Review

Guarding food safety with conventional and up-conversion near-infrared fluorescent sensors

Fang Yang a,c,+ , Junlie Yao a,d,†, Fang Zheng a,e,+ , Hao Peng a,d , Shaohua Jiang b, Chenyang Yao a,d , Hui Du a,d , Bo Jiang a, Stefan G. Stanciu f,+ , Aiguo Wu a,c,+  

a Cixi Institute of Biomedical Engineering, Chinese Academy of Science (CAS) Key Laboratory of Magnetic Materials and Devices & Zhejiang Engineering Research Center for Biomedical Materials, Ningbo Institute of Materials Technology and Engineering, CAS, 1219 ZhongGuan West Road, Ningbo 315201, PR China  
b International Innovation Center for Forest Chemicals and Materials, College of Materials Science and Engineering, Nanjing Forestry University, Nanjing 210037, PR China  
c Advanced Energy Science and Technology Guangdong Laboratory, Huizhou 516000, PR China  
d College of Materials Sciences and Opto-Electronic Technology, University of Chinese Academy of Sciences, Beijing 100049, PR China  
e Department of Nano Science and Technology Institute, University of Science and Technology of China, Jiangsu 215123, PR China  
f Center for Microscopy-Microanalysis and Information Processing, University Politehnica of Bucharest, Bucharest 060042, Romania

highlights

Near-infrared (NIR) fluorescent nanomaterials are highly-promising in the quest for a next-generation of food toxicity sensors.  
Exploiting NIR photoluminescence for food security assessment is effective in detecting inorganic and organic contaminants.  
Perspectives and challenges concerning the use of NIR photoluminescence for food safety detection are discussed.

graphical abstract

Article info

Article history:  
Received 15 December 2021  
Revised 19 January 2022  
Accepted 24 January 2022  
Available online 30 January 2022

abstract

Background: Acknowledged by the World Health Organisation (WHO), over 200 diseases ranging from mild to fatal are linked to the consumption of food products subjected to physical, chemical, or biological contamination. Nevertheless, conventional methods commonly used for the identification of health hazards in foodstuffs have problems coping with the sensitivity requirements imposed by latest-hour regulations in the field. Additionally, their use and availability is wildly limited by aspects such as instrument dimension, prohibitive costs, detection complexity and required operational knowledge.  
Aim of review: This review provides an overview of recent efforts that have focused on the assessment of food contamination based on near infrared (NIR) photoluminescent sensors. Important endeavors that...
have targeted the precise detection of various inorganic and organic contaminants, including hydrogen sulfide, cyanide anions, mycotoxins, antibiotic residues, etc., are presented and relevant challenges that lie en route as stumbling blocks for such sensors to reach the next level of maturity and to become more available, are systematically discussed and enunciated.

Key scientific concepts of review: Ingenious food contamination sensors that rely on conventional or up-conversion photoluminescence in the NIR region represent an emerging topic. To date, such sensors have demonstrated as promising detection candidates, possessing important advantages such as: high efficiency, facile implementation, and convenient flexibility, thereby promising significant contributions to expand the current state of the art in food security.

Introduction

Across their journey through the supply chain, from farm to fork via factory and market, food products can be subjected to various health hazards linked to biological, chemical, or physical contamination that carry deep implications for human health. Over 200 diseases ranging from less severe to fatal ones, such as cancers [1], can be linked to the consumption of food containing pathogenic bacteria, viruses, parasites, or chemical substances. A prominent example that we find relevant to provide in the current pandemic context is the transmission via contaminated food products of the SARS-COV-2 virus [2–3], the pathogen responsible for the unprecedented crisis that is currently affecting the entire planet, accounting for over > 5 million deaths at the time of writing this article, and immeasurable financial losses, in less than 2.5 years since the first reported cases. Also important to mention are the numerous food safety scandals (e.g. prion in beef, clenbuterol in pork and melamine in milk powder) that have continually occurred over the years, which were also linked to severe human health threats accompanied by significant social and economic burden [4–6]. Thus, the advent of more efficient and more reliable solutions that can probe and certify food safety are of utmost importance for ensuring human physical well-being, life quality and the sustainability of worldwide healthcare and financial systems [7]. As a result of WHO’s continuous emphasis on the importance of this field, the development of novel food safety detection technologies that can identify hazardous substances and pathogenic biological organisms in food, is gaining increasing interest. Such technologies can be complemented by others that can remove biological organisms in food, is gaining increasing interest. Such technologies can be complemented by others that can remove

NIR fluorescent sensors that can signal food contamination, with splendid stability, specificity and sensitivity, circumventing the auto fluorescence interference of test samples [15–17]. While the employment of NIR fluorescent organic molecules or nanomaterials to enable food safety detection sensors has acquired remarkable progress, this field is far from being exploited at its full potential.

NIR fluorescent organic molecule sensors, organic fluorophores (e.g. squaraines, cyanines, and bodipy derivatives) and optically tunable mechanisms have been jointly combined to date to result in advanced target-sensitive platforms. To this end, a series of schemes such as electron transfer, protection-deprotection, characteristic spirocyclization, and fluorophore integration have been devised to efficaciously endow organic fluorophores with optically available tunable groups, which provide highly significant optical advantages for sensing, including low fluorescence background, long decay length, or structural and functional variability [18–21]. Meanwhile, driven by the development of nanotechnologies, nanomaterials possessing unique physicochemical properties are substantiated as a welcome component of NIR fluorescent sensors [22–23]. With prominent temporal and spatial sampling, rapid response and enhanced signal readout, a special type of NIR fluorescent nanoparticles (NPs), coined upconversion nanoparticles (UCNPs) blaze a brand new path for food safety determination. Such nanomaterials upconvert energy, meaning that they emit light whose wavelength is lower compared to that of the excitation source; for example, UCNPs excited in the infrared can emit in the visible domain. As a result of their physico-chemical characteristics suitable for sensing (e.g. high luminescence efficiency, long luminescence lifetime, narrow emission peak, large Stokes-Shift, good chemical stability, low cytotoxicity), NIR UCNPs can overcome the performance limitations of traditional organic fluorophores, such as short fluorescent lifetime, broad characteristic spectrum and proneness to photo-bleaching [24–26]. This has led to the emergence of a considerable number of UCNP applications focused on food safety.

In this review, we summarize representative NIR fluorescent sensors in light of their potential to detect usual food contamination sources, including inorganic substances (hydrogen sulfide, bisulfite/sulfite anions, cyanide anions, nitrite anions and heavy metal cations) and organic substances (foodborne pathogens, mycotoxins, antibiotic residues, pesticide residues and biological amines). Subsequently, we discuss challenges and future aims of NIR fluorescent sensors for food safety detection. Altogether, we hope that this review not only paints an illustrative picture of the current state of the art, but can also spark fresh ideas leading to the advent of novel techniques for food safety detection based on NIR technologies, and guide the development of novel sensors with superior performance for future food safety applications.

Inorganic substances

Inorganic substances present in numerous food products are highly relevant with respect to the regulation of metabolic pro-
cesses and of the energy balance. Importantly, the overdose of certain inorganic substances (e.g. toxic metals, metal oxides, salts, sulfides and halides) in foodstuffs may pose danger to the human health, thus identifying such situations is critical. Accordingly, the availability of simple and rapid inorganic substance detection methods as point-of-care devices, or as devices available in relevant health departments is highly desired. In Table 1, we present a number of practical NIR sensors that have been developed so far to identify the presence and dose of inorganic substances in edible substances.

**Hydrogen sulfide**

Hydrogen sulfide (H$_2$S) represents a widely met pollutant compromising food safety and endangering human health [27]. For instance, abnormal levels of H$_2$S result in a high incidence of various severe diseases, such as Alzheimer’s, Down syndrome, liver cirrhosis, or diabetes [28–29]. Although multiple fluorescence methods featuring easy manipulation and real-time imaging have been engaged to monitor H$_2$S, a large proportion of probes are distinguished with short emission wavelength which makes them significantly affected by background fluorescence interference and photo damage [30]. As a consequence, the development of NIR fluorescent technologies that can replace, expand or augment the current methods operating in the visible regime is very important for enabling the determination of H$_2$S contamination with higher specificity and sensitivity.

In recent years, several innovative NIR fluorescent sensors have been synthesized for H$_2$S detection in food samples. In this respect, a sophisticated NIR fluorescent nanosensor integrating switchable chromic Cy7Cl (a cationic cyanine dye) and NIR775 (a NIR fluorescent dye) into a phospholipid polymer to analyze H$_2$S in actual food samples such as red wine, beer and stale egg white (Fig. 1a-b) was reported by Xiao et al. [31]. This work showed that Cy7Cl was qualified as a H$_2$S-reactive chromophore and energy acceptor, and NIR775 efficiently acted as a H$_2$S-inert fluorophore and energy donor, conspicuously triggering fluorescence resonance energy transfer (FRET), an energy transfer process through dipole–dipole interactions between the donor–acceptor pair, and quenching the fluorescence emission of NIR775 at 778 nm. With the permeation of H$_2$S, blue-green Cy7Cl was gradually converted to colorless Cy7SH, which caused fluorescence quenching of Cy7Cl at 810 nm and restored fluorescence emission of NIR775. In addition to this, this simple and precise method satisfied a limit-of-detection (LOD) of 11.0 nM, sufficient to specifically detect H$_2$S among other anionic and sulfur-containing species. Another notable effort is the work of Zhong et al. [32], who reported a hyperchomic NIR fluorescent probe consisting of donor–acceptor fluorophore and 2,4-dinitrophenyl ether moiety capable to monitor H$_2$S in red wine, real water, and living cells. On the one hand, the donor–acceptor construction could red-shift the absorption and emission wavelengths to the NIR region ascribing to intramolecular charge transfer (ICT), a fundamental photochemical process relying on charge flow from a donor to an acceptor. On the other hand, the 2,4-dinitrophenyl ether moiety was found to be highly fit in serving as a H$_2$S recognition probe based on fluorescence quenching. Interestingly, in the presence of HS$^-$, the 2,4-dinitrophenyl ether moiety was induced to release the fluorescent molecule, thereby offering a significant fluorescence response (reduced intensity at 745 nm and enhanced intensity at 640 nm) and a solution color change from colorless to purple blue.

In brief, in these past works, the fluorescence intensity of fluorophores designed to perform in the NIR region had been successfully elevated or decreased, at significant levels, via H$_2$S mediated thiolysis and thiolation. The advantages of NIR fluorescence technologies in terms of Stokes-Shift and signal-to-noise ratio (SNR), enabled thus valuable practical applications for H$_2$S identification.

**Bisulfite/sulfite anions**

Serving as food preservatives, bisulfite/sulfite (H$\text{SO}_3^-/\text{SO}_3^{2-}$) anions validly suppress browning, oxidation, and microbial reactions during the period of storage [33]. Nevertheless, ingestion of these anions can lead to tissue and cell injury, thus inducing

| Table 1 |
|---|
| Notable NIR fluorescent sensors for detecting inorganic substances. |

| Test object | Mechanism | Detection medium | $\lambda_{ex}/\lambda_{em}$ (nm) | Linear range | Detection limit | Applications in foodstuffs | Ref |
|---|---|---|---|---|---|---|---|
| H$_2$S | FRET | PBS solution (pH 7.4, 1x) | 720/778 810 | 0.0367–120 μM | 11.0 nM | beer, red wine, stale egg white, riverine water | 31. |
| H$_2$S | ICT | DMF/H$_2$O (pH 7.4, PBS-HCl 10 mM, v/v = 3/7) | 543/640 745 | 12–38 μM | 3.09 μM | red wine, real water | 32. |
| HSO$_3^-$ | ICT | PBS solution (pH 7.4) | 550/690 | 3.13–200 μM | 0.46 μM | tap water, wine, sugar solution, Chinese liquor granulated sugar, vermicelli crystal sugar, red wine, soft sugar, crystal sugar, sugar granulated sugar sprouting potato, un-sprouted potato, almond, cherry, cherry seed, bitter cassava, Chinese sauerkraut, river water | 38. |
| SO$_3^{2-}$ | ICT | DMSO/HEPES (pH 7.4, 10 mM, v/v = 6/4) | 576/675 | 0–12 μM | 31.6 nm | | 39. |
| HSO$_3^-$ | ICT | PBS solution (pH 7.4, 10 mM) | 670/705 | 0.01–0.15 mM | 0.37 μM | crystal sugar, red wine, wine, soft sugar, crystal sugar, sugar granulated sugar | 40. |
| HSO$_3^-$/SO$_3^{2-}$ | ICT | PBS solution (pH 7.4, 20 mM, with 50% CH$_3$OH, v/v) | 485 | 0–3 μM | 27 nM | | 42. |
| HSO$_3^-$/SO$_3^{2-}$ | ICT | PBS solution (pH 7.4, 10 mM, with 10% DMF, v/v) | 500/717 560 | 0–4 μM | 87 nM | | 43. |
| CN$^-$ | ICT | PBS solution/DMF (pH 7.4, v/v = 1:1) | 490/519 688 | 0–80 μM | 0.075 μM | | 47. |
| NO$_2^-$ | ICT | HCl solution (pH 1.0, 0.1 M) | 567/656 | 0–1 μM | 6.7 nm | | 51. |
| Hg$^{2+}$ | IFE | EtOH/H$_2$O (pH 7.2, 10 mM HEPES, v/v = 2:1) | 547/756 | 0.05–10 μM | 13.5 nm | tap water, tea | 54. |

FRET = Fluorescence Resonance Energy Transfer; ICT = intramolecular charge transfer; IFE = Inner Filter Effect.
asthma and allergies in individuals [34–35]. Among the current methods of HSO3\(^-\)/SO3\(^2-\) detection, several fluorescent probes tend to stand out due to splendid on-site and real-time testing properties [36–37]. Moreover, fluorescent probes distinguished with significant NIR fluorescence response and colorimetric effect in HSO3\(^-\)/SO3\(^2-\) measurement procedures are capable even to optimize the background and enhance the resolution.

The number of NIR fluorescent probes possessing high sensitivity in the detection of HSO3\(^-\)/SO3\(^2-\) molecules, augmented by minimum autofluorescence interference, achieved a sustained and substantial growth. For example, an excellent NIR probe suitable for different types of analyte solutions was constructed to rely on the ICT mechanism (Fig. 1c-e) [38]. In this ingenious chemical sensor implement by Zeng et al., \((E)-3-(4-(dimethylamino)phenyl)acrylaldehyde, a common fluorescent sensor with high fluorescence yield and chemical stability, was utilized as the acceptor, and positively charged 1-Benzylquinolin-1-ium as the donor and mitochondria-targeting component. As the SO3\(^2-\) level improved, a linearly correlated reduction in the fluorescence signal at 690 nm was observed, which simultaneously faded the solution color from bluish violet to colorless. The applicability of this method was demonstrated in various sample types such as sugar, wine, HepG2 cells and even zebrafish, demonstrating its versatility. Another effort important to mention is the work of Duan et al. [39], where a novel NIR probe based on dicyanomethylene-benzopyran and quinolinium was reported to exhibit an extremely fast response (<50 s) in the detection of SO3\(^2-\) molecules, with a LOD of 31.6 nM. To achieve this, dicyanomethylene-benzopyran was chosen as a photostable fluorophore precursor, and quinolinium, possessing an electron-withdrawing ability, was used as a structure block to quench the fluorescence of the obtained probe. Once quinolinium was interrupted by SO3\(^2-\) anions through 1, 4-Michael addition reaction (an organic conjugate addition reaction), a notable chromogenic reaction (from yellow to purple) and an easily measurable NIR fluorescence response (from off to on) could be observed. Importantly, this method was successfully employed to visually detect SO3\(^2-\) anions in very common food samples such as granulated sugar and vermicelli, upon some mild conditions (pH 7.4, 37 °C). In another study that we find important, stabilized hemicyanine skeletons on the basis of IR-780 were designed as a fluorescent probe for HSO3\(^-\) determination in crystal sugar and red wine samples [40]. As HSO3\(^-\) anions increased gradually, HSO3\(^-\) mediated nucleophilic addition reaction towards the carbon atom in the probe was shown to trigger conspicuous fluorescence intensity attenuation at 705 nm with the fading of the blue reaction solution. In addition, this probe, featuring prominent biocompatibility and cell-membrane permeability, was applied for HSO3\(^-\) monitoring in HeLa cells and BALB/c mice, thereby exhibiting great potential for biological research such as in vitro and in vivo imaging.

Different approaches rely on ratiometric NIR fluorescent sensors, which not only exhibit notable SNR advantages, but are also enriched with the attributes of ratiometric fluorescent sensors which measure emission intensities at two disparate wavelengths to offer a self-calibration correction [41]. Such approaches had represented a welcome addition to the family of NIR sensors developed for HSO3\(^-\)/SO3\(^2-\) determination. In an interesting study, a super-assembled probe conjugating electron-donating 7-diethylamino coumarin fluorophore and an electron-withdrawing indolium derivative was found to test HSO3\(^-\)/SO3\(^2-\) anions with evident dual ratiometric and colorimetric signal alterations (Fig. 1f-h) [42]. More specifically, the nucleophilic attack of HSO3\(^-\)/SO3\(^2-\) anions could disrupt the conjugated bond of coumarin-indolium structures and discourage the ICT process, extinguishing this way the NIR fluorescence of the coumarin-indolium hybrid at 667 nm but recovering that of the coumarin moiety at 485 nm. On account of sufficiently low LOD (27 nM), the applications of this probe covered HSO3\(^-\) identification in food and serum samples, as well as
bioimaging of HSO3 anions in living cells. Furthermore, a straight- 
forward detection dipstick system relying on this probe was also 
successfully prepared to enable rapid-response and high-sen-
sitivity HSO3 analysis. In a later effort, the same research group 
devised an azo-coumarin-indolium conjugated probe with longer 
absorption and emission wavelengths via condensation reaction 
[43]. Upon addition of HSO3 anions, the optimized probe was qual-
ified to provide significant ratiometric and colorimetric fluores-
cence effects at 560 nm and 717 nm, respectively, indicating a 
typical ratiometric fluorescence pattern. On the strength of the 
superior response (down to 30 s) and LOD (estimated to be 
87 nM), this probe effectively enabled HSO3 detection in various 
food samples and exogenous/endogenous bioimaging in living 
cells.

In summary, the efforts discussed in this section have not only 
led to the development of NIR fluorescent sensors based on the 
nucleophilicity of HSO3/SO32 anions for HSO3/SO32 measurement 
in foodstuffs, but also introduced a new perspective to design sen-
sors that can be used to address other anion species in cells and 
even animal models. Hence, we find these investigations to repre-
sent an important progress of NIR fluorescent techniques in food 
chemistry.

**Cyanide anions**

Cyanide (CN-) anions, which are generally acknowledged as 
deadly anions, are known to induce cellular respiratory paralysis 
once they become tightly attached to the cytochrome oxidase, even 
at a low dosage [44]. Despite the fact that they represent a serious 
health hazard, extensive applications of CN- anions in various 
industrial processes still exist, generating contaminated industrial 
wastewater, which can pollute foodstuffs [45]. Furthermore, 
cyanogenic glycosides diffusely distributed in food crop species (sor-
ghum, bamboo shoot, almonds, and cassava) can also release CN- 
anions in the case of plant cell rupture caused by improper pro-
cessing [46]. To address the issue of food products contamination, 
an ingeniously ratiometric NIR fluorescent probe was established to 
sense CN- anions in numerous food samples (e.g. bamboo shoots, 
almonds and sprouting potatoes) without elaborate instrumenta-
tion (Fig. 2a-e) [47]. In this work the authors exploited NIR fluores-
cence in a method that differed in terms of working principles from 
ICT based ones; it relied on increasing the conjugation length of the 
probe to reduce the energy gap and realize red-shifted emission 
centered at 688 nm. This CN- detection probe was based on the 
unique nucleophilic function of the CN- anions to electron deficient 
double bonds such as carbon–carbon double bond, carbon–oxygen 
double bond, and carbon–nitrogen double bond. Upon treatment 
with CN- anions, a noticeable ratiometric fluorescence response 
appeared with the fluorescent intensities respectively at 519 and 
688 nm. The ratios of the fluorescent intensities at these two wave-
lengths were found to be closely correlated to the concentration of 
CN- anions, endowing this distinguished probe with the ability to 
accurately measure CN- levels.

Despite promising efforts such as those discussed in this sec-
tion, the number of reported fluorescence based sensors developed 
for CN- detection and analysis in food samples is low, and such 
sensors operating in the NIR domain are even scarcer. However, 
given the commendable results obtained in past related works, 
and their intrinsic advantages, we argue that NIR based methods 
aimed at detecting CN- anions qualitatively and quantitatively 
are in urgent need to enable food safety applications addressing 
this critical problem. The introduction of NIR ratiometric 
approaches, could, to some extent, overcome or alleviate artifacts 
deriving from photo bleaching and probe distribution, which 
would significantly enhance the accuracy of CN- contamination 
assessment.

**Nitrite anions**

As a vital intermediate of the nitrogen cycle, nitrite (NO2-) 
anions are actively under development in food products as additive 
and preservative agents [48]. To some degree, NO2 is a form of bio-
logical nitric oxide (NO, a toxic volatile compound) storage rather 
than a metastable final product [49]. Ascribing to this, excessive 
take of NO2 anions induces adverse effects on the population, 
especially in children and pregnant women, being responsible for 
the production of carcinogenic N-nitrosamines, which can be 
linked to blue baby syndrome and methemoglobinemia [50]. 
Therefore, extending the effectiveness of NO2 quantification 
methodologies, and developing novel methods that are more sen-
sitive compared to current ones, and which can be more conve-
niently implemented, is of extreme value. In this quest, Yu et al. 
[51] introduced a coumarin framework based NIR fluorescent sen-
sor possessing emission capabilities at 656 nm that was estab-
lished via the covalent assembly principle (Fig. 2f-g). Owing to an 
termolecular azo-coupling mechanism, the prepared sensor 
could react with NO2 anions through diazotization in a strong 
acidic environment and afterwards with the newly formed aryldia-
zonium through an electrophilic aromatic substitution reaction to 
test the azo-dye. More interestingly, in this identification pro-
cess of NO2- orange-colored azo-dye was further protonated into 
purple-colored form possessing NIR fluorescence. Additionally, 
the sensor in its initial acidulated state was completely dark, offer-
ing zero background, which significantly augmented the results of 
the performed NO2 analysis in river water, Chinese sauerkraut and 
Escherichia coli samples. The results were found to be consistent 
with measurements performed with the conventional NO2 identi-
fication method, the Griess assay.

Regarding the final step in the Griess assay, azo-coupling with 
activated aromatic rings is undoubtedly a reliable fluorescent sen-
sor strategy for NO2 determination. The combination of this strat-
egy and covalent-assembly principle has significant potential to 
accomplish zero background, effective spectral red-shift towards 
NIR region and optimal detection sensitivity, holding great pro-
mises in food security and basic scientific research.

**Heavy metal cations**

The overwhelming exploitation and usage of metals or ores 
have deep implications for environment pollution and food con-
tamination. This topic has hence attracted the attention and criti-
cisms of the society. Posing a huge threat to human health, 
heavy metal cations should only be present in trace amounts in 
foodstuffs, however levels that exceed the acceptable ones are fre-
quently observed. Such hazard levels can be linked to severe health 
issues such as neural disorders and cognitive deficit which have 
been found to occur after long term ingestion [52–53]. Although 
many traditional methods for heavy metal cations detection exist, 
such as atomic absorption/emission spectroscopy (AAS/AES) and 
inductively coupled plasma mass spectroscopy (ICP-MS), these 
solutions are highly dependent on either complicated pre-
paration or the availability of expensive and bulky instrumenta-
tion. NIR-based biosensors conceived for testing heavy metal 
cations in a highly rapid and low-cost fashion could play a huge 
role in the field. A prominent example of the significant value of 
NIR materials/technologies to address the heavy metal cations 
detection problem is the work of Annavaram et al. [54]. In this 
effort, spirolactam appended rhodamine-B (a fluorescent dye) 
based organic complex-RhDCP and UCNPs (type NaYF4: Yb, Er) 
were combined to constitute a sensing probe for Hg2+ analysis in 
tap water and black tea (Fig. 2h). Once the complexation between 
Hg2+ cations and RhDCP occurred, an internal filter effect (IFE), a 
radiative energy transfer phenomenon involving the absorption
of excitation or emission from fluorophores, would be elicited due to the evident spectral overlap between the absorption and emission bands of UCNPs and RhDCP-Hg\textsuperscript{2+}. By means of an IFE effect, the emission quenching of UCNPs at 547 and 756 nm was triggered. The efficiency of this process was proportional to the concentration of Hg\textsuperscript{2+} cations. Although a wide variety of fluorescent sensors have been reported and applied to date for Hg\textsuperscript{2+}, Fe\textsuperscript{3+}, Al\textsuperscript{3+}, Zn\textsuperscript{2+}, Cu\textsuperscript{2+}, and Pb\textsuperscript{2+} detection [55–56], to ensure food safety. The number of NIR sensors for metal cation detections is very limited. Given the success of the methodology based on the IFE effect reported by Anna-varam et al. [54], we hope that not far from now novel NIR based sensors will be developed to address this pressuring problem.

Organic substances

Organic substances are, in general, adverse for physical health when potentially ingested by humans. Unfortunately, the contamination of foodstuffs with organic compounds is frequent [57–59]. For example, benzoic peroxide exists in flour, formaldehyde in seafood, and organic benzenethiol in drinking water, etc [60–61]. In this context, a wide palette of fast and effective organic matter detection methodologies based on NIR fluorescence have been developed to date [62–63]. Furthermore, the introduction of antibodies and aptamers (short single-stranded DNA, RNA or peptide molecules selected from combinatorial libraries) as solutions to this problem enabled a new class of measurement techniques exhibiting highly specific targeting performance. Compared with traditional antibodies, aptamers are easily chemically synthesized, modified and stored for a large variety of biomolecules, chemical entities or cell targets [64]. In Table 2, we provide an overview of prominent NIR fluorescent sensors that have been developed for the detections of organics, categorized according to the targeted hazardous substances.

Foodborne pathogens

Although largely available and well-established food packaging techniques (e.g. pasteurization and vacuum packaging) offer foodstuffs relatively long preservation time, the contamination of the so packaged food products with foodborne pathogens still occurs, accounting for problematic health issues such as acute emesis and acute abdominalgia [65]. Over the past decade, food infections mediated by various foodborne pathogens such as Salmonella, Listeria, and Escherichia coli have been occurring all over the world [66]. On account of the warning of these events, preventive measures need to be taken, especially in the form of improving the efficiency of the pathogen detection strategies in food samples, and developing new monitoring strategies based on latest generation advanced materials. As one of the advanced identification strategies, NIR fluorescent technologies with almost perfect specificity and sensitivity have been proposed to detect pathogens. For example, a prominent aptasensor method unifying the anti-Stokes type emission of UCNPs (type NaYF\textsubscript{4}: Yb, Tm) with the Stokes type
emission of CdTe quantum dots (QDs) was conducted to simultaneously monitor multiple food pathogens (Fig. 3a-d) [67]. Owing to the upconversion property of UCNPs excited by NIR irradiation (980 nm) and down-conversion property of QDs by ultraviolet (UV) irradiation (325 nm) respectively, the detection system effectively avoided typical issues in conventional methods such as spectral overlap and signal crosstalk. Additionally, the DNA aptamers included in this sensor provided admirable sensitivity and specificity for the enabled bioassay, yielding LOD values of 16 and 28 cfu mL\(^{-1}\) for Staphylococcus aureus and Salmonella typhimurium sensing, respectively.

In brief, NIR-activated foodborne pathogen recognition biosensors proffer an alternative scheme to address the deficiencies of the traditional models such as moderate sensitivity and slow response. Moreover, different combinations of UCNPs and other luminescent units possessing non-overlapping fluorescence emission have broad research prospects and great research value for simultaneous detections of several analytes.

**Table 2**

| Test object | Detection medium | \(\lambda_{ex}/\lambda_{em}\) (nm) | Linear range | Detection limit | Applications in foodstuffs | Ref |
|-------------|------------------|-------------------------------|--------------|----------------|---------------------------|-----|
| S. aureus, S. typhimurium | PBS solution 325/527 (SA), 980/806 (ST) | 50-10^6 cfu/mL | 16 cfu/mL (SA), 28 cfu/mL (ST) | / | red wine, beer, grape juice, | 67. |
| Ochratoxin | borate buffer (pH 8.5) 980/660 | 0.1–1000 ng/mL (standard solution) | 0.098 ng/mL (standard solution), 0.449 ng/mL (wine), 0.108 ng/mL (grape juice), 0.208 ng/mL (beer) | / | | 68. |
| Patulin | PBS solution (10 mM) 980/543 | 0.01–100 ng/mL | 3 pg/mL | / | apple juice | 74. |
| Aflatoxin B1 | PBS solution (pH 7.4, 10 mM) 980/550 | 3.13–125 ng/mL | 0.17 ng/mL | / | peanut | 75. |
| Aflatoxin B1, Ochratoxin A | PBS solution 980/452 (AFB1), 980/660 (OTA) | 0.01–10 ng/mL | 0.01 ng/mL | / | maize | 77. |
| Zearealenone | assay buffer (with BGG and BSA based blocking buffer) 980/800 | 50–500 pg/mL | 20 pg/mL | / | maize | 78. |
| Sulfafquinoxaline | PBS solution 370/552 (QDs), 980/542 (UCNPs) 980/543 | 0–20 ng/mL | 1 ng/mL (standard solution), 8 µg/kg (sample) | / | chicken, shrimp | 83. |
| Enrofloxacin | nuclease-free water 980/543 | 0.976–62.5 ng/mL | 0.47 ng/mL (standard solution), 1.59 ng/mL (sample) | / | milk powder | 84. |
| Sulfafquinoxaline | PBS solution 980/474 | 0.1–100 µg/mL (standard solution), 0.5–500 µg/kg (sample) | 0.1 µg/mL (standard solution), 0.5 µg/kg (sample) | / | shrimp, milk, sea bass, beef, pork, chicken | 85. |
| Enrofloxacin \(\beta\)-lactams, Tetracyclines, Quinolones, Sulfonamides, | PBS solution 980/544 774/789 | 1–10 ng/mL 0.26–3.56 ng/mL (β), 0.04–0.98 ng/mL (T), 0.08–2.0 ng/mL (Q), 0.1–3.98 ng/mL (S) | 0.06 ng/mL 8 ng/mL (β), 2 ng/mL (T), 4 ng/mL (Q), 8 ng/mL (S) | / | fish | 86. |
| | | | | | milk | 87. |
| Diazinon | cyclohexane 980/800 | 0.1–50 ng/mL | 0.05 ng/mL | / | tap water, apple, lake water, pear, green tea powder | 94. |
| Diazinon | water 980/547 980/552 | 0.05–500 ng/mL 0.005–10 µg/mL | 0.023 ng/mL, 0.002 µg/mL (PBS), 2 ng/mL (river water/ fresh cane juice), 20 ng/kg (corn/ rice) | 0.1 µg/mL (tyramine), 0.01 µg/mL (histamine) | pork, bacon, trachitus ovatus, carassius auratus, turbot, cheese, soy sauce, rice vinegar, rice wine | 96. |
| Atrazine | PBS solution (pH 7.4, 0.01 M) 980/483 (tyramine), 980/550 (histamine) | 0.5–100 µg/mL (tyramine), 0.1–100 µg/mL (histamine) | / | / | 100. |

**Mycotoxins**

At present, mycotoxins are widely spread throughout the entire world, representing a significant concern given their strong toxicity even in trace amounts [68–69], which has been the main cause of dramatic outbreaks of various foodborne diseases. A variety of mycotoxins (e.g. ochratoxin, zearealenone, aflatoxin, patulin, and...
deoxynivalenol) coexisting in foodstuffs trigger a potential threat to biological health including skin irritation, immunosuppression, neurotoxicity, and even death [70–71]. Due to the expensive and bulky required equipment along with low screening efficacy, traditional mycotoxin detection methods are inadequate to meet the current requirements imposed by this critical problem at the present stage [72]. NIR fluorescent detection technologies represent a great promise to overcome the limitations of traditional methodologies, by enabling novel mycotoxin measurement tools and instruments that are fast, effective and simple to operate. In the following paragraphs, we discuss several experiments conducted to date that nicely reflect this situation.

On the basis of a nonradiative energy transfer process that occurs between lanthanide cation donor fluorophores and acceptors, NIR excited luminescence resonance energy transfer (LRET) techniques have been developed for intelligent mycotoxin determination. Besides additional quenchers, LRET techniques usually need aptamers to realize specific recognition with the corresponding complementary targets in various mycotoxin detection scenarios. In this respect, a single-step LRET aptasensor comprising Mn²⁺-doped UCNPs (type NaYF₄: Yb, Er) and black hole quencher 3 (BHQ3, a quencher dye) was reported to determine ochratoxin A without complex procedures (Fig. 4a-b) [73]. Interestingly, Mn²⁺ doping hindered the transition of Er³⁺ ions to generate an appropriate red emission which overlapped with the absorption of BHQ3 for LRET activation. As the samples containing ochratoxin A were added, the formation of an aptamer-target complex was observed to diminish the linker length between the UCNPs and BHQ3, significantly improving the LRET effect. To some extent, this aptasensor was endowed with increased quenching efficiency in synchronism with the quantity of ochratoxin A, thereby showing satisfactory capacity for quantitative detection in colored food samples (e.g. wine, beer, and grape juice). Moreover, an intriguing LRET assay based on UCNPs (type NaYF₄: Yb, Er) donors and gold NPs acceptors was designed for exonuclease-catalyzed target recycling patulin measurement [74]. In this research, complementary single-stranded DNA strands, availably connected UCNPs and gold NPs were combined to exploit the controlled quenching of the upconversion luminescence. With the presence of patulin, the quenching effect could be effectively attenuated as patulin was bound to the corresponding aptamer for the construction of the stem-loop structure and for the liberation of UCNPs. Most importantly, additional exonuclease owning specificity to single-stranded DNA was exploited to digest the patulin aptamer selectively, thus releasing patulin for subsequent recycle. By virtue of the remarkable linear range (0.01–100.00 ng mL⁻¹) of the method, accompanied by efficient recoveries (93.33–105.21%), this ingenious LRET assay was successfully employed to sense patulin in apple juice samples. In another notable effort exploiting LRET, Wang et al. developed a method based on aptamer-modified UCNPs (type NaYF₄: Yb, Er) and gold NPs to detect aflatoxin B1 in peanut samples [75]. In the presence of aflatoxin B1, gold NPs attached to the UCNPs were gradually replaced by the aflatoxin B1, thus leading to dose-interrelated fluorescence recovery. By counting the number of luminescent particles on the glass slide surface, this single-particle measurement method successfully led to the readout of the concentration of aflatoxin B1.

In competitive immunoassays, an analyte and a labeled antigen compete for a limited number of antibody binding sites. This allows a precise quantification of the antibody amount that becomes bound with the attached analog antigens [76]. As a handy and sensitive strategy, competitive upconversion-linked immunoassay have made a profound impact on mycotoxin detection. For instance, a NIR-activated immunosorbent method was exploited to simultaneously analyze aflatoxin B1 and ochratoxin A in contaminated maize samples (Fig. 4c) [77].

**Fig. 3.** NIR fluorescent sensors for foodborne pathogen detection. (a) Design of a dual-excitation NIR fluorescent probe for foodborne pathogen detection. (b) Fluorescence spectra changes with Staphylococcus aureus (c) Fluorescence spectra changes with Salmonella typhimurium. (d) Specificity evaluation of a dual-excitation NIR fluorescent probe. Adapted with permission [67]. Copyright 2016, Elsevier.
method adopted artificial antigen-modified magnetic NPs as immunosensing probes and antibody functionalized UCNPs (type NaYF4: Yb, Tm; NaYF4: Yb, Er) as multicolor signal probes. The antibody-antigen affinity was exploited as the link between the two types of NPs. Additional magnetic NPs were found adequate to optimize the overall assay efficacy by separating and purifying the immunocomplexes. Upon laser irradiation at 980 nm, a robust fluorescence signal was generated by the UCNPs, which was very useful for the efficient sensing of small toxin molecules. This approach based on energy upconversion helped overcome the problem of target toxins autofluorescence. Farther, amount of immunocomplexes was reduced as mycotoxin concentrations increased, resulting in lower fluorescent signal recorded from the emitting UCNPs. In a different study, Yang et al. [79] introduced a small portable device as an innovative quantitative analysis platform for real-time and off-site mycotoxin determination (Fig. 4d). This method relied on multicolor UCNPs (type NaYF4: Yb, Tm@NaYF4: Er@NaYF4: Yb, Tm; NaYF4: Yb, Tm; NaYF4: Yb, Er) barcodes and fluorescence image processing algorithms. More concretely, encoded signals from microspheres doped with red/blue/green-emitting UCNPs were identified, which effectually mediated indirect competitive immunoassays that were demonstrated to be efficient for the simultaneous detections of diverse mycotoxins including aflatoxin B1, ochratoxin A, and zearalenone. A proprietary algorithm was used to process the images captured by the portable device, which offered a reliable result about the type and concentration of mycotoxins within 1 min. Such handheld devices are likely to play a huge impact in coming years in ensuring food safety in geographic regions with less developed economies, where the availability of complex specialized equipment and trained operators is limited.

Given that mycotoxin pollution yields huge economic losses to food enterprises, livestock and poultry farms, and food processing industries, finding the best detection strategies is of ultra-high importance. Ingenious methods that rely on NIR fluorescent sensors for mycotoxin detection, such as those discussed above represent a great promise in the quest of enhancing the current state of the art. They were shown to provide very high accuracies and sensitivities, features that directly intertwine with the NIR emission/excitation properties responsible for reduced background. Additionally, NIR based multidisciplinary detection assays can be designed in a myriad of ways, fostering and stimulating further developments in connected technologies such as aptamer probes, target recycling, digital enumeration, peptide design, detection equipment, etc.

Fig. 4. NIR fluorescent sensors for mycotoxin detection. (a) Scheme of single-step LRET aptasensor mediated ochratoxin A detection. (b) Fluorescence spectra changes with ochratoxin A. Adapted with permission [74]. Copyright 2017, American Chemical Society. (c) Scheme of the preparation process and aflatoxin B1/ochratoxin A detection for a NIR-activated immunosorbent sensor. Adapted with permission [78]. Copyright 2011, Elsevier. (d) Design of simultaneous mycotoxin detection based on a small portable device. Adapted with permission [80]. Copyright 2018, The Royal Society of Chemistry.
Antibiotic residues

In animal husbandry, the widespread use of antibiotics including tetracyclines, quinolones, sulfonamides and β-lactams has become a standard as a result of their roles in growth promotion, disease prevention and cure [80]. However, such practices are not always implemented carefully. Using uncontrolled antibiotic dosing levels can lead to significant issues such as increasing the emergence of antibiotic-resistant bacteria or the presence of drug residues in the final product that is marketed, which can cause allergies, and various other health problems, including severe pathologies such as cancers [81–82]. In case antibiotic residues are found above critical limits, the product is regarded as a health hazard and needs to be discarded. Hence, there is a great need for cutting-edge, low-cost, and super-sensitive approaches for testing antibiotics’ signatures in various types of foodstuffs, in different stages along their route from farm to market.

Over recent years, the LRET technology has attracted significant attention, in the context of antibiotics detection given its promising performance in connected applications. Among the relevant efforts conducted on this topic, in a work performed by Hu et al., an UCNP (type NaYF₄: Yb, Er) based luminescence quenching immune chromatographic strip was confirmed to be efficient in monitoring sulfamethoxazole (a sulfonamide antibiotic) in foods of animal origin (Fig. 5a-b) [83]. Upon adding sulfamethoxazole samples, a competition between the free sulfamethoxazole and immobilized sulfamethoxazole-ovalbumin took place in a race to combine with a colloidal gold labeled antibody. In this case, less colloidal gold labeled antibody was captured whereby colloidal gold acceptors were inadequate to quench the luminescence of UCNP donors completely. Overcoming typical problems associated to traditional colloidal gold-based strips, this strip featured low cost, one-step operation and visual result judgment, and was shown to generate an optical signal positively correlated with the targets even at weak intensity. Impressively, the obtained strip revealed detection results highly consistent with those yielded by commercial kits in chicken and shrimp samples, with significantly higher performance. With approximately 13-fold lower LOD (1.59 ng mL⁻¹) than a commercial kit, another LRET based aptasensor consisting of core–shell UCNP (type NaYF₄: Yb, Er, Gd) donors and graphene oxide (GO) acceptors was found to be a highly efficient solution for enrofloxacin (a quinolone antibiotic) analysis in milk powder samples [84]. The core–shell structure and Gd³⁺ doping provided UCNPs with enhanced fluorescence intensity and improved the efficiency of the LRET process. This sensitive and cost-effective aptasensor was found to exhibit splendid specificity, being capable to discard signatures associated to other antibiotic residues that could have resulted in a high false-positive rate.

Immunoaasays represent as well very promising antibiotic detection candidates. In competitive immunoassay format, UCNP (type NaYF₄: Yb, Tm) and magnetic polystyrene microspheres were integrated in a system addressing sulfamethoxazole measurement [85]. Building on the advantages of the simple and fast extraction procedure, not involving organic solvents, recoveries of sulfamethoxazole could be significantly measured in the range of 69.80–133.00% in animal-derived food samples. Particularly, this immunoassay showed equal performance in the analysis of sulfamethoxazole in diluted milk samples with a reported LOD of 0.5 μg kg⁻¹. In another notable work, Fe₃O₄ NPs were ingeniously used to immobilize aptamers as magnetic substrates in a new-style NIR fluorescent hybrid probe, with UCNP (type NaYF₄: Yb, Er) as signal sources (Fig. 5c) [86]. On account of the aptamer recognition process, enrofloxacin quantification was simply realized via reading signal alterations from UCNPs. Showing satisfactory values in accuracy, sensitivity, selectivity, linearity, and precision, the proposed hybrid probe was capable of detecting enrofloxacin in various fish samples, including Spanish mackerel, perch, catfish, and snakehead. As regards multiplex lateral flow immunoassays, a novel NIR label was combined with a monoclonal antibody of broad-specificity for screening different antibiotic residues in milk samples (Fig. 5d) [87]. In this interesting approach, diverse antigens were located in separate test zones of a nitrocellulose membrane as capture agents, completing simultaneous analyses of four antibiotic samples including tetracyclines, quinolones, sulfonamides and β-lactams. By means of analyzing the fluorescence intensity of the NIR label, qualitative and quantitative assessment of antibiotic residues was successfully implemented, with LODs and cut-off values meeting the requirements imposed by EU legislation.

Serious health hazards arise from antibiotics being widely used as food additives in livestock and poultry industries given that significant amounts are not properly absorbed nor excreted in the faeces, causing contamination of the subsequent foodstuffs. Recent efforts such as those discussed above suggest that NIR hybrid sensors integrating multiple functions such as specific recognition, stable fluorescence, and reliable magnetic properties can intelligently transform and significantly improve the antibiotic identification process yielding enhanced contamination control.

Pesticide residues

In modern agriculture, pesticides equipped with prominent insect killing effectiveness are widely applied to protect crops from pests and so ensuring high yields [88]. However, the overuse of pesticides, which is very common [89–90], represents an extremely serious food safety issue as it results in the accumulation of indigestible, and highly harmful, pesticides in the body for long periods of time [91]. Furthermore, inappropriately disposed pesticides might be ingested by humans via different contamination routes including atmosphere, water, and agricultural products, resulting in enormous threats to human health [92], given that even low-doses can result in the installment of various conditions and pathologies [93]. Thus, the advent of novel strategies that overcome the bottlenecks of pesticide detection (e.g. limited storage time, complicated pretreatment and expensive instruments) is highly important, and very urgent. Considering recent results, methods based on NIR fluorescence detection technologies are likely to play a very important role in the next years in the context of pesticide residues monitoring, acting as reliable guardians of food safety.

LRET and immunoassays are probably the most commonly employed NIR fluorescence detection schemes for recognizing pesticide residues. With respect to the former, we find important to mention the effort of Wang et al. [94], where an acetylcholinesterase modulated biosensor featuring an UCNP (type NaGdF₄: Yb, Tm)-Cu²⁺ mixture was manufactured for Diazinon (an organ phosphorus pesticide) determination (Fig. 6a-b). In this platform, thiocholine (considered as an enzymatic hydrolysate of acetylthiocholine) was able to seize Cu²⁺ from UCNP-Cu²⁺, which was accountable for the luminescence quenching of the UCNPs. Since Diazinon irreversibly impaired the enzymatic activity of acetylcholinesterase, the production of thiocholine would decrease greatly in samples containing Diazinon, thus reducing the luminescence recovery. Based on the above mechanisms, this biosensor, featuring a reliable linear detection (0.1–50 ng mL⁻¹) was demonstrated in contaminated environmental and agricultural samples. Analogously, in a different effort, UCNP (type NaYF₄: Yb, Er) and GO were selected as foundations to construct a practical fluorescence sensor for Diazinon analysis in real food samples [95]. Once adsorbed onto the GO surface via a π-π interaction, the aptamer-modified UCNP donors would quench their own luminescence. With the addition of Diazinon, this phenomenon was terminated,
leading to a linear recovery in the fluorescence intensity of the UCNPs. In a different type of approach, a competitive upconversion-linked immunoassay technology was harnessed to result in a highly sensitive system for Atrazine monitoring, a pesticide commonly found in sugar cane juice, rice, corn, and river water samples [96]. In this immunoassay system, anti-Atrazine antibody conjugated UCNPs (type NaYF4: Yb, Er) and antigen conjugated polystyrene magnetic microspheres were utilized as the signal and capture probes, respectively. Interestingly, the antigen was entitled to compete with Atrazine for antibody binding and immunocomplex formation. Upon excitation at 980 nm, the intensity of green fluorescence yielded by the magnetic separated complexes was measured to reflect the count of pesticide residues.

Current forecasts on agricultural economy suggest that the use of pesticides will continue to increase, globally. This will result in higher needs for detection tools that are not only better compared to the current solutions but also more affordable and more easy to use. Detection methods based on NIR fluorescence are expected to be of great help in this quest, as efforts such as those discussed above demonstrated that they could enable specific target analyses in cooperation with various technologies, e.g. enzyme inhibition technology, aptamer technology and immune technology.

Biogenic amines

Known as bioactive nitrogen-containing compounds with low molecular weight, biogenic amines (BAs) including histamine, tyramine, cadaverine, spermine, spermidie, phenylethylamine and putrescine are transformed from protein in foods through microbial amino acid decarboxylase [97]. Adequate ingestion of BAs from various foods (e.g. fruits, vegetables, dairies, seafoods, fermented foods, meat products and beverages) can expedite physiological metabolism, enforce immunity, and improve body constitution. However, improper intake of BAs may bring about diverse reactions, such as abdominal cramps, tachycardia, vomiting, and migraine [98] and can even result in various diseases [99]. Thus, efficient detection approaches are urgently needed for the screening of BAs in daily protein-rich foods.

Recent efforts suggest the potential of NIR based technologies to significantly contribute to BA detection. For example, Wu et al. [100] reported a method for histamine sensing based on a material that was synthesized by coating a layer of molecularly imprinted polymers doped with silver nanoparticles on the surface of UCNPs. In the presence of histamine, the fluorescence intensity of the proposed material was quenched gradually while, conversely, the intensity of Surface Enhanced Raman Scattering (SERS) signals, yielded by the same material, increased gradually. This dual effect led to achieving a histamine LOD of 0.009 mg L\(^{-1}\) for the fluorescence mode, and 0.04 mg L\(^{-1}\) for the SERS mode, showing the huge potential held by dual responsive materials for BA detection. In a more recent effort, an analytical strategy based on the NIR fluorescence of multi-color UCNPs (type NaYF\(_4\): Yb, Tm) labels was developed to detect tyramine and histamine concurrently in meat, fermented products and aquatic origin foodstuffs (Fig. 6c-e) [101]. Upon laser excitation at 980 nm, two types of UCNPs displayed different single emission peaks respectively at 483 nm and 550 nm, laying the foundation for multiple BAs identification scenarios. In addition, magnetic microspheres were linked to the tyramine or histamine coating antigens as capture probes for the competition with analytes. By reason of the simple
competitive immune process that was ingeniously exploited, this
strategy reduced the total test time, saving approximately 10–
20 min of the color development time, and promoted the efficient
detection of the targeted BAs.

At present, the detection of BAs in food samples generally refers
only to the analysis of histamine. However, many foodstuffs con-
tain other BAs, some of which may possibly induce a synergistic
effect to heighten the toxicity of histamine. Therefore, simultane-
ous detection of multi-component BAs is of great significance for
ensuring food safety. Given the flexibility of detection technologies
that rely on NIR fluorescence discussed in this review, we are con-
fident that novel, highly efficient, BA detection schemes will soon
be reported.

Conclusion and perspectives

In conclusion, all NIR fluorescent sensors discussed herein
demonstrate the tremendous potential of such technologies to
ensure food safety. Works reported in recent years show that var-
ious materials capable of NIR fluorescence can be functionalized
for many applications targeting different contaminants and differ-
ent foodstuffs. Nevertheless, it should be noted that so far most
efforts addressing the development of NIR fluorescent sensors
had been focused on biological imaging, whereas food safety meth-
ods based on NIR fluorescent sensors are still in their infancy. Even
though such methods have many unique requirements, some of
them not easy to address, the connected body of work performed
to date suggests that NIR fluorescent sensors will assume in the
coming years a significant role in food safety, once several barriers
to further progress are addressed. Some of the most representative
issues are outlined below:

First, a wide palette of sophisticated NIR fluorescent sensors
have been reported [102–103], and although they present impor-
tant advantages in terms of SNR, the entire elimination of the back-
ground signals in food samples is still a challenge. Therefore,
additional efforts need to be placed on the following designs: (1)
time-gated luminescence performance, (2) unique fluorescence
signal peaks; (3) stability in weak acid or alkali; (4) excellent sen-
sitivity for the target. In this context we find noteworthy to men-
tion that the introduction of functional ligands and polymers is
promising to foster the development of novel NIR fluorescent sen-
sors that will yield important breakthroughs in terms of detection
sensitivity and specificity [104].
Secondly, most NIR fluorescent sensors introduced to date were reported to enable single-species detection, whereas different types of food contaminant sources may co-exist in foodstuffs such as foodborne pathogens and mycotoxins. Obviously, single-species detection is inadequate to match all contaminants in foodstuffs. Multispecies detection would allow to completely rule out the possibility of food spoilage, thus such methods are desperately demanded in the food industry, to effectively safeguard the quality of foodstuffs.

Third, NIR fluorescent sensors should be more practical (e.g. more easy to create, more simple to operate, available in miniaturized, portable and affordable devices) to satisfy the customers and market requirements. For this purpose, continually in situ techniques are well-suited to help individuals obtain the real-time situation of food samples. In parallel, developing fluorescent sensors endowed with color variability upon disparate target concentrations would contribute to naked eye detection or to the implementation of accessible read-out strategies, e.g. test paper designs.

We also find important to mention that an increasing number of multi-modal sensors tactfully integrate multiple detection strategies into a single platform, exploiting in tandem their superiorities, and thus yielding higher detection accuracy, sensitivity and stability. However, such efforts are still tentative when it comes to using NIR based sensors for food safety applications. We anticipate that the development of such combined approaches could play an important role in further consolidating the role of NIR technologies in this field, given that many available tools and methods can significantly augment their use. For instance, nuclear magnetic resonance (NMR), identified as another fast, precise and non-invasive technology can cooperate with NIR fluorescent sensors for improved food safety detection. Such combined approaches would provide more comprehensive food quality information for vegeta-
bles, fruits, meat, and aquatic products. In this respect, NMR parameters are engaged to reflect microbiological growth and effectively verify the reliability of foodborne pathogen detection by NIR fluorescent sensors.

Other NIR fluorescence applications that are highly expected are those referring to the in vivo detection of ingested substances regarded as health hazards. With regard to the timely detection of contaminants, in vivo, in the human body, NIR fluorescent sensors are equipped with unrivaled advantages since UV and visible fluorophores hold limited penetration depth. On the grounds of qualitative and quantitative analysis of data linked to the outputs of NIR fluorescent sensors, physicians could detect the nature of the hazardous substances that was ingested, its amount, and consequently could arrange the corresponding treatment plan to relieve suffering and restore health of patients. Similar approaches based on in vivo probing of NIR fluorescent materials could be of help for researchers in efforts to understand nosogenesis aspects linked to various food contamination sources. In addition, the advent of such methods and applications would play a tremendous role in medicine, which could be extended to the early diagnosis of other non-foodborne diseases such as metabolic syndrome and cancer [105].

We strongly hope that this review will facilitate the future development of highly efficient and versatile NIR fluorescent sensors, by providing an overview of notable recent efforts that have been reported in the field of food safety detection.

Compliance with ethics requirements

This review does not contain any studies with human or animal subjects.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgement

This work was supported by the National Natural Science Foundation of China (51803228, 51873225), the Zhejiang Provincial Financial Support (R5110230). SG Stanciu acknowledges the support of UEFISCDI Grant RO-NO-2019-0601 MEDYCONAI. SGS and FY acknowledge the support of the EsSence CA19118 COST Action, which facilitated fruitful interactions.

References

[1] Hofseth LJ, Hebert JR, Chanda A, Chen H, Love BL, Pena MM, et al. Early-onset colorectal cancer: Initial clues and current views. Nat Rev Gastroenterol Hepatol 2020;17(6):352–64. doi: https://doi.org/10.1038/s41575-019-0253-4.
[2] Anelich L, Ruei R, Farber JM, Parreira VR. SARS-CoV-2 and risk to food safety. Front Nutr 2020;7. doi: https://doi.org/10.3389/fnut.2020.580551.
[3] Prezelj A, Olveza A, Pecar S. Abuse of clenbuterol and its detection. Curr Med Chem 2003;10:281–90. doi: https://doi.org/10.2174/09298670333368310.
[4] Jin HJ, Kim J-C. The effects of the BSE outbreak on the security values of US agribusiness and food processing firms. Appl Econ 2008;40(3):357–72. doi: https://doi.org/10.1080/00036840701873674.
[5] Cheng Y, Liu Y, Huang J, Li K, Zhang W, Xian Y, et al. Combining biofunctional magnetic nanoparticles and atp bioluminescence for rapid detection of escherichia coli. Talanta 2009;77(4):1332–6. doi: https://doi.org/10.1016/j.
[6] Flynn K, Villareal BP, Barranco A, Belc N, Bjomissions B, Bucos V, et al. An introduction to current food safety needs. Trends Food Sci Techn 2019;84:1–3. doi: https://doi.org/10.1016/j.
[7] Chocholoski P, Solich P, Satinski D. An overview of sequential injection chromatography. Anal Chim Acta 2007:600(1-2):129–35. doi: https://doi.org/10.1016/j.
[8] Miao YB, Ren HX, Gan N, Cao Y, Li TH, Chen YJ. Fluorescent aptasensor for chloramphenicol detection using DlE-encapsulated liposome as nanotracer. Biosens Bioelectron 2016;81:454–9. doi: https://doi.org/10.1016/j.
[9] Xing W, Neethirajan S. Ensuring food safety: Quality monitoring using microfluidics. Trends Food Sci Techn 2017;65:10–22. doi: https://doi.org/10.1016/j.
[10] Yaseen T, Pu HB, Sun DW. Functionalization techniques for improving sers substrates and their applications in food safety evaluation: A review of recent research trends. Trends Food Sci Techn 2018;72:162–74. doi: https://doi.org/10.1016/j.
[11] Shephard GS. Determination of mycotoxins in human foods. Chem Soc Rev 2008;37:2468–77. doi: https://doi.org/10.1039/b713084b.
[12] Umesh S, Manukumar HM. Advanced molecular diagnostic techniques for detection of food-borne pathogens: Current applications and future challenges, Crit Rev Food Sci Nutr 2018;58(1):84–104. doi: https://doi.org/10.1080/10408398.2015.1126701.
[13] Fang Yu, Shang J, Liu D, Shi W, Li X, Ma H. Design, synthesis, and application of a small molecular NIR-II fluorophore with maximal emission beyond 1200 nm. J Am Chem Soc 2020;142(36):15271–5. doi: https://doi.org/10.1021/jacs.0c08179.10.1021/jacs.
[14] Luo S, Zhang E, Su Y, Cheng T, Shi C. A review of NIR dyes in cancer targeting and imaging. Biomaterials 2011;32(29):7127–38. doi: https://doi.org/10.1016/j.
[15] Behkhe K, Marhejczyk JE, Brehm R, Wurtz C, Ramos Gomes F, Dullin C, et al. Target-specific nanoparticles containing a broad band emissive NIR dye for the sensitive detection and characterization of tumor development. Biomaterials 2013;34(1):160–70. doi: https://doi.org/10.1016/j.
[16] Rabie H, Zhang Y, Pasquale N, Lagos MJ, Batson PE, Lee K-B. NIR biosensing of neurotransmitters in stem cell-derived neural interface using advanced core-shell upconversion nanoparticles. Adv Mater 2019;31(14):1806991. doi: https://doi.org/10.1002/adma.201806991.
[17] Egawa T, Hanaka K, Koide Y, Ujita S, Takahashi N, Ikegaya Y, et al. Development of a far-red to near-infrared fluorescence probe for calcium ions and its application to multicenter neuronal imaging. J Am Chem Soc 2011;133(36):14157–9. doi: https://doi.org/10.1021/ja205809h.
[18] Hirayama T, Van de Bittner GC, Gray DW, Lusenko S, Chang CJ. Near-infrared fluorescent sensor for in vivo copper imaging in a murine wilson disease.
F. Yang, J. Yao, F. Zheng et al. Journal of Advanced Research 41 (2022) 129–144

Yang M, Zhang Y, Cui M, Tian Yu, Zhang S, Peng K, et al. A smartphone-based detection of metal ions. Sens Actuat B 2016;218:311–8. doi: https://doi.org/10.1016/j.snb.2016.02.105

Allard MW, Bell R, Ferreira CM, Gonzalez-Escalon A, Hoffmann M, Muravu T, et al. Genomics of foodborne pathogens for microbial food safety. Curr Opin Biotechnol 2018;49:224–9. doi: https://doi.org/10.1016/j.copbio.2017.11.022

Kurt H, Yuce M, Hussain B, Budak H. Dual-excitation upconverting nanoparticle and quantum dot aptasensor for multiplexed food pathogen detection. Biosens Bioelectron 2016;81:280–6. doi: https://doi.org/10.1016/j.bios.2016.02.019

Cimbalov A, Alonso-Garrido M, Font G, Manyes L. Toxicity of mycotoxins in vivo on vertebrate organisms: A review. Food Chem Toxicol 2020;137:111161. doi: https://doi.org/10.1016/j.fct.2020.111161

Berthiller F, Creutziger A, Pajtla C, Saenger G, Karlowski P, et al. Masked mycotoxins: A review. Mol Nutr Food Res 2013;57(1):165–86. doi: https://doi.org/10.1002/mnfr.201200764

Plišči-Mesljević A, Mandrevski RA. Ochratoxin a: An overview on toxicity and carcinogenicity in animals and humans. Mol Nutr Food Res 2007;51:1192. doi: https://doi.org/10.1002/mnfr.200709020

Marin S, Ramos AJ, Cano-Sancho G, Sanchis V. Mycotoxins: Occurrence, toxicology, and exposure assessment. Food Chem Toxicol 2013;60:218–37. doi: https://doi.org/10.1016/j.fct.2013.07.047

He T, Wang Y, Li P, Zhang Qi, Lei J, Zhang Z, et al. Nano-based enzyme immunoassay for aflatoxin in agro-products with high tolerance to coelenterate method. Anal Chem 2014;86(17):8873–80. doi: https://doi.org/10.1021/ac500210w

Jo E-J, Byun J-Y, Mun H, Bang D, Son JH, Lee JY, et al. Single-step LRET aptasensor for rapid mycotoxin detection. Anal Chem 2018;90(1):716–22. doi: https://doi.org/10.1021/acs.analchem.7b04827

Wu Z, Xu E, Jin Z, Idrulayaraj J. An ultrasensitive aptasensor based on fluorescent resonant energy transfer and exonuclease-assisted target recycling for patulin detection. Food Chem 2018;249:136–42. doi: https://doi.org/10.1016/j.foodchem.2018.01.025

Wang Xu, Cohen L, Wang J, Walt DR. Competitive immunoassays for the simultaneous detection of antibiotics and carcinogenicity in animals and humans. Mol Nutr Food Res 2011;30(1):35–42. doi: https://doi.org/10.1016/j.bios.2011.08.023

Zheng H, Sheng R, Li H, Ahmad W, Chen Q. Rapid and selective detection of bacillus cereus in food using cdna-based up-conversion fluorescence spectrum copy and aptamer modified magnetic separation. Spectroct Acta Pt A-Molcule Spectr 2022;267:120618. doi: https://doi.org/10.1016/j.saa.2021.120618

Su S, Mo Z, Tan G, Wen H, Chen X, Deshmukh A. PAA modified upconversion nanoparticles for highly selective and sensitive detection of Cu2+ ions. Front Chem 2021;9:41933–44. doi: https://doi.org/10.3389/fchem.2021.41933

Zhong B, Sheng W, Liu Y, Huang N, Zhang W, Wang S. Multiplexed fluorescence immunosensor combined with magnetic separation and upconversion nanoparticles as multicolor labels for the simultaneous detection of tyramine and histamine in food samples. Anal Chim Acta 2020;1130:1137–25. doi: https://doi.org/10.1016/j.aca.2020.07.043

Zheng H, Sheng R, Li H, Ahmad W, Chen Q. Rapid and selective detection of bacillus cereus in food using cdna-based up-conversion fluorescence spectrum copy and aptamer modified magnetic separation. Spectroct Acta Pt A-Molcule Spectr 2022;267:120618. doi: https://doi.org/10.1016/j.saa.2021.120618

Suu S, Mo Z, Tan G, Wen H, Chen X, Deshmukh A. PAA modified upconversion nanoparticles for highly selective and sensitive detection of Cu2+ ions. Front Chem 2021;9:41933–44. doi: https://doi.org/10.3389/fchem.2021.41933

Maddahfar M, Wen S, Hosseinpour Masahki SM, Zhang L, Shimon O, Stenzel B, et al. Stable and highly efficient antibody-nanoparticle conjugation. Bioconjugate Chem 2021;32(6):1146–55. doi: https://doi.org/10.1021/acs.bioconjchem.0c00192

Chen Y, Shimon O, Huang G, Wen S, Liao J, Duong HTT, Maddahfar M, Su QP, Ortega DC, Lu Y, Campbell DH, Walsh BJ, Jin D. Upconversion nanoparticle-assisted single-molecule assay for detecting circulating antigens of aggressive prostate cancer. Cytom A 2021. doi: https://doi.org/10.1002/cyt.a.24564

Fang Yang is currently acting as an Associate Professor at Cixi Institute of Biomedical Engineering, Ningbo Institute of Materials Technology and Engineering, Chinese Academy of Sciences (CIBE-NIMTE) and is involved in multiple research projects related to nanobiomaterials and their biological effect. His Bachelor in Physics (2010), Masters of Physics (2012) and PhD in Chemistry (2016) titles were awarded by the Phillips University of Marburg (PUM) in Germany. His research studies Fang was deeply involved in research: 2008-2012 Research Assistant at the Biophotonics Department of PUM; 2010-2012 Researcher at the Biophysical Chemistry Department of PUM; 2012-2016 full time Researcher and PhD student at the Biophysical Chemistry department of PUM. He has authored more than 30 scientific publications with an H-index 10.
F. Yang, J. Yao, F. Zheng et al. Journal of Advanced Research 41 (2022) 129–144

Junjie Yao obtained his Bachelor degree in Biological Engineering from China University of Mining and Technology in June 2018, and received his Master degree in Materials Physics and Chemistry at Cixi Institute of Biomedical Engineering, Ningbo Institute of Materials Technology and Engineering, Chinese Academy of Sciences (CIBE-NIMTE) in June 2021. His research project focuses on the functional nanomaterials for cancer diagnosis and treatment.

Fang Zheng obtained her Bachelor degree in Materials Chemistry from Anhui Normal University in June 2018, and received her Master degree in Materials Engineering at University of Science and Technology of China in June 2021. Her research project focuses on the magnetic nanomaterials for cancer diagnosis and treatment.

Yao received his PhD from University of Bayreuth, Germany in 2014. Then he worked as Scientific Coworker during 2014-2017 at Neue Materialien Bayreuth GmbH, Germany and TransMTF GmbH, Germany, respectively. In 2017, he was awarded “Jiangsu Distinguished Professor” and worked at the College of Materials Science and Engineering in Nanjing Forestry University. His current research interests include but not limited to the following topics: biased materials, stimuli materials, functional wood materials, high performance fibrous materials, energy storage materials. He has published more than 120 papers with a citation more than 5000 and H-index of 45.

Shaohua Jiang received his PhD from University of Bayreuth, Germany in 2014. Then he worked as Scientific Coworker during 2014-2017 at Neue Materialien Bayreuth GmbH, Germany and TransMTF GmbH, Germany, respectively. In 2017, he was awarded “Jiangsu Distinguished Professor” and worked at the College of Materials Science and Engineering in Nanjing Forestry University. His current research interests include but not limited to the following topics: biased materials, stimuli materials, functional wood materials, high performance fibrous materials, energy storage materials. He has published more than 120 papers with a citation more than 5000 and H-index of 45.

Hui Du obtained her Bachelor degree in Chemical Engineering and Technology from Binzhou University in June 2013, and received his Master degree in Materials Technology and Engineering from China University of Mining and Technology in June 2016. Now he is acting as an engineer at Cixi Institute of Biomedical Engineering, Ningbo Institute of Materials Technology and Engineering, Chinese Academy of Sciences (CIBE-NIMTE). Her research project focuses on the preparation of zinc-doped ferrite nano-materials and their bio-applications.

Bo Jiang obtained his Bachelor degree in Electronic Information Science and Technology from Binzhou University in June 2013, and received his Master degree in Materials Technology and Engineering from China University of Mining and Technology in June 2016. Now he is acting as an engineer at Cixi Institute of Biomedical Engineering, Ningbo Institute of Materials Technology and Engineering, Chinese Academy of Sciences (CIBE-NIMTE). His current research interest focuses on the preparation of nano-materials by laser ablation in liquid.

Shaozhu Jiang received his PhD from University of Bayreuth, Germany in 2014. Then he worked as Scientific Coworker during 2014-2017 at Neue Materialien Bayreuth GmbH, Germany and TransMTF GmbH, Germany, respectively. In 2017, he was awarded “Jiangsu Distinguished Professor” and worked at the College of Materials Science and Engineering in Nanjing Forestry University. His current research interests include but not limited to the following topics: biased materials, stimuli materials, functional wood materials, high performance fibrous materials, energy storage materials. He has published more than 120 papers with a citation more than 5000 and H-index of 45.

Stefan G. Stanciu received the PhD. degree in electronics and telecommunications from University Politehnica of Bucharest (UPB), Bucharest, Romania, in 2011. He was a Postdoctoral Researcher with UPB and ETH Zurich, Zürich, Switzerland. He is currently a Principal Investigator with Center for Microscopy-Microanalysis and Information Processing, UPB. He has coauthored >60 Web of Science journal articles, with >30% as main author, and several book chapters. His research focuses on high- and super-resolution imaging by scanning laser and scanning probe microscopies. He acted as a Management Committee Member in three EU COST Actions dealing with bioimage analysis (NEUBIAS), emerging microscopy techniques (BioBrillouin), and nano sensing (EsSENCe), in the latter serving also as Short-Term Scientific Mission Coordinator. Stefan currently coordinates various research projects that focus on super-resolved imaging of cells, tissues, and advanced materials, and on the development of related image analysis and processing methods, with focus also on artificial intelligence.

Aiguo Wu received his PhD from Changchun Institute of Applied Chemistry, Chinese Academy of Sciences (CAS), China, in 2004. He started his independent career working for NIMTE after taking up his research associate appointment at Northwestern University, USA and his postdoctoral positions at Caltech, USA and University of Marburg, Germany. His research is focused on the synthesis of nanomaterials and their biomedical applications in biosensors, bioimaging, and drug delivery. He has authored over 180 scientific publications and has received some scientific awards and honors. The published papers have been cited by others more than 7000 times with an H-index of 41.