor for the quantitation and detection of *E. coli* 0157:H7, *S. aureus*, *L. monocytogenes*, and *S. typhimurium*. The fluorescence emissions of all the resultant QDs in the MNDs-cell-QD complexes were simultaneously measured with a spectrometer. The limit of detection for the four bacteria was recorded to be 80, 100, 47 and 160 cfu/ml, respectively, in pure culture and 320, 350, 110 and 750 cfu/ml, respectively, in mashed beef. The aptasensor could detect the aforementioned bacteria species in 2.5 h within a rather broad range (101 and 10^4 cfu/mL), demonstrating its ability for multiplex detection of other foodborne pathogens (Xu et al. 2015). Further, Tao et al. (2021) designed a one-step FRET assay to detect *S. aureus* using antibiotic-modified gold nanoparticles as acceptors and aptamer-modified quantum dots as donors. The results showed that the sensor could exhibit a detection limit of 100 cfu/ml and a linear range of 10–5×10^8 cfu/ml (Tao et al. 2021).

Duan et al. (2014) reported a method for the simultaneous detection of *Vibrio parahaemolyticus,* and *S. typhimurium* based on FRET with carbon nanoparticles as acceptors and green- and red-emitting quantum dots as donors. Aptamers for *V. parahaemolyticus* were modified with green-emitting quantum dots, and those for *Salmonella were* modified with red-emitting quantum dots. The LOD of the novel sensor was identified to be 25 cfu/ml and 35 cfu/mL for *V. parahaemolyticus* and S. *typhimurium*, respectively. There was also a linear correlation of the concentration of the two pathogens in the range of 50–10^6 cfu/ml based on quantum dot fluorescence. This method was proposed to be beneficial in detecting pathogens in chicken and shrimp samples (Duan et al. 2015). In another study, dual recognition of *S. aureus* was proposed by Yu et al. (2017) in developing a FRET platform based on vancomycin and aptamer-based bimolecular interactions. This method was linear in the range of 20 and 108 cfu/mL and a detection limit of 10 cfu/mL (Yu et al. 2017). Further, efforts have been made to develop unique, culture-free, rapid, quantitative method for detecting *S. aureus* in minimally processed liquid samples with the help of a smartphone via aptamer-functionalized fluorescent magnetic NPs. Shrivastava et al. (2018) tagged *S. aureus* cells in a detection cassette for magnetic capture and the fluorescent images were created with a smartphone using LEDs as an excitation source. The minimum detectable concentration in peanut milk samples was as low as 10 cfu/ml within a detection time of 10 min (Shrivastava et al. 2018). Liu et al. (2021) prepared a novel fluorescence aptasensor for sensitive and rapid *Listeria monocytogenes* detection in tap water and pasteurized milk samples. In this study, upconversion nanoparticles functionalized with aptamers were utilized to

bind with the bacterial cell by providing a strong fluorescence signal. The results indicated that the aptasensor possessed 8 cfu/ml detection limit with 68 to 68×10^6 cfu/ml of detection range (Liu et al. 2021). High sensitivity with low signal-to-noise ratio and rapid turnaround time are the advantages of fluorescence detection aptamer-based sensors (Aslan et al. 2023). However, covalent labeling of aptamers with fluorophores can be time-consuming and expensiveness (E Wang et al. 2011; Zhang et al. 2023).

Surface plasmon resonance-based aptamer biosensors

The principle of surface plasmon resonance (SPR) has been incorporated into the design of various aptamer-based biosensors for detecting foodborne pathogens (Cooper 2003). This technique is shown in Fig. 4. Recently, Khateb et al. (2020) developed a portable, label-free aptasensor for detecting *S. aureus* in pure culture and artificially contaminated milk samples using nanostructured plasmonic elements. A detection limit of 10^3 cfu/ml was obtained for the milk samples in 120 secs without any pre-enrichment step (Khateb et al. 2020). Further, Wang et al. (2019) immobilized aptamers specific to *S. aureus* and *E. coli* on a planar gold substrate through a polyadenine-mediated immobilization technique, which resulted in surfaces with SPR characteristics. The resultant SPR aptamer-based biosensors showed a limit of detection of 10^5 cfu/ml for *E. coli* and 10^6 cfu/mL for *S. aureus*. However, it was established that a higher aptamer lateral density, together with other technical enhancements, such as decreasing the ionic strength of the aptamer solution, utilization of 10A-polyA as an anchoring group and bromine ion as a back filler, would yield a better result in capturing target bacteria (Wang et al. 2019). Dursun et al. (2022) developed a novel SPR-based aptasensor for the detection of *Brucella melitensis* bacterial pathogen in milk samples. In this study, B70 aptamer was used to specifically bind with the bacteria, which was immobilized with magnetic core–shell silica nanoparticles for the initial purification of the target bacteria in milk. The SPR sensor chip was prepared using B46 aptamers to instantly detect the bacteria in 1 mL of milk sample with a low detection of $27 \pm$ cells (Dursun et al. 2022). In general, SPR aptamer-based sensors help in the detection of food-borne pathogens with excellent chemical stability, high affinity and high selectivity towards specific targets as well as ease for chemical modification (Nguyen et al. 2015). However, limitations, such as multi-detection of analytes and non-specific binding of aptamers are prevalent in SPR-based aptamer sensors (Gaudreault et al. 2021).

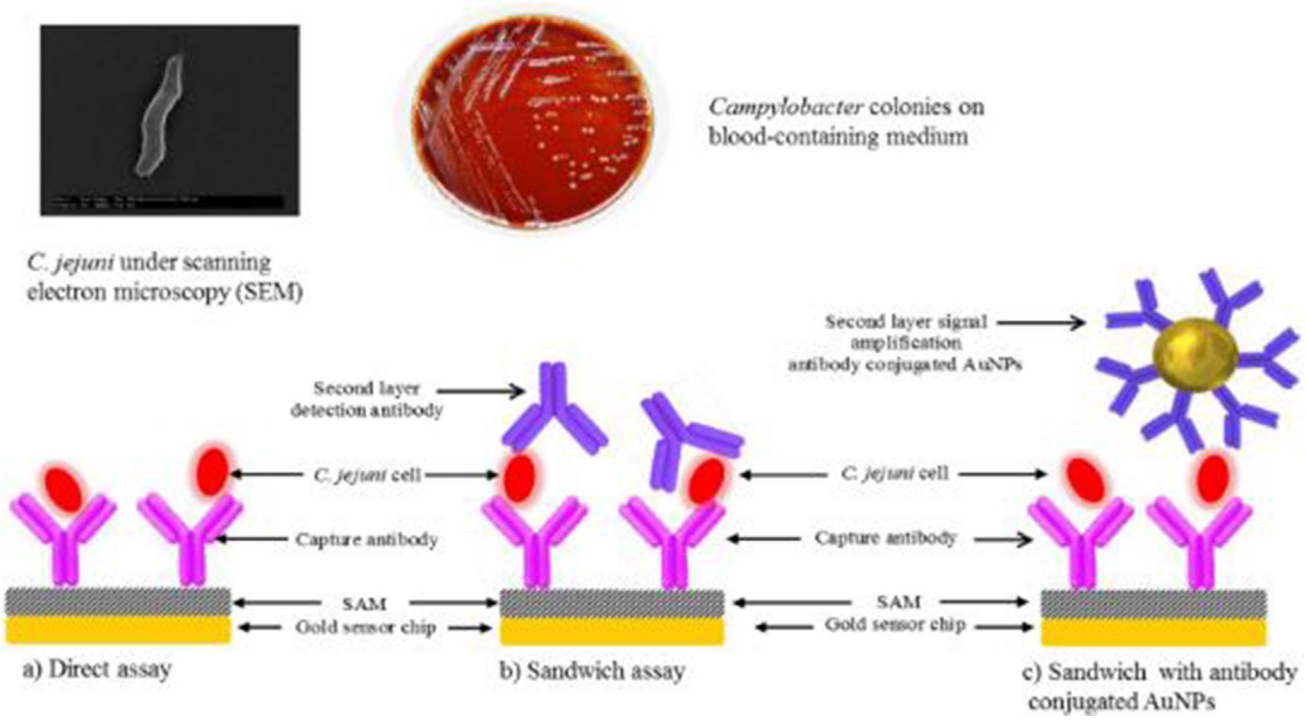

Fig. 4 Detection of *Campylobacter jejuni* using antibody-functionalized surface plasmon resonant gold nanoparticles as SPR-based aptamer-based biosensors via **a** direct assay; **b** Sandwich assay and **c** sandwich with antibody conjugated gold nanoparticles. Reproduced with permission from Masdor et al. (2017), ©MDPI, 2017 (Masdor et al. 2017)

Lab-on-chip aptamer-based biosensors

Lab-on-chip (LOC) aptamer-based biosensors are miniaturized aptamer-based biosensors integrated into a single chip to detect one or more analytes to be beneficial for the biochemical detection and sequencing of DNA (Dkhar et al. 2022). Weng and Neethirajan (2016) developed a rapid, simple and sensitive aptasensor for the detection of food allergen named Ara h1 (a homo-trimeric protein which is a major allergen in peanuts and accounted for 95% of all peanut-allergenicity reactions), using a microfluidic system integrated with quantum dots (QDs) aptamer and functionalized with graphene oxide (GO). The aptasensor used QDs-aptamer-GO composite as probes to undergo alterations in the presence of the target. The resultant miniaturized optical aptasensor exhibited a detection limit of 56 ng/ml within 10 min (Weng and Neethirajan 2016). The same group also developed nanomaterial-enhanced multipurpose paper-based microfluidic aptasensor for detecting food allergens and toxins, including egg white lysozyme, β-conglutin lupin, okadaic acid and brevotoxin. The resultant aptasensor was similar to the previous studies, where GO and specific aptamer functionalized QDs were employed as probes. The assay was performed on the paper-based microfluidic chip, which reduced the sample quantity (10 µL), required reagents and drastically reduced testing time (Weng and Neethirajan 2018). Moreover, a simple paper-based microfluidic aptasensor using a nitrocellulose membrane was developed to detect norovirus, which is a leading cause of acute gastroenteritis and can be transmitted through food and drinks. The results showed that the aptasensor possesses a linear range of 13 ng/ml to 13 µg/ml and a LOD of 4.4 ng/ml and 3.3 ng/mL while utilizing multiwalled carbon nanotubes and graphene oxide, respectively (Weng and Neethirajan 2017). Recently, Costantini et al. (2019) prepared a novel label-free fluorescent aptasensor that are integrated in a lab-on-chip device for ochratoxin A (toxic metabolite released by certain fungal strains) detection in wheat and beer samples. The study showed that the conformation of the aptamer changed when the aptasensor interacts with the ochratoxin A, which eventually leads to a fluorophore release and a decrease in the fluorescent signal detected by the silicon photosensor array positioned underneath the microfluidic network. The lab-on-chip was reported to detect the toxic metabolite in a short time of 5 min with 1.3 ng/ml detection limit and 5–200 ng/ml detection range in food samples (Costantini et al. 2019). Reduced time for analysis, low reagent costs and high-throughput analysis are the advantages of LOC-based aptamer sensors (Nikoleli et al. 2018; Radhakrishnan et al. 2022). However, complexity in the fabrication of the chip with labor-intensive technique and requirement of both trained personnel and expensive equipment are the limitations of these sensor types. All these studies, as summarized in Table 2, showed that aptamers have the potential to detect foodborne pathogens as well as toxic metabolites released by microbes in food with high specificity, selectivity and efficiency.

Table 2 Recent aptamer-based biosensors for the detection of foodborne pathogens

Aptamer	Detection method	Microbe detected	Food product	Limit of detection	References
Peptide aptamer	Optical aptasensor	*E. coli*	Soft drink and fruit juice	27 cfu/ml	Liu et al. (2022)
Peptide aptamer	Colorimetry	*Salmonella*	Milk samples	–	Yi et al. (2019)
SA31	Colorimetry	*S. aureus*	Milk and pork	3 cfu/ml	Zhu et al. (2021)
Peptide aptamer	SERS	*S. aureus*	–	35 cfu/ml	Zhang et al. (2015)
Thiolated peptide aptamer	SERS	*S. typhimurium*	Milk	15 cfu/ml	Duan et al. (2016a)
dsDNA	SERS	*E. coli* O157:H7	–	0.3 cfu/ml	Tian et al. (2023)
Peptide aptamer	Chemiluminescence	*E. coli*	–	2 cfu/ml	Gao et al. (2022)
SA37 and SA81@HRP	Electrochemical	*S. aureus*	Tap water and beef broth	8 cfu/ml	Nguyen and Gu (2023)
Peptide aptamer	Lateral chromatography test strip	Aflotoxin B1 released by *Aspergillus* species	Corn	51 ng/ml	Song et al. (2023)
Peptide aptamer	Fluorescence detection	*Listeria monocytogenes*	Tap water and pasteurized milk	8 cfu/ml	Liu et al. (2021)
B70 and B46 aptamer	SPR	*Brucella melitensis*	Milk	27 cells	Dursun et al. (2022)
Peptide aptamer	Lab-on-chip	Ochratoxin A released by certain fungal strains	Wheat and beer	5–200 ng/ml	Costantini et al. (2019)

Future perspective

Food safety is vital in combating several foodborne infections. Hence, the quest for technologies and methods for rapidly detecting foodborne pathogens is a top priori ty in the research arena. The conventional methods for detecting foodborne pathogens, such as the culture-based methods, are cheap, easy to use and reliable. However, this method is usually slow and requires several days to obtain conclusive results. Further, the sensitivity of this method is greatly reduced in cases where there are low bacterial levels and cannot detect bacteria in the 'viable but non-culturable (VBNC) state (Oliver 2010). Furthermore, PCR is also rapid, accurate, sensitive and specific compared to culture-based methods. This method can even detect minute levels of targets. However, the amplification of extracellular DNA and the dead cells can increase the level of viable bacteria cells, which can lead to false results (Rudi et al. 2005; Umesha and Manukumar 2018). Moreover, reverse-transcriptase PCR (RT-PCR) and PCR combined with biological dyes are currently utilized to detect viable foodborne pathogen accurately (Zeng et al. 2016). In general, RT-PCR is used for mRNA detection with certain limitations, where RNA is tedious to handle, as it is prone to contamination. Also, there must be gene expression of the target pathogen for the process to be successful, but gene expression can change with variation in stress parameters (Barbau-Piednoir et al. 2014). Additionally, several distinct approaches have been developed for detecting foodborne pathogens, including multiplex PCR, DNA microarray, sequencing methods (whole genome and next generation), ELISA, and all its modifications. These methods also have limitations, such as low sensitivity and specificity, long detection time, requirement for purified samples, high cost and requirement of a huge labor force. The limitations of all these methods have demanded highly efficient monitoring techniques, such as aptamer-based biosensors for food pathogen detection (Grumezescu and Holban 2018) in the future. Even though, aptamers possess ability to detect foodborne pathogens, standalone aptamers cannot be employed as biosensors. Immobilization of aptamers onto nanoparticles and electrodes are required to enhance their ability for rapid detection. Thus, development in the field of nanoparticles or nanocomposites and immobilization techniques to combine aptamers with nanoparticles will help in improving the efficacy of aptamer-based biosensors in the future.

Conclusion

Biosensors are currently considered as a prospective future of foodborne pathogen detection due to their numerous advantages, such as excellent sensitivity, selectivity and specificity, rapidity, simplicity and low detection limit. Further, biosensors are used during in situ pathogen detection with accuracy and in real-time, making them suitable for point-of-care monitoring pathogen and industrial applications. However, conventional biosensing based on antibody technologies can have a significant setback. Antibodies require more time and a host to be developed, are temperature sensitive, expensive, and cannot be recovered after denaturation. These limitations have led to the emergence of chemically synthesized oligonucleotides named aptamers for the fabrication of biosensors called aptamer-based biosensors. Aptamers are identified as a solution to most of the limitations exhibited by antibodies. Aptasensor technologies, such as electrochemical, optical, SPR-based (surface plasmon-based), and mass-sensitive (quartz crystal microbalance and acoustic wave) approaches have been developed over the years. Several studies have reported that aptasensor technologies are beneficial for detecting foodborne pathogens on real samples. Thus, these recent studies indicated that aptamer-based biosensors can be developed to possess various advantages for monitoring foodborne pathogens.

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Declarations

Conflict of interest Authors declare that there is no conflict of interest.

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