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Feature Article (by invitation only)

Applications of nanotechnology in food packaging and food safety: Barrier materials, antimicrobials and sensors

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ABSTRACT

In this article, several applications of nanomaterials in food packaging and food safety are reviewed, including: polymer/clay nanocomposites as high barrier packaging materials, silver nanoparticles as potent antimicrobial agents, and nanosensors and nanomaterial-based assays for the detection of food-relevant analytes (gasses, small organic molecules and food-borne pathogens). In addition to covering the technical aspects of these topics, the current commercial status and understanding of health implications of these technologies are also discussed. These applications were chosen because they do not involve direct addition of nanoparticles to consumed foods, and thus are more likely to be marketed to the public in the short term.

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1. Introduction

Nanotechnology involves the characterization, fabrication and/or manipulation of structures, devices or materials that have at least one dimension (or contain components with at least one dimension) that is approximately 1–100 nm in length. When particle size is reduced below this threshold, the resulting material exhibits physical and chemical properties that are significantly different from the properties of macroscale materials composed of the same substance. Research in the nanotechnology field has skyrocketed over the last decade, and already there are numerous companies specializing in the fabrication of new forms of nanosized matter, with anticipated applications that include medical therapeutics and diagnostics, energy production, molecular computing and structural materials. In 2008, nanotechnology demanded over $15 billion in worldwide research and development money (public and private) and employed over 400,000 researchers across the globe [1]. Nanotechnologies are projected to impact at least $3 trillion across the global economy by 2020, and nanotechnology industries worldwide may require at least 6 million workers to support them by the end of the decade [1].

Despite the excitement surrounding nanotechnology and the abundance of funding dollars being poured into it, however, one industry which has been slow to catch on is the food industry. This is not so surprising, as public preference for "natural" food products has historically inhibited the implementation of emergent food technologies, and nanotechnology has been no exception. Indeed, while public opinion about general nanotechnology applications has ranged from neutral to slightly positive [2–5], some studies suggest that consumers remain wary about "nanofoods" [6–9].

Nevertheless, scientists and industry stakeholders have already identified potential uses of nanotechnology in virtually every segment of the food industry (Fig. 1), from agriculture (e.g., pesticide, fertilizer or vaccine delivery; animal and plant pathogen detection; and targeted genetic engineering) to food processing (e.g., encapsulation of flavor or odor enhancers; food textural or quality improvement; new gelation or viscosifying agents) to food packaging (e.g., pathogen, gas or abuse sensors; anticounterfeiting devices, UV-protection, and stronger, more impermeable polymer films) to nutrient supplements (e.g., nutraceuticals with higher stability and bioavailability). Undeniably, the most active area of food nanoscience research and development is packaging: the global nano-enabled food and beverage packaging market was 4.13 billion US dollars in 2008 and has been projected to grow to 7.3 billion by 2014, representing an annual growth rate of 11.65% [10]. This is likely connected to the fact that the public has been shown in some studies to be more willing to embrace nanotechnology in "out of food" applications than those where nanoparticles are directly added to foods [7,11,12].

Despite an explosion of growth in this area, food nanotechnology is still a lesser-known subfield of the greater nanotechnology spectrum, even among professional nanotechnologists. This article

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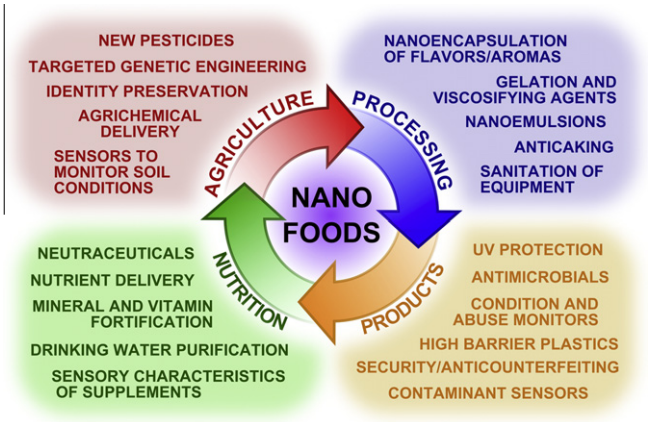

Fig. 1. Nanotechnology has applications in all areas of food science, from agriculture to food processing to security to packaging to nutrition and neutraceuticals. Some potential applications are shown here. The applications which will be reviewed in this article are those in the orange quadrant, which are the most likely to be marketed in the near term.

addresses this knowledge deficit by providing a comprehensive review of current developments in nanotechnology as it applies to foods and food-related systems, focusing specifically on applications which are most likely to enjoy consumer acceptance and regulatory attention in the immediate future. Covered topics include polymer nanocomposites for stronger, higher barrier packaging materials, nanoparticle-based antimicrobials, and sensors/assays that detect contaminants in foods or monitor changes in packaging conditions or integrity. Specific health concerns related to these various applications are also briefly described. The article concludes with a brief overview of the commercial and regulatory outlook of food nanomaterials.

2. Barrier applications of polymer nanocomposites

When food will not be consumed immediately after production, it must be contained in a package that serves numerous functions. In addition to protecting the food from dirt or dust, oxygen, light, pathogenic microorganisms, moisture, and a variety of other destructive or harmful substances, the packaging must also be safe under its intended conditions of use, inert, cheap to produce, lightweight, easy to dispose of or reuse, able to withstand extreme conditions during processing or filling, impervious to a host of environmental storage and transport conditions, and resistant to physical abuse. This is a tall order for any material to fill.

A critical issue in food packaging is that of migration and permeability [13–16]: no material is completely impermeable to atmospheric gasses, water vapor, or natural substances contained within the food being packaged or even the packaging material itself. In some applications, high barriers to migration or gas diffusion are undesirable, such as in packages for fresh fruits and vegetables whose shelf life is dependent on access to a continual supply of oxygen for sustained cellular respiration [15]. Plastics utilized for carbonated beverage containers, on the other hand, must have high oxygen and carbon dioxide barriers in order to prevent oxidation and decarbonation of the beverage contents [15]. In other products, migration of carbon dioxide is far less of an issue than that of either oxygen or water vapor. As a result of these complexities, food products require sophisticated and remarkably different packaging functions, and the demands on the packaging industry will only increase as food is transported over increasingly longer distances between producers and consumers.

Traditional materials for food packaging include metal, ceramic (glass), and paper (cardboard). While these materials are still used, the light weight, low cost, ease of processing and formability, and remarkable diversity in physical properties of organic polymeric materials makes plastics attractive alternatives for the packaging of foods. Polymers which are most frequently used for food packaging include, but are not limited to, polyolefins such as polypropylene (PP) and various grades of polyethylene (HDPE, LDPE, etc.), polyethylene terephthalate (PET), polystyrene (PS) and polyvinyl chloride (PVC). Though polymers have revolutionized the food industry and possess numerous advantages over conventional materials, their major drawback is an inherent permeability to gasses and other small molecules. Some polymers are better than others in this regard. PET, for example, provides a good barrier to oxygen (O_2 permeability = 6–8 nmol m^{-1} s^{-1} GPa^{-1}) , while high density polyethylene (HDPE) fares much worse (O_2 permeability = 200–400 nmol m^{-1} s^{-1} GPa^{-1}) [16].[1] On the other hand, HDPE offers a significantly better barrier against water vapor than PET [16].

In general, permeability of a polymer to oxygen or moisture is dependent on a large number of interrelated factors, including: polarity and structural features of polymeric side chains, hydrogen bonding characteristics, molecular weight and polydispersity, degree of branching or cross-linking, processing methodology, method of synthesis, and degree of crystallinity. Permeability to one migrant can also be complicated by the presence of other migrants. For instance, ethylene–vinyl alcohol (EVOH) exhibits quite excellent oxygen transmission rate (OTR) values under dry conditions, but under very humid conditions (relative humidity >75%) it can possess OTR values more than an order of magnitude higher due to swelling of the polymer and plasticization in the presence of diffused water molecules [17,18]. It is noteworthy that bio-derived polysaccharide (starch) based polymers, which have garnered attention due to their biodegradability, tend to have an even larger dependence of their OTR on humidity level, which has severely limited their usefulness [19]; other thermoplastic biopolymers like polylactic acid (PLA) or polycarprolactones (PCLs) have good tolerance to moisture but less exciting baseline (dry level) OTR values [19].

Because no known pure polymer exhibits all the desired mechanical and barrier properties required for every conceivable food packaging application, complex multilayer films or polymer blends are often utilized. For example, in an application where ultrahigh oxygen barriers are required over a large humidity range, a high oxygen barrier, water sensitive material like EVOH can be sandwiched between two layers composed of a relatively hydrophobic polymer such as polyethylene [20–22]. Direct polymer blending is also a useful approach to achieve desired gas barrier and mechanical properties that cannot otherwise be attained with polymer monolayers [19,23–27], and films with even better, more controllable properties might be achievable with smart-blended coextrusions [28]. Unfortunately, while multilayer films and polymer blending have yielded packaging materials with acceptable gas barrier properties that lack the limitations inherent to many monolayer films composed of ultrahigh barrier polymers, they possess higher production and material costs, require the use of additional additives and adhesives that complicate their regulation by federal agencies, and entail added difficulty when it comes to recycling. As a result, there is still a significant push in the polymer industry to generate monolayer films with improved mechanical and gas barrier properties, particularly those which are composed of biocompatible materials.

Polymer nanocomposites (PNCs) are the latest materials aimed at solving the aforementioned problems. PNCs are created by dis-

[1] PET and HDPE typically have O_2 permeability values ranging from 46 to 62 and 1550 to 3100, respectively, in units of mL mil m^2 day^{-1} atm^{-1}. See Ref. [16] for conversion tables for gas permeability values as well as tables of permeability values and transmission rates for various polymers.

persing an inert, nanoscale filler throughout a polymeric matrix. Filler materials can include clay and silicate nanoplatelets (*vide infra*), silica (SiO_2) nanoparticles [29–32], carbon nanotubes [33–40], graphene [41–43], starch nanocrystals [44,45], cellulose-based nanofibers or nanowhiskers [46–54], chitin or chitosan nanoparticles [55–58] and other inorganics [59–62]. Though enhancing polymer barrier properties is the most obvious application of PNCs in the food industry, PNCs are also stronger [33,63–74], more flame resistant [59,63,68,73,75–81] and possess better thermal properties (e.g., melting points, degradation and glass transition temperatures) [64,71,72,82–84] than control polymers which contain no nanoscale filler; alterations in surface wettability and hydrophobicity have also been reported [85]. Some of these physical property enhancements can be particularly impressive. For example, a layer-by-layer assembly technique was used to fabricate a PNC material composed of clay nanoplatelets dispersed within cross-linked polyvinyl acetate (PVA) that possessed a modulus (stiffness) of 106 ± 11 GPa, almost two orders of magnitude larger than "virgin" PVA and comparable to the stiffness of some grades of Kevlar [86]. A similar fabrication technique was used to engineer clay/poly(ethyleneimine) PNCs that preserved the weave structure of cotton fabrics during extended burning times when used as a coating [87].

In the end, PNCs should offer the food packaging industry better downgauging opportunities, in addition to cost savings and waste reductions, due to the smaller amounts of polymer that need to be used to attain packaging materials with identical or even better mechanical attributes. Nanocomposites may even offer environmental advantages over conventional plastics: when a nanofiller is dispersed within the bio-compatible polymer PLA, the PLA bio-nanocomposite actually has a faster rate of biodegradation than PLA containing no such additives [88].

2.1. Permeability of PNCs

The permeability of polymeric materials to gasses is determined by the adsorption rate of gas molecules into the matrix at the atmosphere/polymer boundary and the diffusion rate of adsorbed gas molecules through the matrix [14,16,89]. The adsorption rate is generally dependent on the rate of formation of free volume holes in the polymer created by random (Brownian) or thermal motions of the polymer chains, and diffusion is caused by jumps of molecular gas molecules to neighboring (empty) holes. Thus the permeability of polymer films is dependant on free volume hole sizes, degree of polymer motion, and specific polymer–polymer and polymer–gas interactions, all of which can be affected by intrinsic polymer chemistry as well as external properties such as temperature and pressure. Of course, the overall rate of gas diffusion is also directly dependant on the film thickness.

The dispersal of nano-sized fillers into the polymer matrix affects the barrier properties of a homogeneous polymer film in two specific ways. The first way is by creating a tortuous path for gas diffusion [89]. Because the filler materials are essentially impermeable inorganic crystals, gas molecules must diffuse around them rather than taking a (mean) straight line path that lies perpendicular to the film surface. The result is a longer mean path for gas diffusion through the film in the presence of fillers, as illustrated in Fig. 2. Essentially, the tortuous path allows the manufacturer to attain larger effective film thicknesses while using smaller amounts of polymer.

The effect of dispersed nanomaterials on the mean path length for gas diffusion has been modeled theoretically. The simplest model, first proposed by Nielsen, assumes that fillers are evenly dispersed throughout the matrix and take the shape of rectangular platelets of uniform size, and supposes that the tortuosity of the path is the only factor influencing the gas diffusion rate [90]. In the Nielsen model, the gas permeability is given by

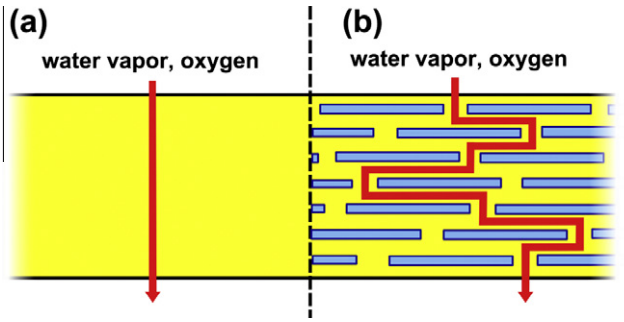

Fig. 2. Illustration of the "tortuous pathway" created by incorporation of exfoliated clay nanoplatelets into a polymer matrix film. In a film composed only of polymer (a), diffusing gas molecules on average migrate via a pathway that is perpendicular to the film orientation. In a nanocomposite (b), diffusing molecules must navigate around impenetrable particles/platelets and through interfacial zones which have different permeability characteristics than those of the virgin polymer. The tortuous pathway increases the mean gas diffusion length and, thus, the shelf-life of spoilable foods.

$$\frac{K_{\text{composite}}}{K_{\text{matrix}}} = \frac{1-\phi}{1+\frac{\alpha}{2}\phi} \tag{1}$$

where the K values represent permeabilities of the composite material and of the matrix in the absence of filler, ϕ is the volume fraction of filler and α is the aspect ratio (length divided by width) of the individual filler particles. This equation shows that as the particles become more anisotropic or plate-like in shape, the barrier effectiveness is expected to increase, a prediction which has been experimentally verified [89]. In practice, the Nielsen model is valid only for small loading percentages ($\phi < 10\%$), as higher loadings result in particle agglomeration, which in turn effectively reduces the mean particle aspect ratio [89] and may affect other properties of the system such as the amount of polymer available to intercalate into the nanoclay galleries and the proportion of "interphase" regions in which the nanoclay surface and any organic modifiers interact directly with the polymeric host material [91]. Improvements on the Nielsen model include adjustments for random positioning of the filler throughout the matrix [92–94], as well as filler shape (e.g., hexagonal [95] or disk [96,97]), size uniformity [94,98], angular orientation with respect to the lateral dimension of the film [99,100], degree of agglomeration or stacking [98,101], and high nanoclay filler contents [91]. Temperature effects have also been studied [91]. In general all of these models predict that large volume fractions or large particle aspect ratios are required to reduce the gas permeability by an appreciable degree. These theoretical considerations have been reviewed in detail [89] and some of the more widely utilized models have recently been tested experimentally over a full range (0–100 vol.%) of nanoclay filler content and modified accordingly [91].

While tortuosity is usually the primary mechanism by which nanofillers impact the barrier properties of PNCs, this is not always the case. The second way that nanoparticulate fillers influence the barrier properties is by causing changes to the polymer matrix itself at the interfacial regions. If the polymer–nanoparticle interactions are favorable, polymer strands located in close proximity to each nanoparticle can be partially immobilized. The result is that gas molecules traveling through these interfacial zones have attenuated hopping rates between free volume holes, or altered density and or size of holes, a fact which has been observed directly via the use of positron annihilation lifetime spectroscopy (PALS) [89,102–104]. In addition, the presence of surfactants or other additives used to efficiently incorporate the filler into the matrix can also

affect the diffusivity or solubility of permeants. The effects of the interfacial regions have been found to be particularly important in polymer matrices that possess very high native gas permeabilities, such as polyolefins [105]. Attempts have been made to model the effect of the interfacial regions [89,106,107] on the diffusivity properties of migrant gasses through polymer films, but the relevant parameters are not always easily measurable.

In any case, each PNC system is different and properties can only predicted generally. These considerations also demonstrate why nanomaterials have been so successful as fillers for polymer composites: compared to micro-scale fillers, nanoparticles have much higher aspect ratios and, due to their high surface area to volume ratios, the interfacial volume element in a PNC film is significantly greater than that of a polymer microcomposite created from the same materials. It is also worth mentioning that gas transport properties can also be modified in the absence of exogenous nanofillers; semicrystalline polymers such as PET and PE have gas permeabilities that are directly related to their degree of crystallinity due to the fact that nanocrystalline regions within the polymer matrix increase tortuosity of gas diffusion and effect changes to the gas transport regions of the interfacial regions [108,109]. In other words, crystalline regions of semicrystalline polymers act as nanoscale fillers. Unfortunately, polymer crystallinity is difficult to measure accurately,[2] and is dependent on numerous processing and structural factors [109], although some recent efforts at controlling polymer crystallinity in nanoscale layered assemblies has yielded some impressively high oxygen barriers [110].

2.2. Structure and barrier behavior of clay and silicate nanocomposites

By far the most promising nanoscale fillers for PNCs are nanoplatelets composed of clays or other silicate materials. The popularity of nanoclays in food contact applications derives from their low cost, effectiveness, high stability and (alleged) benignity. The prototypical clay utilized in PNC applications is montmorillonite (MMT) [$(Na,Ca)_{0.33}(Al,Mg)_2(Si_4O_{10})(OH)_2{\cdot}nH_2O$)], a soft 2:1 layered phyllosilicate clay comprised of highly anisotropic platelets separated by thin layers of water (Fig. 3). The platelets have an average thickness of ~1 nm and average lateral dimensions ranging between a few tens of nm to several μm. Each platelet contains a layer of aluminum or magnesium hydroxide octahedra sandwiched between two layers of silicon oxide tetrahedra. The faces of each platelet have a net negative charge, which causes the interstitial water layer (known as the gallery) to attract cations (Ca^{2+}, Mg^{2+}, Na^+, etc.) and allows for the construction of multi-layer polymer assemblies under appropriate conditions (Section 2.3).

Individual MMT clay platelets possess surface areas in excess of 750 m^2/g and aspect ratios on the order of 100–500 [111]. These structural characteristics contribute to MMT's excellent utility as a filler material for PNCs, typically giving rise to impressive increases in polymer strength and barrier properties with only a few wt.% added to the polymer matrix. However, because they have such large surface energies, clay nanoplatelets tend to stick together, particularly when dispersed in nonpolar polymer environments. Agglomeration of clay platelets leads to tactoid structures (microcomposites) with reduced aspect ratios and, according to the Nielsen model, reduced barrier efficiencies. When polymer–clay interactions are more favorable, or when steps are taken (e.g., sonication [112]) to disaggregate the platelets, intercalated and fully exfoliated PNC structures are formed [64,111,113,114]. Intercalated morphologies are characterized by moderate intrusion of polymer strands into the gallery volume, and the shape of the layered stack is preserved. In fully exfoliated structures, on the other hand, individual platelets are well separated and have extremely favorable interactions with the polymer matrix [115]. These various nanoclay morphologies are depicted in Fig. 4.

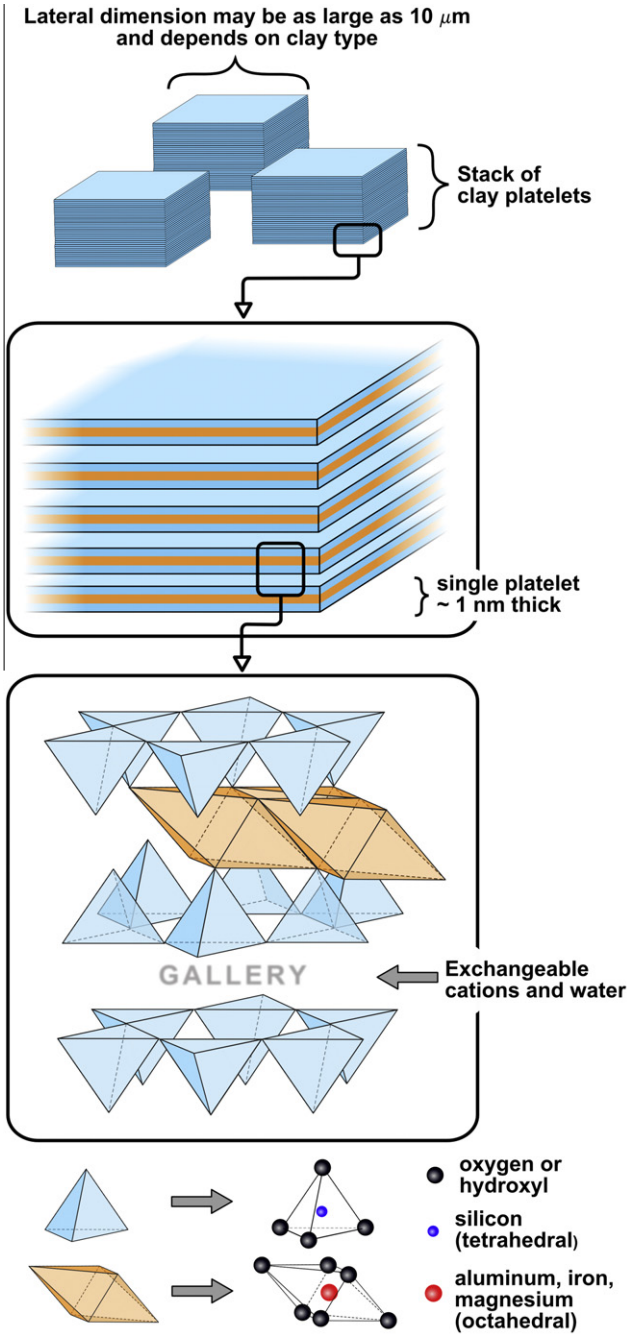

Fig. 3. Structure of montmorillonite (phyllosilicate clay).

MMT is not the only layer silicate material utilized in nanocomposite materials. Related clays such as kaolinite, hectrite and saponite can also be used in PNC applications and the natural structure of these various clays can play an important role in PNC properties. For instance, polyimide nanocomposites containing 2 wt.% of hectrite, saponite, montmorillonite and synthetic mica have water vapor permeabilities of 12.3, 10, 5.86 and 1.16 g mm m^{-2} day^{-1} compared to 12.9 g mm m^{-2} day^{-1} for the

[2] In fact, gas transport rates may be an effective means of estimating polymer crystallinity [106].

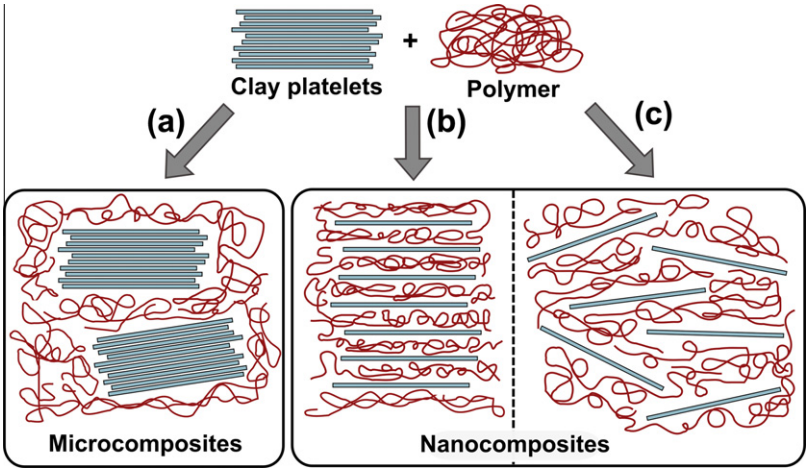

Fig. 4. Tactoid (a), intercalated (b) and exfoliated (c) polymer–clay nanocomposite morphologies.

virgin polymer [116]. Theoretical modeling of this data shows that the variation in H_2O permeability as a function of clay type corresponds well to the natural platelet lateral dimensions for each clay (i.e., there is a nanoplatelet aspect ratio dependency). A similar result has been obtained for oxygen permeability in poly(lactic acid) nanocomposites [117].

The manner in which the polymer–clay nanocomposite (PCNC) is fabricated can play a large role in how the clay platelets are distributed throughout the matrix and, therefore, the barrier properties of the resulting materials. Melt processing, *in situ* polymerization and solution-based processing techniques may be more or less suitable for different filler/polymers systems [118–120], and an excellent review [121] discusses these relationships extensively. As one example, Yeh et al. showed that when MMT platelets are present during *in situ* polymerization of poly(methylmethacrylate) (PMMA), the resulting MMT/PMMA PNCs have better clay exfoliation and thus significantly lower OTR and water vapor transmission rate (WVTR) values (compared to virgin polymer) than when the MMT was incorporated into commercially purchased PMMA by solution dispersion [122]. Pereira et al. recently showed that the type of extrusion method also can have an enormous effect on the final barrier properties of a MMT/polyamide PCNC film, with OTR rates varying over three orders of magnitude for films made of the exact same polymer and filler materials [123]; a similar dependency of mechanical properties on processing method for MMT/polyamide has also been observed [123,124]. In this regard, it is clear that controlling the nanoparticle dispersion morphology (i.e., tactoid, intercalate, exfoliate) is important, as it has an enormous influence on the bulk properties of the PCNC materials [73]. For instance, Gorrasi et al. [125] studied the correlation between nanoparticle morphology and water vapor barrier of a series of MMT/polycaprolactone (PCL) composites, and found that while PCL PCNCs possessing the tactoid (microcomposite) and intercalated nanoparticle structures exhibited diffusion parameters close to those of virgin PCL, fully exfoliated structures led to values that were roughly two orders of magnitude lower.

Unfortunately, efficient delamination of platelets to form fully exfoliated morphologies is hindered by the fact that clay particles are hydrophilic and many polymers of interest (PET, PE, PP, etc.) are hydrophobic [64,120]. Good dispersibility of nanoclay platelets in hydrophobic matrices is typically achieved by functionalizing the polar clay surface with organic ammonium ions bearing long aliphatic chains [70,82,105,126,127]. Note that these organofunctional groups need not be passive spectators: efficient exfoliation of MMT in PMMA and PS polymers can be achieved by functionalizing the MMT particles with an organoammonium ion bearing two styrene groups, which directly participate in an *in situ* polymerization of the matrix [128].

Not surprisingly, PCNC barrier properties depend on the type of organic compatibilizer utilized due to varying effects on nanoparticle morphology. For example, moisture permeability of a MMT/epoxy PCNC material using octadecylamine as an organic modifier is lower than when the modifier is a quarternary alkylamine [129]; in the latter case, dispersed MMT nanoparticles possess a mean interlayer distance (*d*-spacing) of 3 nm, compared to the 8 nm mean interlayer separation of MMT particles functionalized with octadecylamine, resulting in less efficient exfoliation and poorer barrier behavior. A more systematic demonstration of the influence of the modifier on degree of MMT exfoliation and, hence, gas barrier properties is provided by Osman et al., who utilized quaternary ammonium modifiers bearing either one, two, three or four long alkyl (octadecyl) chains [130]: when MMT/polyethylene nanocomposites were fabricated using modifiers having more numerous long alkyl chains, the clay platelets generally had larger *d*-spacing values (inter-platelet separation) due to steric interactions, and thus better gas barriers. MMT clays with better cation exchange capacities also exhibited better degrees of exfoliation within the polymer matrix due to similar steric considerations. When all of the data-sets are combined, a clear inverse correlation between *d*-spacing and oxygen transmission rate is apparent, as shown in Fig. 5. The Osman study is a great example of the power of chemistry and nanotechnology: a clear understanding of the factors involved, combined with the unique chemical properties of nanoscale particles, can lead to impressive control over the physical properties of macroscopic materials.

The first successful example of a polymer–clay nanocomposite (PCNC) was a nylon-6 MMT hybrid material developed by the Toyota Corporation in 1986 [131]. The initial interest in PCNC materials stemmed from gains in strength and fire retardancy, and it was not until over a decade after their first appearance in the literature that their impressive barrier properties were fully realized and PCNC-based food packaging materials development commenced [118]. Over the last 25 years, hundreds of clay-based PNC systems have been reported, and nanoscale clay materials have been successfully incorporated into virtually every important class of synthetic or natural polymer. This body of work is especially exciting in light of the evident success in using PCNCs to improve the mechanical and barrier properties of biocompatible polymers, which in their virgin states are either too brittle or water-sensitive to enjoy widespread commercial use in the food industry. Some

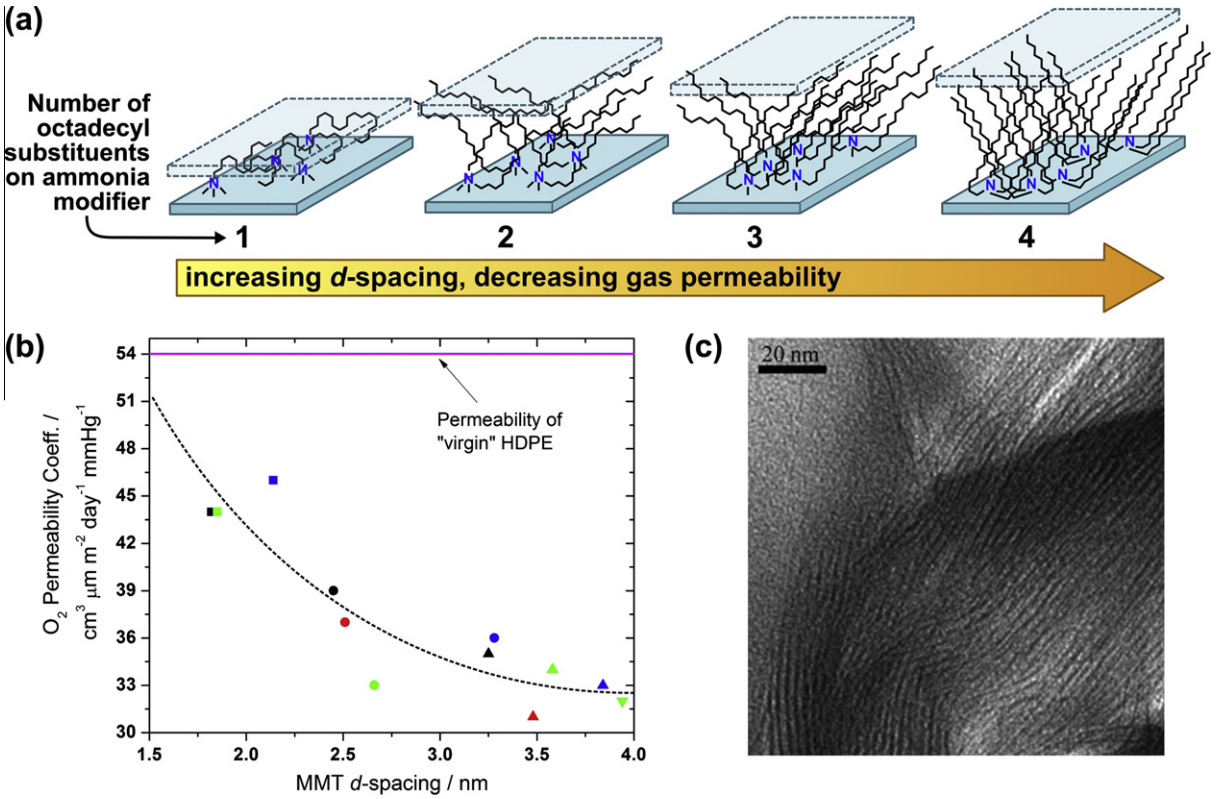

Fig. 5. Effect of clay organic modifier on the macroscopic properties of PCNCs. MMT clays were chemically modified with trimethyl-(octadecyl)ammonium [□], dimethyl-di(octadecyl)ammonium [○], methyl-tri(octadecyl)ammonium [△] and tetra(octadecyl)ammonium [▽] and dispersed within a linear high density poly(ethylene) (HDPE) matrix. Separation between individual platelets (*d*-spacing) increased as the number of long alkyl chains on the modifier increased from 1 to 4 due to steric interactions (a). A plot of measured oxygen permeability coefficient as a function of *d*-spacing for the fabricated nanocomposites reveals a clear inverse correlation between these factors (b). Colors in the scatter plot represent MMT clays with various cation exchange capacity (CEC) [black: 680 µeq/g; red: 880 µeq/g; green: 900 µeq/g; blue: 1000 µeq/g]; a higher CEC results in higher packing density and a larger *d*-spacing. All fabricated PCNCs have better oxygen barriers than the virgin polymer, represented by the pink line. The dashed line is meant only to guide the eye. A TEM image of the 900 µeq/g, dimethyl-di(octadecyl)ammonium sample at 2.8% loading (c) shows good exfoliation of the MMT layers in this system. The image in (c) is taken from Osman, et al. [130] (www.dx.doi.org/10.1039/B417673A). Reproduced by permission of The Royal Society of Chemistry.

clay/polymer examples are provided in Table 1 along with selected oxygen and moisture permeability data. This list is not an exhaustive representation of the work that has been done in this area, and direct comparisons between tabulated values should be avoided due to the dependence of transmission rates on numerous factors which are not disclosed in this table; this table is only meant to illustrate the range of polymer classes that have been studied. Readers interested in a more comprehensive account of specific polymer systems, either biocompatible or otherwise, should consult any of the excellent reviews on the subject [19,64,68,73,111,113,118–120,132–137].

2.3. Brick wall layer-by-layer assemblies

Most PNC fabrication techniques offer only partial control over the filler dispersion morphology within the polymer matrix. As Table 1 showed, while improvements in oxygen and moisture vapor barriers can be achieved in virtually any polymer by clay nanoparticle dispersion, with only a few exceptions these improvements are generally modest. The complicating factor here is attaining complete exfoliation of dispersed clays, which limits the achievable diffusion path tortuosity. While advances have been made toward understanding the factors which influence the degree of clay platelet exfoliation in PNC films, these relationships are complex and difficult to control in practice. Therefore top-down approaches to PNC fabrication are limited in their ability to provide consistently impressive improvements in oxygen and moisture vapor permeabilities.

Layer-by-layer (LBL) assembly [157–161] is a bottom-up strategy to fabricate multilayer film structures with pre-defined component organization at the nanoscale. Multilayer films are constructed as follows (Fig. 6). A prepared substrate (quartz or polymer such as PET, e.g.) is submerged in a solution of a positively charged polymer, rinsed, dried, and then submerged in a solution of negatively charged clay platelets. Each cycle of alternating submerging leads to the formation of a single clay-polymer bilayer, and cycles are repeated until the desired number of bilayers is achieved. Bilayers are held together by electrostatic attraction between the polymer and clay layers, which have opposite polarity.

The impressive flame retardancy [87] and strength [86] of PCNC materials fabricated through LBL methods has already been mentioned. PCNCs formed through LBL assembly have been compared to nacre (mother of pearl) [86], a natural layered mineral/biopolymer substance which is thought to be among the strongest mineral materials produced in nature. LBL-assembled nanoclay/polymer or nano-silica/polymer materials have been found to have superior wettability [162], anisotropic ion transport [163] and anti-reflectivity [164]. For food packaging applications, the most exciting attribute of these materials is their barrier properties, such that they have been envisioned to be potentially useful as ultrathin, flexible, high gas barrier coatings for conventional polymer films.

Grunlan and coworkers have pioneered the use of LBL assembly to fabricate polymer/clay films with high structural order and tailorable oxygen barriers. In two recent studies, they reported LBL assembled films of MMT/poly(acrylamide) [165] and MMT/

Table 1
Some representative polymer–clay nanocomposite systems and their improvement on oxygen and water vapor permeabilities.[a]

Polymer matrix[b]	Type of filler	Clay (wt.%)	$P(O_2)$	$P(H_2O)$	Refs.
PI	OM-MMT	8	13.0	7.4	[138]
	OM-MMT	2	19.8		[139]
PS	OM-MMT	16.7	2.8		[101]
PA	OM-MMT	5.5	>1100		[123]
PET	Na-MMT	5	15.6	1.2	[140]
	MMT [c]	5	2.23	1.15	[141]
PEG	Na-MMT	3–5	10^5–10^{6th} [d]		[142]
PU	OM-MMT	6	0.7–1.3	1.6–1.7	[143]
EVOH	Kaolinite	5	3.0–4.0	1.2	[144]
PMMA	OM-MMT	5	1.83	1.70	[122]
PLA	MMT [c]	5	1.16	1.21	[141]
	OM-MMT	5	1.2–1.9	1.7–2.0	[145]
	Syn. Mica	4	2.8		[117]
PHB	Kaolinite [c]	5	1.26	1.06	[141]
PHBV	MMT [c]	5	1.36	2.16	[141]
PCL	OM-MMT	12		4.87	[146]
PVA	Graphite	5		1.1	[43]
	Na-MMT	6		~3	[147]
PVA[e]	Na-MMT	20	>21[f]		[148]
PVC	SiO_2	3	~1.6	~2.8	[149]
PP	OM-MMT	5	~1.4	~1.7	[150]
	$CaCO_3$	3	~1.4		[151]
HDPE	OM-MMT	4	1.2–1.7		[130]
	OM-MMT	5	2.8–2.9	1.8–2.4	[152]
LDPE	OM-MMT	4.76	2.2		[153]
WG	Na-MMT	4.5		~8 [g]	[154]
CH	OM-MMT	30		1.44	[155]
TPS	Na-MMT	10		~1.7	[156]

[a] Permeabilities are expressed as improvement ratios: the ratio of the gas permeability or transmission rate of the virgin polymer to the gas permeability or transmission rate of the polymer–clay composite, measured at the same conditions. Note that polymer processing and clay incorporation method, as well as polymer MW, organic modifier type, temperature, humidity and film thickness all varied significantly from one study to the next.
[b] For a complete list of abbreviations, see Appendix A.
[c] The surface modification of the commercialized clay filler utilized in this study was reported as undisclosed proprietary information.
[d] The oxygen permeability values for the Na-MMT/PEG films in this study were compared to a literature value for virgin PEO. It is not clear how rigorous of a comparison can be made between these values.
[e] PVA terpolymer modified with 1% itaconic acid.
[f] O_2 permeability was lower than the instrument's ability to determine.
[g] Film cast from solution with pH = 11. Low pH solution gave relative permeability of ~2.3 for same MMT/polymer blend.

poly(ethylene imine) [166] which have oxygen permeabilities and transmission rates below instrument detection thresholds while only being a fraction of a micron thick. For instance, an oxygen permeability of $<2 \times 10^{-9}$ cc m^{-1} day^{-1} atm^{-1} (below the instrument detection limit) was achieved with a 70 bilayer film only 230.75 nm thick, as illustrated in Fig. 6. Oxygen permeability was also found to be dependent both on the number of bilayers in the film as well as the pH of the polymer solution, giving rise to materials whose oxygen transport properties were tailorable to any desired value within a broad range. More impressively, in a follow up study [167], the Grunlan group used a three component (MMT/PAA/PEI) system as the basis for a flexible LBL assembled film which *at a mere 51 nm thick* (four MMT/PEI/PAA/PEI quadlayers) exhibited virtually undetectable oxygen transmission when coated on a PET substrate. For comparison to these values, the oxygen permeability of a 25,400 nm (1 mil) thick film of EVOH, generally considered to be one of the best food-packaging polymers when high oxygen barriers are required, has an oxygen permeability of $2.76–18.70 \times 10^{-6}$ cc m^{-1} day^{-1} atm^{-1} (measured at 0% relative humidity), depending on the degree of EVOH hydroxyl functional group content [16]. In other words, the LBL-assembled nanocomposite films have oxygen permeabilities several orders

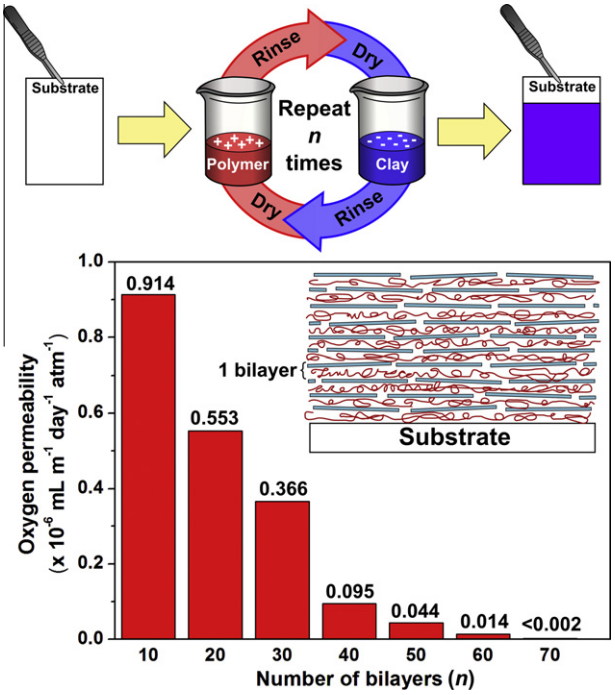

Fig. 6. *Top.* Schematic of layer-by-layer assembly of a positively charged polymer and negatively charged clay to form "brick-wall" multilayer films with ultrahigh oxygen barriers. *Bottom.* Oxygen permeability values for "brick wall" films of various bilayer numbers formed from branched poly(ethylene imine) (PEI) and sodium montmorillonite at pH 10. Actual permeability values are provided on top of each bar. The inset shows a schematic the 10-bilayer film and highlights the excellent exfoliation achievable through this fabrication technique. Adapted with permission from Priolo et al. [166]. Copyright 2010 American Chemical Society.

of magnitude lower than a 1 mil EVOH film while at the same time being over four orders of magnitude thinner.

Note that while the oxygen permeability of LBL-assembled PNC materials are moisture sensitive, they are far less so than conventional polymers. For example, the OTR at 95% relative humidity of a LBL-assembled clay/poly(acrylamide) PCNC remains more than an order of magnitude lower than bare PET. Furthermore, when this system is combined with a high moisture barrier (poly(chlorotrifluoroethylene)), an OTR below 0.005 cc m^{-2} day^{-1} atm^{-1} can be maintained even under very humid (95%) conditions [165]. Cross-linking has also been shown to significantly improve moisture insensitivity of these LBL-assembled nancomposites [167].

The extremely high oxygen barriers exhibited by LBL-assembled clay/polymer materials results from the "brick wall" structure achievable by fabricating the nanocomposites in this fashion [81,165]. The clay platelets are organized in neat monolayers with a well-defined polymeric region in between each monolayer (Fig. 6, inset). This is an efficient way to promote extensive exfoliation of the clay particles within the polymer matrix. In addition, because each particle is essentially oriented perpendicular to the gas migration direction, the tortuosity of the migration path is optimized, as predicted by theory [89]. Such precise control over the clay particle orientation and morphology within a polymer matrix would be nearly impossible to achieve with conventional processing techniques, and thus for PNC food packaging materials that possess good optical clarity and the highest oxygen barriers, LBL fabrication methodologies or other bottom-up strategies may be the wave of the future.

2.4. Current commercial status, safety and outlook

Because PCNC packaging materials are relatively inexpensive to manufacture, there are already numerous companies that have

made them commercially available. Companies such as Nanocor™ offer a wide variety of polymer nanocomposites for purchase in pellet form, and several trademarked product lines exist, such as Aegis™ (Honeywell Polymers), Durethan® (LANXESS Deutschland GmbH), Imperm® (ColorMatrix Corp.), nanoTuff™ (Nylon Corporation of America) and NanoSeal™ (NanoPack, Inc.). A more complete summary of active companies in the field is provided elsewhere [136].

Most commercially available PCNC products are marketed toward a very specific application, including several in the food and beverage industry. PCNC packaging materials have, for example, become popular with beverage manufacturers, such as Miller Brewing Company [133], which has used them to manufacture plastic bottles possessing both high barriers to oxygen and carbon dioxide migration. Other interested parties in PCNC technology include the US Army Natick Soldier Research, Development and Engineering Center (NSRDEC), which has invested considerable time and money researching the potential use of PNC plastics to package meals ready to eat (MREs) for soldiers; in addition to currently creating an enormous amount of waste, MREs have incredibly stringent shelf-life and robustness requirements which PCNC-based packages may be uniquely able to satisfy [168].

Given the number of studies that cite food packaging as a likely endpoint for PCNC research, the number of researchers who have investigated these materials in shelf life or safety experiments using real food components is surprisingly small. One study showed that PCNCs based on PET, PHBV and PHB at 5 wt.% exhibit relative permeabilities ($P_{composite}/P_{polymer}$) of *d*-limonene, a key aroma compound in citrus fruits, of 3.2, 1.6 and 8.8, respectively, indicating that PCNC packaging materials are less likely than conventional plastics to scalp flavors, colors or aroma from foods [141]. More relevant to behavior with real food systems is a 2007 study [151] which showed that total microbial and mold counts on apple slices decreased significantly over a period of 10 days when packaged in $CaCO_3$/iPP PNC films, as opposed to apples stored in neat isotactic PP, which experienced an increase of total mesophilic microflora over the same time period. The study also showed that the apples stored in PNC packaging ripened better due to ethylene gas retention and exhibited less oxidation than those stored in conventional PP packages.

Of some concern is the safety of packaging materials made with PNCs. The main risk of consumer exposure to PNC packaging is through migration[3] of nanoparticles or other substances from packages into packaged foods which are then eaten, yet migration studies of PNC materials are ambiguous and few in number. A 2005 study [169] showed that vegetables in contact with clay/starch nanocomposite films exhibited no trends in their iron and magnesium content, but manifested elevated levels of silicon; the authors alleged that the results demonstrated either no appreciable migration of the constituent elements of the clay nanoparticles into the food, or migration within the limits set forth by then-current European Union (EU) regulations. A separate study showed that Uvitex OB, a commonly used additive to polyolefins approved for food contact use in Europe (2002/72/EEC), has very low release into oil-based and aqueous-based food simulants from a MMT/wheat-gluten PNC film, compared to up to 60% loss in LLDPE films subjected to the same test [170]. This MMT/wheat-gluten film also permitted aluminum and silicon migration into food simulants that was allegedly well within the limits set forth by European regulations, although the authors of this study were careful to point out that the more difficult quantification of nanoparticle migration should ideally be performed. Finally, a 2010 paper revealed that diffusion of triclosan and *trans*-,*trans*-1,4-diphenyl-1,3-dibutadiene (DPBD), two other common additives, was slower in poly(amide)/clay PCNCs than in neat poly(amide) [171].

While the above studies demonstrate that PCNCs may slow down the migration of potentially harmful additives into foods, the body of safety research is at this time fragmentary and incomplete. A theoretical treatment has predicted that montmorillonite particles with surface modification embedded in various polymer matrices are unlikely to migrate into foods from a polymer nanocomposite food contact material in any detectable quantities [172]. Nevertheless, more comprehensive experimental studies need to be done in PCNCs made from common-use food-contact polymers such as PET, especially since some food and beverage companies are already utilizing these materials in their products. More importantly, the availability of clay nanoparticle toxicology data is still lacking, as are developments in strategies to detect and categorize clay and other nanoparticles in complex food matrices. One study determined that exfoliated silicate nanoclays exhibited low cytotoxicity and genotoxicity, even when part of a diet fed to rats (measured acute oral toxicity, median lethal dose, $LD_{50} > 5700$ mg/kg body weight under the conditions probed) [173]; however the authors of this study only tested a single clay type and morphology, so it is unclear whether it can be applied in a general sense. Furthermore, it has recently been shown [170] that PCNC films exhibit enhanced migration of nanoclay components into food simulants when the films undergo high-pressure treatment, a food preservation/sterilization method that is becoming increasingly popular; a follow up study [174] demonstrated that MMT clays undergo undetermined structural or chemical changes under pressures as low as 300 MPa and concluded that "such changes should be taken into consideration when binging [*sic*] montmorillonite–polymer composites into contact with food."

As a result of these considerations, while PCNCs may represent the next revolution in food packaging technology, there are still steps that need to be taken in order to ensure that consumers are protected from any potential hazards these materials pose.

3. Silver nanoparticles and nanocomposites as antimicrobial food packaging materials

Silver has a long history of being used as an antimicrobial agent in food and beverage storage applications. Numerous ancient societies stored wine and water in silver vessels. Web searches on the historic uses of silver reveal anecdotal reports of early settlers placing silver dollars or silver spoons at the bottom of milk and water bottles to prolong shelf life, and of seafaring ships or airliners lining their water tanks with silver to keep water potable for long periods of time. Silver was the sterilization agent for water on the Russian MIR space station and on NASA space shuttles [175], and silver's broad-spectrum antimicrobial activity and relative low cost have made it a candidate as the active disinfecting agent for water in developing countries [176,177]. In 2009, the FDA modified the food additive regulations to permit the direct addition of silver nitrate as a disinfectant to commercially bottled water at concentrations not to exceed 17 μg/kg [178].

Beyond food applications, silver has long been used as an antiseptic. Hippocrates, the "father of medicine", advocated the sprinkling of silver powder on ulcers to expedite healing [179], and silver has been used since World War I (and continues to be used) in wound dressings. Pencils or sticks of hardened silver nitrate (lunar caustic or *lapis infernalis*) were considered essential items in a surgeon's chest as early as the 1600s and silver nitrate solutions were used to treat burn victims of the *Hindenberg* disaster [180]. Though the use of silver as an antimicrobial temporarily fell out of favor after the proliferation of chemicals such as Penicillin,

[3] See Refs. [1–10] of [166] for a general introduction to migration of organic molecules through polymer films.

interest was revived in the 1960s [181] and silver-based pharmaceuticals continue to be used today as topical and ophthalmic disinfectants. Silver sulfadiazine is still considered the treatment of choice for burn victims [182].

Silver has numerous advantages over other antimicrobial agents. Compared to molecular antimicrobials, which are generally targeted to specific organism classes, silver is broad spectrum and toxic (to varying degrees) to numerous strains of bacteria, fungi, algae, and possibly some viruses. Being an element, silver is shelf stable for long periods of time. Conventional wisdom regards silver as safe to humans and other higher order organisms when used responsibly, and silver-based pharmaceuticals have few if any acute or chronic known side-effects at FDA-permitted doses. Silver is reasonably effective at penetrating biofilms, which has been a drawback to many molecular antimicrobials [183]. Furthermore, though bacterial strains which manifest silver-resistance are known and these mechanisms have been studied [175], some researchers have suggested that silver may be less susceptible to the buildup of resistance than molecular antimicrobials [184,185]. This remains an area of some uncertainty. Even so, however, the explosion of interest in silver as a broad-spectrum antimicrobial agent during the last two decades may be in part due to the proliferation of resistance to strong molecular antimicrobials; in that respect, silver has been shown [186,187] to be an effective bacteriocide against antimicrobial-resistant bacterial strains (e.g., MRSA), which have become a concern [188] in hospitals.

Yet perhaps the largest advantage of silver antimicrobials is that silver can be easily incorporated into numerous materials such as textiles and plastics, making it especially useful for applications where broad spectrum, sustained antimicrobial activity is desirable but where traditional antimicrobials would be impractical. This is not only advantageous to the food industry, where silver-containing plastics have been incorporated into everything from refrigerator liners [189] to cutting boards [190,191] to food storage containers [192,193], but it has also been revolutionary to the medical device industry, which has seen a proliferation of silver-coated urinary catheters [194,195], cardiovascular implants [196,197], esophageal tubes [198,199], bandages [200,201], sutures [202] and other instruments [203,204] on which bacterial growth compromises patient survival. To date, the FDA has approved over a dozen silver-containing zeolites or other substances for use as food contact materials[4] for the purpose of disinfection, as well as numerous silver-coated medical devices.

Despite the long history of silver as an antimicrobial, the mechanism of this activity remains a matter of active research. The general explanation offered [185] is that silver kills by at least one of the following mechanisms: (a) interference with vital cellular processes by binding to sulfhydryl or disulfide functional groups on the surfaces of membrane proteins and other enzymes; (b) disruption of DNA replication; and (c) oxidative stress through the catalysis of reactive oxygen species (ROS) formation. However, controversy exists regarding which of these mechanisms is most important. For instance, one study [205] presented evidence which showed that silver binding specifically to membrane proteins disrupts ion and proton transport across the membrane, while another found that Ag ions permeate to the cellular interior, where they interfere with ribosomal activity and disrupt the production of several key enzymes responsible for energy production [206]. With respect to interference of DNA replication, cell wall damage resulting from silver binding to membrane proteins and DNA condensation in *Escherichia coli* and *Staphylococcus aureus* has been observed; the condensation of DNA in response to the presence of Ag ions has been cited as a defense mechanism, which, while protecting the DNA from harm, limits the ability of cells to self-replicate [207]. In contrast, a separate report asserted that Ag complexes of glutamic and tartaric acids actively interfere with DNA unwinding, and suggested that Ag ion binding to enzymes and membrane proteins is a comparatively minor contributor to silver's antimicrobial effect [208]. Gram-negative bacteria (e.g., *E. coli*) are generally more susceptible to silver treatment than Gram-positive bacteria (e.g., *S. aureus*) because transport of positively charged silver ions across the thicker, peptidoglycan-rich outer membranes of Gram-positive bacteria is slow relative to transport across the thinner membranes of Gram-negative specimens [207]. Finally, there is evidence that the antibacterial activity of silver zeolites derives from silver's ability to catalyze the production of reactive oxygen species, which causes cell death by creating oxidative stress [209]; in support of this idea, antioxidant rich *Bacillus* spores are highly resistant to silver antimicrobials, whereas vegetative and relatively anti-oxidant poor *Bacillus* cells are quite vulnerable [210]. It is certainly possible that all of these mechanisms contribute to the antimicrobial activity of silver, which would explain its broad effectiveness as well as the infrequent reports of silver-resistant bacterial strains.

3.1. Antimicrobial activity of silver nanoparticles

It was inevitable given the history of silver as an antimicrobial that the effectiveness of nanoparticulate silver at killing or preventing the growth of microbes would eventually be tested. Since the earliest published reports of the antimicrobial properties of silver colloids, silver nanoparticles (AgNP) have been found to be potent agents against numerous species of bacteria, including: *E. coli* [211–229], *Enterococcus faecalis* [214,222,229], *Staphylococcus* (*aureus* [214,220,222,223,225,226,228,229] and *epidermidis* [214,222]), *Vibrio cholerae* [213,220], *Pseudomonas* (*aeruginosa* [213,214,222], *putida* [230], *fluorescens* [229,231] and *oleovorans* [232]), *Shigella flexneri* [220], *Bacillus* (*anthracis* [223], *subtilis* [219] and *cereus* [229]), *Proteus mirabilis* [223], *Salmonella enterica* Typhimurium [213,220,225,229], *Micrococcus luteus* [225], *Listeria monocytogenes* [229] and *Klebsiella pneumoniae* [214,222,229]. AgNPs are also effective against strains of these organisms that are resistant to potent chemical antimicrobials, including MRSA, MRSE, vancomycin-resistant *Enterococcus* (VRE) and extended-spectrum β-lactamase (ESBL) producing *Klebsiella* [214,222]. In addition, AgNPs are toxic to fungi (e.g., *Candida albicans* [223,229,233,234], *Aspergillus niger* [229,232], *Trichophyton mentagrophytes* [233] and yeast isolated from Bovine mastitis [228]), algae (e.g., *Chlamydomonas reinhardtii* [235]) and phytoplankton (e.g., *Thalassiosira weissflogii* [236,237]), and are inhibitory to at least two viruses (HIV [238] and monkeypox [239]).

There is some disagreement over the manner in which AgNPs are toxic to bacterial cells. The most conservative viewpoint is that silver atoms detach from the surfaces of AgNPs and cause cellular damage by the exact same mechanisms observed for conventional silver antimicrobials. Some studies which show that AgNPs are more toxic than an equivalent amount of dissociated silver ion cite the "Trojan Horse" model for engineered nanoparticle toxicity [240], whereby AgNPs act as efficient vehicles to deliver a large quantity of silver ions to the interior of cells in a short period of time. Support for the hypothesis that AgNPs are simply carriers for Ag^+ is provided by a study which showed that AgNPs are ineffective at slowing the growth of Ag^+-resistant *E. coli* strains [217]. In addition, *E. coli* cells exposed to ~9 nm AgNPs [216] exhibited

[4] There are presently 17 silver-containing substances approved by the FDA for contact with foods resulting from successful Food Contact Notifications (FCNs). These include Food Contact Substances 1, 47, 193, 248, 270, 275, 294, 296, 351, 430, 432, 433, 434, 476, 535, 697, and 793. Of these, only number 430 (a colorant) is not related to the antimicrobial properties of silver. A list of FDA approved Food Contact Substances is currently available at http://www.fda.gov/Food/FoodIngredientsPackaging/FoodContactSubstancesFCS/ucm116567.htm. The above list resulted from a search string of "silver".

the same disruption to trans-membrane potentials and depleted ATP levels observed earlier [205] in *E. coli* cells exposed to $AgNO_3$, albeit at absolute molar concentrations three orders of magnitude lower (μM vs. mM). Importantly, the bactericidal effect is clearly related to the chemical nature of silver, as similarly sized gold nanoparticles have no antimicrobial activity [228].

While AgNPs do likely serve as a source of Ag^+ ions, they may have additional antimicrobial mechanisms. For instance, when normalizing for released Ag^+ concentration, AgNPs have been found to be more toxic to algae than equivalent dosages of $AgNO_3$ [235]. Contrasting the study cited above [217], a separate report found that AgNPs had great effectiveness against silver resistant strains of *P. mirabilis* and *E. coli* and highlighted the fact that particles of different sizes, shapes or other characteristics may behave differently, even in the same system [223]. There is also evidence that AgNP surfaces efficiently catalyze the formation of free radicals in bacterial cells, which can cause cell death through oxidative stress [228].

Yet probably the most striking evidence that AgNPs are toxic to microorganisms via mechanisms that are different than Ag ions comes from an investigation by Morones et al. [213], which showed that the concentration of Ag^+ ions released from AgNPs under the tested conditions was too low to account completely for toxicity of AgNPs. More importantly, these authors were able to demonstrate that AgNPs bind to membrane proteins, forming pits and causing other morphological changes (Fig. 7); AgNPs were also found to react with the phosphorous groups of DNA. Morphological changes (pitting) in cellular membranes as a result of bacterial AgNP exposure were independently observed by Sondi and Salopek-Sondi [227], who further speculated that AgNP binding to membrane surfaces causes leeching of lipopolysacchrides and a subsequent loss of structural integrity and impermeability. The pitted membranes thus become more porous, which disrupts ion and molecular transport and also catalyzes the entry of additional AgNPs into the cellular interior where they can cause further damage to DNA and other cellular components.

Aside from differences in susceptibility between bacterial species (particularly between Gram-negative and Gram-positive specimens [228]), the quantitative toxicity of AgNPs to bacteria varies from study to study and appears to be dependent on numerous factors. For instance, studies have shown that the toxicity of AgNPs increase significantly as the nanoparticle diameter decreases [212–214,217,226,241,242] due to the fact that smaller nanoparticles have larger relative surface areas for Ag^+ release, have higher protein binding efficiencies, and pass through pores in bacterial membranes more easily. Nanoparticle shape is also an important factor [218]: triangular AgNPs have better bactericidal properties against *E. coli* than spherical or rod-shaped particles, which is attributed to the variation in percentage of {1 1 1} vs. {1 0 0} surfaces[5] present in nanoparticles of each respective shape (Fig. 7). It is thought that {1 1 1} surfaces have better binding efficiency to sulfur groups of cellular components [213]. AgNP surface charge [217], solubility and degree of agglomeration [217,227], and surface coating [222,224,243] also influence the antimicrobial properties, and AgNPs may also act synergistically with other present chemicals (e.g., ampicillin) for amplified effect [225]. Unfortunately, in most studies AgNPs are poorly characterized and/or produced by methods which yield nanoparticles of highly nonuniform shape and size, which complicates the elucidation of important structure–function relationships. Additionally, the specific proteins on various bacterial proteins that are more or less susceptible to AgNP reactivity are only recently beginning to be identified [224].

[5] Miller indices, {nlm} refer to the symmetry of the crystal lattice along a given mathematical plane. A plane with symmetry {1 1 1} has a different geometrical arrangement of silver atoms than a plane with symmetry {1 0 0}, which can impact surface reactivity and, apparently, binding to living cells.

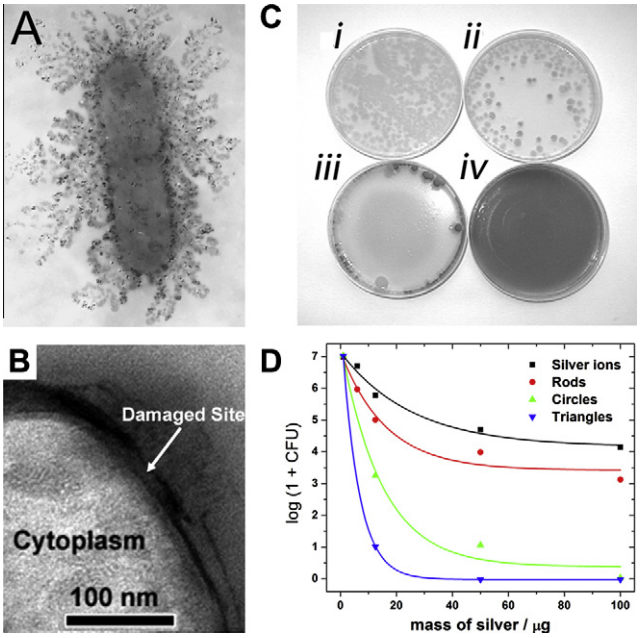

Fig. 7. Mechanisms of Silver Nanoparticle Bacteriocidicity. (A and B) Silver nanoparticles (AgNPs) are lethal to bacteria in part because they damage cell membranes. The figure shows pictures from separate studies demonstrating adherence of AgNPs to and subsequent pitting of the membrane surface of *E. coli*. (C) Due at least in part to damage of cell membranes, the presence of AgNPs reduces *E. coli* growth and viability. Here, a photograph shows growth of *E. coli* on LB plates containing AgNPs at (i) 0, (ii) 10, (iii) 20 and (iv) 50 μg cm^{-3}. (D) Numerous studies have explored factors which influence AgNP lethality. This plot relates the number of bacterial colonies able to grow on plates incubated with various amounts of AgNPs, as a function of AgNP shape. Other factors which influence AgNP antimicrobial efficiency include particle size, surface charge, and the nature of substituents featured on the particles' surfaces. Panels A and C are reproduced from Sondi and Salopek-Sondi [227] with permission. Copyright Elsevier (2005). Panels B and D were reproduced with permission from Pal et al. [218]. Copyright 2007 American Society for Microbiology.

In summary, it is clear that AgNPs are potent broad spectrum antimicrobials: minimum inhibitory concentrations of 2–4 μg/mL for AgNPs with diameters 45–50 nm against *E. coli*, *V. cholerae*, *S. flexneri*, and at least one strain of *S. aureus*, have been reported, which rivals the bactericidal properties of penicillin against nonresistant strains [220]. Furthermore, that potency can be easily manipulated through the unique physical effects offered by nanomaterials. For instance, Akhaven and Ghaderi [244] showed that when silver nanowires are subjected to external electric fields, they have 18.5–63% better antimicrobial potency due to enhanced silver ion production at the wire termini. Also, photoexcitation of AgNPs coated with a thin (1–2 nm) layer of porous silica at visible light frequencies which are in resonance with AgNP surface plasmon bands has been shown by Fuertes et al. [245] to enhance antimicrobial activity against *E. coli* significantly, either through photosensitized ROS generation or photocatalyzed silver ion release; this effect is also reversible, providing a portal into photoswitchable antimicrobial behavior. Studies such as these imply that if intelligently-designed silver nanostructures are incorporated within food storage containers, the application of an external electric field or light source might be able to be used as a controllable and noninvasive sterilization method.

3.2. Polymer nanocomposites containing silver nanoparticles

One of the biggest advantages of inorganic nanoparticles over molecular antimicrobials is the ease with which the former can be incorporated into polymers to form functional antimicrobial

materials [246]. This is especially true due to the controlled release properties of AgNPs [247,248], which can be engineered to remain potent antimicrobial agents for long periods of time. Thus, AgNP/polymer nanocomposites are attractive materials for use in both medical devices as well as food packaging materials to preserve shelf life.

While silver zeolites have been used to create antibacterial polymer composites for some time, AgNP-based nanocomposites offer added stability and slower silver ion release rates into stored foods, which is important for sustained antimicrobial activity. For example, when the antimicrobial activity of an AgNP/SiO_2 nanocomposite material was compared with that of a Ag zeolite and a $AgNO_3/SiO_2$ composite, the latter two materials had more ($\sim$10$\times$) potent acute antimicrobial responses yet the nancomposite allowed for a longer duration of activity [229]. Thus while a zeolite-based material might offer a superior immediate effect, the sustained antimicrobial activity of the nanocomposite would be better suited for the packaging of foods that require long transportation distances or storage times. Note that as in the case of "bare" AgNPs, the AgNP/SiO_2 composite material was found to be effective against a broad spectrum of bacteria and fungi, was more effective against Gram-negative than Gram-positive bacteria, and could be incorporated within a PP polymer matrix for the creation of antibacterial films for food contact applications.

Numerous AgNP/polymer PNCs have been reported in the literature. Sanchez-Valdes et al., for example, coated a five layer (PE/tie/PA-6/tie/PE; PA-6 = polyamide six and tie = maleic anhydride grafted polyethylene) plastic film with an AgNP/polyethylene nanocomposite layer and found antimicrobial activity against the fungus *A. niger*, a common food contaminant [232]. Moreover, they found (see Fig. 8, top) that the activity was dependant on the coating method: methods that gave rise to a rougher surface (and hence more surface area for silver-ion release) had higher activity than those that resulted in a smoother surface. Münstedt and coworkers published several studies on AgNP/PA-6 and /PP PNCs (AgNP particle size $\sim$ 800 nm) which possessed antimicrobial activity against *E. coli* and *S. aureus* as well the fungus *C. albicans*, polychaete worms (*S. spirorbis*), sea squirts (*C. intestinalis*) and algae (*U. intestinalis*) [249–251]. The antimicrobial activity was also found to be dependent on factors which affect silver ion release rate, such as degree of polymer crystallinity [249], filler type (i.e., silver particles, zeolites, etc.) [250], hydrophobicity of the matrix [251] and particle size (i.e., nanocomposite vs. microcomposite) [252]. Colloidal silver particles have also been coated 90–150 nm thick onto paper using ultrasonic radiation, and this coated paper was shown to manifest excellent antimicrobial activity against *E. coli* and *S. aureus*, "suggesting its potential application as a food packing material for longer shelf life" [253]. Other AgNP/polymer PNCs exhibiting antimicrobial activity include versions in poly(acrylamide) [254], PVA [255], PVP [256], PE [257], PMMA [258], PU [259], PEO [260], alginate [261], soda-lime glass [262], silicone elastomer [247], cellulose [263–265], and chitosan [266–271]. The chitosan-based materials are particularly interesting, as chitosan is a polysaccharide with natural antimicrobial properties, which suggests a cumulative antimicrobial effect is attainable. Moreover, chitosan films loaded with AgNPs have also been found to have better tensile and gas barrier properties than virgin films composed of the same material [268,270]. Layer-by-layer assembly approaches have also been used to create antimicrobial Ag-based PNCs [266,272] that have enhanced strength and mechanical properties.

AgNP/polymer nanocomposite materials have been tested with real food systems to determine the effect of AgNP antimicrobial properties on food shelf-life. For instance, Mohammad-Fayaz et al. dipped sterilized carrots and pears into alginate solutions containing biosynthesized AgNPs, forming "edible antibacterial films". They found that the treated carrots and pears had less water loss and higher consumer acceptability (judged on basis of color, texture and taste) over the course of 10 days (Fig. 8, bottom) [261]. In a similar study, fresh asparagus spears coated with AgNP/polyvinylpyrrolidone nanocomposite films had their shelf lives extended to 25 days when stored at 2 °C; in addition to having less weight loss, greener color and tenderer texture, coated asparagus also had less microorganism (psychotrophic bacteria, yeast and mold) growth during this time period [256]. An edible film based on AgNPs dispersed in glycogen has also been reported [273]. Chinese jujube fruit stored in food storage bags composed of AgNP/nanoparticulate TiO_2/polyethylene films were firmer, heavier, and had less decay, less browning and slower ripening over a period of 12 days than fruit stored in control materials [257]. Orange juice stored at 4 °C in LDPE films incorporating P105 (TiO_2 and 10 nm nanosilver mixture) power at 5% loading exhibited statistically significant reduction in *Lactobacillus plantarum* growth

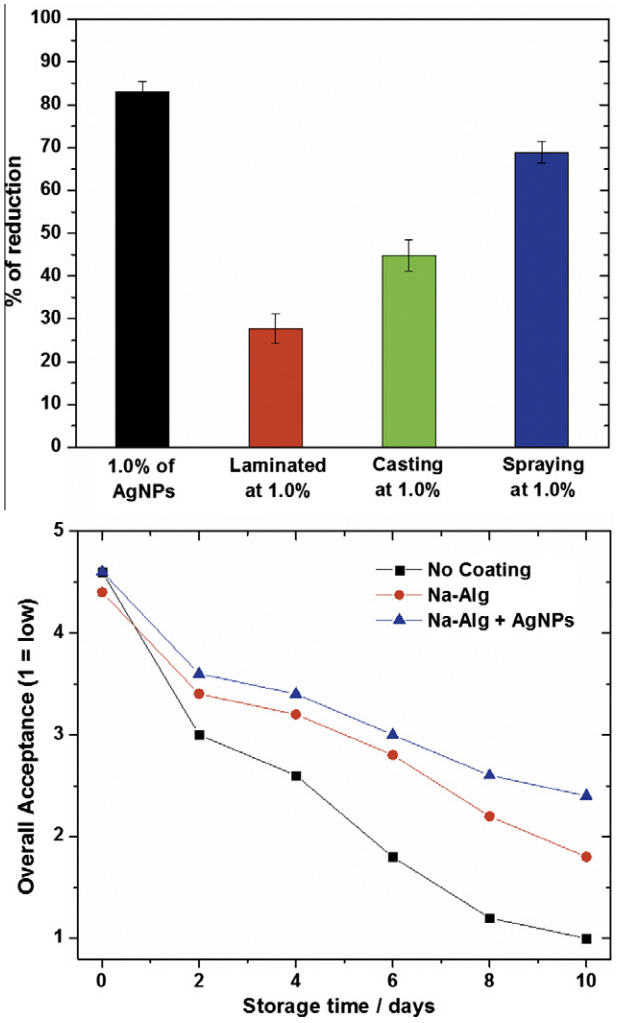

Fig. 8. Effectiveness and consumer acceptability of antimicrobial PNCs. *Top*: Percent reduction after 14 days against the food-spoilage fungus *Asperigillum niger* of $AgNO_3$ suspension (black) and multi-layer polymer films coated with AgNP/polyethylene PNC overlayers using three coating methods. All the PNC films exhibited antimicrobial activity; the strength of the activity depends on the "roughness" of the PNC layer. Adapted with permission from Sánchez-Valdes et al. [232]. Copyright 2009 John Wiley and Sons. *Bottom*: Perceived sensory acceptance (based on texture, appearance, and aftertaste) of carrots coated in AgNP/sodium alginate (Na-Alg) PNC films versus acceptance of suitable controls stored at identical (27 °C) conditions, as a function of storage time. The AgNP films increase the shelf life of fresh produce by reducing microbial growth and decreasing weight and protein loss. Figure created from data reported in Mohammad-Fayaz et al. [261].

over a time period of 112 days [274]. In another kind of application, cellulose pads containing AgNPs generated from silver ions *in situ* have been shown to reduce the microbial levels of exudates from beef meat stored in modified atmosphere packaging [275], and fresh cut melon stored on AgNP-containing cellulose pads had lower microbial counts (mesophiles, psychrophiles and yeasts) and longer microbial growth lag times [265]. In addition, since silver particles catalyze the destruction of ethylene gas, fruits stored in the presence of AgNPs have slower ripening times and thus extended shelf lives [265].

Despite all of these advances in the use of silver nanostructures for food packaging applications, comprehensive studies in various polymer systems are still lacking, and much work needs to be done to elucidate key relationships that influence the antimicrobial strength of various AgNP-based PNC materials.

3.3. Other antimicrobial nanoparticles

The antimicrobial properties of nanoparticles composed of other materials have been investigated. Titanium dioxide (TiO_2) particles in particular are promising [276–282]. Unlike AgNPs, the antimicrobial activity of TiO_2 nanoparticles is photocatalyzed and thus TiO_2-based antimicrobials are only active in the presence of UV light. For instance, TiO_2 nanoparticles have been found to be effective against common food-borne pathogens including *Salmonella choleraesuis* subsp., *Vibrio parahaemolyticus*, and *L. monocytogenes* under UV illumination but not in the dark [276]. Specifically targeting food-packaging materials, Cerrada et al. ultrasonically dispersed TiO_2 nanoparticles throughout EVOH films and observed their effective photo-activated biocidal properties against nine microorganisms (bacteria and yeasts) cited to be involved in food poisoning and spoilage, some of the data for which are shown in Fig. 9 [283]. Another food packaging study showed that polypropylene films coated with TiO_2 nanoparticles inhibited *E coli* growth on fresh cut lettuce [284]. Several researchers have combined the antimicrobial properties of TiO_2 nanoparticles with silver or AgNPs to create films or particles with enhanced antimicrobial activity [257,285,286]. In principle, food packaging films incorporating TiO_2 nanoparticles may have the additional benefit of protecting food content from the oxidizing effects of UV irradiation while maintaining good optical clarity, as TiO_2 nanoparticles are efficient short-wavelength light absorbers with high photostability; this approach to UV protection has already found traction in sunscreens [287], textiles [288–290] and wood varnishes [291,292], although care must be taken as some forms of nanoparticulate titania may photocatalyze polymer oxidation and degradation.

Other nanoscale materials which have been shown to have antimicrobial properties include nanoparticles based on magnesium oxide [293–296], copper and copper oxide [219,297–305], zinc oxide [274,306–316], cadmium selenide/telluride [317–319] and chitosan [320–322], as well as carbon nanotubes [323,324]. Several of these studies [300,308–310,313,316] are targeted specifically at food or food packaging applications, and a recent publication reviewed the numerous classes of nanomaterial antimicrobials targeted for use in drinking water sterilization [325]. In another system, researchers replaced the sodium ions of montmorillonite nanoclays with silver ions and showed antimicrobial activity of these silver nanoclays when dispersed in poly(ε-caprolactone) [326]; nanoclays modified with silver have also been dispersed in poly(lactic acid) to similar effect [327]. Note that complex nanoscale architectures with antibacterial activity have also been developed; for example, Ho et al. covalently attached vancomycin molecules to the surface of gold nanoparticles and showed that they have killing power more potent than vancomycin on its own, even against vancomycin-resistant bacterial strains [328], and Yang et al. functionalized lysozyme-coated polystyrene nanoparticles with selective antibodies and demonstrated efficient bactericidicity against the common food pathogen *L. monocytogenes* [329]. Finally, Bi et al. [330] loaded carbohydrate (phytoglycogen) nanoparticles with nisin (a broad-spectrum antimicrobial peptide produced by *Lactococcus lactis* during fermentation which is frequently used during the manufacture of processed cheeses, meats and beverages) and showed that they exhibit sustained antimicrobial activity against plated *L. monocytogenes* with efficacy that lasts several times longer than free nisin.

3.4. Health impacts of nanosilver-based biocidal materials

As with almost every other class of nanomaterial with commercial applications, research and development of nanosilver has

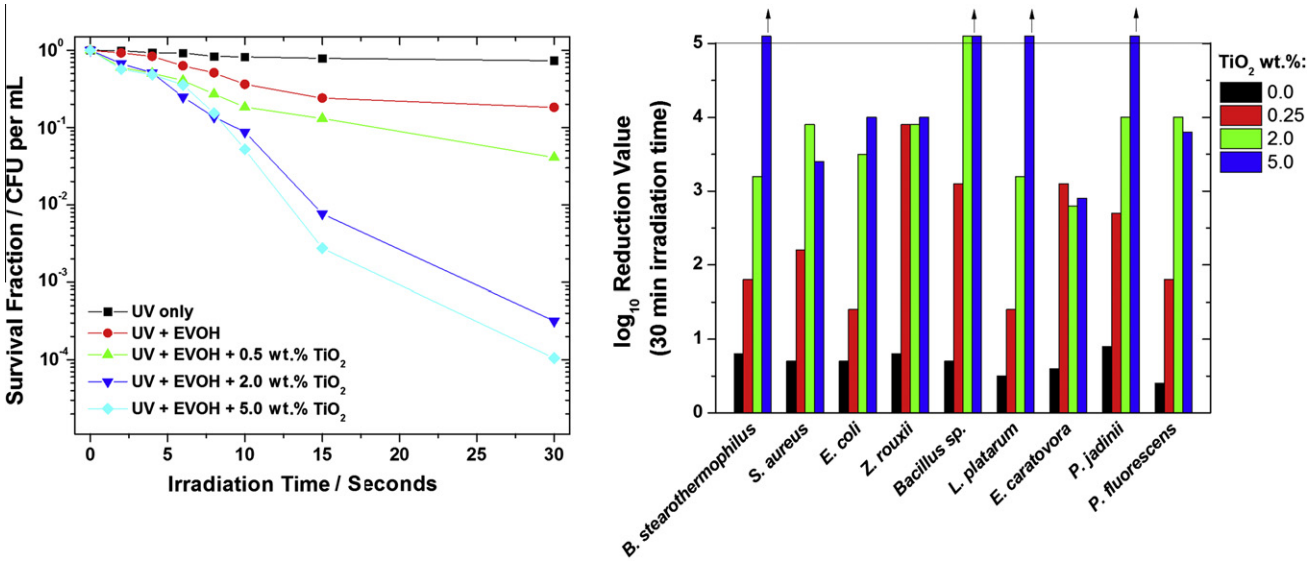

Fig. 9. Photosensitized antimicrobial effectiveness of TiO_2/EVOH nanocomposite materials. *Left:* Survival fraction of *E. coli* suspended in appropriate liquid medium in the presence of TiO_2/EVOH nanocomposite films (several nanoparticle loading percentages) as a function of UV irradiation time. *Right*: Total logarithmic reduction of numerous food-relevant microorganisms after 30 min of irradiation time in the presence of the TiO_2/EVOH materials. Bars with upward-pointing arrows represent samples where the log-reduction was reported as greater than 5. Created using data reported in Cerrada et al. [283].

outpaced our understanding of the potential consequences of the use of this technology. Nanoscale silver particles are currently used in more manufacturer identified products than any other nanomaterial [185]. There are (as of August 2009) at least 259 products which utilize some form of nanosilver for their function [237], ranging from textiles (socks and linens) to cosmetics/hygiene products (toothpastes, make-ups), from appliances (washing machines and refrigerators) to cleaning agents (detergents, soaps), and from kitchen supplies (food storage containers, bakeware, cutting boards) to toys and building materials (paints, caulks, glues). Silver nanoparticles may also make an appearance in commercialized food packaging materials in the future. Unfortunately, the effect of this increase in the use of nanoscale silver on human health and the environment is unclear.

The number of AgNP *in vivo* toxicological studies is still incredibly small, so generalized conclusions about the effects of AgNP exposure via food-relevant routes of exposure remains limited. It is, for example, still unclear to what extent the biochemical pathways which facilitate processing of silver ions apply to AgNPs, to what extent AgNPs pass through the intestinal lining intact or are dissolved into silver ions in the highly acidic environment of the stomach, and to what extent AgNPs can pass through natural biological barriers such as the blood–brain barrier, the placenta or into breast milk. It is also crucial to note that regardless of one's interpretation of the available body of literature, there have been almost no attempts to study the cumulative effects of chronic AgNP exposure, and systematic investigations of the relationship between particle characteristics (size, shape, surface charge, etc.) and toxicity have yet to be performed. Furthermore, while one study was able to demonstrate that silver nanoparticles dispersed within electrospun PVA nanowhiskers were cytotoxic to epidermal keratinocytes and fibroblasts [331], very little is known about how the toxicity of silver or AgNPs is altered when these species are dispersed within plastic coatings. A review of *in vitro* and *in vivo* AgNP toxicological studies provides a more thorough analysis of this topic [332].

In vitro toxicological studies have shown that AgNPs may not be benign to isolated mammalian cells. Human lung fibroblasts and glioblastoma cells exposed to AgNPs exhibit reduced ATP content, increased ROS production, damaged mitochondria, DNA damage and chromosomal aberrations in a dose-dependent manner compared to controls, suggesting that AgNPs have the potential to be cytotoxic, genotoxic, antiproliferative and possibly carcinogenic [333]. AgNPs at low concentrations *in vitro* cause changes to the cell cycle progression of human hepatoma cells, whereas at higher concentrations AgNPs induced abnormal cellular morphology, cell shrinkage, and chromosomal damage to a much worse extent than that caused by similar Ag^+ concentrations, indicating that the toxicity of AgNPs is not only caused by Ag cation release [334]. Exposure of spermatogonial mouse stem cells to 15 nm AgNPs at low (10 μg/mL) levels *in vitro* results in cellular morphological changes and mitochondrial damage, etc., and thus AgNPs may represent a threat to male reproductive health under some conditions [335]. AgNPs also exhibit cytotoxicity to rat liver cells mediated through oxidative stress (e.g., disrupted membrane potentials, ROS formation etc.) at far lower concentrations than particles composed of other metals and metal oxides [336]; AgNP size-dependent cytotoxicity caused by oxidative stress and ROS formation was also demonstrated for rat alveolar macrophages [337]. While at least one AgNP-based dermatological ointment has been demonstrated to be cytotoxic to human fibroblasts and skin/carcinoma cells, causing concentration-dependent morphological changes, signs of oxidative stress, lipid oxidation, DNA fragmentation/apoptosis and, at very high concentrations, necrosis, it has nevertheless been concluded that AgNPs were safe for skin contact at concentrations up to 6.25 μg/mL [338]; however this dosage may be expected to be highly AgNP-size dependent, so the absolute usefulness of this mass-based dosage metric is debatable, particularly since the AgNP characteristics in this study were not disclosed. Despite these reports of AgNP cytotoxicity, some other studies have arrived at contrary conclusions: one group of researchers found that epidermal cells are unaffected by antimicrobial-relevant concentrations of AgNPs [223] and several groups have determined that AgNPs contained in LBL-assembled PNCs or bone-cements cause no observable toxic effects on human osteoblasts under the tested conditions [266,272,339].

While there is a growing number of *in vitro* studies showing that silver nanoparticles are cytotoxic to a variety of mammalian cell types, *in vivo* studies which have investigated the systematic effects of AgNP exposure by oral routes of exposure are more ambiguous. For example, though AgNPs were found distributed in virtually every organ of rats fed a steady nanoparticle diet, there were few toxic effects observed except at the highest concentrations [340,341]. An oral intake study in weaning pigs showed AgNP accumulation in the liver but no acutely toxic effects [342]. On the other hand, lymphocyte infiltration and inflammation has been observed in the livers of mice which were fed nano- and micro-sized silver particles, an effect which was exacerbated when particle diameter was on the nanoscale [343].

It is important to keep in mind that in determining the health impact of a new food contact substance, toxicity information needs to be contextualized by a determination of how readily this substance can become released from packaging materials into various foods substances. Unfortunately, very little work has been done to assess the ability of nanoparticles in general, and AgNPs in particular, to migrate through rigid polymer environments and cross over the packaging/food interface. Šimon et al. [172] used a physicochemical approach to theorize that embedded AgNPs may diffuse from food packaging into foods at detectable levels only when the particle radius is very small (~1 nm), when the packaging is comprised of a polymer with relative low dynamic viscosity (e.g., polyolefins such as LDPE, HDPE and PP), and when there are no significant interactions between the particles and the polymer. Though broad-scope experiments assessing this prediction have not yet been published, at least one study [274] has shown evidence of migration into a food substance, in this case orange juice, from LDPE packaging materials incorporating Ag or ZnO antimicrobial nanoparticles[6]. A more pressing concern, however, may be food contact materials in which the AgNPs are located on the material surface, such that they come into direct contact with the food matrix. In the aforementioned report of AgNPs being incorporated into cellulose pads for use in modified atmosphere packaging of fresh beef [275], for example, the authors found that detectable levels of silver ions leeched into the meat exudates (though not into the meat itself). Even so, systematic attempts to study relationships between particle characteristics, polymer type, food pH/polarity, and, especially, environmental conditions relevant to food production, storage and packaging use (e.g., temperature, pressure, humidity, light exposure and storage time) are decidedly lacking, making it difficult to broadly assess this important aspect of the safety of AgNP-based food contact materials at this time.

As a final note, though the results of some AgNP toxicological studies may appear ominous, they must be kept in perspective. In many studies particles were poorly characterized or not characterized at all, and the relationship between the effects of exposure observed in isolated cells *in vitro* and those in whole organisms is not always clear, particularly when questions remain about nanoparticle toxicology. Moreover, some studies go out of their way to

[6] Only the presence of silver or zinc in the food matrix was reported, so it was not known if whole nanoparticles, nanoparticle aggregates or only trace elements migrated from the packaging material.

sound controversial or to overstate the relevance of their findings. For example, one publication which has garnered some headlines demonstrated that AgNPs interfere with DNA replication during PCR cycles, as well as during reproduction in *E. coli* cells [344]. Yet the study's title ("*Food storage material silver nanoparticles interfere with DNA replication fidelity and bind with DNA*.") implies that the article reports on a toxic effect in a consumer product, when in fact the article has nothing to do with food or food packaging at all. Thus scientists should make a heightened effort to stick to the facts and avoid hyperbolic titles, conclusions or prognostications wherever possible, so as to minimize the likelihood of misleading news agencies or the public about the safety of consumer products that contain nanomaterials.

4. Nanosensors and nanotechnology-based assays for food-relevant analytes

Fresh produce or meats which are either spoiled or unpalatable exhibit odors, colors or other sensory characteristics which can be easily discerned by consumers. When packaging materials prevent extensive sensory exposure, however, consumers must rely on sell-by dates, which are determined by producers based on a set of idealized assumptions about the way that the food is stored or transported. While the sell-by date for a carton of milk may indicate to a consumer that the product should be good for a period of two weeks, this date may no longer be applicable if that milk was stored above its optimal temperature for an hour, either in a delivery truck or in a warm automobile.

The unique chemical and electro-optical properties of nanoscale particles offer solutions to this problem. Through bottom-up engineering, nanomaterials can be devised which are able to detect the presence of gasses, aromas, chemical contaminants and pathogens, or respond to changes in environmental conditions. This not only is useful for quality control to ensure that consumers are able to purchase products which are at their peak of freshness and flavor, but it also has the potential to improve food safety and reduce the frequency of food-borne illnesses. Such technology would obviously benefit consumers, industry stakeholders and food regulators. Some companies (e.g., Ripesense [http://www.ripesense.com] and OnVu [http://www.onvu.com/]) already market nanotechnology products that help consumers determine whether certain foods are likely to be palatable, but most of the work on nanosensors or assays for food-related analytes is still in the early stages of development. This section highlights some of the most recent and exciting work in this area.

4.1. Detection of small organic molecules

Beyond the benefit afforded to supermarket shoppers and food manufacturers, nanotechnology-based sensors have the potential to revolutionize the speed and accuracy with which industries or regulatory agencies can detect the presence of molecular contaminants or adulterants in complex food matrices. Many of these assays are based on observed color changes that occur to metal nanoparticle solutions in the presence of analytes. For example, gold nanoparticles (AuNPs) functionalized with cyanuric acid groups selectively bind to melamine (Fig. 10), an adulterant used to artificially inflate the measured protein content of pet foods and infant formulas; the melamine-induced aggregation causes AuNPs to undergo a reproducible, analyte-concentration-dependent color change from red to blue, which can be used to precisely measure the melamine content in raw milk and infant formula at concentrations as low as 2.5 ppb with the naked eye [345]. A similar approach examined test samples for the presence of melamine by adding in sequential fashion separate solutions of gold ions and

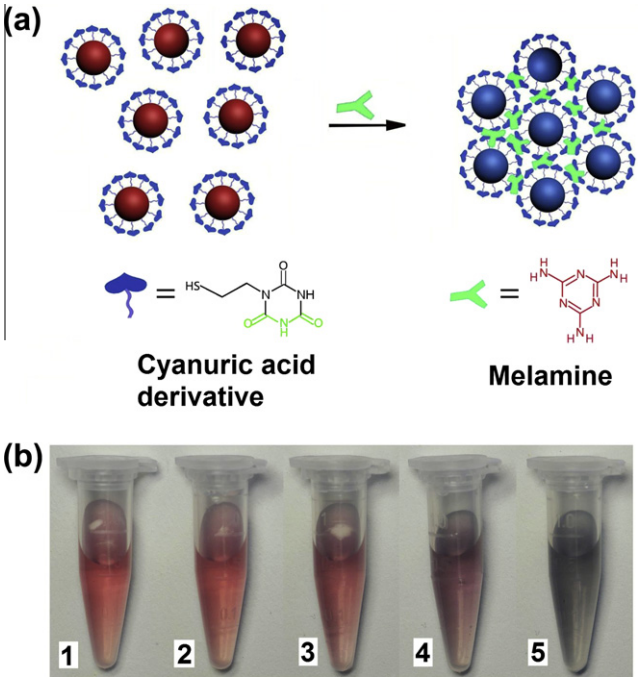

Fig. 10. (a) Schematic showing colorimetric detection of melamine in solution using modified gold nanoparticles (AuNPs). AuNPs are conjugated to a cyanuric acid derivative, which selectively binds to melamine by hydrogen bonding interactions. When bound to melamine, aggregated AuNPs (blue) exhibit different absorptive properties than "free" AuNPs (red). (b) Visual color changes of AuNP-melamine sensor in real milk samples: (1) AuNP solution without any addition; (2) with the addition of the extract from blank raw milk; (3), (4) and (5) with the addition of the extract containing 1 ppm (final concentration: 8 ppb) melamine, 2.5 ppm (final concentration: 20 ppb) melamine and 5 ppm (final concentration: 40 ppb) melamine, respectively. Adapted with permission from Ai et al. [345] Copyright 2009 American Chemical Society.

a chemical reductant [346]. In this system, when melamine is present in a sample, it binds to the reductant and prevents AuNP formation; thus, test samples with no melamine turn fully red during the assay due to AuNP formation via reaction between the gold ions and the reductant. Colorimetric detection of melamine in raw milk using AuNPs and crown-ether-modified thiols with a limit of detection of 6 ppb has also been reported [347].

Other assay systems for small molecules depend on fluorescence rather than absorptive color changes. For instance, a sensor based on a detection methodology called enhanced fluorescence linked immuno-sorbent assay (EFLISA) can be used to detect the presence of gliadin, one of the primary food proteins that cause inflammation in patients suffering from Celiac disease [348]; this system utilizes metal-enhanced fluorescence from rhodamine-labeled anti-gliadin antibodies in close proximity to nanostructured silver island films (SIFs), an approach which could be used to determine the gluten content of gluten-free foods and which could be easily adapted for the selective detection of other protein-based analytes. Another fluorescence-based assay efficiently detected cyanide in drinking water at concentrations as low as 2 nM using fluorescence quenching of gold nanoclusters [349], and a nanoscale liposome-based detector for the contamination of drinking water with pesticides has also been devised [350]. Several protein-based bacterial toxins [351], including bolutinum toxin serotype A [352], have been detected at picomolar (pM) levels using antibody-labeled luminescent quantum dots, which would be useful in food safety and anti-bioterrorism applications. Easy-to-read colorimetric metal nanoparticle detectors have also been developed for numerous other small molecules [353,354], proteins [355,356] and metal ions [357–362],

suggesting that similar strategies could be devised for the convenient detection of a variety of common food adulterants, allergens or contaminants.

Electrochemical detection is another popular method by which nanomaterial-based sensors with applications in the food industry function; compared to optical (colorimetric or fluorimetric) methods, electrochemical approaches may be more useful for food matrices because the problem of light scattering and absorption from the various food components can be avoided. Many electrochemical sensors operate by binding selective antibodies to a conductive nanomaterial (e.g., carbon nanotube) and then monitoring changes to the material's conductivity when the target analyte binds to the antibodies. For example, conduction changes which occur when Microcystin-LR (MCLR), a toxin produced by cyanobacteria, binds to the surface of anti-MCLR-coated single-walled carbon nanotubes are easily detectable down to MCLR concentrations of 0.6 nM, which easily satisfies guidelines set by the World Health Organization for this substance in drinking water [363]; this technique improves the sampling time over traditional MCLR measurement methods (e.g., ELISA) by an order of magnitude. A similar strategy utilizing AuNPs and glucose-sensitive enzymes can be used to measure glucose concentrations in commercial beverages [364], and a reusable piezoelectric AuNP immunosensor has been developed which detects the presence of aflatoxin-B1[7] in contaminated milk samples down to a concentration of 0.01 ng/mL [365]. Other electrochemical systems based on nanomaterials include: an immunosensor based on a cerium oxide nanoparticle and chitosan nanocomposite which detects ochratoxin-A, a food-borne fungal contaminant [366]; detection of staphylococcal enterotoxin B [367] and cholera-toxin [368] using silicon nanowire transistors and carbon nanotubes (CNTs), respectively; and detection and quantification of food colorants[8] (Ponceau 4R and Allura Red in soft drinks [369] and Sudan 1 in ketchup or chili powder [370]) using CNTs and the concentration dependent intensity changes of the colorant-specific oxidation peaks. Note that analytes are not limited to harmful substances: one study showed that CNT-based electrochemical detection in microfluidic devices can be used to measure antioxidant, flavor compound and vitamin content in vanilla beans and apples [371]. Numerous other examples of electrochemical detection of various biomolecules using nanomaterials are provided in a recent review of the topic [372].

4.2. Detection of gasses

Excess moisture and oxygen are leading causes of food spoilage, and yet many assays for vapor or gas content inside of a package require destruction of the package [373–375]. Thus, in processing facilities, packaged foods are tested randomly during a production run, typically one in every 300–400 packages [375], which is time-consuming and costly, yet does not ensure that unsampled packages meet quality and safety standards [376]. The ability to continually and easily monitor the gas content of a package headspace would also provide a means to assess the safety and quality of the contained food long after it has left the production facility, suggesting that noninvasive leak detection and gas content methods would be invaluable [374].

To this end, numerous noninvasive gas sensing methods based on nanotechnology have been devised. Mills and coworkers, for example, have developed a promising photoactivated indicator ink for in-package oxygen detection based upon nanosized TiO_2 or SnO_2 particles and a redox-active dye (methylene blue) [375,377–380]; this detector gradually changes color in response to even minute quantities of oxygen, as shown in Fig. 11. While quantification of the oxygen content within food packages would be difficult with this technology, it nevertheless would provide consumers and retailers an easy, visual method to identify modified atmosphere packages (MAPs) with possible compromised seal integrity. One example of a sensor for moisture content, shown in Fig. 12, is based upon carbon-coated copper nanoparticles dispersed in a tenside film [376]. In humid environments, swelling of the polymer matrix results in larger degrees of inter-nanoparticle separation; these changes cause sensor strips to reflect or absorb different colors of light which can be monitored easily for quick and accurate determination of package moisture levels without invasive sampling. A noninvasive method of measuring carbon dioxide content in MAPs has also been devised, and is based upon lifetime analysis of luminescent dyes standardized by fluorophore-encapsulated polymer nanobeads [381]; notably, this CO_2 sensor has a detection range of 0.8–100%, a resolution of 1%, and only 0.6% cross-sensitivity with molecular oxygen.

Some other examples of gas sensing related to food safety or quality include: detection of gaseous amines, which are indicators of fish and meat spoilage [382], at the parts-per-trillion (ppt) level (theoretical) effected using fluorescence quenching of nanofibrils of perylene-based fluorophores [383,384] or at the ppm level using conductance changes in composites of SnO_2 nanoparticles and TiO_2 microrods [385]; a series of electronic sensors which utilize ZnO–TiO_2 nanocomposites or SnO "nanobelts" to detect the presence of volatile organics, including acetone, ethanol and carbon monoxide [386–388]; and WO_3-SnO_2 nanocomposites to detect the presence of ethylene gas, a hormone responsible for fruit ripening [389].

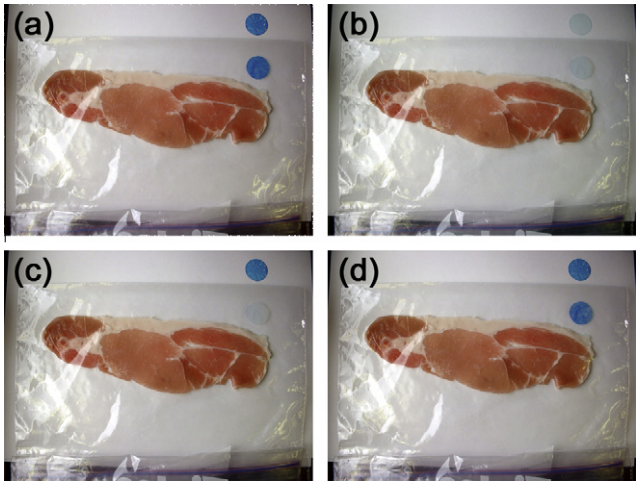

Fig. 11. Photographs of O_2 sensors which utilize UV-activated TiO_2 nanoparticles and methylene blue indicator dye, one placed inside of a food package flushed with CO_2 and one placed outside. In (a) the package is freshly sealed and both indicators are blue. The photograph in (b) shows the indicators immediately after activation with UVA light. After a few minutes, the indicator outside of the package returns to a blue color, whereas the indicator in an oxygen-free atmosphere remains white (c) until the package is opened, in which case the influx of oxygen causes it to change back to blue (d). This system could be used to easily and noninvasively detect the presence of leaks in every package immediately after production and at retail sites. Images taken from [375] (www.dx.doi.org/10.1039/B503997P) – reproduced by permission of The Royal Society of Chemistry.

[7] Aflatoxin-B1 is a toxic and carnicogenic substance found in grains and other food crops contaminated by fungi in the genus *Aspergillus*, as well as in milk produced by animals that eat contaminated feed.

[8] Detection of food colorants would be especially useful because numerous colorant additives, including Ponceau R4 and Sudan 1, have been shown to be carcinogenic in either animals or humans and often show up illegally as adulterants in many imported food products.

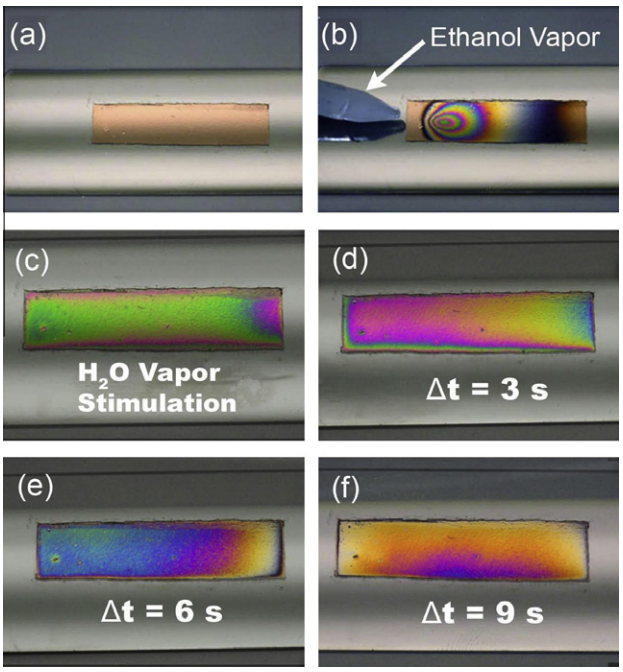

Fig. 12. Moisture sensor which utilizes carbon-coated copper nanoparticles dispersed in a polymer matrix (a). Ethanol vapor exposure results in rapid and reversible iridescent coloration (b). Water vapor exposure swells the polymer, which causes the nanoparticles to exhibit larger interparticle separation distances and thus different observable optical behavior (c). As moisture dissipates (d–f), the sensor reverts back to its native state and appearance. Reprinted with permission from Luechinger et al. [376]. Copyright 2007 American Chemical Society.

4.3. Detection of microorganisms

In 2011, the Centers for Disease Control (CDC) estimated that food-borne pathogens cause approximately 48 million illnesses in the US each year, 128,000 of which lead to hospitalization and 3000 of which result in death [390–392]. The CDC further estimates that reducing foodborne illness by just 1% would keep about 500,000 Americans from getting sick each year.[9] Thus the ability to determine whether food products are contaminated by various bacteria, fungi or viruses that can cause food-borne illnesses remains an important research objective. Detection methods which are fast, inexpensive and require little expertise or training to correctly interpret are especially desirable for "point of care" (i.e., non-laboratory) settings.

Most convenient biological detection methods are based on immunological assays which take advantage of selective antibody-antigen interactions. Nanomaterial-based microbial sensors generally utilize the same strategy, but because they possess unique optical and electrical properties in combination with spacious, easily functionalized surfaces, nanomaterials offer significant improvements in selectivity, speed and sensitivity compared to chemical or biological methods based on macroscale materials. Several authors have reviewed the advantages of nanomaterial-based pathogen sensing in detail [393–395].

As mentioned earlier, a significant problem with sensing in complex matrices such as foods is dealing with sample opacity, light scattering, color and other numerous interferences. Though some all-optical methods have been devised, such as one which used two-photon Rayleigh scattering in conjunction with antibody-conjugated gold nanoparticles to selectively detect *E. coli* [396], most detection strategies in real food systems require isolation of the target organism from the surrounding environment to ensure that signal-to-noise ratios are sufficiently large to observe. Often, a technique known as immunomagnetic separation (IMS) is used to satisfy this requirement (e.g., [397]). IMS uses magnetic particles attached to selective antibodies in combination with a magnet to selectively separate the target analyte from the food matrix prior to detection. Nanoscale magnetic particles are especially useful in this regard due to their extremely high surface-to-volume ratios, which facilitate large analyte capture efficiencies. Captured analytes can then be easily purified and subjected to standard measurement techniques. This approach is illustrated graphically in Fig. 13. For instance, attachment of antibodies selective for *L. monocytogenes* onto functionalized, magnetic iron oxide nanoparticles can be used to efficiently separate the target bacteria from artificially contaminated milk and detect them using real-time PCR analysis [398]. A similar approach has been used to isolate *E. coli* from freshly ground beef with >94% capture efficiency and no interference from other tested bacterial species [399].

Due to the unique electrical and optical properties of nanomaterials, and the ease with which bottom-up engineering can provide multifunctional nanoscale architectures, pathogen detection strategies are increasingly abandoning conventional microbiological analysis methods in preference of a reliance on nanomaterials themselves as the means of detection. The general idea is that not only can the nanoscale magnetic particles be used to bind and isolate analytes from the matrix, but they (or other nanomaterials which constitute parts of multi-component systems) can also be directly detected without the need for time-consuming biological assays. This is particularly easy with microbial detection because the small size of nanoparticles relative to those of the target organisms causes large, readily observable electrical/optical property modulations before and after binding events. It is also worth pointing out that nanomaterials lend themselves well to multiplexing assays, as in the case of a barcode-style method

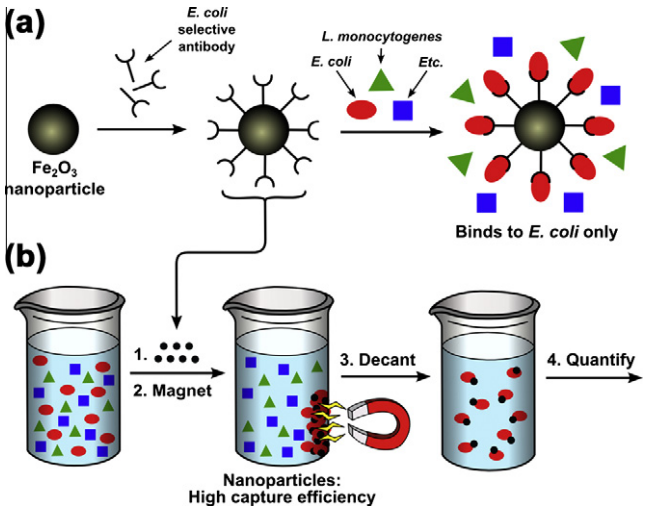

Fig. 13. Schematic illustrating IMS-based detection methods using magnetic nanoparticles. (a) Antibodies selective for specific bacterial strains or species (e.g., *E. coli*) are bound to the surfaces of magnetic nanoparticles (e.g., Fe_2O_3). Only the targeted organisms will bind to the functionalized magnetic nanoparticles. (b) A complex matrix (e.g., food, blood, milk, etc.) contains the target analyte as well as numerous potential interferences, such as other bacterial species, viruses, proteins, food or blood particles, etc. Functionalized magnetic nanoparticles are added to the matrix, where they bind selectively and with high capture efficiency to the target analyte. A magnetic field isolates the analyte-bound magnetic particles, after which the supernatant is then carefully decanted. The remaining material is then subjected to quantification assays. In more sophisticated systems, the magnetic nanoparticles themselves are the means of detection and quantification (see text).

[9] See http://www.cdc.gov/foodborneburden/2011-foodborne-estimates.html [Accessed 05/09/2011].

which utilizes binding of selective antibodies to specific regions of magnetic (and nonmagnetic) multi-metal nanowires for the simultaneous, multiplexed optical detection of bacteria, viruses and protein-based toxins [400].

There are numerous examples which demonstrate the utility of nanomaterials, and in particular magnetic nanomaterials, as vehicles for the simultaneous isolation and optical or magnetic detection of microorganisms. Magnetic nanoparticles can be used to isolate *Mycobacterium avium* spp. *paratuberculosis* from contaminated whole milk and determine the bacterial concentration by observing effects of conjugation-induced magnetic particle agglomeration on the spin–spin (T2) relaxation times of nearby water protons [401]; importantly, this method is not susceptible to interference from other bacterial species that may be present in the matrix. A similar approach that measures changes in the magnetic susceptibility (correlated to changes in particle hydrodynamic volume) of bound and unbound iron oxide particles efficiently detects *Brucella* antibodies in the blood serum of infected cows [402].

One of the most significant advantages of highly-sensitive nanotechnology-based techniques is the reduced incubation and measurement times required for accurate detection. For instance, one research group used sugar molecules attached to nanosized magnetic iron oxide particles to isolate up to 88% of *E. coli* in a sample with only a 45 min incubation time [403]; the *E. coli* were subsequently detected using fluorescent staining. Irudayaraj and coworkers improved upon this approach by using species- and strain-specific antibodies instead of sugar molecules to isolate and optically detect (bench top FTIR/ portable mid-IR) the target organisms in 2% milk and spinach extract [404]. In a separate series of studies, they used magnetic nanoparticles in conjunction with gold nanorods (AuNRs) to separate and detect key food-borne bacteria; here, the magnetic particles facilitate separation while the AuNRs are used for optical detection in the near-infrared. Notably, because AuNRs have length-dependant absorptive properties and efficient light-to-heat energy conversion, they offer the possibility of multiplexed detection (i.e., simultaneous detection of multiple organisms) as well as efficient photoactivated antimicrobial activity via thermal ablation, all from a single multi-component entity [405,406]. Optical colorimetric detection and thermal ablation of *Salmonella* using oval-shaped AuNPs has also been demonstrated [407]. With this in mind, is also worth pointing out that nanomaterials can be useful for the rapid detection of microorganisms after IMS, even IMS performed using conventionally-sized magnetic particles: as an example, Su and Li used IMS to separate *E. coli* from test samples and semiconductor nanocrystals (quantum dots) as fluorescent tags [408]. Their protocol offered a detection range of 10^3–10^7 CFU/mL and total detection time of only 2 h, compared with 18–24 h for traditional bacterial plating/incubation methods.

As with chemical analytes, electrochemical detection of microorganisms is also a popular and efficient method when it comes to nanomaterials. A particularly nice example of this strategy is provided by Wang et al., who fabricated conductive TiO_2 nanowire bundles, coated them with antibodies selective for *L. monocytogenes*, and deposited them between two gold electrodes, as shown in Fig. 14 [409]. In contaminated samples, bacteria bind to the antibodies, which causes a measurable change in impedance across the nanowire bundle. Using this technique, the authors were able to detect as low as 4.7×10^2 CFU/mL *L. monocytogenes* in 1 h without significant interference from other food-borne pathogens; this is a significant improvement over traditional Immuno-Dot Blot analysis, which had a detection limit of 2.2×10^5 CFU/mL. Changes in conductance or resistance across circuits manufactured from or including nanoscale components have also been used to detect members of the *Bacillus* [410], *Salmonella* [411,412], and *Echerichia* [413,414] bacterial genera, as well as viruses [412].

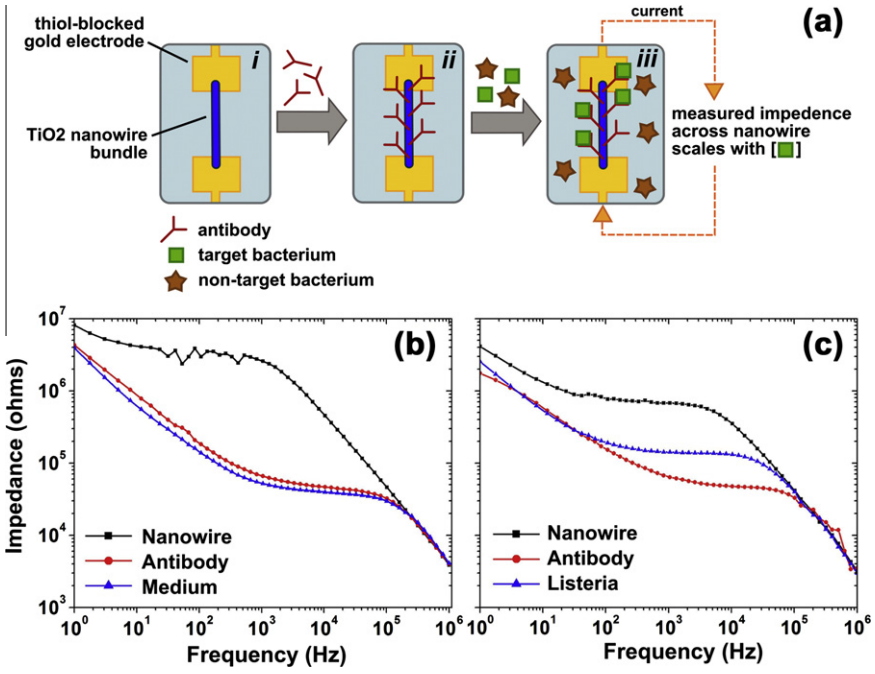

Fig. 14. Impedance-based detection of bacteria. (a) Gold electrodes protected with *n*-butylthiol ligands are connected with a conductive TiO_2 nanowire bundle. Antibodies selective to the target bacterium are then bound to the nanowire bundle. When the sensor is exposed to a complex matrix containing the target organism, changes in the electrical (impedance) properties of the bundle due to bacterium-antibody binding events can be readily observed. (b) and (c) Sample data set illustrating the detection of *Listeria monocytogenes* at a concentration of 4.65×10^3 cfu/ml. Note that exposure to a control medium (b) causes no changes to the impedance across the bundle, but that exposure to the bacteria (c) results in easily observable impedance changes due to immunoselective binding events. Adapted with permission from Wang et al. [409]. Copyright 2008 American Chemical Society.

4.4. Detection by surface-enhanced raman scattering (SERS)

Like infrared spectroscopy, Raman spectroscopy is a particularly valuable tool for the identification and detection or organic compounds because each molecule has a unique pattern of molecular vibrations which gives rise to a correspondingly unique spectral fingerprint. Though Raman spectroscopy has numerous advantages over infrared for molecular identification, a significant disadvantage is that Raman scattering is an extremely weak effect, which limits its usefulness in diagnostic applications. However, it was discovered in the 1970s that roughened metal surfaces can greatly (typically in the range of 4–7 orders of magnitude) increase the Raman peak intensity of analyte molecules in their general proximity. Though the physical origin of surface-enhanced Raman scattering (SERS) is still a matter of some scientific debate, it is known that the effect is at least partially caused by interaction of molecular electronic states with localized electric fields generated by photoexcitation of metal surface plasmons. Because of orientation requirements between the molecular transitions and the plasmon oscillations, SERS enhancement is greatest on surfaces with large degrees of curvature or "roughness". As a result, nanoscale metal structures, such as those comprised of gold or silver, give rise to the most enhanced, and thus practically useful, SERS signals for characterization and detection of analytes.

SERS using nanoscale substrates has proven to be a useful platform for the detection of food-related analytes. For instance, Mengshi Lin and coworkers have pioneered the use of fractal-like or patterned gold nanostructures (Fig. 15) as substrates to detect compounds of interest to food safety, including melamine and its derivatives [415–417], as well as crystal violet and malachite green (~0.2 ppb level) [418], which are two FDA-banned fungicides/antimicrobials often found in fish grown in contaminated waters. With respect to melamine, the authors were able to identify this compound extracted from milk with concentrations as low as 2 ppm [417], and also from artificially contaminated wheat gluten, chicken feed, cakes and noodles [416]. Such a SERS-based detection method might be useful for quick screening of food samples, followed by conventional HPLC analysis for the elimination of false positives. Gold nanoparticles may be used as well for SERS detection of perchlorate (an environmental food and water pollutant) at the nM level in contaminated water samples [419].

In addition to chemical contaminants, SERS can also be used to detect and identify food-borne pathogens, as each bacterial species appears to have a unique fingerprint arrangement of spectral peaks. For instance, single *Bacillus* spores can be detected using SERS and nanostructured gold substrates, and several different *Bacillus* species can be easily distinguished [420]. Silver substrates can be used to rapidly and simultaneously screen for *E. coli*, *L. monocytogenes*, and *S. typhimurium* [421] and gold substrates have been used to identify and discriminate seven food- and water-borne viruses in drinking water, including norovirus, adenovirus, parvovirus, simian rotovirus, coronavirus, Sendai virus and herpes virus, with clear spectral differences even at the strain level and detection limits of 100 particles [422]. In a more recent report, AuNPs, AgNPs and Au–Ag core–shell nanoparticles were used in conjunction with unique Raman reporter molecules for simultaneous detection of multiple organisms via a combination of SERS and UV–Vis spectroscopy [423]; the same research group has also used a combination of magnetic separation with labeled silica-coated magnetic nanoparticles and AuNPs labeled with Raman reporter molecules for multiplexed SERS detection of *S. enterica* serovar *Typhimurium* and *S. aureus* in spinach wash and peanut butter emulsion with a detection limit of 10^3 CFUs/mL [424].

In summary, while the use of SERS and nanoscale materials as a tool to detect the presence of contaminants or pathogens related to food safety is still in its infancy, the early results are very promising in terms of both detection limits and speed of measurement.

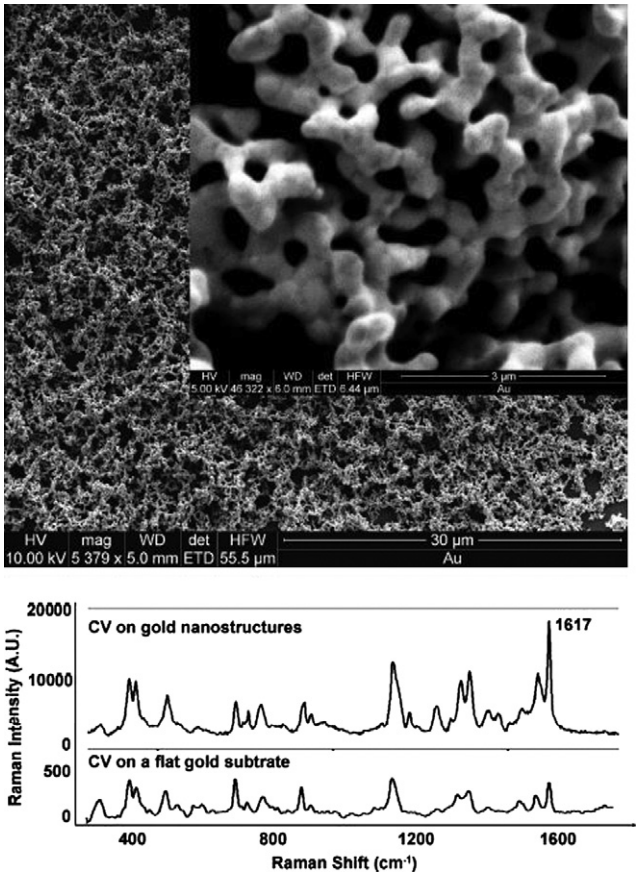

Fig. 15. *Top.* Fractal-like gold nanostructures fabricated from AuNPs for use as a SERS substrate. *Bottom.* SERS spectrum of 2 ppb crystal violet (CV) on gold nanostructures and a "normal" Raman spectrum of 2000 ppm CV on the control (a gold-coated glass slide). Both spectra were acquired under identical Raman instrumental conditions. Note that the spectral intensity for CV on the SERS substrate is effectively 4×10^7 times larger than that of the conventional Raman experiment. Because each chemical compound exhibits a different spectral fingerprint, SERS can be used to quickly and accurately detect a wide range of food contaminents, including living organisms. Reprinted with permission from He et al. [418]. Copyright 2008 American Chemical Society.

5. Outlook

Nanotechnology will likely impact virtually every aspect of the food sector in some way. This review has discussed in some detail a few of the most promising applications, including food packaging materials that possess extremely high gas barriers and antimicrobial properties, and nanosensors which can detect microorganisms or chemical contaminants at surprisingly low levels. Other prospective uses for nanotechnology in foods which were not discussed include, but are not limited to: nanoencapsulants for the delivery of nutrients, flavors, or aromas [425]; more potent pesticides [426][10]; security inks or nanobarcodes to protect against counterfeiting or preserve product identity [427,428]; and nanoparticles which can be utilized in targeted genetic engineering of agriculturally-relevant livestock or plant organisms [428].

[10] See also the US Environmental Protection Agency's webpage on nanomaterials in pesticides, and related guidance documents at http://www.epa.gov/pesticides/regulating/nanotechnology.html [Accessed 06/27/2011].

Despite these potential benefits, the future of "nanofoods" remains uncertain. It is well known that consumers are much more hesitant to accept new technologies in their foods than in other consumer products, and nanotechnology is no exception. While the public currently views generalized nanotechnology applications in a relatively neutral or even positive way, some research suggests that they remain wary about nanotechnology as it is applied in the context of foods. In addition to dreading the health and environmental consequences of nanofoods consumption, consumers are also concerned about ethical or moral issues, including labeling and the right to choose, improvement of human abilities, engineering of living matter, privacy, equitability of socioeconomic distribution and naturalness of the food supply.

As a result of these considerations, public acceptance of food products which incorporate or utilize nanomaterials will be predicated largely on how much trust the public has in industry and the government to protect them from unknown hazards [11]. To that end, openness on industry's part regarding what they're doing and why they're doing it will go a long way toward assuaging public fears about nano-food products. Unfortunately, an editorial article published in the journal *Nature Nanotechnology* recently asserted that "up to 400 companies around the world are researching possible applications of nanotechnology in food and food packaging – and many of them do not want their customers to know this" [429]. Even more foreboding: in a highly publicized report published in 2010 [430], the United Kingdom House of Lords' Science and Technology Committee stated that "far from being transparent about its activities, the food industry was refusing to talk about its work in [nanotechnology]... This is exactly the type of behavior which may bring about the public reaction which [industry] is trying to avert."

The future of nanofoods is also contingent upon the way this emerging technology is handled by regulatory agencies. The enormous potential benefits offered by nanotechnology must be weighed against the potential risks of use and abuse of nanomaterials – and in large part these risks are still being evaluated. When it comes to foods and food packaging materials incorporating nanoscale materials, there are numerous data gaps that need to be filled in order to demonstrate product safety to a wary public. These data gaps include a lack of information regarding: nanomaterial migration through polymer films; the interaction of nanomaterial biomolecules and cellular components; the value of mass-based definitions of dosage in the context of nanomaterials; the interrelationships between nanoparticle characteristics (size, shape, surface charge, etc.) and toxicity or pharmacokinetic properties; appropriate and consistent methods to identify, characterize and quantify nanomaterials in complex food matrices; chronic toxicity of nanomaterials or toxicity following oral routes of exposure; and biodegradability of nanomaterials or the toxicity of nanomaterials to ecologically important organisms.

The goal of this article was to show the reader that nanomaterials offer some exciting benefits to the food industry, including better materials for food packaging and also safer foods on supermarket shelves that have lower incidences of contamination with chemical adulterants and potentially life-threatening microorganisms. The applications reviewed here were specifically chosen because they are the most likely nanofood products to be accepted by consumers in the short-term. Even so, food nanotechnology is still young, and the future of this exciting field is still largely uncertain. Regardless of how applications of nanotechnology in the food sector are ultimately marketed, governed, or perceived by the public, it seems clear that the manipulation of matter on the nanoscale will continue to yield exciting and unforeseen products. We must continue to be stalwart against the potential dangers and ethical questions that the use of this new technology will pose, and successful and safe implementation of these applications will require constant dialogue between the scientists and companies who invent them and the consumers who purchase them. If we succeed in these endeavors, then the benefits of nanotechnology may play an important role in making the world's food supply healthier, safer, and more plentiful.

Appendix A

See Table A1.

Table A1
Abbreviations.

Polymers:
CH: chitosan
EVOH: ethylene-vinyl alcohol
PA: poly(amide)
PCL: poly(caprolactone)
PE, HDPE, LDPE, LLDPE: poly(ethylene), and high, low and linear low density poly(ethylene)
PEG: poly(ethylene glycol)
PEI: poly(ethylene imine)
PEO: poly(ethylene oxide)
PET: poly(ethylene terephthalate)
PHB: poly(hydroxybutyrate)
PHBV: poly(hydroxybutyrate-co-valerate)
PI: poly(imide)
PLA: poly(lactic acid)
PMMA: poly(methylmethacrylate)
PP, iPP: poly(propylene) and isotactic poly(propylene)
PS: poly(styrene)
PU: poly(urethane)
PVA: or poly(vinyl acetate)
PVC: poly(vinyl chloride)
TPS: thermoplastic starch
WG: wheat gluten
Other:
AgNP: silver nanoparticle
AuNP: gold nanoparticle
AuNR: gold nanorod
CEC: cation exchange capacity
CDC: centers for disease control
CFU: colony forming unit
CNT: carbon nanotube
CV: crystal violet
EFLISA: enhanced fluorescence linked immuno-sorbent assay
EPA: environmental Protection Agency
ESBL: extended-spectrum beta-lactamase
EU: European Union
FCN: food contact notification
FDA: (United States) Food and Drug Administration
FTIR: Fourier transform infrared (spectroscopy)
HPLC: high-performance liquid chromatography
IMS: immuno-magnetic separation
LBL: layer-by-layer (assembly)
LOD: limit of detection
MAP: modified atmosphere packaging
MCLR: microcystin-LR
MMT: montmorillonite
MRSA/MRSE: methicillin-resistant *Staphylococcus aureus*/*epidermidis*
NSRDEC: Natick Soldier Research, Development and Engineering Center
OTR: oxygen transmission rate
PALS: positron annihilation lifetime spectroscopy
PCR: polymerase chain reaction
PNC, PCNC: polymer nanocomposite, polymer/clay nanocomposite
ROS: reactive oxygen species
SERS: surface-enhanced Raman scattering
SIF: silver-island film
TEM: transmission electron microscopy
VRE: vancomycin-resistant *Enterococcus*
WVTR: water vapor transmission rate

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