Emergent Materials (2023) 6:15–30
https://doi.org/10.1007/s42247-022-00441-4

REVIEW

Rapid detections of food pathogens using metal, semiconducting nanoparticles, and their hybrids: a review

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Received: 19 September 2022 / Accepted: 14 December 2022 / Published online: 17 January 2023
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Abstract

Over the years, food-borne illnesses possess a major public health concern around the world, especially those in low-income countries and rural areas. In spite of all safety precautions and control measures to prevent the cause of food-borne bacterial pathogens, there are global demands for rapid detection approaches. Although traditional methods for detecting food-borne bacteria are very accurate, they are very time-consuming, expensive, and also need trained personnel. In recent years, nanotechnology-based approaches with different types of organic, inorganic, and hybrid nanomaterials have been proposed to devise novel detection methods for food pathogens. Among these, metal nanoparticles with surface plasmonic properties, semiconducting nanoparticles with photo-luminescence properties, and their hybrids with different polymeric systems have shown popularity in the design of point-of-care testing (POCT)–based food biosensors, and this is the focus of our current review. This review is majorly divided into two sections; the first one is based on the various approaches as quick detection schemes using different types of nanoparticles and their hybrids. Here, we discuss the properties of different types of plasmonic, semiconducting nanoparticles and how these properties have been used to devise the scheme for rapid detection methods. The second part of the review discusses the use of different receptors on bacterial surfaces enabling quick identification. This includes advantages and disadvantages of different types of receptors such as synthetic antibodies, tailspike proteins, and lectins that have been conjugated onto nanoparticles for binding onto targeted pathogens in the detection process.

Keywords Nanoparticles · Biosensors · Antibody · Tailspike protein · Detection · Food-borne diseases

1 Introduction

Food-borne diseases are of emergent concern as they contribute to human morbidity and mortality, necessitating a review of food quality, which is often compromised due to contamination in the presence of pathogens or their respective secreted toxins. Most of the food-borne diseases are caused by bacteria. Common examples are, *Campylobacter jejuni*, *Salmonella enterica*, *Escherichia coli* O157:H7, *Listeria monocytogenes*, *Vibrio* spp., *Staphylococcus aureus*, *Bacillus cereus*, and *Clostridium perfringens* [1, 2]. According to an estimate by the World Health Organization (WHO), 600 million cases and 420,000 death cases due to food-borne diseases are reported worldwide every year, of which 56 million people die each year [3, 4]. Medical diagnostic tools are imperative to understand the extent of the spread of global pandemics related to food-borne diseases. Most food-borne diseases are self-limiting in healthy individuals; however, antibiotics are often prescribed for severe diseases, particularly in immunocompromised patients. Indeed, prior to considering elimination approaches of a specific bacterium, rapid and accurate detection of the concerned etiological agent is essential for implementing effective control measures timely [5, 6].

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Although detection methods such as culture-based, immunological, and molecular biology-based techniques (Fig. 1) are accurate, these processes are time-consuming, expensive, need proper laboratory instruments, and require skilled persons to perform assays. For example, culture and colony-based techniques are being routinely used to detect bacteria and have the advantage of a high degree of reliability. But, these traditional methods are quite time-consuming to perform [7], need almost 2–3 days to obtain initial results, and can extend up to more than 1 week to confirm the presence of specific bacteria [5, 8]. Conventional colony count estimations and DNA amplification-based methods are summarized in Table 1. Nowadays, matrix-assisted laser desorption ionization–time of flight (MALDI-TOF) mass spectrometry is also used worldwide by a number of researchers for rapid and sensitive identification of bacteria in urinary tract infections (UTIs), blood cultures, respiratory tract infections, cerebrospinal fluids, stool samples, etc. [14]. Major drawbacks of this advanced technique is with respect to cost, portability, and requirement of skilled technicians.

A comparison of conventional and rapid detection methods (in Tables 1 and 2) clearly indicates that although conventional methods are sensitive and have accuracy toward detection, none of them are as advantageous as nanoparticle-based smart detection systems. They provide rapid detection of food pathogens and have portability and easy mode of operation (easy to carry the sensory devices to remote site areas for monitoring, and the instruments are operationally easier to handle for a non-technical person with minimal instructions) along with high sensitivity (detection limit of nano-biosensors are less, so as to identify even a very low concentration of pathogens) which in turn provides lots of opportunities in the formulation of POCT nano-devices.

In the past few years, nanotechnology-based approaches have been extensively used for the development of rapid detection schemes for food pathogens due to their small size and large-surface-to-mass ratio which facilitate the interaction with the bacterial cell wall and their metabolites in a better way by improving the sensitivity of bacterial detection [24]. Different types of nanomaterials with large surface-to-volume ratios and multi-functionality have been proposed to devise detection methods in different biological entities (Fig. 2a and b). Plasmonic, colorimetric, and photoluminescence-based detection methods have been widely implemented for rapid POCT-based detection of food pathogens in recent years [20, 29, 30]. These detection methods mostly involve the conjugation of specific receptors, either synthetic

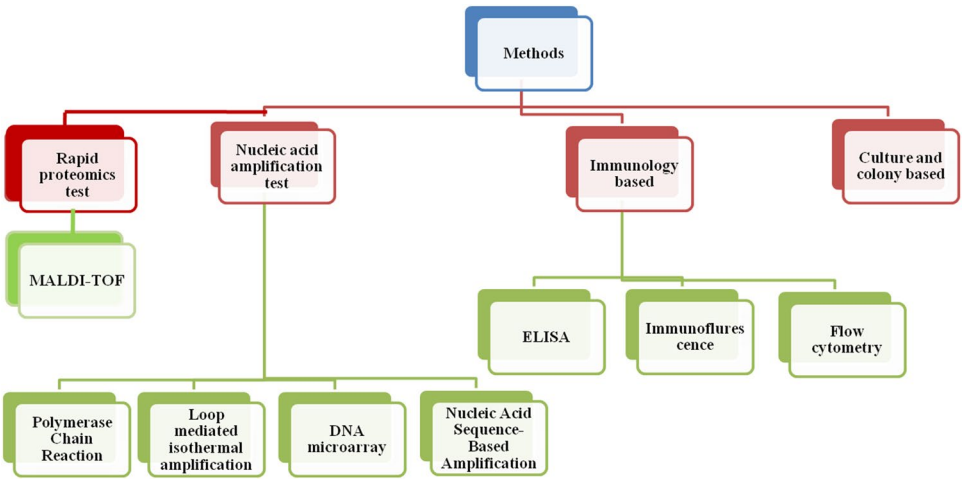

Fig. 1 Various methods used for the detection and identification of bacteria in food

Table1 Different methods used for the detection of food pathogens

Methods	Target pathogen	Limit of detection	Response time	Reference
Colony count estimation	*E. coli*	-	Up to 24 h	[9]
	Listeria moncytogenes	-	Up to 7 days	
Multiplex PCR	*Salmonella enteritidis*	10^3 cfu/ml	24 h	[10]
Real-time PCR	*Salmonella enterica*	0.1 cfu/g	10 h	[11]
Nucleic acid sequence–based amplification technique (NASBA)	*Salmonella enteritidis*	10 cfu/reaction	26 h	[12]
Loop-mediated isothermal amplification method (LAMP)	*Vibrio parahaemolyticus*	10 cfu/reaction	16 h	[13]

Table 2 Rapid detection of food pathogens using different types of nanomaterials

Types of nanoparticles		Targeted organisms	Surface functionalized	Mode of detection	Detection Time	Limit of detection	References
Metallic	AuNP	*Escherichia coli* O157:H7	Polyclonal Antibodies	Electro-chemical biosensor	45 min	10^1 cfu/ml	[15]
	AuNP	*Salmonella*	TSP	UV–vis absorption and fluorescence spectra	-	-	[16]
	Fe_3O_4	*E.coli*	Anti-*E.coli* antibody	Fluorescence	1 h	10 cfu/ml	[17]
	Fe_3O_4	*E.coli*	T7 bacteriophage	Colorimetric detection	10^4 cfu/ml in 2.5 h 10 cfu/ml in 6 h	10 cfu/ml	[18]
	AgNP	*S. aureus*	Biotinylated primary anti-*S. aureus* aptamer	Sandwich immunoassay (electrochemical immunosensor)	-	10–10^6 cfu/ml	[19]
Bimetallic	SiO_2@Au core–shell NPs	*S. aureus*	Phage S13′	Dark-field microscopy imaging	15–20 min	8×10^4 cfu/ml	[20]
	Fe_3O_4@ Al_2O_3 MNPs	*Acinetobacter baumannii*	Tail fibers of bacteriophages ϕAB2 and ϕAB6	Matrix-assisted laser desorption/ionization mass spectrometry	10 min	~10^4 to 10^5 cells/ml	[21]
Semiconducting	SWCNT–gold NP nanohybrids	*S. typhimurium DT104*	Rhodamine 6G (Rh6G)-modified monoclonal AC04 antibody	Surface-enhanced Raman scattering	15 min	10^5 cfu/ml	[22]
	Quantum dots to carbon nanoparticles	*Vibrio parahaemolyticus* and *Salmonella typhimurium*	Aptamer based biosensor	Dual florescence resonance energy transfer from QDs to carbon NPs	80 min	25–35 cfu/ml	[23]

(e.g. antibody) or natural (DNA, protein, bacteriophages, enzyme, etc.) onto nanoparticle surface in order to increase the sensitivity of the detection systems.

Our review primarily discusses about various types of POCT detection methods using different types of nanoparticles and their hybrids. The review has two parts. The first part discusses the principle of detection methods based on the color-tunable properties of plasmonic, semiconducting nanoparticles, and their hybrids. The second one is based on the use of different types of bio-recognition elements, synthetic antibody, tailspike proteins, and bacteriophages and their conjugation onto nanoparticle surfaces which enables the detection of specific pathogens precisely. Moreover, the advantages and disadvantages of synthetic and natural receptors are also discussed. Finally, we focus on the limitation of different detection methods and speculate a future perspective of a possible rapid detection approach for foodborne bacteria.

2 Different types of nanoparticles and their applications in detection of food pathogens

Nanoparticles used for rapid detection can be broadly divided into three categories, namely metal, semiconducting, and their hybrids such as polymer nanocomposites.

2.1 Types of nanoparticles and their detection principle

2.1.1 Metal nanoparticles

Metallic nanoparticles are very popular due to their surface plasmonic color-tunable properties and have wide-range applications in different sectors [31]. Surface plasmon resonance (SPR) is the resonant oscillation of conduction electrons at the interface of metal nanoparticles stimulated by incident light. The surface plasmon properties can be tuned

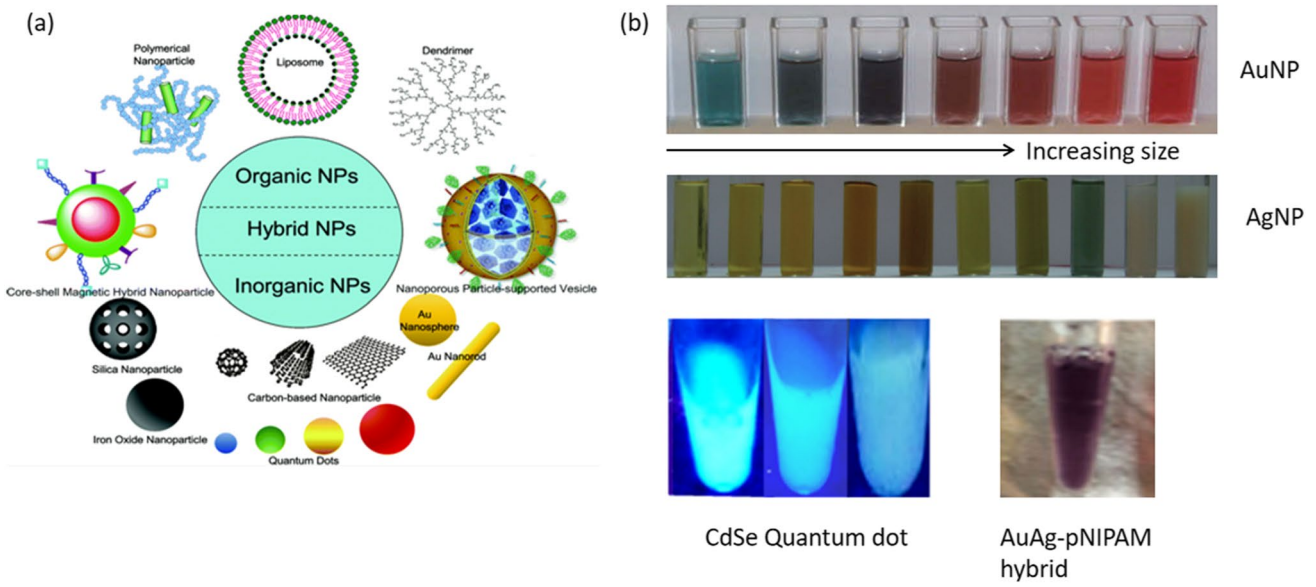

Fig. 2 **a** Image showing a few such examples of different types of nanomaterials with other small particles based on their size (source: Ding H M et. al., 2018 [25]). **b** Various distinct colors are shown by AuNP (source: Huang X et. al., 2010 [26]), AgNP (source: Mukherji S et. al., 2019 [27]), and semiconducting nanoparticles (source: Belza J et. al., 2021 [28])

over a broad-wavelength range by controlling the morphology, shape, and size of nanoparticles. Moreover, any changes in the dielectric environment around the particle surface also strongly affect the color-tunable properties due to shift in surface plasmon resonance making it a very suitable candidate in pathogen detection. Metal nanoparticles are usually prepared by the chemical reduction method by adding a reducing agent in the reaction mixture containing metal-ion precursors. The larger surface area of metal nanoparticles enables them to adsorb small molecules and can also be modified with various chemical functional groups. They can easily conjugate with ligands, antibodies, proteins, etc. leading to a wide range of applications in biomedical and environmental sectors [32, 33]. Gold, silver, and their bi-metallic composites are widely used in different biomedical applications due to their distinct surface plasmonic properties.

Most label-free LSPR (localized surface plasmon resonance) sensors work by means of direct assays. Aptamers present in the solution conjugate with the AuNPs and act as a stabilizer by preventing AuNP aggregation. Hence, no change in color. When target bacterium is present, aptamers will not be able to prevent AuNPs aggregation anymore because of the strong interaction between aptamers/antibodies and target bacterium. AuNPs start to aggregate which ultimately leads to a color change from red to purple as illustrated in a scheme below (Fig. 3a). There are certain limitations in direct assay where protein molecules present in different food samples might lead to false detection of bacteria as they prevent aggregation of metal nanoparticles specifically AuNPs by stabilizing them. Kim H S et. al. (2017) [34] and Kim YJ et. al. (2018) [35] successfully demonstrated an LSPR-based indirect assay for the detection of food-borne bacteria in their studies. When target bacterium is present, aptamers readily form complexes with it because of strong interaction, and the reaction mixture is subjected to centrifugation. All aptamer–bacterium complexes are present in the pellet after centrifugation. Now, when AuNPs are added to the supernatant, they will readily start to aggregate due to absence of aptamers that help the AuNPs to stay in a non-aggregated mono-disperse form. This leads to a rapid color change from red to purple which is shown in a schematic in Fig. 3b. In the absense of target bacterium, free aptamers present in the supernatant will act as stabilizer that will prevent salt-induced aggregation of nanoparticles, and hence, no change in color is seen.

Metal nanoparticles are firstly functionalized with receptor biomolecules specific to target analyte, and when they come in contact with target pathogens, a change in binding-induced refractive index is observed accompanied by a shift in the surface plasmon resonance peak. This leads to a change in color of metal nanoparticles which can be employed as rapid POCT-based detection of food pathogens. The surface plasmon resonance peak shift of metal nanoparticles in response to the target pathogen is shown in a schematic in Fig. 4a. Iron nanoparticles (FeNPs) have magnetic responsive properties that can be integrated with plasmonic nanoparticles in order to use for quick separation and detection applications [37, 38]. In addition, metal nanoparticles can have bi-metallic properties where two different types of nanoparticles can be fused having both properties preserved.

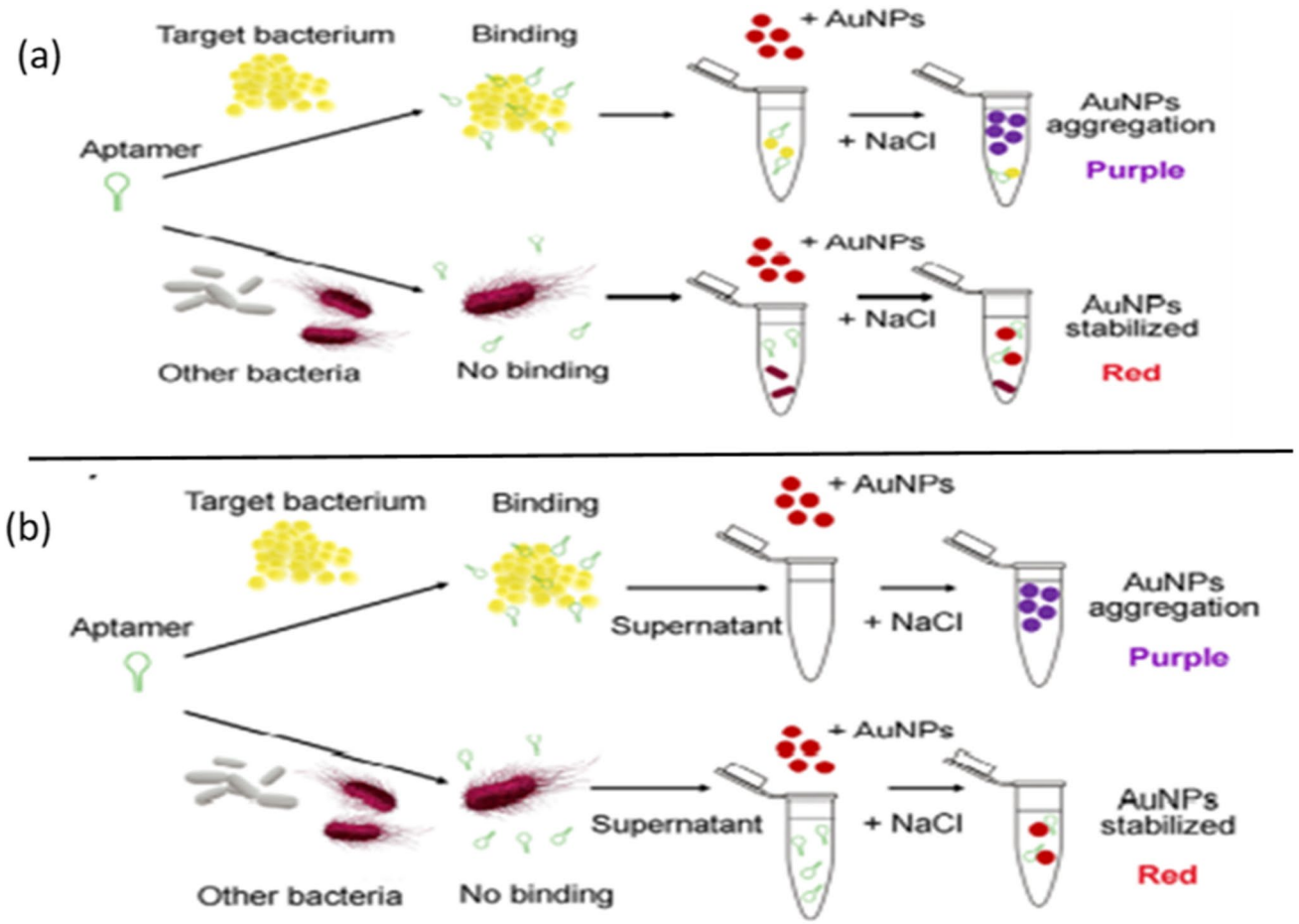

Fig. 3 Schematic representation of **a** direct assay and **b** indirect assay for the detection of food-borne bacteria (source: Marin M et. al., 2021 [7])

Bi-metallic nanoparticles are much more advantageous compared to monometallic nanoparticles due to their higher catalytic properties, enhanced thermal conductivity, better optical properties, etc. [39, 40].

2.1.2 Semiconducting nanoparticles

Semiconducting NPs are fluorescent materials that exhibit a variety of quantum phenomena as well as size-dependent material characteristics that can be used in a variety of applications [41–43]. Quantum dots (QDs) and carbon dots (CDs) are two examples under this category. Quantum dots are nano-sized crystalline clusters [44] that can be made from semiconductor materials such as indium phosphide [45], cadmium selenide [46], cadmium sulfide [47], cadmium telluride [48], or gallium arsenide [49]. These materials are quite useful for bio-imaging, labeling, and sensing because of their exceptional properties, such as high quantum yield, high molar extinction coefficients, high resistance to photo-bleaching, and exceptional resistance to photo and chemical degradation [50]. On the other hand, carbon dots are of less than 10 nm, quasi-spherical crystalline graphitic nanoparticles that are widely used due to their unusual structure and photophysical features [51] and have been proposed as potential carriers for biological research. The use of carbon nanotubes, magnetic nanoparticles, and quantum dot-based nanoprobes for in vivo focused imaging can pave the way for faster, less invasive, and thorough identification of bacteria enabling better diagnosis. When fluorescence semiconducting nanoparticles absorb photons from incident light, they move onto an electronically excited state. As the excited molecules return to their ground state, they emit a photon of lower energy corresponding to a longer wavelength than the absorbed photon which is attributed to the characteristic color shown by these nanoparticles. These nanoparticles can be functionalized with receptor biomolecules, and when they come in contact with a specific target analyte, a change in fluorescence intensity and peak shift is recorded. This unique property can be exploited for the rapid detection of food pathogens which is shown in Fig. 4b.

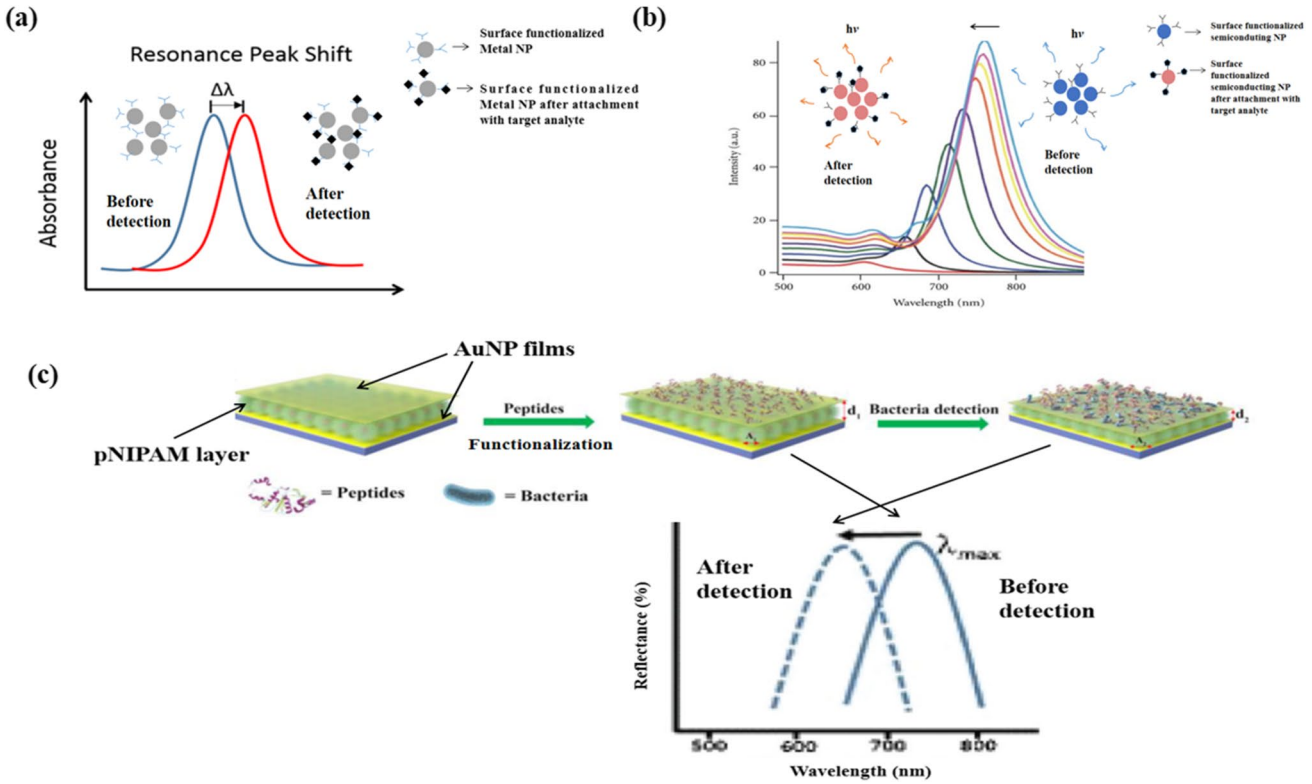

Fig. 4 **a** Metal nanoparticle–based detection of food pathogen by monitoring resonance peak shift in absorbance spectra. **b** Semiconducting nanoparticle–based detection of food pathogen by change in % intensity and peak shift fluorescence spectra. **c** AuNP@pPNIPAM etalon–based (source: Xia X et. al., 2022 [36]) detection of pathogen by monitoring capacitance change in response to pressure changes in the etalon and corresponding change in reflectance

2.1.3 Hybrid nanoparticles

Hybrid systems are nanostructures with a combination of different organic–inorganic and organic–organic materials forming a functional structure in a nanoscale dimension with desired properties. One such type of hybrid nano-system is polymer-hybrid. These particles can be more advantageous as they are custom-made synthetic polymers [52]. Among several stimuli-responsive polymeric materials for nanocomposite systems, PNIPAM(Poly(N-isopropylacrylamide)) has a commendable responsive behavior [53]. It is a stimuli-responsive microgel that is usually preferred for the preparation of hydrogels compared to any other polymeric system. PNIPAM matrix is capable of volume phase transition by controlling temperature, pH, pressure, and ionic strength [54, 55].

Mutharani B et al. (2020) evaluated various physical and chemical properties of PNIPAM microgels and hybrid NP microgels [56]. For encapsulation of nanoparticle in polymer matrix, PNIPAM is cross-linked for microgel formation leading to the synthesis of hybrid nanomaterials. This makes them exhibit remarkable properties such as increased catalytic activity due to morphologies with highly active facets [57, 58]. The use of hybrid nanoparticles (a combination of soft matter and nanomaterials) are in recent trends as major researchers are using it in different sectors due to its mixed property, extremely large surface-to-volume ratios [59], and multiple functions [60–62]. Shu T et al. (2022), in one of their recent studies, showed how multi-responsive microgel/nanoparticle hybrid systems can be used successfully as optical sensors [63]. These hybrid systems can be designed by sandwiching a layer of PNIPAM between two thin films of AuNP. These films are functionalized with receptor biomolecules, and when they come in contact with a specific target analyte, sandwiched PNIPAM layer undergoes a volume change which leads to a change in capacitance of the etalon and a change in reflectance as shown in Fig. 4c.

2.2 Implementation of detection principle in food pathogens

Detection methods include colony count estimation, multiplex and real-time PCR, nucleic acid sequence amplification, and various other immunology-based techniques (Fig. 1). Although these techniques provide accuracy in data, they are too time-consuming (up to 24 h or more), expensive, and require skilled persons to conduct the test. On the other

hand, nanoparticle-based detection techniques are cost-effective, less time-consuming, and also do not require any high-end instrument to provide accurate data. Detailed analysis of different conventional and nanoparticle-based detection techniques are shown in Tables 1 and 2 respectively.

2.2.1 Detection of *S. typhimurium*/*Vibrio parahaemolyticus*

Duan N et. al. (2013) [64] evolved a singular approach, primarily based on FRET (fluorescence resonance energy transfer) for the simultaneous detection of *Vibrio parahaemolyticus* and *Salmonella typhimurium*. They used each green and red emitting quantum dots, modified with amine aptamers as energy donors and carbon nanoparticles (CNPs) as acceptors of energy in the FRET system. The gQD-aptamer is used to detect *V. parahaemolyticus*, and the rQD-aptamer is used to detect *S. typhimurium*. Optimized concentrations of both the shade QDs-aptamer were taken with the aid of thinking about their fluorescence depth and binding saturation and were taken in the ratio of gQDs-aptamer to rQDs-aptamer as 1:2.5. When CNPs were added to free QDs, the fluorescence quenching effect is very negligible, but when CNPs were added to QDs-aptamers, the fluorescence quenching effect is highly efficient. When the solution of QDs-aptamers and CNPs comes in contact with the target bacteria, the aptamers preferentially attach to bacteria and form the QDs-aptamer-target complex (Fig. 5a), which would not adsorb onto the surface of CNPs due to the weakening of л stacking between CNPs and aptamer. Thus, higher the target bacteria concentration, stronger the fluorescence intensity (F). The fluorescence signals of QDs-apt at different concentrations of specific bacteria are shown in Fig. 5b. They have also found that for both *V. parahaemolyticus* and *S. typhimurium*, linear ranges were 50–106 cfu/ml with a detection limit of 25 cfu/ml and 35 cfu/ml, respectively.

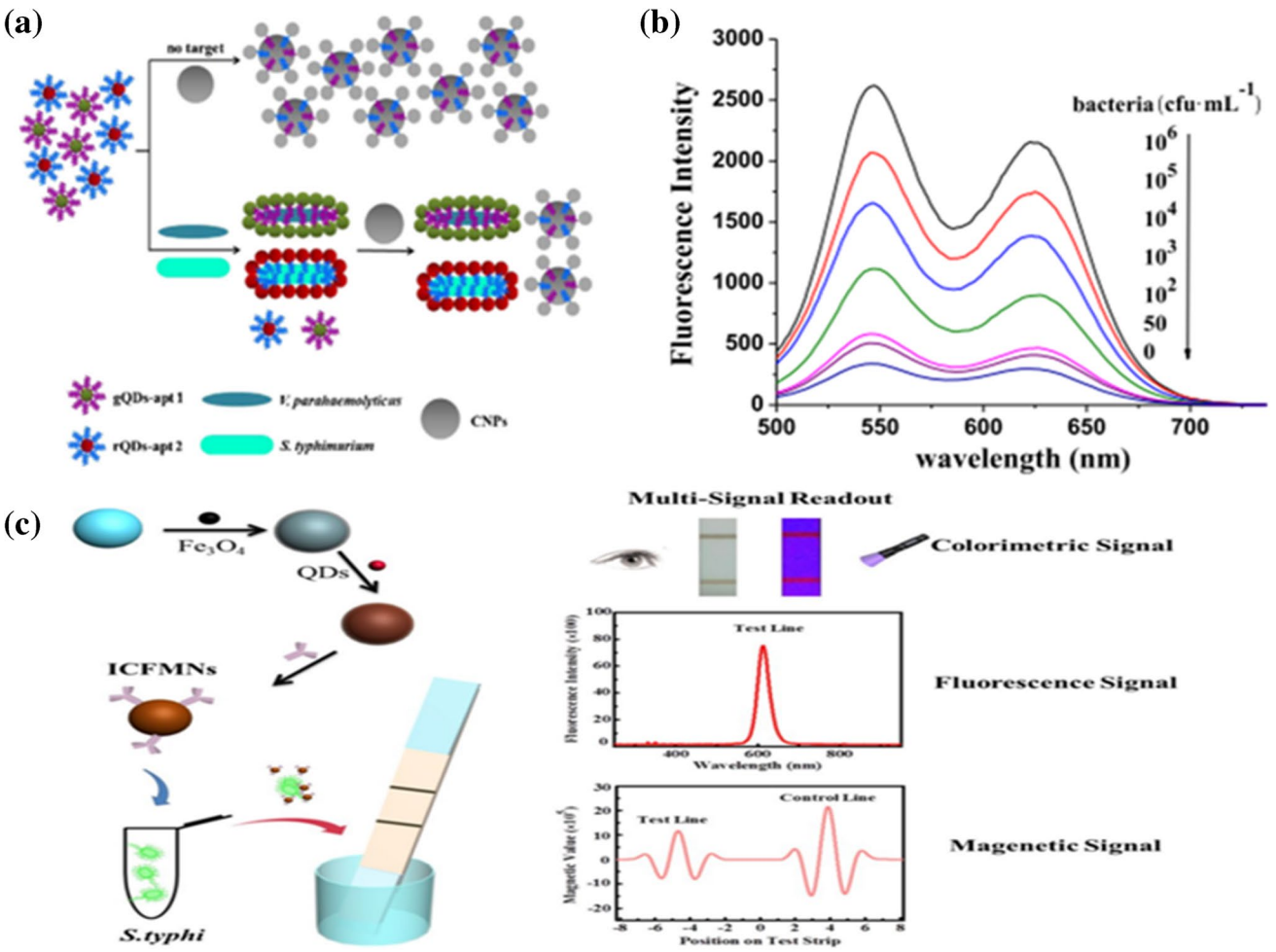

Fig. 5 **a** Schematic representation of dual FRET energy transfer from QDs-aptamer to CNPs. **b** Graphical representation of fluorescence intensity with wavelength at different concentrations of pathogens (source: Duan N et. al., 2015 [23]). **c** Colorimetric and quantitative detection of *S. typhimurium* using CFMN-based hybrid material (source: Hu J et. al., 2018 [65])

2.2.2 Detection of *E. coli*

Mohamadi E et al. (2017) [66] used photoluminescence properties of CdSe-QDs for the rapid detection of *Escherichia coli* (*E. coli*) which is a common pathogen present in food products. They collected specific bacteria and suspended them in PBS buffer solution and thereafter mixed the suspension with CdSe-EDC mixture in order to obtain QD-tagged *E.coli* (Fig. 5b). This study focuses on using a synthesized CdSe-QDs and how it can be used as a fluorescent probe for detection of food-borne pathogen *E. coli* in agar medium and groundfish substrates. This method also has great potential and can be used in food safety measurements.

2.2.3 Detection of *S. typhimurium*

Hu J et al. (2018) [65] in their study showed a rapid POC colorimetric detection of *S. typhimurium* using a hybrid material which was an assembly of Fe_3O_4 and quantum dots. This technique is based on a combination of properties shown by metallic magnetic nanoparticles and semiconductor nanoparticles. They used Pst-AAm-COOH nanospheres and performed a layer-by-layer assembly of poly (ethylene imine) and Fe_3O_4 or quantum dots over it. This hybrid material, CFMN (colorimetric-fluorescent-magnetic nanospheres), had an outer silica layer for more stability and was also further functionalized with carboxyl groups for antibody coupling. Fe_3O_4 and quantum dots provide strong magnetic and fluorescent signals respectively. *S. typhimurium* was tagged with the nuclear dye Hoechst 33,342 which showed blue fluorescence, and CFMN material showed red fluorescence under UV light. By using this CFMN material, they formulated a lateral flow immunoassay (LFIA) chip (Fig. 5c) that, in contact with *S. typhimurium*, changes color to brown. There is also the appearance of a red fluorescence band on the test line which indicates the presence of S. *typhimurium*. The change in the magnetic signal of the *S. typhi*/CFMN complex provided the quantitative analysis of *S. typhimurium* with a detection limit of 3.5×10^3 cfu/ml. This multi-signal CFMN-based LFIA chip holds great potential for food safety.

2.2.4 Detection of *E. coli*/*Salmonella aureus*

Yamada K et al. (2016) [67] developed a multi-junction sensor based on a single-walled carbon nanotube (SWCNT) which is a great semiconductor for the rapid detection of multiple food-borne pathogens. They have created a chip containing a 2×2 array of gold tungsten wire coated with polyethylenimine (PEI) and SWCNTs and functionalized it with streptavidin and biotinylated antibodies. Initially, they measured the current across the four junctions of the chip, then they calculated the change in current across different junctions under the influence of different concentrations of pathogens. They checked the effect of change in current for pure *E. coli* and pure *S. aureus* and also did the simultaneous detection of both. With an increase in the concentration of pathogens, the resistance across each junction of the 2×2 array increases. Ultimately, this changes the electrical properties of the SWCNT sensor as resistance is inversely proportional to current, and with an increase in concentration, the electric current value decreases. So, the detection of food pathogens can be achieved by measuring the change in current across the junction of the SWCNT-based chip.

2.2.5 Detection of *V. parahaemolyticus*

Wu S et. al. (2015) [68] in their study showed a similar colorimetric aptamer-based bacteria detection technique. AuNPs were modified with horseradish peroxidase (HRP) enzyme, and then two different aptamers Apt1 and Apt2 were added to the HRP-modified AuNP. Apt2 is conveyed by magnetic nanoparticles. A magnetic field was applied to the solution which helped in the formation of AuNPs-HRP-Apt1-Target-Apt2-MNP complexes. This complex can detect *V. parahaemolyticus* bacteria in presence of tetramethylbenzidine (TMB) and H_2O_2 by giving a colorimetric signal which was in proportion to the bacterial concentration present in the sample having a limit of detection up to 10 cfu/ml. When the target pathogen is absent, the AuNPs-HRP-Apt1 complex is free and does not form any further complex with Apt2-MNPs and hence cannot be detected by a magnet. So, no signal can be observed upon the addition of TMB to the solution.

3 Surface functionalization with bio-receptors

Appropriate functionalization of nanoparticles has greatly enabled accuracy for the detection of various food-borne bacteria. Therefore, it is important to understand the functionalization procedure. Briefly, the nanomaterials are further functionalized to execute modifications on their surface to enhance the efficiency of binding to target bacteria by minimizing the off-target binding and making these materials more efficient in several translational applications including the detection and the identification of bacteria and other pathogens (Fig. 6). The functionalization of different nanoparticles plays an important role in health-related applications as it completely depends upon both the chemical and physical interaction between the ligands and nanoparticles [69]. Most importantly, it is the linking property and the physicochemical adsorption property which leads to effective modification of the surface chemistry of the nanoparticle to enhance its activity and proved to be a significant

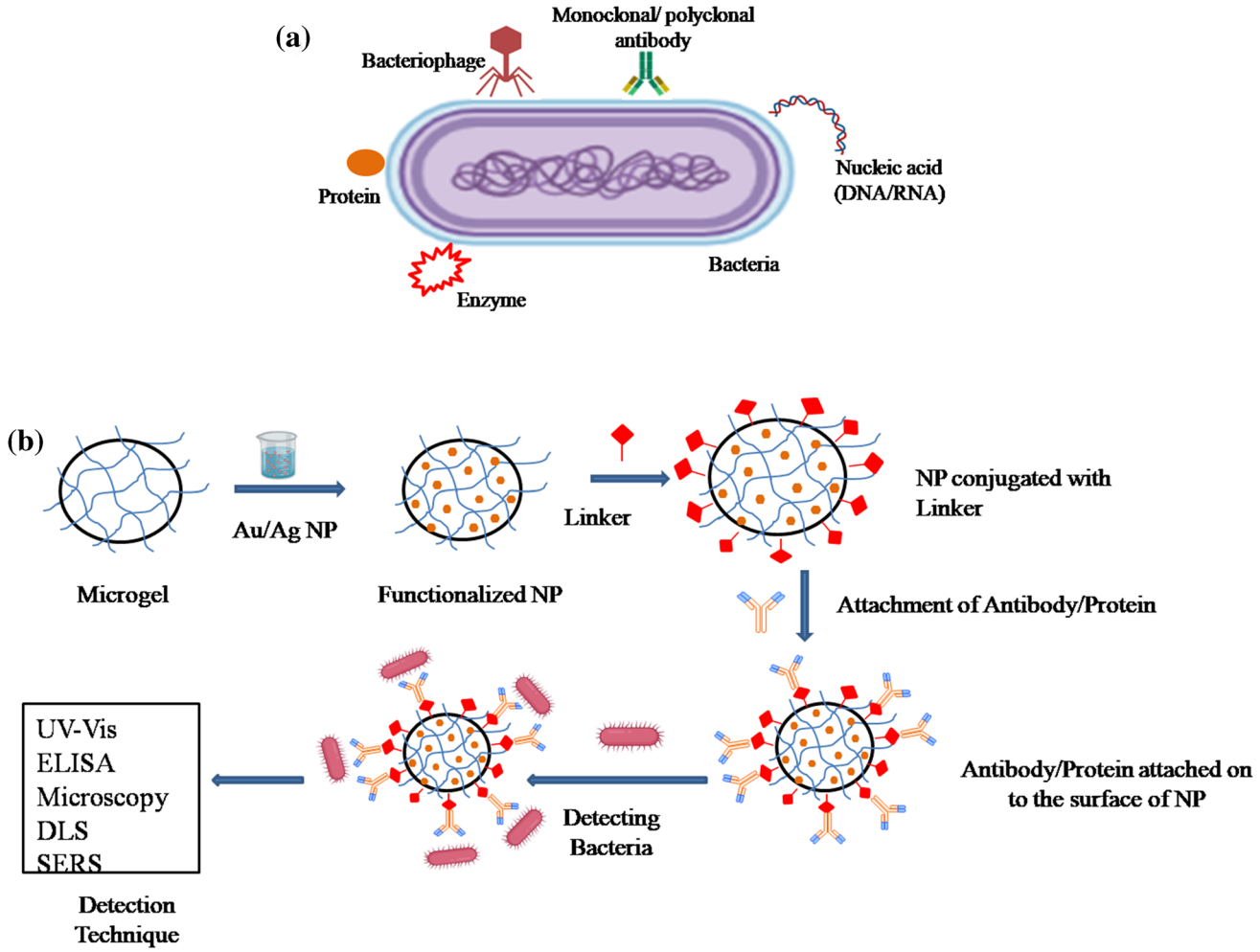

Fig. 6 **a** Various types of bio-receptors used for detection. **b** Schematic diagram showing the detection of bacteria using different techniques

addition in increasing the specificity of detection of bacteria. Generally, the functionalization of the surface of nanoparticles is performed by conjugation with several bio-molecules or bio-receptors.

Bio-receptors or biological recognition elements have been widely studied for the development of quick approaches for food-borne pathogens in order to minimize the drawbacks caused due to conventional methods. These novel pathogen molecular approaches are being developed for a variety of characteristics of detection, including sensitivity, speed, selectivity, viable cell discrimination, and applicability for in situ analysis. A bio-receptor is a molecular moiety that helps in the recognition of the species using a biological mechanism as they help in the attachment of the analyte of interest to the sensor so that it can be measured. They also facilitate the incorporation of specific properties on the surface of the NPs by increasing the surface-to-volume ratio [70] causing less toxicity, high efficiency, and stability [69] in contrast to the conventional NPs that are unstable over a period of time and have high toxicity level [71]. Bio-receptors can be divided into various types such as antibodies, enzymes, nucleic acids, proteins, biological structures, or cells; bio-mimetic, bacteriophage, and tailspike proteins (TSP) (Fig. 6a). In this section, we give an overview of different biological molecules on bacteria that can be used as targets for detection along with describing both advantages and disadvantages.

3.1 Enzymes

Enzymes are one of the initial generations as bio-recognition elements and are extensively used in the research field due to its high commercial availability and due to its simple isolation and purification process from various sources. The major advantages of using enzymes are their great sensitivity, direct visibility, and long-term stability [72]. However, there are significant drawbacks to utilizing enzymes as labels, such as several assay stages and the risk

of endogenous enzyme interference. Many enzyme-based detection methods are easy to examine as they do not require any expensive or difficult equipment [73]. However, enzyme stability remains a challenge, and the capacity to maintain enzyme activity for a prolonged time is a concern [74].

3.2 Antibodies

Antibodies are frequently used as bio-receptors due to their selective nature. These molecules act as a potent analytical tool, and their capacity to recognize molecular structures (antigens) on bacteria [73, 75] is due to their lock and key model of interaction [76]. According to literature, directly assembled AuNPs onto SPR chip surfaces instead of labeling them with antibodies in order to enhance the SPR signal as a label-free detection system by genetically fusing GBP to Staphylococcal protein A acts as a novel crosslinker [77]. Based on the advantages of AuNP, a novel and sensitive assay for the analysis of *Staphylococcus aureus* (*S. aureus*) and *Lactobacillus* (spp.) using antibodies were developed. Here, synthesized AuNPs were conjugated with antibodies using NHS-EDC coupling [78]. Some of the major advantages of using antibodies as bio-receptors are specificity, affinity, and limit of detection around 10–100 cfu/ml [79]. Disadvantages of using antibodies as bio-receptors are its purity, expensive, cross-reactivity, ineffective in high temperatures, type of sample used, unstable in case of structure and composition, and difficulty to develop.

3.3 Nucleic acid

The use of DNA (deoxyribonucleic acid) and RNA (ribonucleic acid) are also bio-recognition elements based on its complementary base pairs that are the genetic materials of an organism, and these are self-replicating [73]. According to Lee K J et. al. (2018) [80], the detection of both negative and gram-positive bacteria can be done by using a nuclease-responsive DNA probe. The advantages of using these molecules are cost-effectiveness and stability in structure and composition. The major disadvantage is that they do not provide any information regarding the viability of identified cells because they cannot distinguish between DNA generated from live and dead cells.

3.4 Bacteriophages and their components

Bacteriophages have recently been used as bio-recognition components to identify a variety of harmful bacteria. Phages are viruses that connect to specific receptors on the bacterial surface and inject their genetic material inside the organism. These particles range in size from 20 to 200 nm [81]. Phages use their tailspike proteins to identify bacterial receptors. As the identification is so specific, it can be used for bacterial typing, paving the way for the creation of particular pathogen detection methods. Bacteriophage tail apparatus has an ability to bind with an array of cell surface structures like LPS (lipopolysaccharides), different components of the cell wall, and proteins. As per Huan Peng et al. (2018) [82] bacteria can be detected easily using phages when combined with AuNP. Here, the capsids of chimeric phages are thiolated, and when these phages are incubated with the bacterial sample, it leads to subsequent aggregation.

Basic advantages of using bacteriophages as bio-receptors are their specificity, easy to amplify, cheap, resistant to temperature, pH, organic solvents, and also their resistance towards the adverse extracellular environment [83]. Some of its limitations are optimization of phage size, capture efficiency, overexposure to the surface-immobilized phages causing bacterial lysis, large size, and expression of binding units on the phage's surface for specific binding to bacteria [83].

Phage TSPs have been proposed as an alternative bacterial recognition probe, demonstrating that they can overcome the limitations of whole bacteriophages. Due to the smaller size of the molecules, phage TSPs have a better capture efficiency. Furthermore, genetically expressing desirable tags on TSPs can improve their affinity and binding properties. For instance, using silica-encapsulated Raman-reporter embedded (SERS) nanoprobes, named nano-aggregate embedded beads (NAEBs), when conjugated with tailspike protein (TSP) of *Salmonella* enable a highly specific and ultrasensitive optical transduction platform for detection [16]. TSPs have a number of advantages over antibodies and whole-phage methods, in addition to their high level of stability [84–86]. Increased storage stability, no influence of virulence factor, yield in high quantity, and easy manipulation are also some of the major advantages for the use of TSPs over whole bacteriophages [81]. A few others include portability, high specificity, production of results in real-time, speed of response, and multiple pathogen detection in case of both laboratory and field.

4 Conjugation of bio-receptor onto the surface of nanoparticles

Non-covalent (reversible) and covalent (irreversible) conjugations are the two primary categories of conjugation procedures. Each approach has its own set of advantages and disadvantages, so the conjugation method selected is determined by the intended usage [87]. Hydrophobic contacts, electrostatic, and ionic interactions are different types of non-covalent interactions in which bio-receptors or other functionalized groups are nonspecifically adsorbed onto nanoparticles while the nanoparticles remain negatively charged, ensuring their colloidal stability [88, 89].

The covalent conjugation procedures [90, 91] employ binding of antibodies directly to the surface of nanoparticles using a mediator linker, or via adapter molecules like (strept) avidin and biotin [92, 93]. A condensation reaction can be used to produce amide bonds when carboxylic groups are treated with primary amines. As a result, a water-soluble carbodiimide (such as EDC, 1-ethyl-3-(3-(dimethylaminopropyl)-carbodiimide) is typically utilized. The activated group is reactive toward primary amines after creating an intermediate product with the carboxylic moiety. Active ester compounds (N-hydroxy-succinimide; NHS) can be employed to create amide linkages in the presence of primary amines on the particle surface [92]. This amide bond links the primary amine of the lysine residue of protein or antibody with the carboxylic group of the NP. EDC is utilized to activate the carboxyl group on the surface of nanoparticles to form a cross-linker in the EDC/NHS activation chemistry used for covalent conjugation. The resultant intermediate can attach to the antibody's main amines, but it is unstable and hydrolyzes easily. Sulfo-NHS is combined with EDC to produce a more stable amine-reactive intermediate that binds to the antibody's main amines (Fig. 7). This mode of conjugation technique is widely accepted. A review by Chen J et. al. (2017) [95] focused on the synergistic relationship between pathogen recognition components (i.e. protein/antibodies) and nanomaterial surface conjugation [95]. Addressing a similar context in this review, we refer to the term "surface functionalization" as the immobilization of the recognition element on the nanomaterial surface.

A few disadvantages of using the non-covalent conjugation method are the need for a high concentration of antibodies for the preparation of antibody–NP conjugates, the biological response being difficult to control due to electrostatic attraction between the conjugates, random orientation of antibodies on the nanoparticle surface, change in pH affecting the binding efficiency and, lastly, influence of other similar molecules replacing the bio-receptors during the procedure [92, 96, 97].

In the following (Table 2), we will be mainly emphasizing on the biological importance of plasmonic and photoluminescence nanoparticles in the detection/identification of food bacterial pathogens.

Surface modification of NPs refers to the conjugation of bioreceptors or chemicals onto the surface to enhance the characteristics and strike the target with high accuracy [98, 99]. According to previous studies, when metallic nanoparticles (AgNPs, AuNPs, Fe_3O_4) are conjugated with antibodies or phages, they can easily detect different pathogens (*Escherichia coli, Pseudomonas aeruginosa, Vibrio cholerae, Xanthomonas campestris, Lactobacillus spp., Staphylococcus aureus,* etc.) [77, 78, 82, 16]. These functionalized NPs have excellent physical features, such as anti-agglomeration, better optical qualities, anti-corrosion, biocompatibility, solubility, biodistribution, and non-invasive nature [100, 101]. Through surface modification, functionalization improves the qualities and features of nanoparticles, improves efficacy, and reduces toxicity levels of NPs [70].

Although functionalized NPs have a number of advantages for their use, there are limitations during the synthesis of such particles as well as using them for detection purposes. One of the major factors affecting bacterial detection is accuracy during surface modification [102, 103]. Synthesis and attachment of the proper size and shape of these particles are also a critical step that affects detection [103].

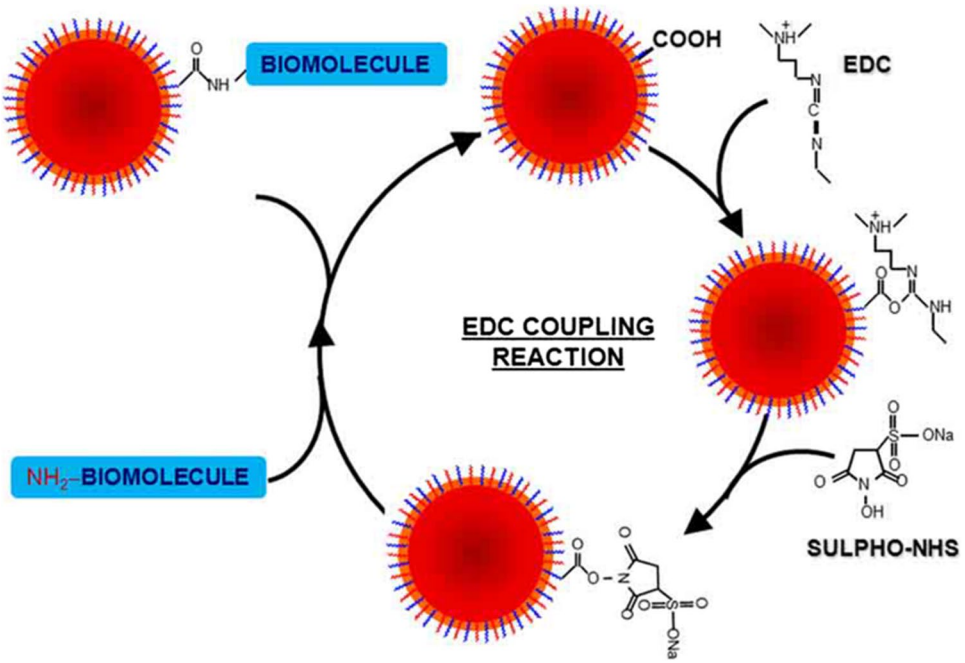

Fig. 7 Schematic diagram showing surface functionalization of NPs using EDC/NHS conjugation method with bio-receptors for detection of bacteria (source: Conde J et al., 2014 [94])

Functionalized NPs can be toxic too [104]. These major limitations can be partly overcomed by maintaining suitable environmental factors such as pH and temperature, to avoid change in the behavioral factor of the functionalized NPs [103, 105]. Furthermore, a proper bio-distribution, biocompatibility, proper retention, less cytotoxicity, and proper clearance time are also essential factors to reduce the drawbacks of functionalized NPs [103].

5 Conclusions

Infections caused by food pathogens are of global health concern and result in significant mortality and morbidity. Over recent years, there is a growing demand all over the world to use rapid diagnostic methods which are cost-effective, simple, and affordable for deadly chronic infectious diseases such as diabetes, tuberculosis, malaria, and diarrhea (106–108) as these are the leading problems in tropical and sub-tropical developing countries where sanitation and hygiene are a major cause for concern [109–111].

The use of metal, semiconducting, and their hybrid nanoparticles are considered as advanced quick detection approaches for food-borne bacterial pathogens as discussed in this review article. Smart detection of bacteria using such type of nano-enabled sensing approaches is a boon to mankind as currently available conventional culture-based approaches lead to delayed treatment procedures by health professionals to cure diseases caused due to use of contaminated food. It is sure that such kind of nanoparticles hold a great promise to develop sensors for bacterial detection both in laboratory settings as well as in body fluids in vivo by tracking these organisms in vivo. To implement these nano-based techniques for detection, surface functionalization of nanoparticles is the most critical challenge although the method includes a few drawbacks like stability and lacking monodispersity with proper shape and size due to self-aggregation. A single step during the functionalization of the NPs should be considered. Along with this the size range of NPs and controlled functionalization with desired molecules should also be considered for its use as nanoprobes. Another concern is that the functionalized nanoparticle-based approaches for the quick detection of food-borne pathogens have not been successfully applied for clinical practice due to the lack of evidences on efficient targeting ability, biocompatibility, clearance, proper bio-distribution, and toxicity [112] causing inconsistency and uncertainty in obtaining regulatory approval. Therefore, appropriate strategies should be developed to focus on techniques for the synthesis of highly reproducible functionalized nanoparticles which can be multi-dimensionally useful in different biological sectors, including clinical settings.

In the early years of nanotechnology research, the primordial focus was to efficiently fabricate nanostructures. Two of the predominant methods to fabricate nanostructures "Top-down synthesis and Bottom-up synthesis" were established by material scientists [113]. Later, these methods were exploited for pioneering nano-biosensor research and development. The small size and large-surface-to-mass ratio of nanomaterials facilitates the interaction with bacterial metabolites and bacterial cell wall. Further, the flexibility of nanomaterials to mold its shape (e.g., nanotubes, nanowires, nanorods, nanoparticles, cantilevers, and nanoarray) for desired bacterial interaction plays an important role in improving the sensitivity of bacterial detection [23]. Such small-scale interactions subjugate the alteration of the bacterial physicochemical properties [114]. Our analysis in this review, the first of its kind, provides ample evidences on currently existing nano-hybrid-based methods for bacterial detection, especially from the food-borne origin (although these techniques can be used for bacterial detection in other sources too). The article will throw light on scientific community to achieve knowledge on this and may prompt smart researchers to open up new avenues for developing better specificity and sensitivity-based approaches for bacterial detection.

6 Author's perspectives

Antibody functionalized poly (N-isoproplyacrylamide)-*co*-poly(acrylic acid) (PNIPAM-PAA)-based microgels encapsulated with gold nanoparticles serve as an innovative approach for various translational applications due to the presence of tags, high sensitivity, and specificity for target bacteria [115]. Particularly, there are several drawbacks for the detection of pathogens using the established streptavidin–biotin chemistry. Furthermore, antibodies are difficult to manufacture in large quantities, require considerable expertise, and are dependent on animal experimentation [116, 117]. Due to such concerned difficulties while using antibodies, bacteriophage tailspike proteins (TSP) have become popular alternative tools. Bacteriophages have naturally evolved in a way to precisely attach to specific bacterial strains/genera [118] as antibody analogs. Two important reasons for using tailspike protein instead of antibodies are its specificity toward a specific bacteria and cost-effectiveness in comparison to antibodies. Several disulfide bonds and post-translational changes are observed in few large-sized antibodies, which are multimeric proteins. These might require complex eukaryotic machinery to create them in an active state. Furthermore, a majority of investigations has demonstrated that for these compounds to be clinically effective, significant doses must be injected. As a result, the production of therapeutic antibodies require the

use of very large cultures of mammalian cells followed by time-consuming purification procedures, all carried out in accordance with GMP guidelines. This results in enhanced production cost and restricts the widespread use of these drugs. The entire process requires high technical expertise as it involves protein or cellular engineering. Therefore, the use of TSP instead of antibody may be a better option for bacterial detection due to the higher degree of specificity and comparatively less cost than the former. Additionally, TSPs exhibit significant stability, sensitivity, reproducibility, and enhancement compared to antibodies, and technologies based on TSPs do not require cold chain transport as some are thermostable [119]. We can even use this in the detection of diarrhea in rural areas where there is no proper laboratory facility. More importantly, the TSP-based method can be a POCT detection approach for early diagnosis of diarrhea. According to our view, specific bacterial pathogen can be directly visualized under UV light if magnetic nanoparticles conjugated with TSP tagged with quantum dots are used. This research focuses on current advancements in the detection of food-borne pathogens along with concepts and applications of modern rapid technologies used as rapid detection methods that are generally efficient in terms of time, sensitivity, specificity, and labor savings.

The entire world is now highly blessed with the use of wireless internet that enables the communication of personal health information wirelessly and through smartphones. Application of the Internet of Things (IoT) has become a widespread tool playing an essential role in real-time pathogen detection and monitoring using a smartphone and sharing data with other points via an Internet server. We assume that the future application for the IoT may turn its gear to the Internet of Nano-Things (IoNT) in which nanoscale devices are interconnected and are connected to the IoT. Hopefully, the successful implementation of such cutting-edge technology will embark a new horizon for easy detection and identification of bacteria.

Author contribution PSM designed the studies, supervise, and formulate the work plan of review and its revision, writing, and corrections. BRS provided valuable suggestions and idea to improve the review, writing, editing, and corrections. MM: original draft preparation, writing, editing, and referencing. AGM and BP contribute significantly to the writing, editing, and referencing of the section on the use of nanomaterials for the detection of food pathogens.

Funding This work is partially supported by BIRAC, COE, DBT, Govt. of India and ICMR (Indian Council of Medical Research), Government of India.

Data availability Not applicable.

Declarations

Ethical approval Not applicable.

Consent to participate Not applicable.

Consent for publication Not applicable.

Competing interests The authors declare no competing interests.

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