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Applications of Phage-Based Biosensors in the Diagnosis of Infectious Diseases, Food Safety, and Environmental Monitoring

Umer Farooq, Muhammad Wajid Ullah, Qiaoli Yang and Shenqi Wang

Abstract

Environmental pollution and food safety are becoming serious concerns to human health in developing countries. To combat such issues, researchers have developed different approaches for on-spot detection and screening of infectious disease, caused by pathogens and toxins in food and water samples. One such approach is the development of phage- and phage-component-based sensors that are highly specific, sensitive, rapid, efficient, cheap, and portable analyte screening platforms. Such sensors overcome the limitations of conventional screening approaches. This chapter highlights different food and environmental contaminations and represents the potential of phage-based biosensor for bacterial detection. It summarizes different applications of phage-based sensors in the fields of food safety and environmental monitoring and highlights current challenges and perspective. In general, this chapter brings together the technologies related to phage-based sensors and food and environmental safety, by compiling the efforts of engineers and scientists from multidisciplinary areas.

Keywords: bacteriophage, biosensor, infectious diseases, food safety, environmental monitoring

1. Introduction

Many pathogenic bacteria like *Streptococcus*, *Mycobacterium*, *Pseudomonas*, *Salmonella*, *Shigella*, etc. are causing different diseases in humans, resulting in several outbreaks and epidemics of diseases worldwide. Every year, millions of individuals get infected by these bacteria, while the common sources of infections are clinical, food-borne, airborne, and/or waterborne [1]. Clinical, food, and environmental contaminations are the eternal challenges worldwide in the healthcare systems and food safety and environmental monitoring. Irrespective of comprehensive struggles to fight such pathogenic bacteria, the numbers of clinical, food, and environment-related diseases are increasing every year [2]. As a solution to the problem, the development of biosensors especially phage-based biosensors for bacterial detection in clinical, food, and environmental samples has remained a hot topic since the last few decades. Phages in biosensor proved themselves as unique bio-probes, owing to their selectivity, specificity, and

withstanding harsh environmental conditions. Establishing phage-based biosensors for application in food safety and environmental monitoring is a motivating and interesting research topic and is the urgent need of this modern era. The key point is to enhance phage-based cheap recognition tools with maximum levels of selectivity, consistency, and sensitivity with minimum times of assay. Significant struggles have been dedicated on enhancing the transducer surface of biosensor for improved detection and sensitivity. Phage-based bio-probes have been used in transducer development for several analytical approaches to offer specific and selective detection. Bacteriophages as a bio-probe have been successfully applied for bacterial detection in clinical samples (urine) [3], food samples (milk, tomatoes) [4], and environmental samples (river water) [5]. Furthermore, different analytical approaches relying on phage-based bio-probes have been reported like electrochemical [6], bioluminescence [7], fluorescence [8], mass spectrometry [9], magnetoelastic [4], surface plasmon resonance [10], lateral flow assay [11], etc. In the following context, we will review biosensor transduction platforms involving phage-based probes for transducer development to detect infectious bacteria in the field of food and environmental safety monitoring [12]. In this chapter we will highlight applications of different phage-based analytical approaches for bacterial detection in clinical, food, and environmental samples.

2. Phage-based biosensors for infectious pathogen detection

Bacteriophage as a bio-probe has been used in different transduction platforms for detection of pathogenic bacteria, which are briefed as follows:

2.1 Phage optical biosensors

Optical phage-based sensors owing from their reasonably rapid screening, sensitivity, and flexibility to a broad-ranging assay situations have been extensively explored for bacterial detection. Optical methods are classified into two core subclasses on the basis of their working principles, label-free and labeled. The best frequently used optical methods for bacterial screening are fluorescence spectrometry [8], surface plasmon resonance (SPR) [10], and bio- or chemiluminescence [13]. In the subsequent subsection, our focus is on phage bio-probe-based optical biosensors for detection of pathogens with special emphasis on food safety and environmental monitoring. **Figure 1** represents a reporter phage-based optical sensing scheme.

2.1.1 Phage-SPR-based sensors

Surface plasmon resonance (SPR) works on the principle of oscillation phenomenon that happens between the interfaces of any two materials. The change in the refractive index close to the sensor surface caused by contact of target analyte in the medium with the bio-probe (phage) present on transducer surface is measured by SPR biosensors. Phages have been widely immobilized as bio-probes on the surfaces of SPR transducers to offer facility of specific recognition of bacterial detection. The immobilized phage on SPR transducer successfully detected *E. coli* K12 [15], *S. aureus* [16], methicillin-resistant *Staphylococcus aureus* (MRSA), and *E. coli* O157:H7 [17]. Typically, the LOD was ranging from 10^2 to 10^3 CFU/mL. Phage RBPs have been utilized as bio-probes in SPR approaches for specific bacterial screening, such as Singh et al.'s activated gold-coated plates, by immobilizing genetically engineered tailspike proteins from P22 phage to demonstrate selective, specific, and real-time *Salmonella* detection with 10^3 CFU/mL sensitivity [18].
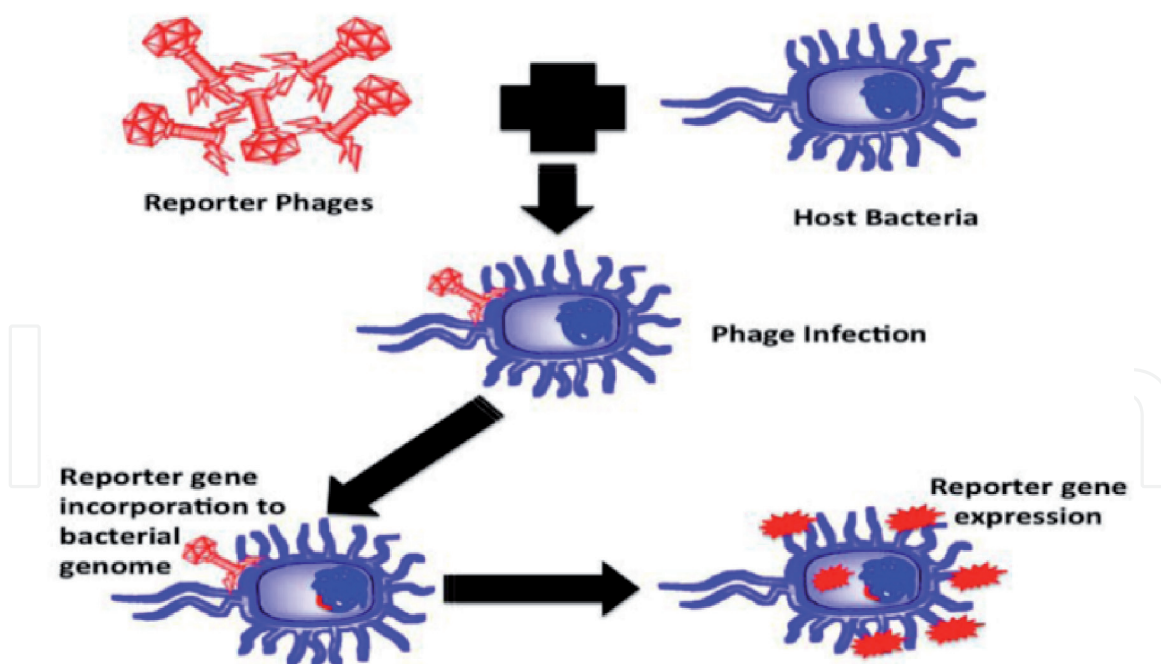
Figure 1.
A graphical representation of target pathogen detections based on reporter phage, adapted from [14].

2.1.2 Phage-bioluminescence sensors

For bacterial quantitative detection in samples, bioluminescence analyses that are rapid, sensitive, and simple are used by assessing the emitted light from intracellular components. Bacterial lysis is the first step of this type assays, to discharge intracellular cell components followed by reaction with luciferase and are screened by bioluminescent. A lytic bacteriophage is involved as a bio-recognition probe for target bacterial detection following lysis. Infectious bacteria like *E. coli* and *Salmonella Newport* were detected by an adenosine triphosphate bioluminescence assay using lytic bacteriophage as bio-probe lysis of target bacterial cell [19]. The sensitivity was enhanced 10–100-folds by addition of adenylate kinase as an alternate cell marker, while less than 10^4 CFU/mL of *E. coli* was reported in ‘1 h [19]. Later it was demonstrated that the quantity of discharged adenylate kinase from lysed cells is dependent on the growth stage, bacterial type, the infection time, and the phage type [20].

2.1.3 Phage-SERS-based sensors

An innovative Raman method, i.e., surface-enhanced Raman spectroscopy (SERS), is enhancing the intensity by vibrational absorbance of definite elements when they are near the surface of nano-organized noble metals by the influence of numerous orders of magnitude. The improved intensity of SERS method is dependent on the molecules' capability to release a Raman signal and the contained fields of plasmon in their neighborhood [21]. For instance, a report stated a phage-SERS biosensor for *E. coli* detection using phage immobilization on nano-figured thin sheet of silver over substrates of silica (**Figure 2**) [22] established by exploitation of metallic nanosculptured thin silver film. The silver film exterior is activated by self-assembled monolayer of 4-aminothiophenol and glutaraldehyde for T4 immobilization to screen *E. coli*. As a reporter molecule, 4-aminothiophenol monitored the Raman band enhancement. Other reports of phage-SERS-based biosensors have been reported and are briefed in **Table 1**.
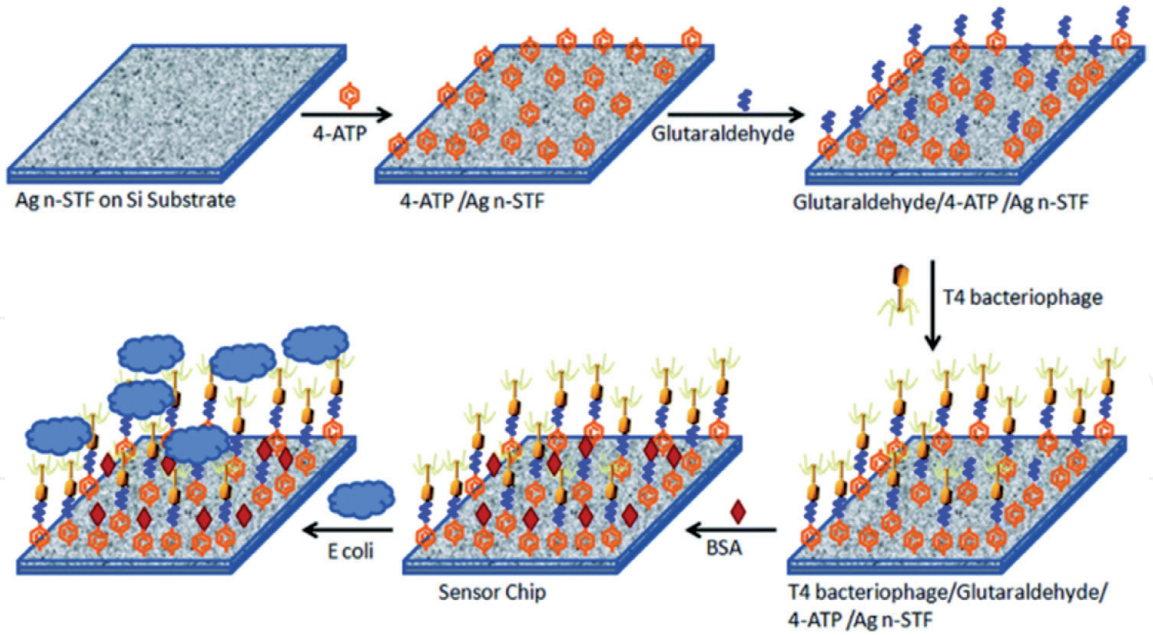
Figure 2.
Schematic representation of phage-SERS-based sensor. Adapted from [22].

Transducer	Phage-based bio-probe	Target bacteria/ analyte	Sample	Detection limit	Ref.
SPR	T4 phage	*E. coli K12*	PBS	7×10^2 CFU/mL	[15]
	T4 phage	*E. coli O157*:H7	PBS	10^3 CFU/mL	[17]
	BP14 phage	MRSA	PBS	10^3 CFU/mL	[17]
	scFv phages	*L. monocytogenes*	—	2.10^6 CFU/mL	[53]
	12,600 phage	*S. aureus*	—	10^4 CFU/mL	[16]
Luminescence	*lacZ* T4 phage	*E. coli* B	Water	10 CFU/mL	[7]
	SJ2 phage	*S. enteritidis*	—	10^3 CFU/mL	[20]
	Pap1 phage	*P. aeruginosa*	Milk, urine	56 CFU/mL	[3]
	Lytic phage	*Listeria innocua*	—	>10^4 CFU/mL	[54]
	Shfl25875	*S. flexneri*	Stool	10^3 CFU/g	[55]
LFA	B4 phage	*B. cereus*	Buffer	1×10^4 CFU/mL	[11]
	Gamma phage	*B. anthracis*	—	2.5×10^4 CFU/mL	[56]
	T7 phage	*E. coli*	Broth	10^3 CFU/mL	[47]
Fluorescent	P22 phage	*S. typhimurium*	Milk	1 CFU/24 mL	[57]
	P-*S. aureus*-9	*S. aureus*	PBS	2.47×10^3 CFU/L	[58]
	Wβ phage	*B. anthracis*	Soil	10^4 CFU/g	[50]
	O157-IOV 4	*E. coli O157*:H7	Milk	4.9×10^4 CFU/mL	[59]
	PP01 phage	*E. coli* O157:H7	Apple juice	1 CFU/mL	[60]
	PDPs	TNT	—	10 μg/mL	[61]
	T7 phage	*E. coli*	LB broth	10 CFU/mL	[62]
QCM	Filamentous phage	*S. typhimurium*	—	10^2 CFU/mL	[35]
	Wild-type	*E. coli* K12	—	10^3 CFU/mL	[6]
	T4 phage	*E. coli*	Milk	Few CFU/mL	[9]

Transducer	Phage-based bio-probe	Target bacteria/analyte	Sample	Detection limit	Ref.
SERS	T4 phage	*E. coli B*	Buffer	150 CFU/mL	[22]
	Phage 12,600	MRSA	—	—	[63]
	P9b phage	*P. aeruginosa*	Clinical samples	10^3 CFU/mL	[64]
	A511 phage	*L. monocytogenes*	—	6.1×10^7 pfu/mL	[65]
Magnetoelastic	E2 phage	*S. typhimurium*	—	5×10^2 CFU/mL	[66]
	JRB7 phage	*B. anthracis*	—	Spores	[67]
	E2 phage	*S. typhimurium*	Romaine lettuce	5×10^2 CFU/mL	[68]
	Phage	*S. typhimurium*	—	1.5×10^3 CFU/mm^2	[69]
Amperometric	B1-7064 phage	*B. cereus*	—	10 CFU/mL	[70]
	M13 phage	*E. coli TG1*	—	1 CFU/mL	[71]
Impedimetric	T4 phage	*E. coli*	—	10^4 CFU/mL	[72]
	T2 phage	*E. coli B*	Broth	10^3 CFU/mL	[73]
	Lytic phage	*S. Newport*	—	10^3 CFU/mL	[74]
	Gamma phage	*B. anthracis Str*	Water	10^3 CFU/mL	[75]
	T4 phage	*E. coli B*	Water, milk	800 CFU/mL 100 CFU/mL	[76]
	Endolysin Ply500	*L. monocytogenes*	Milk	10^5 CFU/mL	[77]

SPR, surface plasmon resonance; scFv, single-chain variable fragment; MRSA, methicillin-resistant Staphylococcus aureus; PBS, phosphate-buffered saline; TNB, trinitrobenzene; TNT, trinitrotoluene; QCM, quartz crystal microbalance; QD, quantum dot; SERS, surface-enhanced Raman spectroscopy; LFA, lateral flow assay; HRP, horseradish peroxidase; CFU, colony-forming unit; PFU, plaque-forming unit; E. coli, Escherichia coli; S. arlettae, Staphylococcus arlettae; B. anthracis, Bacillus anthracis; P. aeruginosa, Pseudomonas aeruginosa; S. flexneri, Shigella flexneri; S. Newport, Salmonella Newport; S. typhimurium, Salmonella typhimurium; S. aureus, Staphylococcus aureus; LB, Luria-Bertani broth.

Table 1.
Applications of phage/phage components in detection of infectious pathogen and other deadly analytes related to food safety and environmental monitoring, where transduction platform used, target analyte/bacteria, sample processed, and limit of detection are briefed with reported literature.

2.1.4 Phage-fluorescent sensor

In fluorescent-phage-based sensor techniques, fluorescently stained phages are utilized as marking agents for the detection of bacterial cells. Fluorescently labeled phages are identified followed by binding to specific host bacterial cell. The composite of bacteriophage-bacteria is then sensed by means of flow cytometry or epi-fluorescent filter approach. A combination of immunomagnetic separation with fluorescent method is detected between 10 and 10^2 CFU/mL of pathogenic bacteria *E. coli* O157:H7 after 10 h augmentation in artificially contaminated milk [23] and 10^4 CFU/mL in sample of broth medium [24]. Additional improvement in the sensitivity of this method was reported by using fluorescent quantum dots (QDs) for phage labeling [25]. Also fluorescent-based sensors have been used for bacterial toxin recognition. Phage display was applied to choose a peptide (12-mer) that was able to attach to *staphylococcal enterotoxin B* (SEB) that is responsible for food poisoning [26]. This approach permitted toxin sensing and detected 1.4 ng of SEB/sample well with the help of fluorescence immunoassay and involved a fluorescently stained SEB binding bacteriophage. Also array-based sensors have been established following the same principle for simultaneous detection of

Bacillus globigii, MS2 bacteriophage, and also SEB [27]. The typically reported sensitivity until now is about 20 CFU/mL by epi-fluorescent microscopic platform [25] and is 1 CFU/mL by flow cytometric recognition approach [28].

2.1.5 Phage-colorimetric sensors

Sensing based on changes in color allows the use of simple diagnostic systems like spectrophotometers, or even involving smartphones, and both of them are comparatively common and feasible. Designed colorimetric phage-based biosensors are mostly based and integrated on the utilization of reporter bacteriophages that carry genes coding for reporter enzymes. The foremost colorimetric sensor based on phage was to detect *Salmonella* ice nucleation sensor using reporter gene *inaW* [29]. Expression of ice nucleation protein was induced upon infection, interrupting the cell, and was consequently observed by the addition of an indicator dye (orange colored) [30]. Other serviceable reporter genes that have been successfully used with various colorimetric substrates are *celB* and *lacZ* segments encoding β-galactosidase and β-glycosidase [31]. More recently enhanced phage-based colorimetric technique has been reported to be integrating and coupling with novel technologies like surface plasmon [32], macroscope and smartphone [33], and lateral flow assay [11]. Other colorimetric phage-based biosensors established in recent years are briefed in **Table 1**.

2.2 Phage-based micromechanical sensors

Representative micromechanical biosensor (magnetoelastic) is expressed in **Figure 3**, involving E2 phage for detection of *S. typhimurium* on tomato and spinach leaves. Further micromechanical-phage-based biosensors are briefed in the following context.

2.2.1 Phage-QCM-based sensors

Quartz crystal microbalance (QCM) sensors are mass-based sensors that are highly sensitive with the ability of detecting nanogram variations in mass. QCM
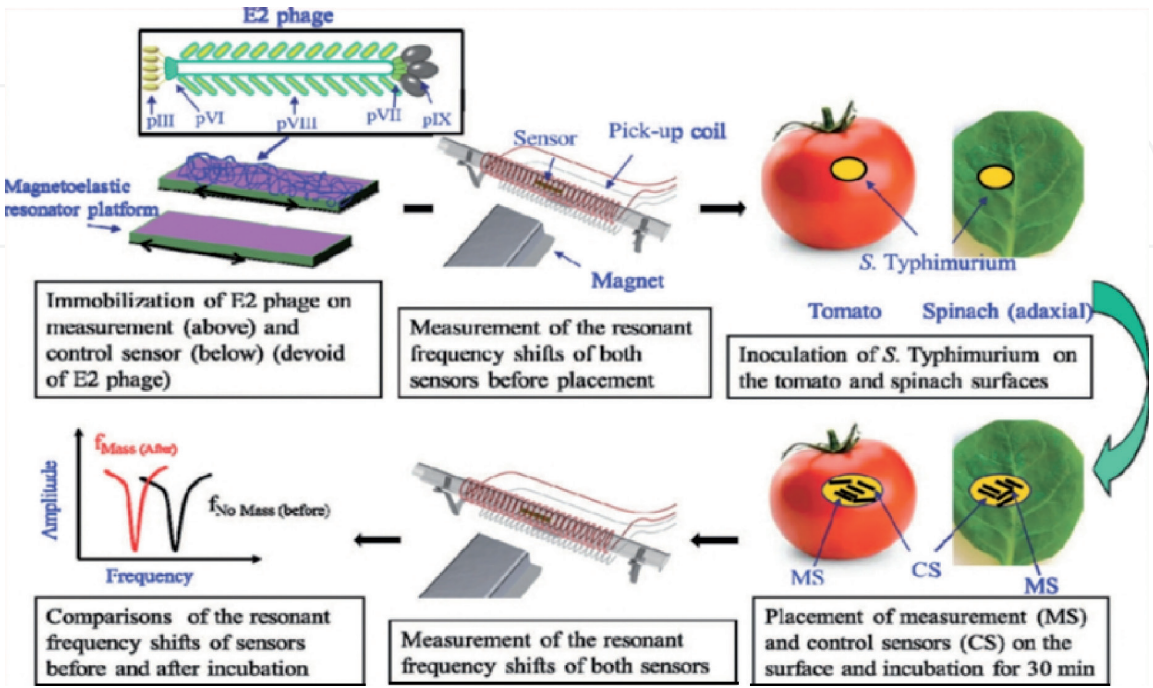

Figure 3.
Schematic representation of S. typhimurium *detection on tomato and spinach leaves on magnetoelastic-E2 phage-based biosensor system, adapted from [34].*

biosensors are functionalized by a very thin piezoelectric film having both sides coated with two conductive electrodes. Mechanical resonance is stimulated by electrical field application through the quartz crystal.

Consequently, QCM-based biosensors could be established to quantify the mass of many target analytes by immobilization of individual bio-probes on the surface of sensor. Phages as bio-probes can be conjugated with QCM biosensors for selective screening of bacterial cells. For instance, physically adsorbed bacteriophages around 3×10^{10} PFU/cm^{-2} on the surface of piezoelectric transducer provided a very rapid and sensitive platform for *Salmonella typhimurium* detection. This immobilized bacteriophage on QCM biosensor had a LOD of 10^2 CFU/mL having a broad linear range of 10^0–10^7 CFU/mL and a quick reaction and detection time of less than 3 min [35]. Other reports of phage-based QCM sensor applications in detection of infectious bacteria in food safety and environmental monitoring are briefed in **Table 1**.

2.2.2 Phage magnetoelastic sensors

Magnetoelastic sensors are prepared from materials having magnetoelastic property, i.e., magnetism and elasticity, and they contract/extend on excitation by alternative-current-magnetic field. The resonance frequency depends on the viscosity/mass adjacent to the surface of the resonating material. Magnetoelastic devices are used for detection of biological and chemical analytes by integration of bio-probes like phages on the biosensor surface and might be functional in gaseous, static, liquid, or flowing condition [21]. Likewise, E2 bacteriophage was genetically modified for specific detection of *S. typhimurium* in samples of food [36], on spinach leaves [37], and in apple juice, tomato, or milk [38], and all these magnetoelastic biosensors displayed outstanding selectivity and specificity. In addition, E2 bacteriophage-based magnetoelastic biosensors expressed tremendous stability when exposed to severe environmental conditions [39]. ME-lytic phage-based biosensor was reported to detect MRSA bacteria. In the evaluation based on varied immobilization times (10, 30, 90, 270, 810, and 2430 min) and bacteriophage concentrations (10^8–10^{12} PFU/mL), lytic phage binding to ME sensor surface was established for optimal conditions. The optimal immobilization time and concentration in PFU/mL for effective binding of phage to ME sensor surface was calculated as 30 min and 10^{11} PFU/mL, respectively. This ME-based biosensor approach was used successfully for detection of MRSA bacteria with LOD of 10^3 CFU/mL [40].

2.3 Phage-based electrochemical biosensors

A schematic representation of electrochemical biosensor of nanoflowers—AuNPs and Thi-phage composite—for *E. coli* detection is illustrated in **Figure 4**.

2.3.1 Phage-amperometric biosensors

Among the electrochemical detection methods, amperometry has been most commonly used for detection of pathogenic bacteria and offered an improved sensitivity platform related to other electrochemical approaches. Electrochemical amperometric biosensor involves a working electrode (having bio-probe) and a reference electrode. For current production in the analyte sample, a bias potential is passed on these electrodes. The produced current is directly dependent on the degree of electron transfer that fluctuates with changes in analyte's ionic concentration. Simply, amperometric sensors detect ionic changes in the solution by determining the variations in electric current. Several approaches have been established for detection of foodborne pathogenic bacteria based on phage-amperometric
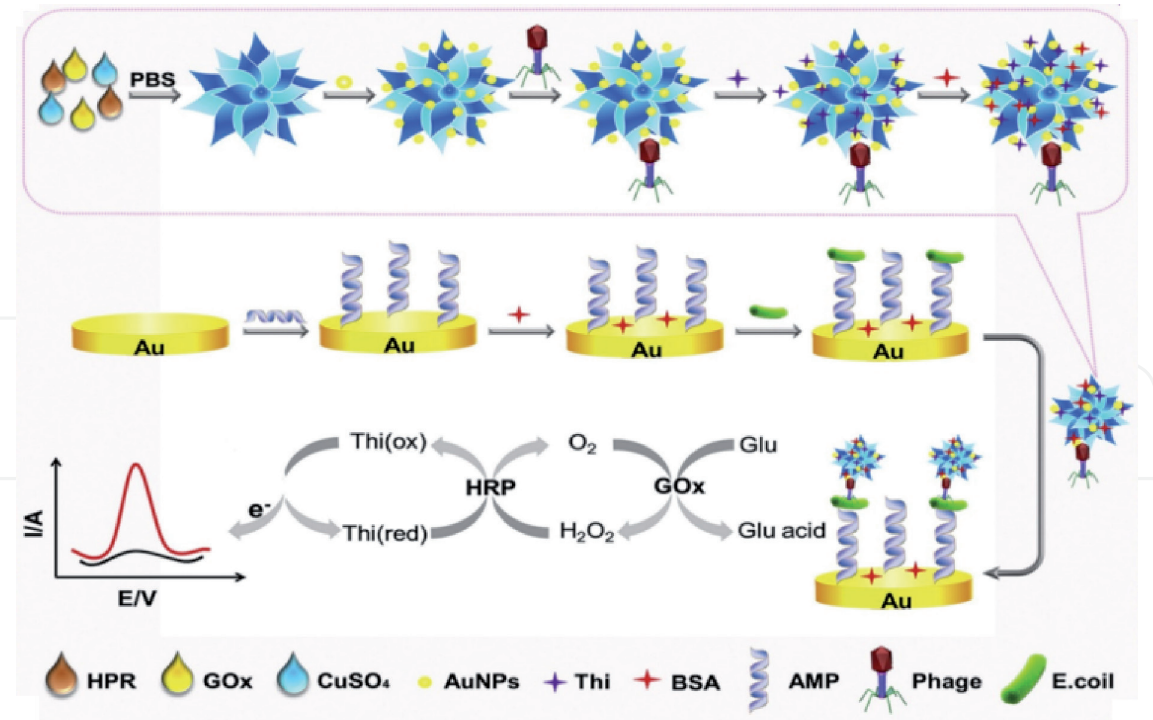
Figure 4.
Illustration of the establishment of composites (nanoflowers—AuNPs and Thi-phage) and E. coli *electrochemical screening, adapted from [41].*

biosensors. Amperometric method integrated with bacteriophage typing was reported to specifically detect bacteria like *E. coli* K12, *Bacillus cereus, and Mycobacterium smegmatis* [42]. The working principle of this biosensor was phage infection that resulted in bacterial cell lysis, subsequently releasing bacterial cell contents, like enzymes and other cell debris, into the test sample. This enzymatic release can be sensed and measured involving particular substrate. The reaction product is oxidized or reduced at working and reference electrodes, resulting in current generation [43].

2.3.2 Phage impedimetric sensors

Electrochemical impedance spectroscopy (EIS)-based sensors determine the fluctuations in impedance as a result of interactions between bio-probe and the analyte. EIS-based sensors have been utilized for bacterial detection by observing the variations on interface of solution-electrode because of the microbial capture on the biosensor surface. The target analyte binding on the sensor surface typically raises the impedance because of the insulating behavior. Phages have been utilized as a sandwiched cross-linker between bacterial cell and the electrode surface. An effective phage-EIS-based platform was reported for recognition of *E. coli* bacterial cells by T4 bacteriophage immobilization on the surface of activated carbon screen-printed electrode with LOD of ~10^4 CFU/mL [44]. By increasing bacterial concentration, a decrease in impedance was observed, which was differing from ordinary binding of intact bacterial cells on EIS biosensor. The motive behind this type of observations was because of the lytic activity of bacteriophages that directed cell lysis and the release of ionic cellular contents and alternatively a rise in conductivity. The detection was specific, and they confirmed the specificity by using *Salmonella* as a negative control. Other reports of impedimetric phage-based detections are summarized in **Table 1**.

3. Phage-based biosensors in food safety and environmental monitoring

Bacteriophage-based biosensors have been established for broad range of applications in food and environmental contaminant detection, for example, pathogens, toxins, and other environmental pollutants. Pathogens causing food contaminations are the supreme common objects of bacteriophage-based biosensors. One more field wherever bacteriophages are utilized as bio-recognition probes is clinical diagnostics of infectious diseases as explained in Section 2. **Table 1** sums up various whole phage/phage component-based biosensor applications in food safety, environmental monitoring, and infectious disease diagnosis. As this chapter does not cover all the reported methodical explanations and applications, therefore interested bibliophiles are referred to the latest literature. For potential future on-site applications, few of the most recent phage-based biosensors for pathogen detection in food and water are briefed as follow.

3.1 Food safety

Magnetoelastic (ME) phage-based biosensor was compared with TaqMan-based qPCR for *Salmonella typhimurium* detection on cantaloupe surface. LOD of both approaches was calculated by successive inoculation of cantaloupe surfaces with *S. typhimurium* suspensions. LOD of *S. typhimurium* was 2.47 ± 0.50 log CFU/2 mm^2 and 1.35 ± 0.07 log CFU/2 mm^2 area of cantaloupe surface and 6.28 and 2.41% by ME phage-based biosensor and qPCR, respectively. This comparison revealed that phage-based ME biosensor is more encouraging and an on-site applicable method to detect *S. typhimurium* on fresh fruit and vegetable surfaces [4]. In another report that was based on fluorescence imaging, *Salmonella* detection was reported involving bacteriophage-derived peptides that bind to *Salmonella enterica* (serotype Typhimurium) cells. In this report, ME biosensor coated with C4–22 phage was used to evaluate and detect *Salmonella* in/on chicken meat. In the case of on-surface detection approach, phage C4–22-based biosensor confirmed *Salmonella* binding capacity 12 times higher than control with no-phage-based sensor, while *Salmonella* cells at concentration of 7.86 × 10^5 CFU spiked per mm^2 area. In the case of in-chicken meat approach, phage C4–22 biosensors were inserted at varied depths below the surface of chicken meat (0.1, 0.5, 1.0 cm) after inoculation of *Salmonella* on the surface. The latter approach presented 23.27–33% of *Salmonella* cell absorption up to 0.1-cm deep under the surface [45].

P. aeruginosa was detected by lytic phage PaP1 displaying high specificity. For label-free *P. aeruginosa* detection, ECL biosensor involving PaP1 was developed. Biosensor was fabricated on glass carbon electrode surface through deposition of PaP1-conjugated carboxyl-graphene. Adsorption of PaP1 tail fibers and baseplate to bacterial cell wall resulted in a decrease of ECL signal, since the accumulation of non-conductive bio-complex on electrode surface disrupted the electron transfer. ECL signal dropped linearly with 1.4 × 10^2–1.4 × 10^6 CFU/mL concentration of *P. aeruginosa*, with biosensing time of 30 min and very low LOD of 56 colony-forming units per mL. With the help of this biosensor, *P. aeruginosa* was quantified in milk with varying values of recovery from 78.6 to 114.3% [3]. Similarly, phage P100 and magnetic particle composite were established to separate *L. monocytogenes* from food samples. Varied sized magnetic particles (150, 500, and 1000 nm) were used for phage P100 immobilization either physically or chemically. The coupling ratio of composites was investigated, and the capturing efficiency of *L. monocytogenes* was evaluated for each composite. The authors reported that composites developed by physical immobilization of P100 attained a greater efficiency of capture and

selectivity toward *L. monocytogenes*. These composites of phage and magnetic particles were further used to selectively isolate *L. monocytogenes* from real sample of food like whole milk and ground beef [46].

3.2 Environmental monitoring

For *E. coli* detection in water, a group of authors established and reported a rise in sensitivity of lateral flow assay based on T7 phage amplification. The assay was founded on phage-based reporter proteins: maltose-binding protein and alkaline phosphatase with 10-folds and 100-folds increased sensitivities, respectively. The increased sensitivity enabled *E. coli* detection of 10^3 CFU/mL in broth while 100 CFU/100 mL of *E. coli* in inoculated river water. Such combination of phage-based diagnosis on paper fluidics offer new platforms to establish innovative detection techniques owing to sensitivity, robustness, and specificity and are personal friendly [47]. Additional improvement in the sensitivity of this method was reported by using fluorescent quantum dots (QDs) for phage labeling. QDs increased the stability and intensity of luminous signal and also enhanced the sensitivity of epifluorescence microscopy and flow cytometry-based detection platforms. The phage head was modified with biotin tagging peptide. The QDs coated with streptavidin were permitted to become bounded to biotinylated bacteriophages. By this approach, detection limit of for *E. coli* was only 20 CFU/mL in water with detection time of 60 min [5].

Similarly, on the basis of phage fluorescent-based detection assays, *Salmonella* in sea water was detected with the help of genetically modified bacteriophages P22 with assay time of 1 h and LOD of 10 CFU/mL [48], while TNT and TNB 1 ng/mL were detected in water with the help of phage display-selected scFv [49]. Likewise, 10^4 CFU/g of *B. anthracis* in soil was detected with the help of Wβ phage involving fluorescence assay [50]. A magnetoelastic biosensor involving JRB7 phage as a bio-recognition element detected 104 spores/mL of *B. anthracis* in water [51], while impedimetric biosensor based on *S. arlettae* specific phage detected 200 CFU/mL of *S. arlettae* in river water [52].

4. Other representative applications

Despite the abovementioned applications of phage-based biosensors, **Table 1** highlights some other representative applications of phage-based biosensors in detection of pathogenic bacteria, food safety, and environmental monitoring.

5. Conclusions and prospects

Without any doubt, environmental monitoring and food safety are the main universal worries that we humans have to oppose and are constantly struggling to take them over. In this chapter, we evidently demonstrated the applications of reported promising platforms of phage-based sensors in the screening of food- and environment-related contaminants. We reviewed demonstrative phage/phage components applied in sensors' development for diagnosis of food pollutants specifically comprising pathogens and toxins. By collaboration with engineers and scientists from multidisciplinary area to design a field applicable sensor and make advancements in phage-based sensors for food safety and environmental monitoring, we expect that this chapter might bring together the technologies related to application of phage-based sensors, in food and environmental safety, and infectious disease

diagnostics. In short, applications of phage-based biosensors in the fields of food safety, environmental monitoring, and infectious disease diagnostics are vital.

Acknowledgements

Acronyms and abbreviations

Abs	antibodies
CFU	colony-forming units
E. coli	*Escherichia coli*
EIS	electrochemical impedance spectroscopy
ELISA	enzyme-linked immunosorbent assay
HRP	horseradish peroxidase
ITNAA	isothermal nucleic acid amplification
IUPAC	International Union of Pure and Applied Chemistry
LB	Luria-Bertani broth
LFA	lateral flow assay
LOD	limit of detection
OTA	ochratoxin A
PBS	phosphate-buffered saline
PCR	polymerase chain reaction
PFU	plaque-forming unit
PSA	prostate-specific antigen
QCM	quartz crystal microbalance
QDs	quantum dots
qPCR	quantitative polymerase chain reaction
RBPs	receptor-binding proteins
scFv	single-chain variable fragment
SEB	staphylococcal enterotoxin B
SERS	surface-enhanced Raman spectroscopy
SPR	surface plasmon resonance
TNB	trinitrobenzene
TNT	trinitrotoluene
TZP	tetragonal zirconia polycrystal
BCCP	biotin carboxyl carrier protein
CBM	cellulose-binding module
SOCP	small outer capsid protein
ME	magnetoelastic

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