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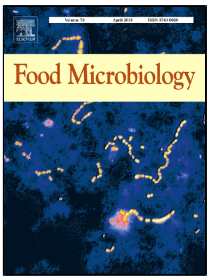

Nanotechnology: review of concepts and potential application of sensing platforms in food safety

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Nanotechnology: review of concepts and potential application of sensing platforms in food safety

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ABSTRACT

In recent years a number of new nanotechnology based platforms have been developed for detection of wide variety of targets including infectious agents, protein biomarkers, nucleic acids, drugs, and cancer cells. Nanomaterials such as magnetic nanoparticles, quantum dots, carbon nanotubes, nanowires, and nanosensors like giant magnetoresistance (GMR) sensors are used to quantitatively detect biomolecules with, experimentally, relatively good accuracy. There has been a growing interest in the use of magnetic fields in biosensing applications. Because biological samples have no ferromagnetic property and therefore there is no interference with complex sample matrix, detection of infectious agents from minimally processed samples is possible. Here, we provide a brief overview of the recent emergence of nanotechnology-based techniques for the detection and monitoring of foodborne diseases. In addition, the potential applications and future perspectives of nanotechnology on food safety are discussed. Ultimately, the review is expected to stimulate and provide directions to the development and application of nanotechnology-based tests for the early detection, and eventual control of foodborne diseases.

Keywords:
Nanotechnology, nanoparticle, biosensor, foodborne illness, food safety

1. Introduction

Foodborne illness or food poisoning is a global public health concern affecting both mostly developing, and up to certain extent, developed countries. Early and accurate detection of foodborne illness is prerequisite for preventing, controlling, and mitigating the impact of potential outbreaks. Traditional laboratory methods for detection of food borne illness depend mainly on culture and biochemical identification of microbial agents [1, 2], nucleic acid detection by polymerase chain reaction (PCR) [3-7], immunological detection such as enzyme linked immunosorbent assay (ELISA) and lateral flow immunoassay [8-13], or chromatography methods for detection of toxins and chemical contaminants [14]. Although those traditional methods are relatively sensitive and specific for the detection of microorganisms and tested

analytes, arguably, most of these tests are laborious, time-consuming and require skilled laboratory personnel [1, 15], which make them incompatible for point-of-care testing.

Nanotechnology is a rapidly expanding field involving nanomaterials. Nanotechnology has applications in different areas of food safety from food processing to assays for detection of contaminants. Nanomaterials have been used to remove contaminants [16, 17], as antimicrobials [18, 19], and as antioxidants [20]. In addition to sensors for detection of pesticides, chemicals, heavy metals, food borne pathogens and toxins, nanotechnology is also used in extraction techniques to adsorb trace amounts of pesticides [21, 22].

Nanotechnology-based detection methods have the potential for providing a number of advantages over conventional laboratory methodologies. Technologies that utilize nanoparticles in conjunction with electrochemical or optical detection modalities offer rapid, sensitive, and cost effective methods that permit miniaturization and automation for point-of-care testing. During the last decade, there have been a number of promising steps towards the development and application of novel nanotechnology. The unique properties of nano-devices and nanomaterials in conjunction with appropriate ligands offer unique opportunities to develop ultrasensitive detection strategies. Among these, nanoparticles, quantum dots, nanotubes, nanowires, and spin valve nanosensors such as Giant Magnetoresistor (GMR) have been used to detect infectious agents, protein biomarkers, as well as chemicals and heavy metals [23-28]. Foodborne illness can arise from consumption of contaminated food, whether it be with foodborne pathogens and their toxins or pesticides and other chemicals. The present review will focus on recent advancements in application of nanotechnology on food safety, mainly on sensing platforms used for detection and monitoring foodborne pathogens and toxins. Detection of chemical food contaminants using chemical nanosensors and methods to remove contaminants using nanotechnology are reviewed elsewhere [29, 30].

2. Nanotechnology in food safety

In recent years, the use of nanotechnology in food safety has gained increasing attention. Nanotechnology based detection systems vary in their mechanisms and designs but they share the same goal, that is, timely and accurate detection of trace pathogens or other contaminants [31].

2.1 Magnetic Nanoparticles

Magnetic nanoparticles (MNPs) are <100 nm particles that can be manipulated by an external magnetic field. Biosensors using MNPs have attracted considerable interest in clinical and medical applications for decades by virtue of unique advantages they offer over conventional detection methods. Most biological samples exhibit negligible magnetic properties, and thus highly sensitive measurements can be performed in visually obscured and minimally processed samples [32]. MNPs are biocompatible, nontoxic, inexpensive to produce, environmentally safe, physically and chemically stable [33]. This section will focus on the use of MNPs for *in vitro* detection of foodborne pathogens and toxins.

In very small MNPs, magnetization can randomly flip polarity under the influence of thermal fluctuation; in other words, these MNPs exhibit properties of superparamagnetism [34]. Superparamagnetic property occurs in single domain MNPs of size around a few nanometers to tens of nanometers in diameter, depending on the material used [35]. These superparamagnetic nanoparticles (SPNs) display negligible remnant magnetic moments in the absence of an external magnetic field, and their magnetic moments grow as the external field increases. This property prevents SPNs from aggregating in physiological solutions, reducing the risk of particle aggregation during solution based assays. A commonly used magnetic nanoparticle is superparamagnetic iron oxide nanoparticles (SPIONs), typically used for immunoassays by modifying their surfaces with appropriate ligands that can bind to specific target of interest.

2.1.1 NMR-based detection platform

The nuclear magnetic resonance (NMR) properties of MNPs is used for *in vitro* detection of biomarkers and pathogens. In using NMR properties as a detection platform, MNPs work as proximity sensors to modulate the spin-spin relaxation time of surrounding water molecules. When applied with an external magnetic field, MNPs generate local magnetic dipole fields that efficiently destroy coherence in the spin-spin relaxation of surrounding water protons. NMR-based detection platform exploits this property of MNPs to modulate the spin-spin T_2 relaxation time of targeted biological samples. The conjugation of MNPs to biological or molecular targets causes shortening of the transverse relaxation time T_2 and a faster decay of magnetic resonance signal. There are two detection mechanisms in NMR-based assays. Magnetic relaxation switching (MRSw) is exploited for detecting small molecules such as nucleic acids and proteins

by employing target-induced aggregation/disaggregation of MNPs. MRSw assays do not require removing unbound MNPs and therefore decreases assay time. For detecting larger biological targets like bacteria and cells, functionalized MNPs will specifically bind to cell biomarkers (see Figure 1). To ensure optimum detection sensitivity unbound MNPs are removed by washing. Change of T_2 relaxation time (ΔT_2) is directly proportional to the number of MNPs bound to its target.

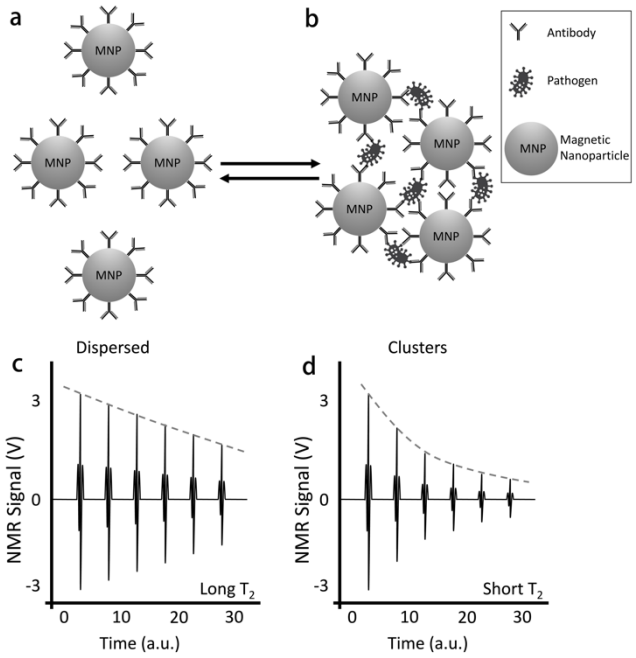

Figure 1. MRSw assays detect changes in the organizational states of MNPs in solution. (a) MNPs in dispersed state. (b) MNPs aggregate forming clusters. (c) Long T_2 relaxation time from dispersed MNPs. (d) Short T_2 relaxation time from MNP clusters.

Detection of *Listeria monocytogenes* in milk powder and lettuce using NMR has recently been reported [36]. *L. monocytogenes* is a foodborne pathogen usually found in raw and processed foods. The specific binding between *L. monocytogenes* and antibody-modified MNPs resulted in clustering of MNPs. The aggregation of bound MNPs changed T2 relaxation time, which was measured using a MRSw based assay. The detection limit of this assay was as low as 3 CFU/mL and the assay requires less than an hour to complete the test. The same authors also reported the detection of *Cronobacter sakazakii,* a bacterium that causes rare but fatal foodborne infection in infants by contaminated powdered infant formula, using the same method and

achieved a detection limit of 1.1 CFU/mL in less than 2 h [37]. Wang, S., et al. demonstrated the detection of *Salmonella enterica* (*S. enterica*) from milk with a detection range of 5×10^3 – 10^6 CFU/mL [38]. A novel assay using miniaturized NMR device has been developed to detect *Salmonella* nucleic acid (mRNA) in the blood of infected patients [39, 40]. In this assay, a magneto-DNA nanoparticle system is utilized which is a promising method for low bacterial load detection from infected individuals. The detection limit of the assay, in spiked blood, was found to be 0.01 CFU/mL for *S.* Typhimurium and 1 CFU/mL for *S. typhi* and *S. paratyphi*. Given the capacity for low-level detection using this system, it is anticipated that a point-of-care NMR system may provide the means for a rapid and easy-to-use diagnostic platform, offering highly sensitive testing of foodborne pathogens, and enabling real-time tracking and mapping of pathogen spread in communities.

2.1.2 Search coil based detection platform

Another application of using MNPs for immunoassays is based on their nonlinear magnetization properties [41-43]. A search coil system (Figure 2) records the nonlinear magnetic responses of MNPs travelling through external magnetic fields generated at two frequencies f_H (high frequency, typically several kHz to tens of kHz) and f_L (low frequency, typically tens of Hz). The signal response, proportional to the amount of MNPs, is recorded at combinatorial frequencies $mf_H \pm nf_L$, where n and m are integers.

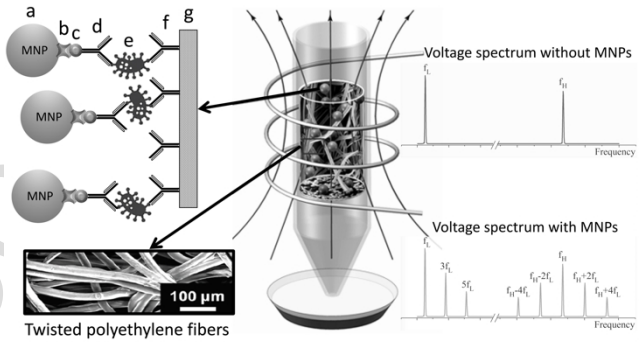

Figure 2. Detection of MNPs by their non-linear response at combinatorial frequencies from the whole volume of the 3D filters made of twisted polyethylene fibers and functionalized with capture antibody located inside a pipet tip. Sandwich-type immunoassay structure: a. MNP; b.

streptavidin; c. biotin; d. tracer antibody; e. antigen; f. capture antibody; g. 3D filter surface. (Figure modified from [44])

A method to detect Staphylococcal enterotoxin A (SEA) and Toxic shock syndrome toxin (TSST) from milk without any sample preparation was developed using search coil based detection platform [44]. In this test system, a sandwich-type immunoassay structure is used (Figure 2). The testing platform consist of a nontransparent 3D porous filter structure made of twisted polyethylene fibers, which provides a large reaction surface, enables quick reagent mixing, and antigen capture by immunofiltration during the assay. The 3D filter surfaces are functionalized using capture antibodies prior to packing into pipet tips. A liquid sample (like unprocessed milk) is filtered through the pipet tip to capture SEA/TSST antigen, followed by a washing to remove any unbound proteins. Finally, biotinylated antigen specific antibodies and streptavidin-coated MNPs are dispensed to detect antigens bound to the filter. MNPs bound to the 3D fiber surface serve as labels, which are assessed by placing the pipet tips into a search coil system. The non-linear magnetic response generated by the MNPs is proportional to the number of antigens present in the sample. The detection limit of this search coil based detection platform in an express mode with 150 µL sample volume, which takes 25 minutes to complete, is 0.3 ng/mL for *SEA* and 0.1 ng/mL for *TSST*. In a high-volume mode, which takes 2 hours to complete, detection limits are 10 ng/mL for *SEA* and 4 ng/mL for *TSST* [44]

In addition to the above pathogens, MNP based platforms have been also developed for rapid detection of Shiga-like toxin 1 (SLT-1) from complex cell lysates of *E. coli* O157:H7 and ham/juice samples [45], Listeria from spiked lettuce samples [46], and for simultaneous detection of four major foodborne pathogens- *E. coli* O157:H7, *Salmonella enterica, Vibrio cholera,* and *Campylobacter jejuni* [47]

2.1.3 Giant Magnetoresistance Nanosensors

In addition to their interaction with water protons, the local magnetic dipole field from MNPs can also be detected by magnetic field sensors based on giant magnetoresistance (GMR) effect, which is often observed in a structure with alternating ferromagnetic and nonmagnetic layers. The scattering of electrons passing through the GMR layers depends on the magnetization orientation of ferromagnetic layers. The electrons experience more scattering if the magnetizations are oriented in an antiparallel manner, leading to a much higher resistance than

those oriented in a parallel orientation. In typical GMR structures, the magnetization direction of one ferromagnetic layer is fixed by applying a field during deposition or annealing process, while magnetization direction of the other ferromagnetic layer can rotate freely under the influence of an applied magnetic field [48]. To realize the detection of biological analytes, the sensor surface is functionalized with capture antibodies, target antigens and MNP-tagged detection antibodies [23]. The specific reaction between antibodies and their cognate antigens leads to a one-to-one correspondence between the number of antigens and the number of MNPs on the sensor surface. Upon application of an external field, the stray field from captured MNPs are picked up by the GMR sensor, resulting in a resistance change proportional to bound antigen concentration (Figure 3). Compared to other sensing techniques, GMR sensors possess advantages of low cost, high sensitivity, and the capability of real-time signal readout [49]. In addition, GMR sensors can be arrayed for simultaneous detection of multiple analytes.

A multiplex sensing platform for the detection of food allergens was demonstrated by Wang et al.[50]. Peanut allergens Ara h1 and Ara h2, and wheat allergen Gliadin were chosen as the analytes, which react with corresponding antibodies spotted on the sensor surface. The detection antibodies conjugated with biotin were then bound to streptavidin magnetic nanoparticles through the biotin-streptavidin reaction. A real-time binding curve was obtained, whose saturation value was used to determine the concentration of each allergen. This sensing platform exhibited significantly lower limits of detection compared to current commercially available food allergen methods. The limit of detection for Ara h1, Ara h2, and Gliadin was 7.0 ng/mL, 0.2 ng/mL, and 1.5 ng/mL, respectively with little to no cross-reactivity with other allergens. Mycotoxins such as aflatoxin-B_1, zearalenone, and HT-2 were also detected using similar detection schemes with a detection limit of 50 pg/mL [51].

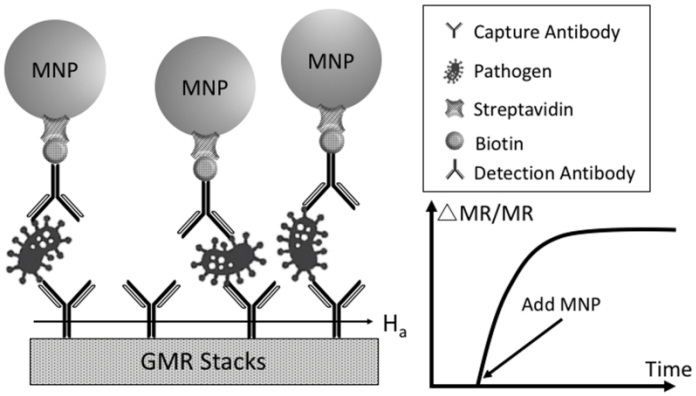

Figure 3. Schematic illustration of the sandwich structure on GMR sensor surface and real-time signal change.

2.2 Non-magnetic Nanoparticles

2.2.1 Localized Surface Plasmon Resonance

Surface plasmon resonance (SPR) is a commonly used optical detection technique for label-free biological sensing. In SPR, a polarized monochromatic light beam is passed through a prism and reflected from the thin metal film (typically gold) on a glass slide, which is in contact with the liquid solution of interest. The surface plasmon resonance is achieved when the frequency of the incident photons striking the metal film matches the natural frequency of the oscillating surface electrons on the metal surface. The angle of incident light can be varied to achieve SPR which, in an experimental point of view, is when the incident angle is equal to the SPR angle. At this point, a nearly complete attenuation of reflected light intensity is achieved. Since the shift of the resonance frequency is proportional to the change in the surface concentration of species adsorbed on the metal surface, real-time binding measurements can be achieved by acquiring the change of optical reflectivity with time [52]. Although SPR technology is well-developed, the instrumentation employed in this technique is expensive and complex to operate [53].

To realize instrumentation for point-of-care medical diagnosis, localized SPR (LSPR) has been developed. Here charge density oscillation can be excited by coupling to the excitation light due to their confinement in the subwavelength nanoparticles. LSPR with ultra-low limits of detection has been achieved for the detection of pathogenic bacteria. A copper-capped nanoparticle array with silica cores was proposed whose plasmonic properties can be tuned by altering the thickness of the copper shell [54]. The nanoparticles were functionalized with species specific single

stranded DNA probes which were subsequently conjugated with target DNAs generated by PCR. Seven pathogenic bacteria including *S. aureus*, and *Enterococcus faecalis* were tested, with a limit of detection of 10 fM of DNA. Despite the low limit of detection stated above for DNA detection, the sensor performance was not as efficient in whole cell detection of *Salmonella* using antibodies, which was attributed to the significantly larger size of the bacterial cells compared to the gold nanoparticles (AuNPs) used in this assay [55].

This effect can be further enhanced by utilizing nanostructures with sharp features. Star-shaped Au nanoparticles were synthesized by Lee et al [56]. It was found that multiple nanogaps can exist in each cluster of nanostars, which amplifies the signal via plasmon coupling. The nanostar clusters exhibited up to 460-fold higher field density than Au nanosphere clusters of similar mass. Nanoparticles with other shapes were also demonstrated, such as nanorice [57] and nanocrescents [58].

2.2.2 Nanoparticle-Assisted Colorimetry

Colorimetric tests are one of the simplest of detection techniques used for biological targets. By utilizing the chemical reaction involving color change, the existence of target analyte can be determined either qualitatively by visualization or quantitatively using colorimeters. However, the efficiency of color conversion in traditional colorimetry is relatively low, which lowers the sensitivity of the device. To solve this problem, nanoparticle-assisted colorimetry was developed [59]. By introducing nanoparticles into the sensing matrix, the surface area on which color precursor molecules are located can be increased significantly.

The detection of *invA* gene of *Salmonella* by combining DNAzyme probe self-assembled gold nanoparticles and polymerase chain reaction (PCR) was demonstrated by Luo et al [60]. A capture probe immobilized on a plate was used to form a sandwich structure, through hybridization between target sequence, capture probe, and a detection probe using functionalized AuNPs. In the presence of hemin, the detection probe could form a G-quadruplex/hemin complex, which served as catalyst for the oxidation reaction mediated by H_2O_2, leading to a dramatic color change. The limit of detection was 3 x 10^3 CFU/mL. Besides DNA detection, AuNPs have also been coupled with antibodies for the detection of *Salmonella* Typhimurium [61].

2.2.3 Quantum Dots

Although widely applied, traditional fluorescence detection with organic fluorescent dyes often exhibits overlapping emission peaks and high sensitivity to photobleaching. Quantum dots (QDs) are semiconductor nano-size crystalline clusters, which are highly resistant to photobleaching and chemical degradation [62]. The bandgap energy of QDs is inversely proportional to their size, which results in narrow and tunable emission bands, independent of the excitation wavelength [63]. QDs are available with different sizes having wide range of emission wavelength, which enables its use in multiplex analysis.

QDs, coupled with immunomagnetic separation (IMS), were employed in multiplex detection of *E.coli* and *Salmonella enteritidis* [64]. Magnetic beads and QDs coated with corresponding antibodies and bound to target antigens were concentrated using a magnet. The fluorescent intensities generated by capturing different concentrations of bacteria were measured with a working range of 5 x 10^2 to 5 x 10^4 CFU/mL for *E. coli* and 4 x 10^2 to 4x 10^5 CFU/mL for *S. enteritidis*. QDs for simultaneous detection of foodborne bacteria in food matrices has also been reported [65, 66]. A recent report demonstrated the detection of parathion, a pesticide, using functionalized graphene quantum dot (GQD) based electrochemical immunosensor with a detection limit of 46 pg/L [67].

Besides fluorescent tags, QDs are also used as fluorescence resonance energy transfer (FRET) donors. Within the Forster distance (1 to 10 nm), fluorescence emitted by donor molecules can be quenched by the acceptor through an energy transfer process. Graphene quantum dots (GQDs) and AuNPs were employed as energy donor-acceptor pairs for *S. aureus* gene detection [68]. Here GQDs were conjugated with capture probes and AuNPs were conjugated with reporter probes complementary to different regions of *S. aureus mecA* gene. Upon hybridization of target oligonucleotides with complementary nucleotide pairs, GQDs and AuNPs were brought together, leading to quenching of fluorescence intensity. By measuring the change of fluorescence intensity of the solution, *S. aureus* target oligo was detected. A schematic illustration of the FRET process is shown in Figure 4. The limit of detection of this technique was around 1 nM.

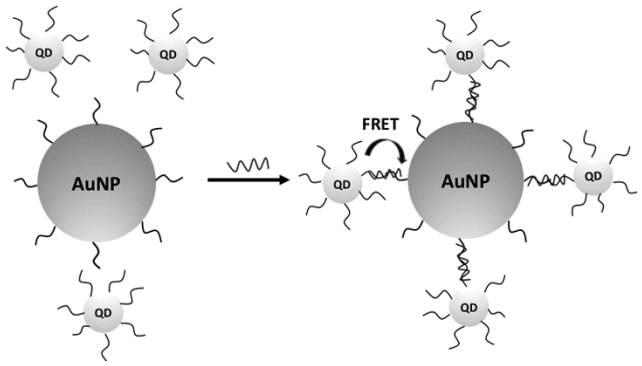

Figure 4. Schematic illustration of FRET process between AuNPs and GQDs. GQDs conjugated with capture probe and AuNPs conjugated with reporter probe.

2.3 Carbon Nanotubes

Carbon nanotubes (CNTs) are allotropes of carbon with a cylindrical nanostructure. Typically, CNTs have diameters of several nanometers and lengths up to several millimeters. These cylindrical carbon molecules have attracted considerable interest because of their unique electronic and mechanical properties, which make CNTs a promising candidate to improve electrochemical biosensor performances [69]. The large surface area of CNTs allows immobilization of ligands for molecular recognition and meanwhile serves as sensing element that allows electrical communication between the underlying electrode and the conjugated antigen-antibody complexes.

Jain, S., *et al*. covalently attached monoclonal antibodies to *Salmonella* on single-walled carbon nanotubes (SWNTs), which are used to modify the glassy carbon (GC) electrode surface used for the detection of low concentration of *Salmonella* [69]. This SWNT *Salmonella*-specific immunosensor analyses the formation of antigen-antibody complexes by measuring change in electrochemical properties (i.e. charge transfer resistance and impedance) of the sensor afforded by the insulating properties of the bacterial cell membrane. Yamada, K., et al. have integrated antibody coated SWNTs into a disposable junction sensor for detection of *Escherichia coli* K-12 (*E. coli* K-12) [70]. Gold tungsten wires coated with polyehylenimine and SWNTs were aligned to form a crossbar junction, and the binding of *E. coli* K-12 and antibodies is monitored by changes in electrical current. The limit of detection of this sensor is 10^2 CFU/mL with a detection time of less than 5 mins. Lerner, M.B., *et al*. covalently bound anti-*Salmonella* antibodies onto CNT-field effect transistors (CNT-FETs) for detection of *Salmonella* in nutrient

broth solutions [71]. They showed that the ON-state current of the functionalized sensor is sharply decreased by exposure to *Salmonella* at concentrations as low as 10^3 CFU/mL of broth. CNT-FETs have been broadly used as highly specific sensors based on antibody-antigen type immunoassays [72, 73]. Furthermore, CNT-FETs are compatible with the long-term goal of integrating a large array of diverse biosensors into a lab-on-a-chip system. Another study demonstrated the optical CNT immunosensor for detection of Staphylococcal enterotoxin B (SEB) in food [74]. Figure 5 shows a CNT-FET based biosensing system.

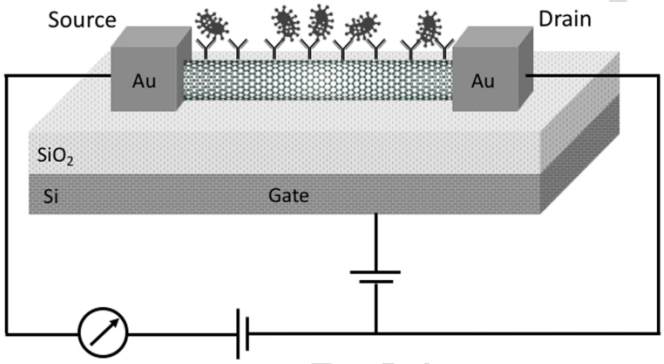

Figure 5. Schematic illustration of detection mechanism for biosensing using CNT-FETs. CNTs are fabricated on Si substrate capped with a SiO_2 layer. Gold contacts serving as source and drain are deposited after the CNT growth. Anti-pathogen antibodies (receptors) are functionalized on the surface of CNTs. The binding event of pathogens to the receptors changes the electrical properties of CNTs. One can detect the presence of pathogens by monitoring the electrical properties of the CNTs.

CNTs loaded with antibodies or enzymes have been widely used as detection probes for immunoassays. However, they are not sensitive enough for detecting pathogens at ultra-low concentrations and require specific conjugation of different antibodies for the detection of different analytes. ConA-CNTs-HRP bioconjugates obtained by functionalizing CNTs with concanavalin A (ConA) and horseradish peroxidases (HRP) are used as a universal nanoprobe for the detection of pathogens and amplification of detectable visual signals [75]. ConA is employed as the recognition element, which can specifically recognize sugar epitopes on the surface of cells and HRP serves as the signal amplification unit by repeated reaction between

biotinylated anti-HRP antibody and avidin-HRP. The ConA-HRP universal nanoprobe can be applied to detect different pathogens by changing the corresponding capture antibodies on the inner surface of 96-well polystyrene plates. This multiple-cycle signal amplification strategy has been demonstrated for detection of *E. coli* O157:H7 in meat samples with a detection limit of 10^2 CFU/mL [75].

CNTs are not only used for detecting foodborne pathogens, but also used for removing and inactivating pathogens. The use of co-polymer poly(propionylethyleneimine-co-ethyleneimine) (PPEI-EI), functionalized multi-walled carbon nanotubes (MWNTs), as coating material on filters for capturing *E. coli* cells from aqueous solutions was demonstrated by Wang, S., et al [76]. This CNT-assisted capturing of *E. coli* was achieved at flow rate of 0.5 mL/min with a capture efficiency of higher than 4 log (up to 6 log or larger). CNT platforms show potential for high-performance biosensing and application as a detection device for foodborne pathogens.

2.4 Nanowires

Like nanotubes, nanowires also have high surface-to-volume ratio and, furthermore, they have attracted substantial research efforts because of extremely high sensitivity of carrier mobility to variations in the electric field at their surface [77].

TiO_2 nanowire bundle for the detection of *Listeria monocytogenes* has been developed [78]. The surface of TiO_2 nanowire bundle is immobilized with monoclonal antibodies to specifically capture *L. monocytogenes*. *Listeria* cell wall has a net negative charge on its surface at pH 7.0, thus, the specific binding of the *Listeria* cell to the TiO_2 nanowire bundle causes significant change in electrical conductance and this impedance measured is reflective of the number of organisms bound. This TiO_2 nanowire bundle based impedance immunosensor is able to detect *L. monocytogenes* at concentrations as low as 4.7×10^2 CFU/mL with an overall detection time of 50 min. In separate report, polyaniline nanowire-based direct-charge transfer biosensors were used for detection of the foodborne pathogen, *Bacillus cereus* [79]. The working principle is similar; in that binding of antigen to its cognate antibody affects the flow of electron charge in the polyaniline nanowire and results in increased resistance, which is recorded. The limit of detection in this design is reported to be 10^1-10^2 CFU/mL using pure cultures of *B. cereus* with a detection time of only 6 min.

Semiconductor nanowires work as the gate in a field-effect transistor (FET), the nature of one-dimensional morphology of nanowire offers better sensitivity over planar FETs. Binding of biomolecules onto the surface of nanowire results in depletion/accumulation of carriers in the whole nanowire. However, this binding of biomolecules only occurs on the surface of a planar FET. Thus, nanowire-based sensors are significantly more sensitive than their planar counterparts and, furthermore, have shorter response times [80]. The efficiency of sensor arrays with highly ordered n-type silicon nanowires (SiNW) for ultra-sensitive biosensing purpose were investigated [81]. These SiNW array sensors were functionalized with peptide nucleic acid (PNA) capture probes, which exhibited the expected surface-charge-induced resistance response upon hybridization with synthetic DNA oligonucleotides.

Nanowires have been actively used in clinical applications. ZnO nanowire hybrid architectures has been reported for detection of breast cancer-related volatile organics [82] and uric acid levels in the serum of Parkinson's disease patients [83]. Si nanowires have been used for the detection of circulating tumor cells [84], cancer risk biomarkers [85], and cardiac troponin I (cTnI) [86].

3 Conclusions and future directions

Nanotechnology has enormous potential in the field of medicine both in therapeutic and diagnostic applications. The application of nanotechnology in food industry has great benefit for food safety, where there is a need for rapid, real time, simple and cost-effective method to detect contamination of foodborne pathogens, toxins and chemicals. Nanotechnology can provide high-throughput and portable diagnostic platforms for screening pathogenic microorganisms and toxins directly from food samples in field and point-of-care clinical settings. Several of these technologies offer multiplexing capabilities for simultaneous testing of multiple analytes with exceptionally high sensitivity that can significantly reduce the cost of testing and detection time. Table 1 provides a summary of nanotechnology based detection techniques for foodborne illness. In recent years, nanotechnology based tests are being improved continuously with the integration of automation and microfluidic systems, which combines all necessary sample handling and analysis steps in a simple hand held biosensing device.

Although nanotechnology methods for detection of food contaminants has several advantages over conventional laboratory methods in terms of assay time, sensitivity, portability

and cost, successful implementation of these techniques in food industry as a universal sensor for different types of food samples is challenging due to inherent complexity of food samples. These technologies have been evaluated with actual food samples obtained from the field, but have only been tested with limited type of foods. Evaluation with large number and different variety of food samples and comparison with well-established methods may help to address this challenge.

Table 1. Comparison of nanotechnology-based methods for detection of foodborne pathogen.

Technique	Nanomaterial	Assay time	Target	Sensitivity	Evaluated matrices	Ref.
NMR	Fe/Fe_3O_4 NPs	40 min	*L. monocytogenes*	3 - 10^3 CFU/mL	Milk powder, lettuce	[36]
	Silica-coated Fe_3O_4 NPs	2 h	*C. sakazakii*	1.1 - 1100 CFU/mL	Milk powder, Cheese	[37]
	Fe_3O_4 NPs	30 min	*S. enterica*	5×10^3 – 10^6 CFU/mL	Milk	[38]
	Fe_3O_4 NPs	3.5 h	*Salmonella* nucleic acid	0.01 – 1 CFU/mL	Blood	[39]
Search Coil	Fe_3O_4 NPs	2 h	SEA TSST	10 pg/mL 4 pg/mL	Milk	[44]
	Fe_3O_4 NPs	25 min	SEA TSST	0.3 ng/mL 0.1 ng/mL	Milk	[44]
LSPR	Slica NPs	*NA*	*S. aureus*	10 fM	Pure culture	[54]
	AuNPs	*NA*	*E. coli* O157:H7	10^7 CFU/mL	Pure culture	[55]
Colorimetry	AuNPs	5 min	*Salmonella*	3×10^3 CFU/mL	Pure culture	[60]
	AuNPs	5 min	*Salmonella*	1×10^3 CFU/mL	Pure culture	[61]
QDs	CdTe	2 h	*S. enterica*	5×10^2 CFU/mL	Pure culture	[65]
	CdTe	2 h	*S. enteritidis*.	10^3 CFU/mL	Juice	[68]
CNTs	SWNTs	4 h	*Salmonella*	1.6×10^4 CFU/mL	Pure culture	[69]
	SWNTs	5 min	*E. coli* K-12	10^2 – 10^5 CFU/mL	Pure culture	[70]
	CNT-FETs	45 min	*Salmonella*	10^3 – 10^8 CFU/mL	Broth	[71]
	CNTs	*NA*	*E. coli* O157:H7	10^2 – 10^6 CFU/mL	Meat	[75]
Nanowires	TiO_2 nanowire	50 min	*L. monocytogenes*	4.7×10^2 CFU/mL	Pure culture	[78]
	Polyaniline nanowire	6 min	*B. cereus*	10^1 – 10^2 CFU/mL	Pure culture	[79]

GMR	Fe_3O_4 NPs	15 min	Ara h1	7 ng/mL	Pure culture	[50]
	Fe_3O_4 NPs	15 min	Ara h2	0.2 ng/mL	Pure culture	[50]
	Fe_3O_4 NPs	15 min	Gliadin	1.5 ng/mL	Pure culture	[50]
	Fe_3O_4 NPs	15 min	HT-2	50 pg/mL	Pure culture	[51]

Conflict of interest

Dr. Jian-Ping Wang has equity and royalty interests in, and serves on the Board of Directors and the Scientific Advisory Board, for Zepto Life Technology LLC, a company involved in the commercialization of GMR Biosensing technology. The University of Minnesota also has equity and royalty interests in Zepto Life Tech LLC. These interests have been reviewed and managed by the University of Minnesota in accordance with its Conflict of Interest policies.

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Highlights

- Nanotechnology platforms have been developed for detection of variety of targets
- We reviewed nanotechnology for the detection and monitoring of foodborne diseases
- Discussed the potential applications of nanotechnology on food safety