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C0065 Emerging Nanomaterials for Analytical Detection

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Chapter Outline

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s0010 1. ANALYTICAL CHEMISTRY ROLE IN FOOD ANALYSIS

p0010 Quality control in food and beverage industry is important to ensure that product characteristics are acceptable to consumers. Chemical analysis is essential for monitoring food attributes such as composition, structure, sensory attributes, microbiological status and nutritional characteristics. In addition, chemical analysis is fundamental for the rational identification of main factors and their interrelations possibly affecting the properties of food. Thus, analytical chemistry has an important role in the development and application of analytical methods for the study of the properties, content and food contaminants.

p0015 Organic and inorganic compounds, heavy metals and pathogenic microorganisms can be toxic for the consumer; so they must be identified in order to prevent diseases and even death. The assurance of food quality is an important challenge for the production and distribution of food. According to the WHO, the quality assurance of food requires security measures in all from harvesting, production, transport, process, storage, marketing and food preparation areas [1].

p0020 New analytical methods and techniques are required for a reliable, fast, highly sensible, selective, quantitative, easy handling, low cost and real time analysis. Chromatography methodologies are the typical methods used for food analysis; however, colourimetric and electrochemical methods have arisen as quick detection methods. Among techniques with high specificity, the bioanalytical techniques are one of the most promising; these are based on the use of biological recognition agents. In recent decades, optical and electrochemical techniques have made use of biosensors, which substantially improve the analytical response. In this chapter, we summarize some important aspects of biosensors.

p0025 IUPAC states that 'a chemical sensor is a device that transforms chemical information, ranging from the concentration of a specific sample component to total composition analysis, into an analytically useful signal. Chemical sensors usually contain two basic components connected in series: a chemical (molecular) recognition system (receptor) and a physicochemical transducer'. Biosensors are 'chemical sensors in which the recognition system uses a biochemical mechanism'. Likewise, 'an electrochemical biosensor is a self-contained integrated device, which is capable of providing specific quantitative or semiquantitative analytical information using a biological recognition element (biochemical receptor) which is retained in direct space contact with an electrochemical transduction element' [2].

p0030 Furthermore, the use of nanomaterials (NMs) and nanotechnology represents a new trend in the development of new analytical methods. Nanotechnology is already recognized as an important tool for the construction of new devices, such as biosensors, and also brings improvements in the performance of chromatography, lab-on-a-chip devices and other analytical platforms. Moreover, NMs have been employed as labels to track a signal, either optical or electrochemical. In the next section, we describe the different NMs, their characteristics and their main applications in quality assurance of food and beverages.

s0015 1.1 Opportunities of Using Nanomaterials

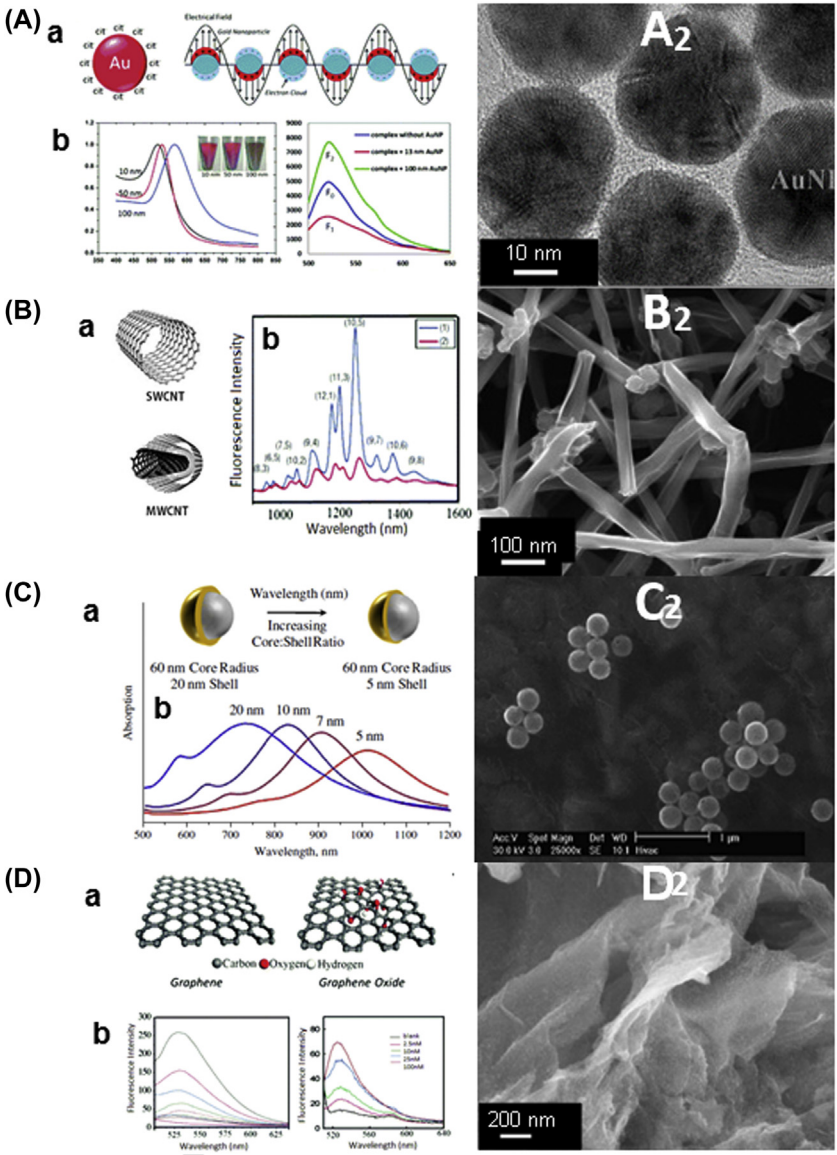
p0035 The development of new analytical methods based on nanotechnology has been a great success. The use of NMs as nanoparticles (NPs), nanotubes (NTs), nanorods, nanowires, nanodiamonds and quantum dots (QDs) has contributed to the creation of new powerful tools applicable in different areas of the food industry, such as the development of 'intelligent' packaging materials, food preservation and quality assurance.

p0040 NMs have numerous applications in food industry including their use as antioxidants, masking-flavour agents, nutrient encapsulation control, release control of nutraceuticals, vitamins or flavours and the construction of nanosensors for the detection of pathogens and chemical contaminants [3]. In the scope of food microbiology, nanobiosensors have great relevance since they reduce the pathogen's analysis time from days to hours or even minutes. Nanobiosensors are based on the use of NMs for the immobilization of enzymes, antigens and nucleic acids over a transducer surface in order to promote direct electron transference, causing an amplification of the analytical signal generated by the biorecognition events. In addition, NMs can be also used as signalling tools (labels) in nanobiosensors such as those based on electrical, optical, mass change and other kind of responses.

p0045 The success of the NMs used as analytical tool lies in their electrical, mechanical, conductive, magnetic and optical properties, which largely depend on their synthesis procedure [4,5]. Certain properties such as size, shape, surface area, aggregation states, charge, chemistry and reactivity of NMs are essential and necessary when evaluating their potential, toxicity, stability and physicochemical behaviour for applications in qualitative and quantitative analysis. Different NMs have been used for these purposes, being the most reported: gold NPs, carbon nanotubes (CNTs), QDs and graphene (GR) (Fig. 1). The most important characteristics of these materials are described in the following section.

s0020 *1.1.1 Gold Nanoparticles*

p0050 Gold nanoparticles (AuNPs) are the most used and are reported by Michael Faraday since the 18th century. AuNPs can easily be synthesized and functionalized, they have high chemical stability and low toxicity and excellent



f0010 **FIGURE 1** (A). (a) Absorption spectra correspond to the nanoparticles. *(From L. Sutarlie, K.M. Moh, M.G.L. Lim, S. Lukman, E. Cheung, X. Su, Plasmonics 9 (2014) 753 with permission from Springer.)* (A_2) Transmission electron microscopy images of synthesized AuNPs with average size of 15 nm. *(From S. Halldorsson, E. Lucumi, R. Gomez-Sjoberg, R.M.T. Fleming, Biosens. Bioelectron. 67 (2015) 595–600 with permission from Elsevier.)* (B) Illustration of CNT quenching: fluorescence spectra. *(From B.C. Satishkumar, L.O. Brown, Y. Gao, C.-C. Wang, H.-L. Wang, S.K. Doorn, Nat. Nanotechnol. 2 (2007) 506 with permission from Nature Publishing Group.)* (B_2) SEM of MWCNT. *(From I. Cesarino, F.-C. Moraes, M.L.V. Lanza, S. Machado, Food Chem. 135 (2012)*

electronic, redox and optical properties [14,15]. Optical properties of these NPs can be related to their size [6], so the transmission electron microscopy is an essential tool when characterizing this material in terms of its size, morphology and dispersion (Fig. 1A).

p0055 Synthesis of AuNPs can generally involve a 'top-down' approach or a 'bottom-up' approach. The top-down synthesis is based on reducing the size of an initial material. It can involve physical or chemical methods such as mechanical milling/ball milling, chemical etching, thermal ablation/laser ablation, sputtering and others. Top-down synthesis has the disadvantage of producing defects on the structure's surface, which is a major limitation due to the fact that physicochemical properties are associated with the surface structure. On the other hand, with the bottom-up approach the AuNPs obtained are more homogeneous [16].

p0060 Due to its high surface area, AuNPs are very reactive and aggregation is favoured, producing an undesired passivation of the surface, so pretreatments are important to prevent this aggregation or precipitation, for example, protecting AuNPs surface. There are many methods reported in literature to protect AuNPs such as the use of citrates, functionalization with thiolated compounds, encapsulation with microemulsions and dispersion in polymer matrixes. From the synthesis process, it is possible to control some characteristics of NPs: size, monodispersion, morphology and surface chemistry. The latter is particularly important when considering the applications of AuNPs for the construction of catalysts, nanosensors and biosensors whose activity strongly depends on the AuNPs chemistry surface [17]. Likewise, properties of NPs not only depend on size, but also on the shape; and physicochemical, electric and optical properties along with catalytic activity and selectivity are highly dependent one of each other.

p0065 Nowadays, among the most important applications of AuNPs is the design of electrochemical and optical biosensors, due to the improved electron's transference they present, the high ultraviolet−visible (UV−Vis) absorption coefficient, the small size (up to 100 nm) and consequently large surface area per unit of mass and biocompatibility compared to other particles [18,19]. Integration of AuNPs in analytical methods and techniques represents an

873−879 with permission from Elsevier.) (C) Optical resonances of gold shell-silica core nanoshells as a function of their core/shell ratio. (C_2) SEM images of nanoshells. *(From S.J. Oldenburg, R.D. Averitt, S.L. Westcott, N. Halas, J. Chem. Phys. Lett. 288: 243−247, 1998 with permission from Elsevier.)* (D) Illustration of GRO quenching: fluorescence spectra GR *from S. He, B. Song, D. Li, C. Zhu, W. Qi, Y. Wen, L. Wang, S. Song, H. Fang, C. Fan, Adv. Funct. Mater. 20 (2010) 453−459 with permission from WILEY* and fluorescence spectra graphene oxide *from R. Yang, Z. Tang, J. Yan, H. Kang, Y. Kim, Z. Zhu, W. Tan, Anal. Chem. 80 (2008) 7408 with permission from American Chemical Society.* (D_2) SEM image of MRGO. *(From S. Yan, T.-T. Qi, D.-W. Chen, Z. Li, X.-J. Li, S.-Y. Pan, J. Chromatogr. A 1347 (2014) 30−38 with permission from Elsevier.) MWCNT,* [Q10] multiwalled carbon nanotubes; *SWCNT*, single-walled carbon nanotubes.

important strategy to increase sensitivity and selectivity, which represents a great technological improvement for the in situ monitoring and real-time analysis of chemical compounds and pathogenic contaminants.

s0025 ### 1.1.2 Quantum Dots

p0070 QDs are conductive or semiconductive NPs with diameters between 1 and 20 nm and contain 100 to 100,000 atoms per NP [20]. The most reported QDs are based on CdSe, CdTe, ZnSe, CdS, CdSe@ZnS (core shell QDs) and InP. Nowadays, new carbon-based QDs have been proposed which, in contrast to traditional QDs, are safer and nontoxic [21].

p0075 As all NMs, QD properties such as size, shape and surface chemistry depend on the synthetic route. Among the different physical and chemical synthetic processes, the colloidal chemistry is the best method for the synthesis of nanocrystals with appropriate surfaces to provide high luminescence efficiency, narrow size distribution and ability to interact with specific species. The surface modification with suitable ligands can help to prevent the agglomeration of QDs, which controls some properties of the nanocrystals in solution, including size, distribution, stability as well as their crystalline structure.

p0080 QDs present optical, electrical, thermal and mechanical characteristics, some of these include high quantum yield (>20%), high molar extinction coefficients, broad absorption spectra, narrow and symmetric emission bands [30−50 nm], generally long photoluminescence (PL) decay times (often >10 ns), large effective stokes shifts and high resistance to photobleaching and chemical degradation [22]. They are also thermally and chemically stable and have good biocompatibility. The properties of these NMs are attributed to their small size and large electron confinement, which means that they can be used for many different applications including photovoltaic, thermal, development of light emitting diodes, fluorescence linked immunoassays, fluorescence resonance energy transfer assays, immunosensors, DNA probes and enzymatic labels or isotopic labels [23].

p0085 In general, the use of QDs is attractive as an analytical tool for the detection and quantification of a great variety of analytes. Because of their unique fluorescent properties, QDs can be used as labels to improve detection limits, sensitivity and specificity in optical and electrochemical methods.

s0030 ### 1.1.3 Carbon Nanotubes

p0090 CNTs were discovered in 1991 by Iijima [24]. These generally present micrometre lengths and diameters below 100 nm, with surface areas in the range of 150−1500 m^2/g [25]. CNTs can be considered as sheets of GR rolled into a cylinder and covered by fullerene structures, whose properties can change depending on the synthesis route, and particularly on the rolling direction [26]. CNTs can be single-walled (SWCNTs), double-walled or multiwalled (MWCNTs) and can be easily functionalized with different organic or

inorganic molecules to achieve greater selectivity in the analysis of different chemical species [27–29].

p0095 CNTs usually offer certain interesting advantages compared to spherical NPs for biotechnological applications. For instance, NTs have large internal volume (in relation to the NT dimensions), which can be filled with any chemical substance or biochemical species wanted, from small molecules to proteins. Furthermore, NTs have different internal as well as external surfaces, which may be chemically or biochemically functionalized [30].

p0100 CNTs have high mechanical strength, high elasticity, high thermal conductivity, and high chemical and thermal stability and can present semiconductor, metal or superconductor properties [31]. In addition, they present unique optical properties as small band-gaps, and PL in the near-infrared region (NIR) [27]. In the electroanalysis field, their unique electrochemical properties are used to improve the analytical parameters of quantification methodologies.

p0105 Nowadays, CNTs have found many applications, such as DNA sequencing, drug delivery, batteries and fuel cells, nanoreactors and also the development of new sensors and biosensors for monitoring of different analytes; this last has had great success over the past decades. CNTs have many advantages when used for the construction of biosensors, for example, due to their small size and large surface area, they exhibit an excellent electronic transference. Also, immobilization of proteins is improved in order to retain its biological activity.

p0110 CNTs have also been used as tools for adsorption and separation of various compounds. Analytical techniques such as capillary electrophoresis, microchip capillary electrophoresis and some chromatographic techniques have employed CNTs as stationary phase with excellent results [27].

s0035 *1.1.4 Graphene and Other Nanomaterials*

p0115 GR is the carbon structure with sp^2 hybridization in two dimensions (Fig. 1D). It is also known as a single carbon sheet and is the main component of other important allotropes. These carbon sheets can be stacked to form a 3-D graphite or rolled to form NTs or fullerenes. Novoselov reported for the first time the synthesis of a single layer of GR [32]. This material exhibited high stability and crystallographic quality with excellent thermal, electrical and mechanical properties, due to the π conjugation [33]. GR has an analogous structure to benzene and polycyclic aromatic hydrocarbons, so the chemistry of these compounds is similar; but a discriminative factor in GR is the formation and/or breaking of conjugated C–C bonds in the basal plane and the C–H bonds on the edges.

p0120 The characterization of GR properties is achieved using scanning probe microscopy (used to study thickness), atomic force microscopy (used to measure mechanical properties) and scanning electron microscopy (employed for morphological studies, Fig. 1. D_2). Raman spectroscopy has been recently

used to determine the thickness of the sheets obtained by mechanical exfoliation [34].

p0125 In general, the main properties of GR are great surface area (2630 m^2/g), high electron mobility (15,000 cm^2/v s), high thermal conductivity: 5000 W/m K, transmittance of about 97.7%, high conductivity ($\sim 104\ \Omega^{-1}\ cm^{-1}$). GR can support a current density about six times higher than that of copper; the electronic characteristics of this material are mainly due to its topology, because of the size of the films at atomic levels, the electron transport can be ballistic at submicrometre distances [35–37].

p0130 Another kind of NMs is core shell NPs (Fig. 1C). These NMs commonly consist of magnetic NPs as core and metal/metal oxide as shell which have attracted extensive attention because of their unique properties such as super magnetism, nontoxicity, biocompatibility, ease synthesis, high specific surface area, chemical stability, electrochemical activity and high electron mobility (115–155 cm^2/V s), which are beneficial for the kinetics of electron transport [38]. The most popular is Fe_3O_4@ZnO where coprecipitation deposition is involved in its synthesis, and also solvothermal methods for Fe_3O_4 magnetic NPs.

p0135 Magnetic nanoparticles (MNPs) have a size of about 50 nm and supraparamagnetic properties. Their ability to separate target molecules from other compounds by the simple use of a permanent magnetic field makes them attractive materials for the fabrication of sensors. MNPs commonly consist of magnetic elements such as iron, cobalt and nickel and their chemical compounds. As stated before, Fe_3O_4 NPs are the most prevalent materials because they have no toxicity, good biocompatibility and do not retain residual magnetism after the removal of external magnetic field. MNPs can be functionalized by groups, eg, -OH, -COOH, $-NH_2$ [39], suitable for further modifications by the attachment of various bioactive molecules for different applications, eg, antibodies or aptamers.

p0140 MNPs are usually integrated with detection techniques for food analysis, as in the polymerase chain reaction (PCR), high-performance liquid chromatography (HPLC), liquid chromatographic-mass spectrometric (LC-MS), electrochemical and optical biosensors. The use of MNPs into conventional detection techniques can make them simple, rapid, highly selective and sensitive [40–44].

s0040 2. BIOSENSING TECHNOLOGIES

p0145 Among the various applications of NMs, their use in the construction of biosensors has been one of the most important. NMs are used for modifying the transducer's surface (with favourable effects on the sensitivity) improving the catalytic effect as well as for an efficient functionalization and immobilization of biological materials [45,46].

p0150 Biosensor technology has certain advantages due to the possibility of massive production of these devices (and thus reducing the analysis costs), use

of sample volumes on the order of microlitres or even nanolitres, short analysis time and multiple analysis (detection of several analytes simultaneously).

p0155 Analytical success of biosensors lies on both, the proper selection of biological material (enzyme, antibodies, DNA, aptamers, cells, bacteria and even tissues) as well as the strategy employed for the immobilization, and not just the biological material but the used NM, in order to prevail its physicochemical characteristics. In particular, when it comes to electrochemical biosensors, an incorrect strategy could affect the catalytic properties of NMs, producing low selectivity due to a high imposed potential.

p0160 There are various classifications for biosensors such as DNA sensors, aptasensors and immunosensors among others (Fig. 2), in which NMs have been used as labels in the detection of a specific analyte, either a chemical contaminant or a pathogen agent [46,47]. The advantage of using NMs in biosensing technology stands in general improvements of analytical performance of the fabricated devices.

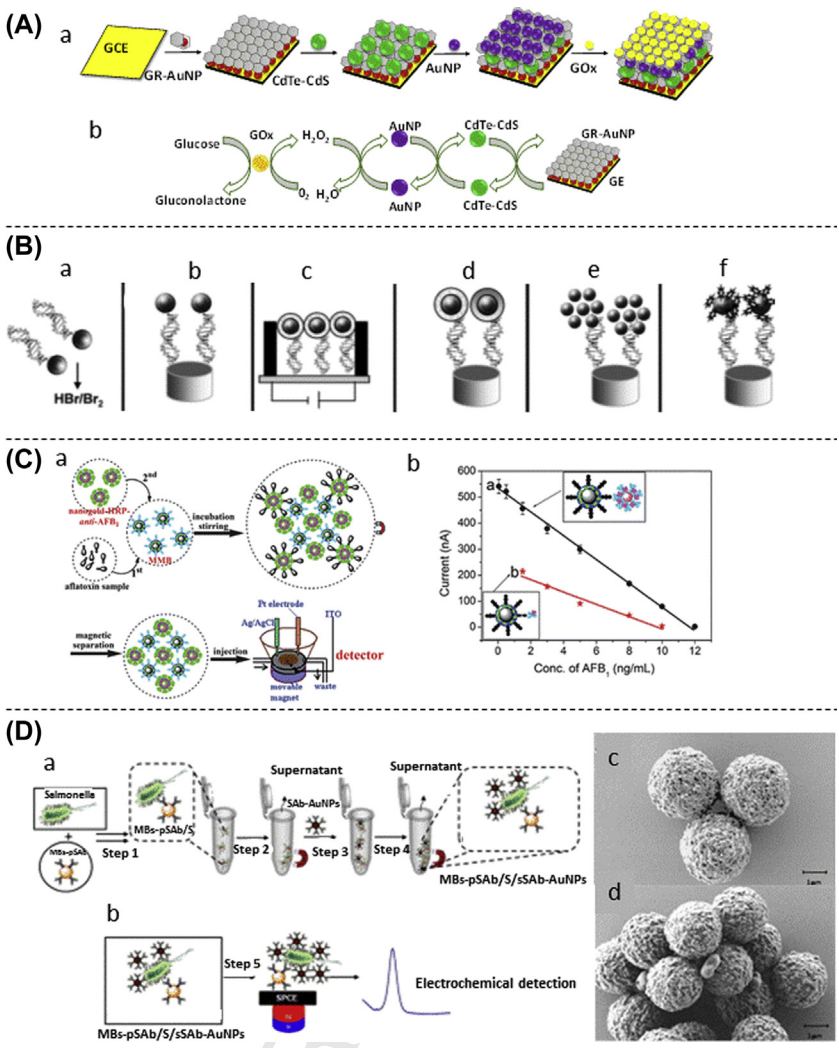
p0165 Usually, in routine food analysis it is necessary to evaluate chemical substances like sugars, alcohols, amino acids, flavourings, colourants, pesticides, as well as to control pathogen microorganisms and mycotoxins [48]. The interest in quality control related to pathogens is due to cases of foodborne diseases. For example, it has been reported that *Salmonella* causes 31% of the deaths related to food, followed by *Listeria* (28%), *Campylobacter* (5%) and *Escherichia coli* O157:H7 (3%) [49]. In this context, biosensor technology represents fast and simple analytical methods enabling food monitoring along the entire food production chain (until delivery to the consumer), and helping to prevent and avoid the spread of diseases and even death.

p0170 Thus biosensing technology and integration of NMs represent in food industry a great alternative considering the analysis required for control and quality assurance of food. Development of biosensors has evolved in order to construct fast, sensitive, reliable and inexpensive devices, so the integration of new materials as NPs, carbon NTs and QDs, among other NMs, is a breakthrough in food diagnostics using specific and efficient transducers. In the following sections, we present a review of these NMs applied to the development of biosensors useful in the quality assurance of foods. Table 1 summarizes the favourable properties, roles of each NM in transducer-based biosensors, as well as the challenges that need to be taken care of for sensor design [50].

s0045 2.1 Batch Devices

s0050 *2.1.1 Gold Nanoparticle-Based Biosensors*

p0175 Electrochemical biosensor's response is essentially based on the change in current, voltage, potential difference or impedance due to oxidation and/or reduction of chemical or biological molecules; this change can be measured with the aid of an appropriate two or three electronic system.



f0015 **FIGURE 2** (A) Procedure for fabrication of (a) GOx/AuNP/CdTe-CdS/G-AuNP/GE, (b) enzymatic reaction. *(From G. Zhiguo, Y. Shuping, L. Zaijun, S. Xiulan, W. Guangli, F. Yinjun, L. Junkang, Electrochim. Acta 56 (2011) 9162–9167 with permission from Elsevier.)* (B) Schematic procedure of the different strategies used for the integration of gold nanoparticles (AuNPs) into DNA sensing systems: (a) previous dissolving of AuNPs by using HBr/Br_2 mixture followed by Au (III) ions detection; (b) direct detection of AuNPs anchored onto the surface of the genosensor; (c) conductometric detection; (d) enhancement with silver or gold followed by detection; (e) AuNPs as carriers of other AuNPs; (f) AuNPs as carriers of other electroactive labels. *(From M.T. Castañeda, S. Alegret, A. Merkoçi, Electroanalysis 19 (2007) 743–753 with permission from Wiley-VCH.)* (C) Schematic illustration of the MMB and the nanogold-HRP-anti-AFB1, and (b) measurement process of the competitive immunoassay method linear curves of the developed immunoassay toward AFB1 standards by using various detection antibodies: (a) nanogold-HRP-anti-AFB1 and (b) HRP-labelled anti-AFB1. *(From D. Tang, Z. Zhong, R. Niessner, D. Knoop, Analyst 134 (2009) 1554–1560 with permission from Royal Society of Chemistry.)* (D) Schematic (not in scale) of Salmonella (S) detection. (a) Principle of the assay. (b) Electrochemical detection of MBs-pSAb/S/sSAb-AuNPs onto screen-printed carbon electrode captured with a magnetic field (step 5) by using DPV technique. SEM images of MBs-pSAb: before (c) and after (d) incubation with 10^5 cells/mL of Salmonella. *(From A. Afonso, B. Pérez-López, R. Faria, L. Mattoso, M. Hernández-Herrero, A. Roig-Sagués, M. Maltez-da Costa, A. Merkoçi, Biosens. Bioelectron. 40 (2013) 121–126 with permission from Elsevier.)*

[Q11]

t0010 **TABLE 1 Nanomaterials Used for Constructing Dual-Transducer Biosensors**

Nanomaterial	Favourable Properties	Major roles in Design	Challenges	Other Remarks
Quantum dots	Tunable fluorescence	FRET donor (more preferential)	Cytotoxicity	Surface functionalization is required to increase aqueous solubility
	Photostability	FRET acceptor	Fluorescence blinking	Biocompatibility
	Emission brightness		No standard synthetic protocol	
Metal NP	LSPR absorption	Fluorescence quencher/ enhancer	Nonspecific aggregation (eg, during particle surface modification or assaying procedures)	Size-dependent optical behaviour (eg, absorption dominates for AuNPs <80 nm; scattering for any larger ones)
	Light scattering	Fluorescence polarization amplifier		Various other particle shapes (eg, rods, plates, triangles, stars) to provide tunable absorption spectra
	Facile surface modification (eg, Au–thiol interaction)	Carrier for DNA barcode or chemiluminescence (CL) reaction catalysers		
	Intrinsic affinity to ssDNA and proteins through coordination chemistry			

Continued

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TABLE 1 Nanomaterials Used for Constructing Dual-Transducer Biosensors—cont'd

Nanomaterial	Favourable Properties	Major roles in Design	Challenges	Other Remarks
Graphene, GO, CNT	Optical quenching	Fluorescence quencher	Nonspecific adsorption	GO is more commonly used than intact graphene
	Different binding affinity with ds- and ssDNA	Enzyme mimicking	CL reaction catalyser	
Carbon nanodot	Tunable fluorescence Facile synthesis Low fabrication cost	FRET donor	Lack of thorough understanding on physical and chemical properties	Usually need further surface modification (eg, ligand attachment or solid capping layers) for efficient emission

AuNP, gold nanoparticles; *CNT*, carbon nanotubes; *FRET*, fluorescent resonance energy transfer; *LSPR*, localized surface plasmon resonance; *NP*, nanoparticles.
From N. Li, X. Su, Y. Lu, Analyst 140 (2015) 2916–2943. © The Royal Society of Chemistry.

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p0180 In particular, the use of AuNPs for the modification of electrodes generates a microenvironment similar to the natural system of redox proteins, giving these molecules better orientation. Also AuNPs reduce the insulating effect of the protein and allow direct electron transfer.

p0185 The construction of a biosensor can include several steps such as the electrodeposition of AuNPs, followed by physical adsorption of biological material [51], a polymer can sometimes be used for encapsulating the biological material used. However, physical adsorption may lead to low reproducibility, so it is necessary to use other strategies.

p0190 Among reported strategies employed to integrate the AuNPs-protein (enzyme) conjugate (Fig. 2A), are the following: self-assembly technology [52], layer-by-layer (LBL) assembly technique (based on electrostatic interactions [53] and polymer-nanoparticle composites [54]. A feature of these composites is that the polymer helps to preserve bioactivity in extreme conditions, in these circumstances, the AuNPs exhibit good affinity for the enzyme and a very stable composite is obtained. Special applications have been reported by the inclusion of AuNPs in carbon paste electrodes, where the NM creates a microenvironment suitable for the complete and direct transfer of electrons of different redox proteins [55,56].

p0195 AuNPs have been used as labels in the detection of pathogens, using as recognition agent DNA or antibodies [34]. The strategy in the construction of DNA biosensor is based on nucleotide hybridization using a capture probe immobilized over the sensor surface (Fig. 2B), where the analyte of interest can be detected due to a hybridization event, the complementary probe is usually labelled with AuNPs, enabling electrochemical detection [57]. AuNPs have the same use in aptasensors, where aptamers are used as target-recognition element and NPs as transducer or signal amplifier [58].

p0200 Some biosensors used for the detection of chemicals important in food quality are summarized below. Antioxidants are important in food industry because they retard oxidation processes in food; usually in food manufacturing. Synthetic antioxidants are used for this purpose [59]; however, an excess of these chemicals can be harmful to health. Synthetic antioxidant analysis is generally performed by conventional techniques, but with disadvantages of time-consuming analyses and requirement of sample pretreatment. Development of electrochemical sensors based on AuNPs provides a competitive alternative for analysis of antioxidants. A proper design in the construction of these sensors has allowed the simultaneous detection of up to three synthetic antioxidants with lower detection limit (LOD) in the order of ng/mL (Table 2). These results are comparable with traditional techniques such as HPLC-time-of-flight mass spectrometry (HPLC-TOFMS) and gas chromatography−mass spectrometry (GC−MS). This type of sensor was used for the detection of synthetic antioxidants in commercial oil samples and validated against the HPLC methodology [60]. The success of this sensor is strongly associated with the strategy used for the immobilization, in this sense, electrodeposition results

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t0015 **TABLE 2 AuNP-based Biosensors for the Detection of Some Compounds of Interest in Food Quality**

Analyte	Technique	Biosensing Surface	Sample	Lower Detection Limit	References
Part I					
Butylated hydroxyanisole (BHA) Butylated hydroxytoluene (BHT) Butylated hydroquinone (TBHQ)	Linear sweep voltammetry (LSV)	AuNPs	Oil	BHA 0.039 μg/mL BHT 0.080 μg/mL TBHQ 0.079 μg/mL	[60]
Methyl parathion	–	AuNPs-MWCNT/methyl parathion hydrolase	Garlic	0.3 ng/mL	[61]
Phenol Catechol Caffeic acid Chlorogenic acid Gallic acid [Q6] Protocatechualdehyde	Amperometry	AuNPs/Tyr	Wine	2.1×10^{-7} M 1.5×10^{-7} M 6.6×10^{-7} M 70×10^{-7} M 20×10^{-7} M	[63]
Pesticide formetanate hydrochloride (FMT)	–	AuNPs/Lac	Mango Grapes	9.5×10^{-8}	[72]
[Q7] Malathion Chlorpyrifos Monocrotophos Carbofuran	–	AuNPs/AChE	Cabbage Lettuce Leek Pakchoi	5 0.05 nm 0.05 nm 0.1 nM 2.5 nM	[74]

Antioxidants Isoflavone glycosides	HPLC	AuNPs	Soya supplements Boiled soya bean Tofu	125 ng/mL	[77]
Phenol	Amperometry	AuNPs/Lac	Wine	0.006 mM	[78]
Phenol total	Amperometry	AuNPs/Lac	Tea Alcoholic beverages	0.1 μm	[79]
Ochratoxin A (OTA)		AuNPs	–	20 nM	[47]
	Impedimetry	AuNPs/aptamer	Beer	0.02 nM	[80]
	Cyclic voltammetry	AuNPs	–	30 pg/mL	[81]
Part II					
Atrazine	Conductimetry	AuNPs/Ag-Ab	Red wine	–	[75]
Cyanides	Piezoelectric quartz crystal (PQC)	AgNPs	Drinking water	2.2 μg/L	[82]
Sugar Glucose	Amperometry	AuNPs/GOx/graphite		0.1 mM	[64]
		AuNPs/GOx	Beer	–	[83]
		SNS-NH_2/AuNP/GOx	Fizzy with orange Coke Lemonade Ice tea Peach juice	0.21 mM	[71]
		AuNPs-silica	Soft drink	360 nM	[84]
	Chronoamperometry	AuNPs-PANI	–	2.5 μM	[85]

Continued

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TABLE 2 AuNP-based Biosensors for the Detection of Some Compounds of Interest in Food Quality—cont'd

Analyte	Technique	Biosensing Surface	Sample	Lower Detection Limit	References
Salmonella typhi	Nano test-strips	AuNPs	Rice, corn and wheat	2 μg/mL	[86]
Salmonella	Amperometry	MBs-pSAb/S/sSAb-AuNPs	Milk	143 cells/mL	[67]
Salmonella enteritidis	EIS	Self-assembly onto gold NPs	–	600 CFU/mL	[87]
Bacillus cereus	Voltametry	Bc-AuNPs-chit-GCE	–	10 CFU/mL	[76]
Escherichia coli O157:H7	Chronoamperometry	MBs–pECAb/AuNPs–sECAb	Meat Water	10^3 CFU/mL 10^4 CFU/mL	[88]
Aflatoxins	Impedance	GO/Py(DPB)/AuNPs	Peanuts, rice, milk, soya bean	1 fM	[89]
		AnAb/AuNP-Lcys	Soya fermentation	18 CFU/mL	[90]
Ochratoxin	DPV	OTA-BSA-AuNPs	–	0.86 ng/mL	[91]

AuNP, gold nanoparticles; *BSA*, albumin from bovine serum; *MWCNT*, multiwalled carbon nanotubes.

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to be the best technique since it allows the control of size and dispersion. Deposition time and the used potential are crucial for obtaining homogeneous NPs size. This strategy has been implemented for the analysis of different compounds [61,62]. Another commonly used technique is the physical adsorption, but problems have been reported in the reproducibility, uniformity and size of the AuNPs deposited layer. Antioxidants such as phenols (phenol, catechol, caffeic acid, chlorogenic acid, gallic acid, protocatechuic aldehyde) have been analysed with a variety of electrochemical biosensors based primarily on AuNPs with enzymes such as tyrosine (Tyr) and lacasse (Lac) [63]. It has been reported that the electrodeposition of AuNPs followed by immobilization of the enzyme via cross-linking with glutaraldehyde results in an efficient biosensor which is able to detect and quantify up to six different types of phenols in different commercial wines. Biosensor stability and sensitivity are associated with the presence of the NPs, which act as nanoscale electrodes electrically communicated with the enzyme and the transducer. These biosensors have demonstrated to be useful in the analysis of antioxidants present in foods like juices, wines, vinegar, oil, tea, among others (Table 2) [63].

p0205 On the other hand, modifications in food composition during storage is an important aspect in food industry, especially when considering the main carbohydrate constituents, such as glucose and fructose, which could be responsible of food-browning processes. For this reason, glucose monitoring is important as it is an indicator of food freshness. Considering this, biosensors based on nanocomposites have been reported for glucose analysis (Fig. 2A); generally, a combination of AuNPs and glucose oxidase (GOx) is used [54,55,64]. The composite may contain nafion or teflon polymers to encapsulate and protect the enzyme, these polymers have a permeability characteristic that allows good interaction with the substrate. It has been reported that the NP's size is a contributing factor on the orientation of the enzyme: generally, a size of 5−50 nm for gold particles allows free orientation of the enzyme, which promotes easy electron transfer between the electrode and the enzyme [68]. Moreover, it has been demonstrated that the use of 10 nm AuNPs enhances amperometric response [69,70]. The application of AuNPs could increase the rate of mediated electron transfer, providing an improved sensitivity with a low LOD.

p0210 These biosensors have shown an LOD of 17 μmol/L with high stability (lifetime of about 3 months) due to the presence of AuNPs. The analytical results were validated with traditional methods such as spectrophotometry. AuNP-based biosensors have been applied for the detection of glucose in a variety of food products such as juice, cola drinks and tea [71].

p0215 Other important chemicals concerning food quality are pesticides, since their presence in foods can cause toxic effects in human health. Pesticides that are considered strong contaminants are organophosphates (OPs), N-methyl carbamates, triazines, chloroacetanilides, pyrethrins, pyrethroids. These pesticides are

used in agriculture, so they are absorbed by fruits and plants that will later be used as food.

p0220 Pesticides such as carbamate, formetanate hydrochloride are usually used in fruits like grapes, mango, potato, onion, citrus, bean, watermelon, pepper and tomato. As an alternative to ultraperformance liquid chromatography−tandem mass spectrometry (UPLC−MS/MS) used in the detection of this pesticide, a biosensor as detector was developed based on the immobilization of laccase on an electrode modified with AuNPs. This strategy allowed the detection of pesticide residues in fruits such as mango and grapes [72].

p0225 Among the most commonly used pesticides are the organophosphorus. To quantify them, various biosensors based on acetylcholinesterase (AChE) have been proposed. It was found that the immobilization of this enzyme on AuNP electrodeposits combined with chitosan (chit)-calcium carbonate provides a favourable and biocompatible microenvironment enhancing the detection. Moreover, it has been found that electrodeposition and a combination of CNTs/NPs [61,73] improves the electrocatalytic activity and help to stabilize the enzyme. With this architecture, response times and LODs are improved [74].

p0230 Atrazine is another important contaminant present in fruits such as grapes. For the detection of this herbicide, immunosensors based on antibodies using AuNPs as labels have been developed. Detection of very low concentrations of atrazine is possible because of the signal amplification caused by the NM. The method is attractive because it is inexpensive, has no matrix effects and presents low analysis times (48 samples can be analysed in 5 h), this biosensor has been used for the detection of atrazine in wine [75].

p0235 Trends in food quality control related to the detection of pathogens are oriented to minimize analysis times. Traditional methods for microorganism's analysis such as morphological and biochemical identification are performed in 2−7 days until confirmation. Other methods such as RAPD (random amplified polymorphic DNA-PCR) require expensive instruments and consumables. In this sense, biosensors can generate quick responses when predicting the existence of microorganisms in real time analyses.

p0240 To date, there have been reported different strategies involving biosensors for pathogens such as *E. coli, Staphylococcus aureus, Bacillus, Salmonella [67], Vibrio parahaemolyticus, Campylobacter jejuni* and *Listeria monocytogenes* (Table 2) [67,86−88,91].

p0245 Thus affinity biosensors are the most employed for the detection of microorganisms, eg, *Bacillus cereus* (*Bc*) bacteria occurring in various foods such as vanilla sauce, custards, soups, rice, pasta, meat, vegetables and dairy products. The immunosensor used to determine these bacteria are based on a monoclonal antibody as recognition agent. A glassy carbon electrode (GCE) is used in which a monolayer of CS is placed on its surface, then AuNPs are electrostatically adsorbed on it and finally the antibody is placed to generate Bc-AuNPs-Chit-GCE. The reported LOD for the bacteria is 10 CFU/mL, demonstrating that this biosensor can be used in quality assurance of foods [76].

p0250 The development of an immunosensor capable of detecting *Salmonella* in milk has also been reported. Biosensor construction is based on the incubation of *Salmonella* (S) with magnetic particles (MBs) modified with the specific primary antibody related to the bacteria (PSAb), generating the conjugate MBs-PSAb. During this step, the bacteria is captured and retained in this conjugate. Subsequently, the system MBs-PSAB/S is captured by applying a magnetic field. Finally, the MBs-PSAB/S is incubated with AuNPs modified with the secondary antigen (SSAB-AuNPs). The bacteria are then detected by differential pulse voltammetry using a screen-printed electrode and a magnet to collect the conjugated MBs-PSAB S/SSAB-AuNPs (Fig. 2C) [67]. The analysis time is estimated in 1:30 h.

p0255 *Escherichia coli* O157:H7 has also been analysed in meat and water samples. Detection has been carried out by using an anti-*E. coli* O157−magnetic beads conjugate (MBs−pECAb) as a capture platform and sandwiching it afterwards with AuNPs modified with secondary antibodies (AuNPs−sECAb), the detection is achieved by using an electroanalytical technique with screen-printed carbon electrodes (SPCEs). LODs of 148, 457 and 309 CFU/mL were obtained for a synthetic solution, minced beef and tap water samples, respectively. When compared with a commercial lateral-flow kit, electrochemical immunoassay performance presented clear advantages such as specificity and reproducibility [88].

p0260 Immunosensors represent a very good strategy for the detection of mycotoxins [72,73,92], it has been reported that about 25−50% of crops worldwide are contaminated by aflatoxigenic fungi [93], so early analysis is a key to ensure food safety. A strategy for mycotoxin detection is based on the incorporation of AuNPs and polyclonal antibody to extracellular antigen from *Aspergillus parasiticus*. For the immobilization of these components in the biosensor, an AuNPs/L-cysteine (Lcys) monolayer is prepared (Fig. 2B). The developed immunosensor has high sensitivity, good recovery and reproducibility for the direct detection of aflatoxigenic Aspergilli during fermentation of soya bean meal [90].

s0055 *2.1.2 Quantum Dot-Based Biosensors*

p0265 The combination of QDs with biomolecules provided new opportunities for the design of biosensors useful in food analysis, due to the characteristics of these NMs, whose chemical, electrical and optical properties can be manipulated and adapted by changing their size, shape and composition.

p0270 In the design of biosensors, QDs can be used as platform for the immobilization of the biomolecule or as recognition label material.

p0275 QDs promote electron transfer and stability of biological materials when used as surface modifiers for transducers, examples of these materials are enzymes, DNA, aptamers and antibodies. To date, QDs have been tested as a platform for the immobilization of enzymes such as GOx, Lac, horseradish peroxidase (HRP), among others.

p0280 To evaluate the advantages of QDs in the architecture of biosensors, Jian Du et al. developed three devices for the detection of glucose using AuNPs and QDs (CdS, ZnS). In this research, variables such as NP size, conductivity, rate constant (Ks) and sensitivity were analysed. The values obtained for the conductivity corroborated the NP's nature. It was determined that AuNPs have better conductivity when compared with CdS or ZnS, although the latter showed better electron transference and the highest sensitivity [94]. Electrochemical and photoelectrochemical techniques were compared and the analysis indicated that the increase in sensitivity is evident when this last technique is used.

p0285 Another biosensor based on a ZnS-QDs mixture, which is used as platform for the immobilization of GOx, exhibits a low LOD (3 μM) using the method with a GOx/Chit/ZnS-CdS/PGE architecture.

p0290 In general, QDs can be used for the immobilization of enzymes taking advantage of different strategies, eg, self-assembled monolayer (Table 3). This strategy is used in the detection of ascorbic acid (one of the most common antioxidants) and is based on the modification of an electrode with a cysteine self-assembled monolayer and coated with functionalized QDs. With this biosensor (Lac/CdTe/Cys/Au), very low LOD are obtained (1.4 μM), furthermore, the biosensor showed good repeatability and stability [95]. Among the most recent strategies reported, the use of QDs in combination with GR stands out; graphene quantum dots (GRQDs) have been used for the determination of total polyphenols in red wine [molybdenum disulphide (MoS_2)] [96].

p0295 Moreover, due to its composition and surface, QDs can be easily modified, immobilized and bound to molecules (eg, DNA, oligonucleotides, aptamers and antibodies).

p0300 At present, QDs are a good alternative for multianalyte detection [97−103]. The multiscreen strategy based on QDs employs a biorecognition agent (Fig. 3A and C), usually antibodies, and QDs of different compositions [97]; the most used are CdS, CuS and PbS [98]. For example, in the case of bacteria, multiscreening is based on marking each bacterium (antibody) with a QD constituted by a different metal (Cd, Cu, Pb), each specie will have a defined and particular analytical signal. In the case of electrochemical immunosensors, discrimination between signals is possible with the use of a voltammetric technique, where each metal has a particular redox potential. *Escherichia coli*, O157:H7 *Campylobacter* and *Salmonella* have been detected with this type of immunosensor, the antibodies are labelled with CdS, PbS, CuS [99] and the analysis is performed using square-wave voltammetry. *Escherichia coli* is associated with the Cd reduction potential (−0.7 V), *Campylobacter* with PbS reduction potential (−0.5 V) and *Salmonella* with the reduction potential of Cu (−0.7 V), the construction of the immunosensor is described in Fig. 3B. LOD for *Salmonella*, *Campylobacter* and *E. coli* were 400, 400 and 800 cells/mL, respectively. It was demonstrated that the inclusion of CNTs significantly increases sensitivity. With this immunosensor, simultaneous detection of these

t0020 **TABLE 3 QD-Based Biosensors for the Detection of Some Chemical Species of Interest in Food Quality**

Analyte	Technique	Biosensing Surface	Sample	Lower Detection Limit	References
Ascorbic acid	Amperometry	Lac/CdTe/Cys/Au	–	1.4 μM	[95]
Escherichia coli *Campylobacter* *Salmonella*	SWASV	MWCNT-PAH/SPE *E. coli*-CdS *Campylobacter*-PbS *salmonella*-CuS	Milk	400 cells/mL 400 cells/mL 800 cells/mL	[99]
Salmonella Typhimurium *Salmonella*	Fluorescence	QDs	Milk Chicken Carcass wash water	13 cells/mL 10^3 cells/mL	[101] [103]
E. coli	Fluorescence	SiO_2NPs	Water	3–5 cells	[105]
E. coli *S. Typhimurium*	Fluorescence	QDs	–	10^4 CFU/mL	[106]
Chloramphenicol	Electrochemical	QDs	Milk	0.0054	[102]
Polyphenol	Electrochemical	MoS_2 nanoflakes/GRQDs/Lac	Red wine	0.32 μM	[96]
	Fluorescence	QDs	–	–	[104]

QD, quantum dot; *SWASV*, square-wave anodic stripping voltammetry.

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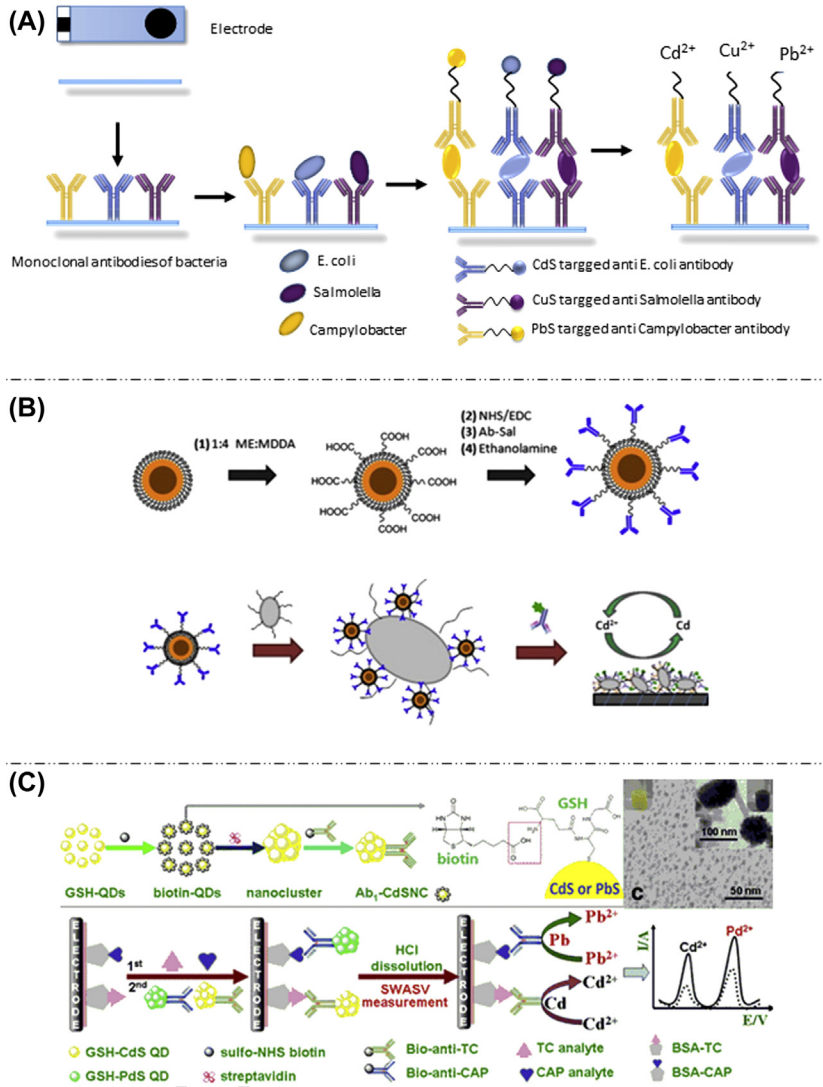

f0020 **FIGURE 3** (A) Multiplexed detection of pathogens using nanocrystal antibody conjugates and SWCNT-PAH/SPE. *(From S. Viswanathan, C. Rani, J. Ho, Talanta 94 (2012) 315–319 with permission from Elsevier.)* (B) (a) Formation of the polyallylamine (ME-MDDA) SAM-functionalized nanoparticles linked to anti-*Salmonella* antibodies. (b) Representation of labelled electrochemical determination of *Salmonella typhimurium*. *(From M. Freitas, S. Viswanathan, H.P.A. Nouws, M.B.P.P. Oliviera, C. Delerue-Matos, Biosens. Bioelectron. 51 (2014) 195–200 with permission from Elsevier.)* (C) (a) Schematic illustration of synthesis and bioconjugation of metal sulfide nanoclusters (CdS used as an example), (b) electrochemical measurement of multiplex immunoassay, and (c) transmission electron microscopy image of metal sulfide quantum dots (CdS used as an example) (*Insets*: TEM image of CdS nanoclusters, and the corresponding samples). *(From B. Liu, B. Zhang, G. Chen, D. Tang, Microchim. Acta 181 (2014) 257–262 with permission from Springer.)*

[Q15] [Q12]

three pathogens in milk is possible, demonstrating its potential for quality control in food industry (Table 3).

p0305 Detection of pathogens using QDs and Fe@AuNPs stands out (Fig. 3C), because of the very low detection limit obtained (13 cells/mL). The inclusion of these NPs (13 nm) with magnetic properties improves sensitivity and analysis times (~1 h). This immunosensor is functional for the detection of *Salmonella* in milk [101].

p0310 Antibiotic residues in dairy products represent a constant concern in food quality control; usually these chemicals are analysed by techniques such as HPLC, ELISA and GC−MS. As an alternative, it has been proposed that an immunoassay using QDs for the analysis of tetracycline (TC) and chloramphenicol (CAP), which consist on the immobilization of TC and CAP conjugates with bovine serum albumin on the surface of a GCE, modified with AuNPs. Anti-TC and anti-CAP monoclonal antibodies are functionalized with CdS and PbS. Detection is performed by square wave anodic stripping voltammetry, the construction of the immunosensor is described in Fig. 3D.

s0060 *2.1.3 Carbon Nanotube-Based Biosensors*

p0315 Because of the electrical and electrochemical properties of CNTs, these materials are ideal for the construction of transducers for biosensors. CNTs as part of electrochemical biosensors have been implemented in different architectures as described in the following sections.

o0010 **1.** Carbon paste electrodes and nanotubes (CNTPEs). CNTPEs are constructed with a mixture of graphite, CNT and a mineral oil [107]. Biological material is added to the mixture too (usually enzymes) [108,109]. These composite electrodes take advantage of the improvement on the electron transference due to the presence of CNT.

o0015 **2.** Modified electrodes with CNTs. These electrodes are associated to the modification of conventional carbon or metal electrodes (Au, Pt, ITO, etc.). The most common technique used for the modification is physical adsorption. CNT adsorption sometimes involves the mixture with a polymer such as poly(glycidyl methacrylate-co-vinylferrocene), Chit, polypirrole, polyaniline (PANY), among others. In general, polymers help the CNT dispersion promoting the electron transference, sensitivity and stability. CNTs have also been used for immobilization of biomolecules; however, the most effective method is the growth of CNTs on the metal substrate, achieving an arrangement of the CNTs which substantially improve the electronic transference. Moving from randomly aligned mixtures of NTs to well-ordered arrays can enhance their electrical conductivity [110]. To promote the catalytic activity of CNTs, it has been reported the use of metal or semiconductor NPs in the electrode's modifications. [Q2]

o0020 **3.** LBL self-assembling modification. This technique involves alternate adsorption on the electrode's surface of polyelectrolites with opposite

charge, through electrostatic interactions. LBL self-assembling modification is not only used for the modification of electrodes with CNTs, but for immobilization of biomolecules as well. Among the advantages of this technique are its simplicity, the minimum quantity of reagents used, and minimization of protein denaturation.

p0335 Different strategies for the construction of CNT-based biosensors using enzymes as recognition agents have been reported, enzyme immobilization is a crucial step for the proper functioning of the biosensor. Some of the reported strategies include the following:

o0025 **1.** Physical adsorption. CNTs are dispersed on the surface of conventional electrodes, usually glassy carbon (GCE), and then a solution containing the enzyme is used to cover the electrode's surface and is allowed to dry. In spite of being a simple and fast technique, this strategy presents some disadvantages: low amount of adsorbed enzyme, leaching, lack of homogeneity of the enzyme on the electrode surface and low reproducibility. The incorporation of CNTs has solved some of these problems since they favour enzyme's adsorption. The adsorption technique has been employed for the detection of different analytes including phenol compounds [111] and OPs [112].

o0030 **2.** Covalent binding. This technique allows direct attachment of the enzyme on the electrode via covalent bonds, which enables the direct electron transference to the enzyme's active site [113].

o0035 **3.** Electropolymerization. This is an attractive and well-controlled method for immobilizing enzymes on the surface of electrodes. This technique consists on mixing the enzyme with a monomer and applying an optimum potential to induce the polymerization. The incorporation of the enzyme in the matrix is often promoted through electrostatic interactions. The benefits of this technique lie in the control of the chemical system; to produce thin layers, polypyrrole is commonly used for these purposes [114,115].

o0040 **4.** Encapsulation. This technique allows the immobilization of the enzyme through the use of hydrogel or sol−gel materials, it can be carried out from a modified electrode with CNTs followed by the deposition of the hydrogel containing the enzyme. Alternatively, CNTs can be incubated with enzymes and then incorporated into the hydrogel or sol−gel matrix and finally deposited on the electrode [116].

p0360 Recently, new developments involving CNTs for the detection of proteins, antibodies and DNA have been reported [117]. CNTs play a double role as transducers and recognition agents, amplifying the analytical response. In food analysis, these sensors are essential in determining the presence of contaminants or pathogens.

p0365 Due to their size and excellent electrochemical properties, CNTs continue attracting interest in the field of biosensors development. It has been

demonstrated that CNT-based biosensors have electrochemical properties superior to most conventional electrodes, their use for the determination of chemical species such as, sulphites, glucose, pesticides, polyphenols and microorganisms is of great significance for food analysis. This section points out the advances reported using these CNT-modified biosensors to detect different compounds associated with the quality control of food (Table 4).

p0370 Sulphites are one of the most common additives in food and beverages technology. They help to preserve colour and flavour during preparation, storage and distribution. The properties of sulphites are mainly associated with their reducing power; they can also inhibit bacterial growth. The most common sulphites used in foods are sulphur dioxide, sodium sulphite, sodium and potassium bisulphite, sodium and potassium metabisulphite. However, there have been reports of allergic reactions and intolerance to foods containing this additive, so the quantification of sulphite is a parameter that must comply with the regulations of the FDA (Food and Drug Administration). The quantitative method recommended by the Association of Analytical Chemists is based on an acid−base titration [118], which despite being a low-cost method, has some limitations such as the high analysis times and errors associated to interferences. Electrochemical methods arise as very good alternatives because they do not require sample pretreatment even if it is a suspension or it is coloured. Generally, the method is based on electrochemical oxidations or reductions using conventional electrodes, although there are some drawbacks such as poor sensitivity and high errors due to interferences. A new alternative based on the use of carbon paste electrodes chemically modified with MWCNT has been highly successful in the quantification of sulphite in water, vinegar, juices, alcoholic beverages and wines [115,119−124].

p0375 Different configurations involving polymers, CNTs and NPs have been reported, with LODs for sulphite in the order of nanomolar concentrations [121]. The inclusion of hybrids (Fig. 4A) containing different NMs (CNT-AuNPs, CNT-QDs, CNT-GR) highly improves sensitivity [122], where CNTs favour the electrocatalytic activity and reduces fouling of the electrode's surface. To date, few biosensors based on CNT have been developed for the detection of sulphite, in spite of its better selectivity. Sulphites are indirectly quantified when using these biosensors, the role of CNTs in this device is related to improved half-life time (90 days), response time (3 s) and low detection limit.

p0380 Carbohydrate analysis is a great concern in food industry; a clear example is the quantification of glucose, fructose and maltose which are very important in the fermentation of wine and beer. To date, diverse configurations of biosensors for the detection of glucose have been proposed, CNTs have been used in a great variety and complex configurations [125−129]. An interesting configuration is the double-stranded DNA (dsDNA); its aim is to support the CNTs and to maintain the bioaffinity of the recognition agent even after being exposed to extreme conditions [125]. The biosensor is constructed from the dispersion of

t0025 **TABLE 4 Carbon Nanotubes in Food Analysis**

Analyte	Technique	Biosensing Surface	Sample	Lower Detection Limit	References
Part I					
Sulphite	SWV	CP/MWCNT	Red Grape juice or red wine samples	16 μM	[119]
	SWV	GCE/PAH/MWCNTs	Vinegar, pickle water, coconut water and shredded coconut	4.2 μM	[120]
	SWV	BFCNPE	Drinking water	90 nM	[121]
	Amperometry	CNTs-PDDA-AuNPs/GC	Fruit juices and red wines	0.03 mg/L	[122]
	DPV	PPO-AuNPs-MWCNTs-PAH/GCE	White and red wine	0.4 μmol/L	[123]
	Amperometry	SOx/AuNPs/Chit/MWCNT/PANI/Au	Juices and alcoholic beverages	0.5 μM	[124]
Glucose	Amperometry	GCE/bCNT-dsDNA/[PDDA/GOx]n	Beverages	50 μM	[125]
		ITO/PB/(chit/MWCNT/GOx]$_6$	–	0.05 mM	[126]
		GOx/amino terminated-MWCNT	–	8.0 μM	[127]
		GCE/[MWCNT-Polyhys/GOx]5/Naf	Milk	2.2 μM	[128]
	Chronoamperometry	Composite GOx/meso-HAP/meso-TiO_2/MWCNT/GCE	Fruit juice	2 μM	[129]
Maltose	Amperometric	AG/PyOx/Chit–MWCNT	Beer	–	[130]
Total phenolics	DPV	Polyeugenol/MWNT/GCE	Red and white wine	0.21 μM	[131]

Gallic acid	Chronoamperometry	MWCNT/GCE	Cognac and brandy	0.19 μM	[132]
Tannic acid	DPV	SWNTs/GC	Tea Beer	8 nM	[133]
Part II					
Carbaryl	Chronoamperometry	GC/MWCNT/PANI/AChE	Cabbage, broccoli and apple	1.4 μM	[9]
Cethomyl				0.95 μM	
Organophosphorus	Amperometry	f-MWCNT/poly(SNS-NH2)/AChE	–	0.09 mM	[135]
Carbofuran	Amperometry	GS-PEI-Au/MWCNTs/GC	Vegetables	0.03 ng/mL	[136]
Organophosphate	Amperometry	PDDA/AChE/PDDA/CNT/GC	–	0.4 pM	[137]
Histamine	Amperometry	Polysulfone/MWCNT/ferrocene	Sardines	1.7×10^{-7} M	[138]
Xanthine	Amperometry	P(GMA-Co-vfc)/MWCNT/XO	Fish, meat	0.12 μm	[139]
Ochratoxin A	Amperometry	SWCNTS		24.1 nM	[140]
Mycotoxin	DPV	MWCNTS	Beer and wine	1.7 μg/L	[141]
Aflatoxin b	DPV	AFB1-BSA-SWNTS/CS/GCE	Corn powder	3.5 pg/mL	[142]
	Potentiometry	Covalent binding to SWCNTs	Milk	5 CFU	[143]
	DPV	MWCNT-CHI-BI/fDNA-tDNA-sDNA-CDsNPS	Beef	1.97×10^{-14} M	[146]
Staphylococcus aureus	DPV	MWCNTCHI-BI/fDNA−tDNA−cDNA−PBS	Beef	3.17×10^{-14} M	[147]
Salmonella spp.	Amperometry	DWCNT	–	8.9 CFU/mL	[148]

AG, α-glucosidase; *BF*, benzoylferrocene; *cDNA*, capture DNA; *DPV*, differential-pulse voltammetric; *DWCNT*, double wall carbon nanotube; *fDNA*, fixing DNA; *tDNA*, target DNA; *PAH*, poly(allylamine hydrochloride); *PDDA*, poly(diallyldimethylammonium chloride); *PyOx*, pyranose oxidase; *SWV*, square-wave voltammetry.

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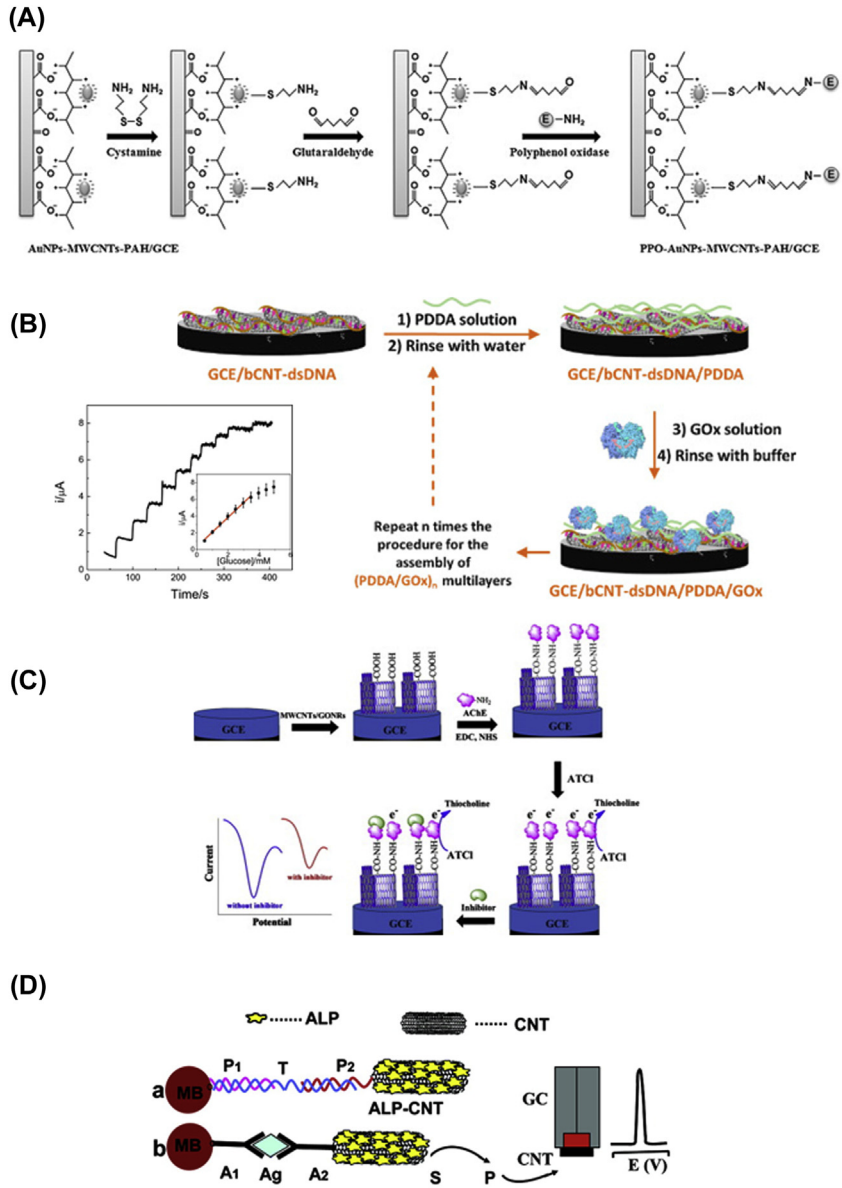


f0025 **FIGURE 4** Schematic illustration of the different steps of: (A) preparation of the PPO-AuNPs-MWCNTs-PAH/GCE biosensor for sulfite. Not drawn in to scale. *(From E. Sartori, F. Vicentini, O. Fatibello-Filho, Talanta 87 (2011) 235–242 with permission from Elsevier.)* (B) Glucose biosensor using bamboo-like MWCN dispersed in double stranded calf-thymus DNA as a new analytical platform for building layer-by-layer based biosensors. *(From E. Primo, F. Gutierrez, M. Rubianes, G. Rivas, Electrochim. Acta 182 (2015) 391–397 with permission from Elsevier.)* (C) Stepwise amperometric biosensor fabrication and principle for pesticide determination. *(From Q. Liu, A. Fei, J. Huan, H. Mao,*

CNTs with dsDNA, which is placed on the electrode's surface, then the electrode is immersed into a solution of polydiallyldimethylammonium (PDDA) followed by immersion in a solution of the enzyme GOx, until multiple layers are obtained. The technique used for the development of the dsDNA-CNT biosensor is shown in Fig. 4B.

p0385 The challenge in the construction of such biosensors is to find the optimum immersion time and number of layers that allow the highest sensitivity and stability of the biosensor. The use of hybrid composites with NMs is a good strategy to improve detection limits when quantifying glucose [129], as demonstrated when used in fruit juices, milk and other beverages (Table 4).

p0390 Maltose is a component of food, such as commercial sugar, beer and milk. Enzyme sensors can accomplish this and several studies have been made in order to develop maltose biosensors. Usually two enzymes are used to construct maltose sensors, one hydrolyses maltose and the other oxidizes glucose, as alternative a new bi-enzymatic system was designed by coimmobilization of α-glucosidase (AG) and pyranose oxidase (PyOx) and the integration of CNT for maltose analysis. This biosensor is suitable for maltose detection in beer [130].

p0395 Other chemical species important in preserving food quality are polyphenols [130–133], which have also been analysed with CNT-modified electrodes. Gallic and tannic acids are some natural polyphenolic compounds usually used in the production of beer, wine, candies and meat products because of their antioxidant properties. These can be analysed according to its oxidation signal with an electrode modified with SWCNT, the very low detection limit (8 nM) and the simplicity of this device makes the method comparable with the official HPLC one [133].

p0400 Pesticide detection and quantification has motivated the development of biosensors based on CNT [134–137] in combination with enzymes such as AChE (Fig. 4C) [134], butyrylcholinesterase, laccase and methyl parathion hydrolase. In the construction of these biosensors, the immobilization of enzymes is achieved using Chit because of its low toxicity and biocompatibility. Polymers have been used along with NMs such as gold or iron NPs, which have been included using the layer by layer adsorption or electrodeposition techniques. Moreover, the construction of CNT-based immunosensors for the detection of pesticides has been a great success because of its high specificity.

K. Wang, J. Electroanal. Chem. 740 (2015) 8–13 with permission from Elsevier.) (D) Analytical protocol: (a) Capture of the ALP-loaded CNT tags to the streptavidin-modified magnetic beads by a (1) sandwich DNA hybridization or Ab-Ag-Ab (2) interaction enzymatic reaction. (b) Electrochemical detection of the product of the enzymatic reaction at the CNT/GCE; Magnetic beads (MB), DNA probe (P1); DNA target (T1); DNA probe (P2) first antibody (A1); antigen (Ag); secondary antibody (A2); S and P, substrate and product, respectively, of the enzymatic reaction; GCE; CNT, layer. *(From J. Wang, G. Liu, M. Jan, J. Am. Chem. Soc. 126 (2004) 3010–3011 with permission from American Chemical Society. Publications.) CNT*, carbon nanotubes; *GCE*, glassy carbon electrode; *MWCNT*, multiwalled carbon nanotubes.

[Q13]

So far, immunosensors for the detection and quantification of carbofurans and atrazine have been developed. Biosensors based on hybrid nanocomposites have improved the detection limits, which have been reported in the order of pg/mL.

p0405 Biosensors based on CNTs have been successfully used to quantify pesticides as carbaryl [9], monocrotophos, chlorpyrifos, dichlorvos, carbomate, carbofuran, parathion, methyl parathion (MP), triazophos, pirimicarb and atrazine in fruits (grape, apple), vegetables (cabbage, broccoli, tomato) and potable water (Table 4).

p0410 In addition to the parameters already discussed, the effect of the methods used for the synthesis of CNTs used in pesticide biosensors has been studied, particularly MWCNT for the detection of *p*-nitrophenol. It was demonstrated that MWCNTs obtained by vapour deposition have better response and greater stability with respect to those obtained by arc discharge. Here a GCE is modified with MWCNT and OPH enzyme. The construction consists of two layers, the first of MWCNTs dispersed in nafion and the second of the enzyme dissolved in nafion. Amperometry is used to quantify paraoxon and MP, both LOD and sensitivity are better for the first pesticide due to the selectivity of the enzyme [112].

p0415 Biosensors based on nanobiomaterial hybrids have had great success for the detection of pesticides such as carbaryl [9], a carbamate pesticide, which is highly effective in controlling insects, consequently, highly employed in agriculture. A concern about this pesticide is the long-term accumulation in the biosphere, since it represents serious risks to human health due to its high toxicity related to the inhibition of AChE, a key enzyme for many functions in the central nervous system. A biosensor has been reported for the quantification of this pesticide based on the modification of glassy carbon by an electropolymerization process with PANI and MWCNT; the immobilized enzyme is AChE. This device exhibits a detection limit in accordance with the established standard regulations in Brazil, and is used in the analysis of fruits and vegetables (Table 4), the results are comparable with the traditional HPLC method [9].

p0420 As already mentioned, a very important matter in food is the analysis of pathogens; biosensors based on CNT, DNA, antibodies; thus aptamers have resulted a very good alternative for the detection of these harmful species.

p0425 To date, genosensors have arisen as rapid methods for the detection of pathogens. Such methods are based on the use of a DNA probe (capture probe), which is functionalized with thiol groups (SH) for its immobilization on the electrode's surface. Moreover, the probe is functionalized with a label which may be an NP with redox properties (Fig. 4D). When the electrode's surface is modified with CNTs, genosensor conductivity and sensitivity are favoured [143−148].

p0430 The analytical response and stability of the genosensor depends on the materials used for the modification of the electrode's surface with CNT, for

this purpose, polymers as Chit have been used. This design can detect *E. coli* and *S. aureus* using the so-called 'sandwich structure', which is based on the hybridization of the capture probe with a specific fragment of the pathogen's gene (fDNA-tDNA-sDNA-NPs) [145,146].

p0435 Thus, the use of CNTs as a platform for the detection of pathogens has been very versatile in combination with nafion, teflon, epoxy polymers, Chit, polypirrol (Py) and poly(ethylenedioxythiophene). In order to improve and facilitate the immobilization of biocomponents in some polymers, $-NH_2$ functional groups are used. Another advantage of using CNT-polymer composites is the homogeneity of the surface which is related to the stability and biocompatibility of the recognition agent [144].

p0440 Advantages of CNTs in biosensor's architecture are related with the improvement of detection limits when determining pathogens, eg, a bioassay based on CNTs and the immobilization of LBL for the detection of *E. coli* O157:H7 achieved a detection limit of 250 CFU/mL (Table 4). This biosensor presents no interference when used for the analysis of milk samples, with no significant differences when compared and validated with the ELISA methodology [144].

p0445 Recently, aptamers have been reported for the recognition of pathogens such as *E. coli* and *Salmonella*, due to its highly specific not only to proteins but also to metals and organic molecules. [Q3]

s0065 2.1.4 Graphene and Other Nanomaterials

p0450 Recently, biosensors have been considered for the production of novel systems using NMs as GR, carbon-QD (CQDs) and core shell NPs.

p0455 GR has been used in the construction of electrodes and transducers in biosensors. GR has great electrochemical properties, some of them are chemical stability, low cost, wide potential window, electrochemically inert and their electrocatalytic activity for several redox reactions.

p0460 Surfactants have been used in some research regarding GR and sensors due to their ability of changing the electrical properties of the electrode's interface and so, the electrochemical processes. This is due by the surfactant's adsorption on the electrode's surface and/or its aggregation into supramolecular structures [147].

p0465 Polymers have also been used with GR to improve some material properties, eg, nafion can serve as an antifouling [148], Chitosan is used in combination with GR to improve permeability and adhesive strength [149–153].

p0470 Modification of electrode's surface with GR and biorecognition elements is usually done through composites. It has been reported that the use of GR in sensor construction is inexpensive and can be produced on a large scale in comparison with other carbon NMs such as CNTs [154].

p0475 It has been demonstrated that GR-based biosensors have electrochemical properties that are equal or even superior compared to other electrodes, therefore its use for food quality. In subsequent sections, advances reported in

literature regarding the use of these GR-based biosensors for food content and composition are presented.

p0480 Enzymes as recognition agents for biosensors based on GR have been proposed considering different construction strategies and the fact that enzyme immobilization is a crucial step for the appropriate response of biosensors. As discussed in the past sections, the most important immobilization techniques are adsorption technique, covalent binding, electropolymerization, LBL.

p0485 Phenolic compounds have been determined using tyrosinase-based biosensors. A novel GR-nanosheets matrix for biosensor's construction was proposed, where the enzyme is immobilized with glutaraldehyde. LOD where obtained compared to those reported with other methods based on GR sensors [155].

p0490 Among the different strategies to improve the quantification of phenolic compounds like chlorophenols, an interesting proposal is the combination of carbon, GR and β-cyclodextrin (β-CD) (cD/GRs/CPE); quantification of 2-chlorophenol (2-CP) and 3-chlorophenol (3-CP) can be easily achieved with detection limits of 0.2 y and 0.09 μM, respectively. This sensor was successfully used in real water samples [156]. Its success is based on the presence of the β-CD due to its nanocavities and supramolecular recognition, which in combination with GR increases the surface area. The success of this configuration depends on the formation of inclusion complexes with the pesticide.

p0495 Interesting proposals are reported in literature using biosensors for pesticide determination, where no enzyme is used. A GR/CNT/CS sensor has been reported to detect OPs like MP, the detection limit obtained was 0.5 ng/mL, much lower compared to sensors using enzymes. Reproducibility and stability also improved and the interference analysis resulted satisfactory. In general, the sensor presented high sensitivity and fast response times [157]. In other report, a cobalt (II) oxide (CoO)-reduced graphene oxide (rGO) based sensor for the detection of carbofuran (CBF) and carbaryl (CBR) is developed. This sensor has excellent electrocatalytic behaviour and it was successfully applied for the simultaneous detection of CBF and CBR in fruits and vegetables [158]. Other reports in literature conclude that β-CD acts like an adsorbent for the preconcentration and electrochemical detection of MP. The analytical characteristics of this sensor are comparable to others based on enzyme structures, β-CD reduces significantly GR aggregation and keeps an effective surface area, so the strong π-electrons de-location can strongly interact with π electrons of MP. This induces superconductivity and a fast electron-transference resulting in an excellent electrochemical response [147].

p0500 Combination of GR with metal NPs has proved to improve detection limits with values ranging picomolar concentrations [154]. Composites are used to construct these biosensors, where chemically reduced GR sheets (RGR) and AuNP with poly-(diallyldimethylammonium chloride) (PDDA) are used to produce a nano-hybrid AuNP/RGR.

p0505 Recently, new sensors based on carbon QDs, also called C-Dots, have been reported. A great advantage of C-Dots is its low toxicity, making them a very attractive material for the development of sensors. These NMs have been used to detect one of the most common pesticides: MP, where C-Dots with zirconia (ZrO_2) are electrodeposited. The detection limit resulted to be 0.056 ng/mL and it was used for detection of this pesticide in rice samples [159].

p0510 Actually, different GR-based biosensors have been reported for *E. coli* detection, through the GR functionalization. The proposed biosensor is a combination of GR/CNT [160] and GR oxide nanosheets, which improves the capture of the bacteria compared to the GR alone [161,162].

p0515 Other strategy of biosensors use a sulphate-reducing bacteria (SRB) which is sensitive through the anti-(SRB) antibody (Ab) [163,164] or also, aptamers can be used, as reported for the detection of *S. aureus* [165]. This sensor is particularly based on GRO and AuNPs linked by single-stranded DNA (rGOssDNA-AuNPs) which works as an amplification system to improve LOD.

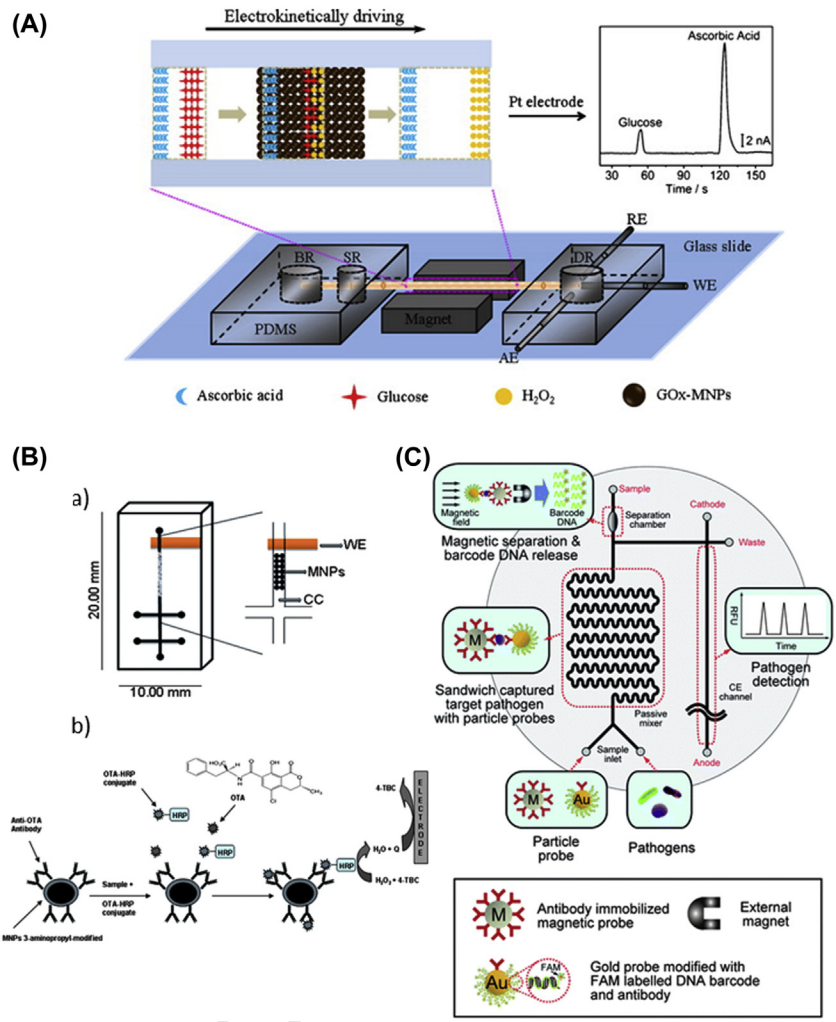
p0520 Trends in several analyses are focussed on the development of composite biosensors based on NMs and enzymes as recognition agents.

s0070 2.2 Lab-on-a-Chip (Microfluidics)

p0525 In the late 1980s, with the evolution of several microfluidic structures, the 'micro total analysis systems' (μTAS) (also called lab-on-a-chip) emerged. These microsystems integrate injection, reaction, separation and analyte detection in a unique device. The advantages of these microsystems in chemical analysis are portability, small sample volumes (nanolitres), high sensitivity, high stability, short analysis times, low cost per analysis and less laboratory space.

p0530 There are different types of lab-on-a-chip devices [166−174]; one of the most important is the capillary electrophoresis microchip (CE microchip), which consists on a reservoir (where the sample is loaded, injector) and a microchannel (where the electrophoretic separation of the analytes is performed). Generally, the microchannel and reservoirs are manufactured using photolithography. In a typical configuration of a CE microchip (both simple cross-T and a twin-T injectors) channels vary from 10 to 100 mm, with a separation length in the range of 3−10 cm (Fig. 5A). Usually microchips can be constructed with glass, quartz or polymers such as poly(methyl methacrylate) (PMMA), polycarbonate (PC), and poly(dimethylsiloxane) (PDMS) which is the most used. Recently, paper has been reported as substrate. Diverse applications have demonstrated the functionality of electrochemical sensors coupled to these microsystems.

p0535 Nowadays, microfabrication technologies and nanotechnology offer great compatibility, so intelligent integrated systems can be constructed with the inclusion of electrochemical sensors. The use of NMs in these microsystems allows the improvement of separation stages, eg, using pseudostationary



f0030 **FIGURE 5** (A). Scheme representation of the construction and analytical procedure of GOx−MNPs. *AE*, auxiliary electrode; *BR*, Buffer reservoir; *DR*, detection reservoir; *RE*, reference electrode; *SR*, sample reservoir; *WE*, working electrode. *(From J. Sheng, L. Zhang, L. Jianping, H. Ju, Anal. Chim. Acta 709 (2012) 41−46 with permission from Elsevier.)* (B) (a) Schematic representation of microfluidic immunosensor. *CC*, central channel; *WE*: Au working electrode. All measurements are given in millimetres, (b) representation of the biochemical immunoreaction. *(From M. Fernández-Baldo, F. Bertolino, G. Fernández, G. Messina, M. Sanz, J. Raba, Analyst 136 (2011) 2756−2762 with permission from Royal Society of Chemistry.)* (C) Schematic diagram of an integrated PMMS-CE microdevice which performs a DNA barcode assay and a capillary electrophoretic separation for multiplex pathogen detection. The PMMS-CE microdevice consists of a passive mixer for target capture with particle probes, a magnetic separation chamber for isolating and purifying the target complexes, and a capillary electrophoretic microchannel for detecting barcode DNA strands to identify target pathogens. *(From J. Jung, G. Kim, T. Seo, Lab.* [Q14] *Chip 11 (2011) 3465−3470 with permission from Royal Society of Chemistry).*

phases in the microchip-based capillary electrochromatography, besides these can be used to improve detection and sensitivity.

s0075 *2.2.1 Nanoparticle-Based Lab-on-a-Chip*

p0540 Several NMs can be used to modify the microchannels in the lab-on-a-chip systems, the most used are AuNPs and CNTs [167]. In particular, NPs have several functions as part of microchips, these can be used as support or for concentrating and/or separating the analyte. These devices can act as biological and molecular recognition systems improving the analysis methodologies.

p0545 AuNPs used as stationary phase on microchips was first proposed by Pumera et al. [168]. The use of NMs allows a significant improvement in mobility, resolution and selectivity. It has been reported that the number of theoretical plates can be doubled compared to systems without NPs. Several investigations are based on this principle, which involves coating the walls of microfluidic networks with polymer and adding NMs that adsorb on such modified walls. This method has been applied to DNA analysis [169].

p0550 Moreover, MBs have been used to generate bioreactors in the microchannel. This bioreactor is based on the immobilization of an enzyme through covalent bonds on the MBs, and then these particles are introduced into the microfluidics channel. Care must be taken when functionalizing the microchannel with MBs because aggregates can block the channel and interfere with the detection.

p0555 Some advantages of using MBs are handling the bioreactor zone in the microchannel through the magnet and regeneration of the bioreactor by replacing the MBs in order to renew them. Based on this principle, MBs have been used in the construction of a bioreactor for detecting carbofuran [170]. AChE is immobilized on the MBs, incubating for 24 h, and then the last ones are introduced into the microchannel and then the electrochemical detection is performed. Indirect quantitation of the pesticide is made through the inhibition of the enzyme. The main advantage of this microsystem is the low detection limit that can be achieved ppb.

p0560 Another interesting strategy employed is the use of an on-chip sandwich immunoassay strategy based on the functionalization of NPs with antibodies. This strategy has been used for detection of some mycotoxins, eg, Ochratoxin A in apples with a detection limit lower than that obtained with the traditional ELISA methodology [174]. Fig. 5B shows the representative diagram of lab-on-chip sandwich configuration for immunoassay.

p0565 Recently, a new barcode DNA assay has been proposed for the detection of target proteins or nucleic acids with high sensitivity. This analysis is based on the use of thiolated barcode DNAs, and two particle probes: magnetic microparticles (MMP) with the recognition element and AuNP with a second recognition element to form a sandwich structured immuno-complex (MMP-target-AuNP); then the dehybridization of the barcode DNA from the NP

probes is done. Fig. 5C shows a schematic representation of the steps involved in the DNA barcode assay for the detection of pathogens like *S. aureus*, *E. coli* and *Salmonella typhimurium*. The application of DNA barcode assay substantially increases sensitivity and presents detection limits in the range of attomolar concentrations.

p0570 Because of their optical properties, QDs have been used as labelling biomolecules in microfluidic systems. Typically, QDs can be attached to protein assemblies for protein detection via a streptavidin-biotin link or a DNA link bridge. QDs are used to enhance the performance and analytical characteristics of fluorescence, optical and electrochemical detectors, but there are few real applications on lab-on-a-chip based on QDs for food analysis. Table 5 summarizes some analysis based on lab-on-a-chip.

s0080 *2.2.2 Carbon Nanomaterial-Based Lab-on-a-Chip*

p0575 CNTs have demonstrated great advantages when used in food analysis, eg, increasing the analytical signal (due to its active surface area) [175], improving selectivity (due to their electrocatalytic properties) and high reproducibility.

p0580 CNTs are used in the lab-on-a-chip devices as stationary phase. This NM improves the separation of various compounds such as DNA fragments, polycyclic aromatic hydrocarbons and phenolic compounds. The separation is associated with $\pi-\pi$ interactions between the aromatic rings of the solute and the sp^2 hybridized aromatic rings of the CNT, as well as with oxygen-containing groups.

p0585 CNTs are used with hydrogel polymers to produce a stationary phase. The durability of the hydrogel as well as the separation efficiency is favoured especially with SWCNT. In general, CNTs have different surface areas and impurities such as metal particles, amorphous carbon and different functional groups from sample to sample. That is an inconvenience for stationary phase development.

p0590 The integration of CNT-based electrochemical detector in microfluidic separation systems is a promising alternative to their traditional sensitivity problems that arise from the extremely low volume samples introduced.

p0595 Thus microfluidic devices may use different CNTs as SWCNT or MWCNT. Antioxidants such as vitamins, isoflavones and vanilla have been analysed using a lab-on-a-chip coupled to a detector with CNTs. Analytical peaks presented high resolution and using MWCNT, high sensitivity is achieved compared to other systems without CNTs, making this system suitable for food analysis (Table 5).

s0085 3. CONVENTIONAL ANALYTICAL TECHNIQUES

p0600 Chemical analysis has evolved with the arrival of NMs, as they have been used in different areas of analytical chemistry, including spectroscopy, electronic detection and separation techniques beside sensors and biosensors.

t0030 **TABLE 5 NMs-Based Lab-on-a-Chip Used in Food Analysis** [Q8]

Technique	Nanomaterial	Analyte	Sample	Lower Detection Limit	References
Electrochemical	MWCNT	Polyphenols Vitamins Vanilla flavours Total isoflavones	Vitamin C Polyphenols Apple	2 μM 12 μM 11 μM 0.8 μM	[176]
Electrochemical	MWCNT/SPE	Polyphenol	Fruits	7.1 μM	[177]
Optical	CNT	Staphylococcal enterotoxin B	Soya milk	0.1 ng/mL	[178]
Electrochemical	Fe_3O_4/MWCNTs/β-CD	Hypoxanthine	Meat	0.3×10^{-8} M	[179]
Electrochemical	MNPs	Ochratoxin A	Apples	0.05 μg/kg	[174]
Electrochemical	MWCNT/PEI/GCE	Herbicides	ND	9 μM	[180]
Electrochemical	MWCNT/PEI/GCE	Phenol	ND	4.2 μM	[181]
Electrochemical	MWCNT/NiNP	Sugar	Herb	0.32 μM	[182]
	rGRO/CuNP	Carbohydrates	Food	1.64 μM	[183]
Electrochemical	MWCNTs/PMMA	Lignans	Herb	0.26 μM	[184]
Electrochemical	MWCNT/PEI/GCE	Antioxidants, acids	Wine	3.2 μM	[185]
Electrochemical	MWCNT/EVA	Coumarin derivatives	Herb	0.27 μM	[186]
Electrochemical	MWCNT/PET	Flavonoids	Peanut hulls	4.2 μM	[188]
Electrochemical	SW and MWCNT/SPE	Antioxidants	Fruit	12 μM	[189]

CNT, carbon nanotubes; *GCE*, glassy carbon electrode; *MNPs*, magnetic nanoparticles; *MWCNT*, multiwalled carbon nanotubes; *ND*, not detected; *PMMA*, poly(methyl meth-acrylate).

10065-COAC-9780444635792

s0090 3.1 Nanomaterial-Based Chromatography

p0605 The chromatography is a physical separation technique for mixture resolution relying on the distribution of the analyte between a stationary phase and mobile phase. In a single step process, it can separate a mixture into its individual components and simultaneously provide a quantitative estimate of each constituent. The analytical efficiency of a chromatography method depends not only on adequate separation but also on suitable detection.

p0610 NMs offer several advantages for separations due to their unique properties, in particular a high surface-to-volume ratio, which can facilitate mass transfer and increase separation efficiency. Compared to silica, the most commonly used packing material, NPs exhibit chemical stability over a wide pH range. NMs consisting of metal oxides, polymers, CNTs, QDs and fullerene NMs are either used directly as the packing material or to modify this last in columns for applications in gas and liquid chromatography, capillary electrophoresis, and electrochromatography. NMs can also act as a pseudostationary phase.

p0615 Recently, monolith columns in combination with NMs have been used for separations. Nanosized metal organic frameworks are also used for separating different analytes. Different magnetic NPs can be used for concentration of analyte and separations, where the analyte detection usually occurs by some type of spectroscopic or electrochemical technique.

p0620 QDs have been implemented as part of fluoroimmunochromatographic technique for MP determination at picogram level by using thiol-stabilized CdTe-QDs as fluorescent probes in a flow-injection analysis system comprising an immunoreactor column packed with immobilized anti-MP IgY antibodies [189].

p0625 On the other hand, SWCNT-hydroxypropyl-β-cyclodextrin (HP-β-CD) was used as stationary phase for the liquid chromatographic separation of organic compounds, the $\pi-\pi$ interaction and the hydrophobic interaction in the stationary phase is improved by introducing the SWCNTs [187]. The SWCNTs make it possible to extend the application range on the newly prepared stationary phases for HPLC.

p0630 Currently, the sensor array used to distinguish between different compounds is the gas sensor array, also called 'electronic nose', which is modelled directly on the olfactory system. It can detect the odour of molecules as vinegar to form a 'fingerprint' database through the use of an array of broadly cross reactive sensors in conjunction with pattern recognition methods. This method has been established by chemiluminescence liquid sensor array (electronic tongue) based on NMs for the discrimination of eight vinegars.

s0095 3.2 Nanomaterial-Based Optical Techniques

p0635 So far, the NMs have been used in fluorescence spectroscopy, surface plasmon resonance (SPR) spectroscopy, localized surface plasmon resonance (LSPR)

spectroscopy, surface-enhanced Raman spectroscopy (SERS), and mass spectrometry, IR, NPs in nuclear magnetic resonance (NMR) spectroscopy, magnetic resonance imaging (MRI), and infrared spectroscopy. In this section, only NM's applications for SPR and fluorescence techniques are discussed.

s0100 *3.2.1 Surface Plasmon Resonance Spectroscopy*

p0640 SPR spectroscopy is based on detecting changes in refractive index that occurs in thin metal films, usually Au, as the result of chemical reactions or a recognition event. When a small change is detected in the refractive index on the analyte−metal interface, information about molecular interactions can be obtained by measuring an optical property (intensity, phase and polarization of light). In the early 1980s SPR was first proposed for the direct monitoring of specific antigen−antibody interactions.

p0645 In SPR sensors, changes in plasmonic resonance signals in the metal thin film are strongly dependent of the refractive index of the medium. The sensitivity of the method is limited by the change amount in the refractive index at the metal surface and the minimum SPR displacement is detected due to the recognition event between the receptor and the analyte.

p0650 The SPR technique has limitations when the analyte is present in very low concentrations and when analysing small molecules. NMs, particularly metal NPs, can help to amplify the analytical signal. Coupling between the localized surface plasmon of metal NPs and the surface plasmon wave of the metal film was found to increase the shift in the SPR spectrum.

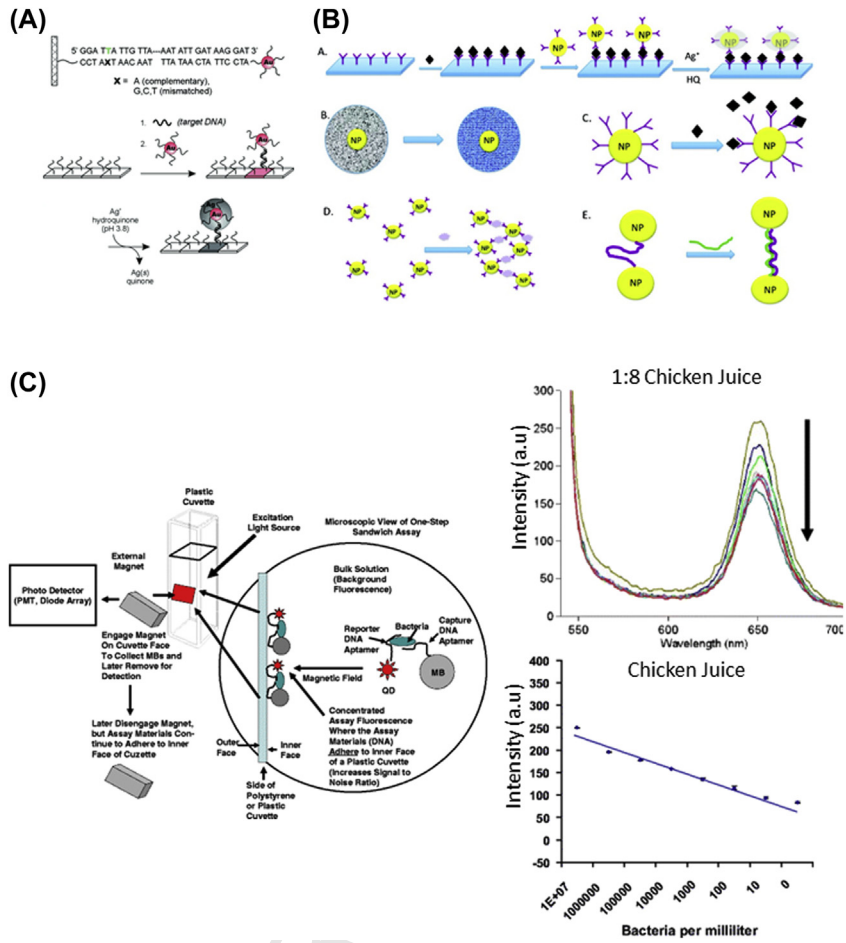
p0655 A sandwich assay strategy has been proposed, where a molecular receptor is on a surface. The analyte binds to the surface, and then the receptor-functionalized metal AuNPs can also bind to the analyte at the surface, this means that the AuNP will not bind to the surface if the analyte is not present (Fig. 6). Absorbance/scattering or visual colour of the AuNP is directly correlated with the amount of analyte present in the solution. In general, all analytes can be analysed based on this principle; however, there are several strategies for amplifying the signal to improve the detection limits [190,191].

s0105 *3.2.2 Spectroscopy Using Gold Nanoparticles*

p0660 NPs and gold nanorods are common NMs used to increase the SPR signal due to their optical properties such as the refractive index, this property depends on the size, shape and chemical composition of the NP (Table 6).

p0665 Modification of the metal film with AuNPs is a good strategy to amplify the signal. NPs can be deposited directly onto the surface to form a nanocomposite, or chemically by cross-link.

p0670 AuNPs can be used to form a biomolecular conjugate using a secondary biomolecular probe sandwich assay with the metal surface, in order to increase the sensitivity and detection limits of SPR sensors [192]. The detection limit is enhanced 10^6 times when using AuNPs [193] whereas using nanorods leads to an



f0035 **FIGURE 6** (A) Schematic representation of different NP LSPR-based sensing mechanisms. *(From T. Taton, C. Mirkin, R. Letsinger, Science 289 (2000) 1757–1760 with permission from AAAS.)* (B) (a) DNA assay, (b) AuNPs as labels with Ag deposition using hydroquinone (HQ) for signal amplification, (c) LSPR bulk refractive index (RI) sensing, (d) LSPR sensing of local binding events, (e) LSPR aggregation based sensing. *(From F. Zamborini, L. Bao, R. Dasari, Anal. Chem. 84 (2012) 541–576 with permission from American Chemical Society Publications.)* (C), (a) Schematic representation of the self-assembling plastic adherent aptamer-magnetic bead plus aptamer quantum dot sandwich assay and magnetic collection system. (b) Spectrofluorometric response of adherent *Campylobacter* assays in chicken juice. *(From J.G. Bruno, T. Phillips, M.P. Carillo, R. Crowell, J. Fluores. 19 (2009) 427–435 with permission from Springer.) LSPR*, localized surface plasmon resonance. [Q16]

improvement of about 10^3 times. However, sensitivity of the system decreases as the size of the probe becomes smaller than the target molecule [194].

p0675 Due to its high extinction coefficient, NPs are used as labels for visual, light scattering or absorbance detection. The most used NPs for this purpose

t0035 **TABLE 6 Summary of Nanoparticles and Their Refractive Index Sensitivities**

Particle	Type	λ_{max} (nm)	Sensitivity (nm/RIU)
Au nanoring	Ensemble	1300	691
Au nanostar	Single	725	218
Au nanodisk	Ensemble	820	327
Au nanotube	Ensemble	650	225
Au triangle@SiO_2	Ensemble	1250	727
SiO_2@cushell	Ensemble	610	67.8
Ag triangle	Ensemble	1093	1096
AuNP dimer	Ensemble	650	471.15

From F. Zamborini, L. Bao, R. Dasari, Anal. Chem. 84 (2012) 541−576 with permission from ACS Publications.

are AuNPs and AgNPs because they present absorption in the visible region and can be easily functionalized.

p0680 A strategy for DNA signal amplification is the 'scanometric' DNA microarray [190]. To amplify the signal of the AuNPs hybridized at the surface, silver ions are reduced to metallic silver with hydroquinone at the surface of AuNPs, this process increases the signal by a factor of 10^5. Based on this, *E. coli, Enterobacter cloacae, Bacillus subtilis, S. aureus* have been detected using AuNPs as labels [195].

s0110 *3.2.3 Spectroscopy Using Quantum Dots*

p0685 Use of QDs have a lot of advantages due to their optical properties eg, the absorption spectrum shows the simplicity to perform multiplex analysis, since it can be excited with a single light source to multiple wavelengths, compared with dyes which are limited to a small region. Multiple analysis allows the evaluation of several parameters in a single run, which reduces the time and cost of the analysis.

p0690 Fluorescence detection based on QDs has been used for biological detection, through the conjugation of QDs with specific DNA. In addition, QDs have been used in the detection of heavy metals using the 'turn off' mode, as it can reduce the risk of a false positive.

p0695 Fluorescence is one of the most popular analysis methods due to its high sensitivity and very low detection limits. However, the main disadvantage of this technique is that fluorophores can undergo photobleaching and have a short stability times. Using NMs with this technique is desirable due to its optical properties, better when compared with organic fluorescent dyes. NPs

tend to have greater stability and higher luminescent intensity. The most important feature is that emission is limited and symmetrical, and NPs are also tunable in size, shape and composition, so they can be used in the detection of biomolecules and heavy metals [140,196–212].

p0700 There are two strategies for 'turn-on' and 'turn-off' detection, when initially fluorescence detection is deactivated turn-on detection occurs, usually through the process of fluorescent resonance energy transfer (FRET), and returns through the interaction with the analyte, which separates the fluorophore and the excitation agent. FRET is a process involving the distance dependent energy transfer from a donor molecule to an acceptor molecule through dipole–dipole interactions.

p0705 In the case of NPs, these are used as FRET donors and the dye serves as an acceptor molecule. The proximity between the actor molecule and the NPs decreases the emission intensity of these last ones and increases the intensity of the acceptor. In 'turn-on' sensors, fluorescence of NPs is deactivated by the interaction with the acceptor molecule or the proximity to the surface, so the fluorescence loss is proportional to the analyte concentration. The most used NMs are QDs and metal NPs, and less frequently used are CNTs.

p0710 It must be remembered that the semiconductor QDs have emission in the NIR. Most commercially available QDs have a semiconductor core, usually a mixture of Cd, Zn, Se, Te, In, P and/or As, the size of these NPs is usually 2–10 nm in diameter. This core is surrounded by a cover, usually another semiconductor material and may include a polymer outer layer.

p0715 Recently, a new type of nanosized carbon particulates like CQDs, with similar size to conventional quantum has been reported [196]. Their use has been significantly increased because of their nontoxic nature, good dispersion in water along with competitive fluorescent properties similar to the toxic metal-based semiconductor QDs. This NM is a new option for *E. coli* and cholesterol detection.

p0720 Integration of QDs and DNA aptamers were developed against $MgCl_2$-extracted surface proteins from *C. jejuni*. The two highest affinity aptamers were selected for use in a magnetic bead (MB) and QD-based sandwich assay scheme (Fig. 6D). The assay exhibits specificity, sensitivity and detection limits of 10–250 UFC colony forming unit (CFU). This strategy may help to prevent major foodborne pathogen outbreaks.

s0115 *3.2.4 Spectroscopy Using Carbon Nanotubes*

p0725 Immunosensing based on CNT was designed for the analysis of a marine (palytoxin, PlTX) toxin, it is usually detected in seafood. The electrochemiluminescent device was developed by preparing a ruthenium-based complex linked to an anti-PlTX polyclonal antibody (pAb). The quantitative detection of PlTX is performed measuring the intensity of the emitted light under excitation conditions. This immunosensor shows a detection limit within subnanograms per millilitre of solution, which is better than reported by HPLC

coupled to mass spectrometry or fluorescence polarization. This device is suitable for detection of mussels and microalgae [213].

s0120 *3.2.5 Surface-Enhanced Raman Spectroscopy*

p0730 Recently, a nano-enabled SERS technique is finding its way into food-related applications. It is a technique capable of measuring samples within minutes, with minimal sample preparation. So, the development of NMs has significantly contributed to Raman spectroscopy techniques. The low sensitivity of SERS can be overcome if a suitable nanostructured surface is used as a substrate to perform SERS [197,214–216]. In the presence of suitable nanostructures, SERS can improve the technique sensitivity to 10^{15} times, leading the potential of this technique for single molecule or single cell detection.

p0735 In Table 7 a review of NM-based optical techniques for some analytes of interest in food science and industry is presented.

s0125 4. CONCLUSIONS AND PERSPECTIVES

p0740 Quality control of food draws the attention of both the institutions responsible for regulating and researchers because of their intimate relationship with human health; hence, the need to generate fast, accurate and reliable information on the quality and safety of foodstuffs.

p0745 Due to these requirements, conventional analytical techniques in recent years have been adapted with new strategies to improve stability, sensitivity, detection limit and the selectivity of the method.

p0750 With the arrival of NMs to the analytical chemistry, chemical and biological analysis techniques have found more opportunity areas. Inclusion of NMs in spectrophotometric techniques and electrochemical separation has improved substantially these techniques when considering sensitivity, specificity and detection limits where femtomolar concentrations can be achieved. In biochemical analysis, detection of pathogens can be made in minutes, thanks to the integration of NMs in biosensors.

p0755 In this sense, the design and development of sensitive devices, which can detect contaminants in food and/or food chain is a vital issue. Their low toxicity and low cost make NMs ideal for the development of new analytical devices with potential applications in food science and industry, eg, carbon QDs.

p0760 Biosensors based on NMs are considered forefront devices representing a great alternative to conventional analytical methods such as HPLC, UV–Vis, fluorescence, electrochemical, among others, as they are able to provide solutions to analytical problems easily, quickly and inexpensively, although this depends on the food area and the analyte considered.

p0765 The unique properties of NMs have enabled their application with great success in microfluidics, promoting the multiscreen for detection of analytes in complex matrixes and with similar structures and even for the detection of pathogens.

t0040 **TABLE 7** Nanomaterials-Based Optical Techniques [Q9]

Technique	Nanomaterial	Analyte	Sample	Lower Detection Limit	References
ECL	TiNT	Choline	Milk	0.01 μM	[198]
	CdS	Hypoxanthine	Fish	5 nM	[199]
FL	CdTe/CdS	Glucose	–	1.8 μM	[200]
	QD	*Campylobacter*	Chicken	2.5 CFU	[201]
	SiO_2	*Salmonella*	Bacteria	3 fM	[202]
	SWNTs	Ochratoxin A	Beer	24.1 nM	[140]
	CdSe/ZnS	Diquat herbicide	Oat grains	0.01 mg/kg	[203]
	β-CD—CdSe/ZnS	Vanillin	Sugar Milk	0.99 mg/mL	[204]
	CdSe/ZnS	Melamine	Milk	0.15 mg/kg	[205]
	CdTe	Melamine		0.02 mg/L	[206]
		Choline		0.1 μM	[207]
		Acetylcholine		10 μM	[207]
	Silica-NPs	Soya protein	Soya milk	0.05 mg/mL	[208]
	Mn:ZnSe	OPs	Milk	1.3×10^{-11} M	[209]
	AuNPs	Streptomycin		47.6 nM	[210]
Colourimetric	AuNPs	Streptomycin		71.3 nM	[210]

10065-COAC-9780444635792

Surface plasmon resonance	Magnetic nanoparticles (MNPs)	Peanut allergen Ara h1	Cocoa	0.09 μg/mL	[211]
	MNPs	Ochratoxin A	Wine	0.94 ng/mL	[212]
Surface-enhanced Raman spectroscopy	MNPs	Ovalbumin	Milk	5 μg/mL	[214]
	AgNPs	*Escherichia coli*		10^3 cells/mL	[215]
	AuNPs	Pesticides	Apple juice and cabbage	2.5 ppm	[216]

AuNPs, gold nanoparticles; *OPs*, organophosphates; *QD*, quantum dot.

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p0770 The development of biosensors based on NMs represents a significant opportunity area with the emergence of new materials with mechanical, electrical and optical properties of a higher quality than the current ones. As a result, carbon-based NMs draw special attention in order to create new devices as carbon − QDs and GR. On the other hand, new electrodes have emerged based on AuNPs chains. In this regard, there are no reports indicating their use for detecting food substances, but there are some for glucose detection with optimal results and representing promising opportunities for future developments with applications in food analysis.

p0775 The use of nanotechnology supports the development of new analytical devices. A challenge in this regard, is a massive device production without changing the NM properties.

p0780 Another challenge in the use of NMs is related to the detection and monitoring of real samples in real time, along with the inclusion of these new devices and methods in already standardized and regulated methods, considering the official legislations.

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Non-Print Items

Abstract:
This chapter revises the recent trends in the use and applications of nanomaterials (NMs) in analytical detections with special interest in food quality control. The most important NMs such as gold nanoparticles, quantum dots, carbon-related nanomaterials and their properties are introduced. We show how analytical science is taking advantage of such materials to either develop new analytical methods or improve the existing technologies. Biosensing, in both batch and lab-on-a-chip formats, is one of the most important analytical technologies that is in the forefront of such interesting applications. The use of these materials in some conventional analytical techniques such as chromatography between others also is discussed. Examples related to such NMs application in real food samples with interest for quality control as well as detection of various interesting compounds such as glucose, amino acids, DNA (normally present in food) or other species that are usually of interest to be detected for safety reasons (bacteria, toxins) are discussed. Aspects related to the improvements of analytical performance in terms of detection limits, stability, selectivity, etc. using various NMs and detection technologies also are discussed.

Keywords: Analytical methods, Biosensors, Carbon nanotubes, Food analysis, Lab-on-a-chip, Nanomaterials, Nanoparticles, Quantum dots.