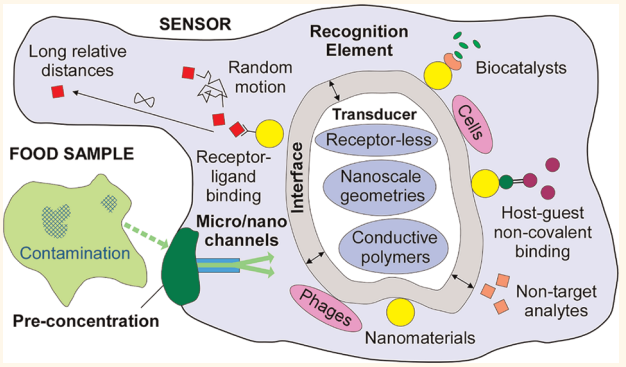
Critical Issues in Sensor Science To Aid Food and Water Safety

R. H. Farahi,[†] A. Passian,[†,‡,*] L. Tetard,[†] and T. Thundat[§]

[†]Oak Ridge National Laboratory, Oak Ridge, Tennessee 37831-6123, United States, [‡]Department of Physics, The University of Tennessee, Knoxville, Tennessee 37996-1200, United States, and [§]Department of Chemical & Materials Engineering, University of Alberta, T6G 2 V4 Edmonton, Canada

ABSTRACT



The stability of food and water supplies is widely recognized as a global issue of fundamental importance. Sensor development for food and water safety by nonconventional assays continues to overcome technological challenges. The delicate balance between attaining adequate limits of detection, chemical fingerprinting of the target species, dealing with the complex food matrix, and operating in difficult environments are still the focus of current efforts. While the traditional pursuit of robust recognition methods remains important, emerging engineered nanomaterials and nanotechnology promise better sensor performance but also bring about new challenges. Both advanced receptor-based sensors and emerging non-receptor-based physical sensors are evaluated for their critical challenges toward out-of-laboratory applications.

The safety of our food and water may arguably hold the greatest socio-economic impact[1] compared to other threats to national and international security, while at the same time being the most vulnerable.[2] While the complex strategy to manage food and water safety is being debated and defined, it is universally agreed that one critical ingredient is *information*. Real-time, comprehensive data on the state of our food and water supply will allow shortened times for assessment of damage, comprehension of causal relationships and traceability, determination of actions for remediation, and notification of the affected populations.[3] In order to obtain the information needed to achieve these objectives, an extensive monitoring system integrated throughout the food chain would be ideal. Yet, how close we are to achieving such a system is unclear. In recent years, the numbers of papers related to food and water sensors (FWSs) have exploded, covering a vast amalgamation of multidisciplinary technologies. However, shared trends among current FWS development appear to be the capitalization of nanotechnology and emerging nanomaterials. By considering key issues such as the delivery of complex food samples to the sensor with minimal preparation, operation in adverse field conditions, overcoming nonspecific responses, understanding recognition–transducer communication, and understanding the ramifications of incorporating nanotechnology (Figure 1), we aim to focus on the critical issues common to all types of FWS. Therefore, no effort is made in reviewing the vast numbers of current sensor technologies *per se*.

The Role of Nanotechnology. Nanotechnology is a common thread in a majority of the new developments in FWS. Predominant nanomaterials used in biosensors are nanoparticles (gold, silicon, magnetic composite, polymer),[4] nanowires (gold, polymer, composite), nanoporous surfaces,[5−7] carbon allotropes (notably nanotubes), and quantum dots.[4] Naturally small or downscaled systems with various geometries offer several unique advantages in FWS: (1) high surface-to-volume ratios, which allow greater effective functionalized sensing surface area in a compact form;[6,8−11] (2) high sensitivity due to their small size;[12−14] (3) unique optical and electrical properties;[15] (4) fast response due to high elastic (spring) constants; and (5) highly localized detection of entities of comparable size. However, each of these advantages is intertwined with a set of challenges. For example, high sensitivity due to a small transducer surface produces challenges such as significantly reduced probability of interacting with the analyte.

* Address correspondence to passianan@ornl.gov.

Published online May 07, 2012
10.1021/nn204999j

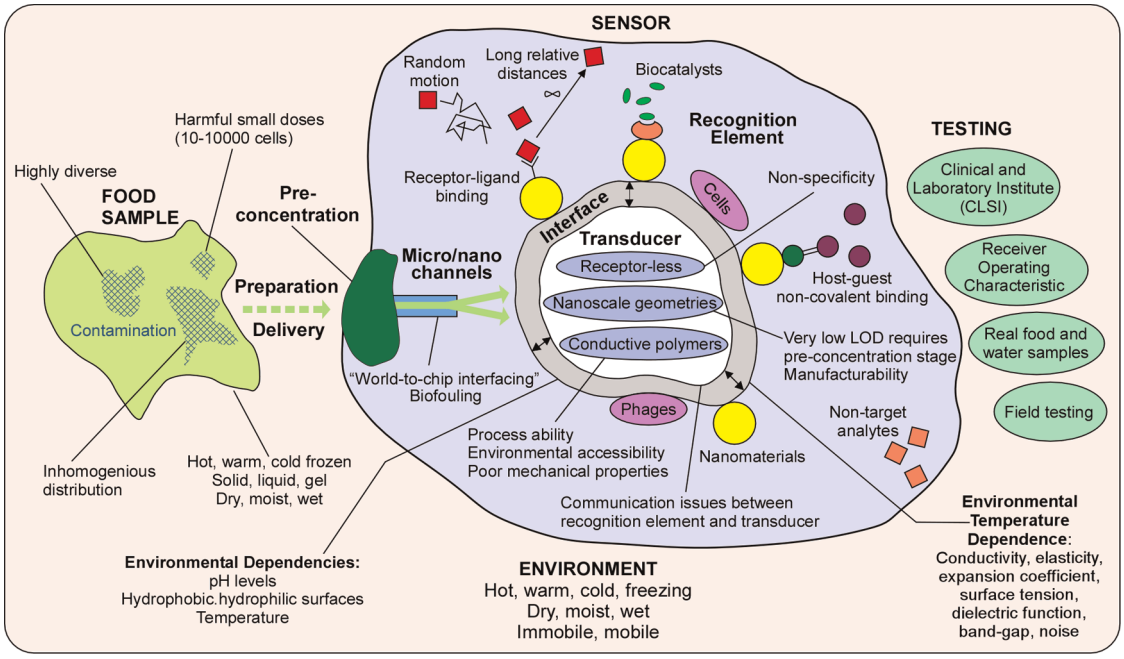


Figure 1. Critical issues in food and water sensors. A sensor is described as a tightly bound combination of two components: the recognition element and the transducer.

Thus, advantages gained by a reduction in size must be balanced with realistic measurement times in order to avoid the need for a preconcentration stage. In practical settings of FWS, the joint merits of "trace amount detection" (*e.g.*, as measured in parts per million or parts per trillion) and "miniaturized sensor" can therefore only be meaningful if a preconcentration stage can be devised; otherwise, lengthy measurement times may subject the system to debilitating noise. Nevertheless, very few preconcentration technologies[16,17] are under development for FWS. Here, as a somewhat relevant example, we consider the detection of trace amounts of explosives molecules[17] in a given real-world environment using a microsensor with a surface area that is far too small to offer sufficient "scattering cross section". Thus, the probability of an interaction event between a single sensor and a random target molecule is dramatically reduced, leading to practically infinite measurement times. Circumvention to this low probability was attempted by first introducing a (cold) collection platform on which the target molecules are physisorbed. After sufficient adsorption time, the molecules coalesce into small droplets, which can be propelled toward the sensing stage *via* the so-called Marangoni flow (convection by virtue of surface tension gradients).[18] As a result of this elaborate preconcentration phase, the effective microsensor area was increased by 10^4 without compromising sensitivity.[17]

> Nanotechnology is a common thread in a majority of the new developments in food and water sensors.

Another serious consideration when dealing with small objects such as carbon nanotubes (CNTs), which naturally form bundles due to strong intrinsic van der Waals attractions, is the separation, manipulation, and translocation of individual nanostructures for feasible device manufacturability.[19] Furthermore, often overlooked stochastic as well as deterministic forces that are generally weak macroscopically can be non-negligible microscopically. An example of the former is Brownian agitation, while an example of the latter is the Knudsen forces arising as temperature gradients can be established over length scales that are proportional to a characteristic length scale of the object, which in turn can be proportional to the mean-free-path of the constituent molecules of the surrounding environment.[20] For example, at room temperature, the mean-free-path of the molecules making up the air is approximately 65 nm. For a nanostructure that has a characteristic dimension of the same size, such as the diameter of a nanosphere or the length of a nanowire, any local temperature gradients can lead to substantial forces exerted on the object that can interfere with the sensing operation.

Emerging Nanomaterials—Conducting Polymers. Emerging nanomaterials such as conducting polymers are demonstrating potential for biological and chemical transducer platforms for FWS due to their ability to be functionalized with biological recognition elements, direct electrical signal transduction, and biocompatibility.[13,21,22] Conducting polymer nanoparticles[8] and

nanowires[12] have been functionalized as molecular imprinted polymers (MIP), phage functionalized for *Salmonella*[23] and *Escherichia coli* O157:H7 detection,[10] and antibody functionalized for viral[24] and bacterial[11] immunosensing. However, known complications to using conductive polymers in FWS are their difficult processability (infusibility and insolubility in organic solvents), poor mechanical properties (low spring constant), high resistance, high actuation voltages, and susceptibility to environmental conditions (humidity, ions, pH, CO_2, *etc.*).

Emerging nanomaterials such as conducting polymers are demonstrating potential for biological and chemical transducer platforms for food and water sensors due to their ability to be functionalized with biological recognition elements, direct electrical signal transduction, and biocompatibility.

Micro/Nanofluidics Integration. Micro/nanofluidic and digital micro/nanofluidic systems enable measurements of small sample volumes, thus offering the prospect of scaling devices down to "lab-on-a chip" platforms, automation of multiple analytical procedures, increased sensitivity, lower costs, and easier operation.[25,26] For detecting biological pathogens and parasites, the primary advantage is significantly reduced sample populations, thereby eliminating the need for skilled operators to perform enrichment and culturing steps that could take 2 to 4 days to complete prior to the actual testing.[27] Given these advantages, microfluidic systems are becoming prevalent in FWS,[28−36] with optical-based transduction systems incorporating microfabricated optical waveguides.[30,31] However, working with microfluidic systems can be extremely difficult. The most serious practical limitations confronting microfluidic systems are biofouling and "world-to-chip" interfacing.[37]

In addition, understanding the physics of the flow for proper design, operation, and interpretation of the measurements is not without challenges.[38] The Navier−Stokes equation is known to break down for confined fluids, where slip flow and temperature jumps can occur. Given the complexity of the analyte−sensor configurations, proper modeling of the fluid−structure interactions requires nontrivial fluid dynamic considerations in the range from continuum down to atomistic approaches.[39] These problems are aggravated for food and water samples, where field input conditions are already far less than ideal.

Diverse Priority Target Analytes. The diversity of molecular species to be detected by FWS is enormous, shown in Figure 2. For example, in the United States, *Campylobacter*, *Salmonella*, *Listeria monocytogenes*, and *Escherichia coli* (*E. coli* O157:H7) are considered the primary foodborne pathogens[40] and continue to be the focus of FWS research.[23,32,41−45] Worldwide, emerging water-borne pathogens responsible for illnesses include *Vibrio cholerae* O139, enterohemorrhagic *E. coli* O157:H, chlorine-resistant *Cryptosporidiumare*, and multi-drug-resistant *Pseudomonas aeruginosa*[46] driven by forces such as population growth, translocation, and socio-economic unrest.[47] Meanwhile, toxin sensor development[5,48−52] remains relevant because, although food sterilization methods can deactivate many proteinaceous toxins, heat-stable small molecule toxins such as mycotoxins and saxotoxins can still be toxic in cooked foods.[53] Recently, claims that ricin could viably be used as a biological weapon on urban populations have been disputed;[54] nevertheless, new ricin sensors continue to be reported.[55−58] Additionally, detection of pesticide[59] contamination in food and water remains a priority due to its toxic effects and persistence in the environment[60] caused by residue, drift, and unintended effects on nontarget species. Thus, given the multiplicity of contaminants, FWS characteristics must be tailored for the particular analyte and its acceptable level of concentration, the food source, environmental stresses, and ease of operation.

Complex Food Matrices and Input Conditions. The ultimate goal and challenge of the FWS is to function in *field* conditions, whether in agricultural settings, food processing facilities, or consumer venues. These real-world conditions present a number of obstacles for reliable and rapid assays of food. For example, consider that food and beverage matrices are complicated substances containing protein, fats, carbohydrates, preservatives, and other constituents that can appear in raw, processed, and precooked arrangements.[61] Furthermore, the distributions of biological and chemical contaminants are not homogeneous in food and water. Small numbers of harmful microorganisms (10−10000 cells) can be an infectious dose, while nonharmful strains may be copresent.[61] The unfavorable sensing environments of farms, factories, and transportation containers make it difficult for sensors to operate with stability, where temperature, pressure, mechanical, chemical, and electromagnetic parameters can vary grossly. Even if a sensor is thermally stable, food and food sources vary in water content, structure (liquid or solid), and temperature, requiring the sensor to be effective in wide operating ranges. Sample preparation must be negligible or minimal for unattended operation in the field. In typical

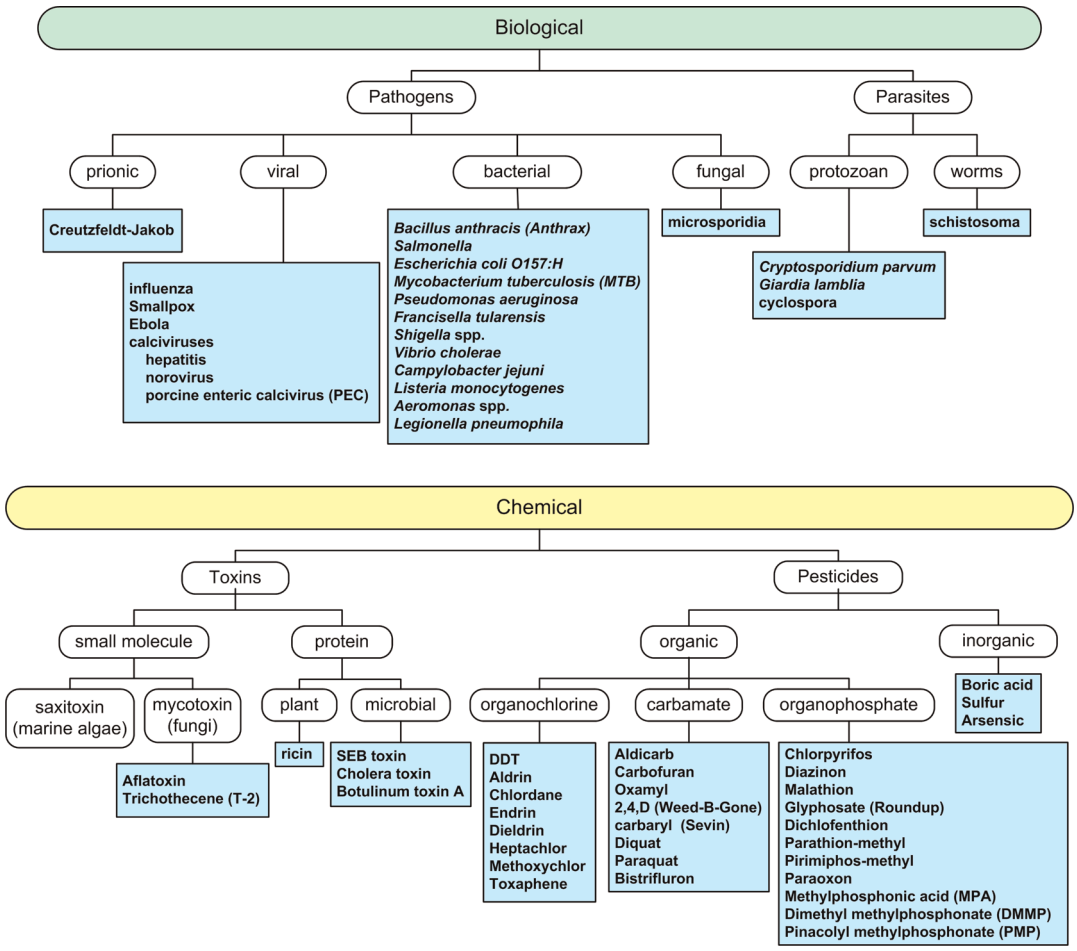


Figure 2. Hierarchical categorization of priority target analytes for food and water. The boxes in blue contain specific examples of pathogens, parasites, toxins, and pesticides.

laboratory experiments, food samples must be prepared and delivered to the sensor region, for example, through a fluidic system enabled with concentration and filtration control. Practical FWS must be designed to operate in environmental conditions with a high nontarget analyte background and biological milieu without highly skilled operators and precisely contrived input conditions. Given these challenges, FWS development must embrace a multidisciplinary approach that incorporates a host of recognition and transducer technologies to satisfy very different target-sample scenarios.

Potential Recognition Technologies. Biological-based receptors (biological sensors) are by far the most conspicuous recognition technology discussed in terms of FWS, followed by chemical-based receptors (chemical sensors), charted in Figure 3. However, direct receptor-less (physical) sensors, rarely mentioned in the context of FWS yet, could be an important contributor for future devices. For receptor-based sensors, receptor material is coated over the transducer, thereby "functionalizing" the transducer to respond to a particular aspect of the specific biological or chemical species. However, in physical sensors, the inherent properties of the sample are measured directly and, if sufficiently distinct, the measurement can be used to identify the analyte. This could prove to be an extremely powerful alternative, where the "usual" need for wet chemistry (enzymatic conversion, receptor–ligand binding, biomimetics using aptamers or molecularly imprinted nanomaterial, *etc.*) is absent. While here we do not make a distinction between "point" sensors and "standoff" sensors,[62,63] it is understood that any remote detection is to be considered a receptor-less approach.

> The ultimate goal and challenge of the food and water sensors is to function in field conditions, whether in agricultural settings, food processing facilities, or consumer venues.

Biocatalysis ("lock-and-key" model)[34,51,64,65] and receptor/ligand binding[6,9,11,15,24,30,35,41,66,67] are mature technologies that offer

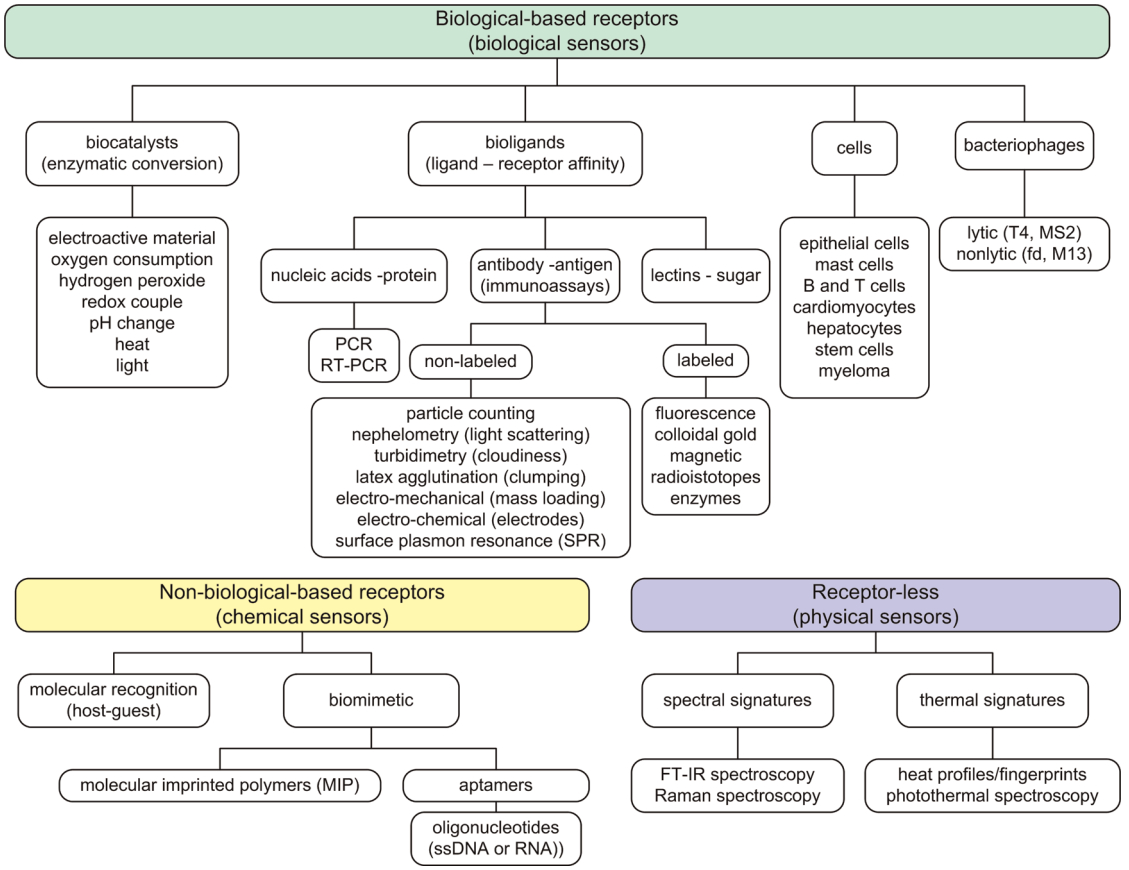


Figure 3. Stratification of potential recognition technologies for food and water sensing. The recognition element is generally described as a substance that produces a biological, chemical, or physical response to the presence of a stimulus (target analyte). Biologically based receptors, often called biological sensors, biosensors, or bioreceptors, use a bioactive macromolecule as the recognition element to sense a limited group of molecules or chemicals that are not necessarily biological in origin. Non-biological-based receptors for FWS are often called chemical sensors or chemosensors or chemoreceptors and, through molecular recognition, have high affinity and selectivity for inorganic and organic molecules, including proteins. While significantly more tenacious to exploit and to develop, receptor-less technologies are also potential FWS.

highly selective identification of molecules and continue to be the recognition method of choice for FWS. Moreover, the cellular response based on the biochemical pathways of whole cells has emerged as a powerful method to detect pathogens and toxins, such as the mammalian cell-based biosensor by Banerjee *et al.*[43,68] Additionally, sensors utilizing bacteriophage (phage) can identify bacterial pathogens by capitalizing on phage-display technology.[10,69,70] Recent non-biological-based FWS have employed aptamers[42,71,72] and molecularly imprinted polymers (MIP)[8,12] as artificial biomimetic receptors.

Persisting issues, for example, in the case of interpretation of the response from a self-assembled monolayer (SAM), call for potential alternatives that bypass chemistry in receptor-based sensors. Challenges in achieving robust and stable recognition through functionalized coatings have led to interest in non-receptor approaches that capitalize on inherent material responses such as unique spectral and thermal fingerprints of analytes. Recent examples include *Bacillus anthracis* identification with nonfunctionalized (coatingless) microcantilevers *via* photothermal and thermal processes,[73] chemical warfare agent detection with microheaters,[74] and heat profiling of explosives with microcalorimetric sensors.[75,76] However, thus far, due to a lack of strong specificity governed by the nature of the particular spectroscopy employed, these promising techniques remain immature as FWS.

Recognition–Transduction Communication. The susceptibility of material properties to environmental parameters *via* various electrochemical, electromagnetic, thermodynamic, and nanomechanical couplings offers a host of potential transducers for FWS, listed in Table 1. Ideally, the transducer should be dependent on the original response of the recognition element and, through amplification and filtering, be able to produce a minimum detectable signal (limit of detection). A prevailing mismatch between transducer sensitivity and uncompromisable recognition has led to a sensor technology state where extremely sensitive (attogram[77] and zeptogram[78] detection limits) transducers are available while recognition elements remain grossly inferior. As a result, for sensitive platforms such as surface acoustic wave (SAW), quartz crystal microbalance (QCM), microcantilevers,

TABLE 1. Potential Transduction Methods and Platforms for FWS[a]

transduction method	transduction mechanism	platform example
electrochemical	electrochemical change between two electrodes measured as:	• micro/nanofluidic-based systems
	1. capacitive	• microelectrodes (micropipets)
	2. amperometric or voltametric	• MEMS electrodes (microcantilevers)
	3. potentiometric	• interdigitated transducer (IDT) electrodes
	4. impedance or resistance	• non-carbon nanowire electrodes
	5. conductance	• carbon nanotube and nanofiber electrodes
	6. electrochemiluminescence	• field-effect transistors (FET)
	7. calorimetric (heat)	• surface acoustic wave (SAW) devices
electromechanical	mechanical change due to mass loading and change in surface tension measured as:	• quartz crystal microbalance (QCM)
		• tuning forks
		• microcantilevers — passive, active (piezoresistive, piezoelectric)
	1. static mode — bending	• conducting polymer ribbons — polyaniline, polypyrrole
	2. dynamic mode — bending, resonance frequency shift	• carbon nanotubes and carbon nanofibers
optical	optical transduction by measuring:	• fiber-optic-based systems
	1. light scattering	• photonic waveguides
	2. fluorescence	• interferometry
	3. chemiluminescence	• microfluidic flow cytometry
	4. colorimetry	• Fourier transform infrared (FT-IR) spectroscopy
	5. evanescent waves	• fluorescence resonance energy transfer (FRET)
	6. thermo-optic heat	• surface plasmon resonance (SPR) and SPR spectroscopy
		• surface-enhanced Raman spectroscopy (SERS)
		• differential optical heterodyne

[a] The signal transduction platform converts (transduces) the response of the recognition element into a quantifiable signal through electrochemical, electromechanical, or optical processes. It is generally agreed that selectivity is primarily governed by the recognition element, while sensitivity is predominantly influenced by the transduction mechanism.

surface plasmon resonance (SPR), and others to rise above the transducer status and be appreciated as sensors, a paradigm shift is needed in the status of recognition chemistry and physics. Further complexity for cases where the above mismatch has been eliminated lies with the interfacial communication between the transducer and the recognition element. Recent work indicates that, despite the availability of high-sensitivity transducers and reasonably robust recognition elements (within a laboratory setting), the interpretation of the signal, that is, the transfer of the response to the transducer, is far from trivial.[79]

Nonspecificity Factors. Often the discourse on nonspecific adsorption or binding of analytes centers on molecular recognition, viable *versus* nonviable cells, and pathogenic *versus* nonpathogenic strains;[80] however, other factors contributing to the overall sample–sensor pair behavior must also be considered. While transducers are generally highly sensitive, they are inherently and often notoriously nonspecific. Often, the transducer itself will respond to the environmental parameters or respond in a nonspecific manner to the same stimuli that the recognition element is to convey to the transducer. Such parameter couplings add substantial complexity to the interpretation of the signals. Decoupling of the various parameters of a sample–sensor pair so as to minimize the reception of "false positives" is particularly important not only in data reliability but also in quantitative data interpretation. For example, the many temperature-dependent properties (conductivity, elasticity, expansion coefficient, thermoelastic damping, surface tension, dielectric function, band gap, noise, *etc.*) relevant to many transducers and/or recognition elements must not interfere with the wide temperature range specific to food and water samples. Or, even for the same temperature, other factors can include the change in pH, hydrophobic/hydrophilic surfaces of the transducer, and mechanical stress.[23] Thus, transducer sensitivity should ideally be accompanied with specificity for the unique response of the recognition element without significantly responding to other environmental variations. This can be particularly challenging for meeting the criteria of "field-deployable" FWS. For example, while stochastic processes often set the ultimate limit of detection, in certain cases, the Brownian or thermomechanical noise of the sensor may be reduced with the cost of significant complexity in either the electronics by using feedback or temperature control by using cooling elements.

Testing and Reporting Consistency. As sensing capabilities continue to improve, testing conditions must become more rigorous and the direct use of real-world samples in real-world operating scenarios (*e.g.*, spinach,[41] tomatoes,[70,81] milk,[82] and beef[83]) will be more common. Horgan *et al.* suggest that, although the performances of new sensing methods are described in terms of specificity, sensitivity, and limits

of detection, sensor assessments should also consider following test guidelines from organizations such as the Clinical and Laboratory Standards Institute (CLSI).[22] FWS could also be assessed by Receiver Operating Characteristic (ROC) analysis, similar to ROC evaluation of immunoassay biosensors for medicine.[84] Ultimately, each sensor technology strives to reach a superior ROC status. An ideal FWS with a ROC curve that could survive arbitrary field testing would indeed be a remarkable achievement.

Future Outlook. In the future, we expect to see both more hybrid systems, brought about by the almost limitless combinations of transducer platforms and recognition elements, and more scalable versions of conventional analytical tools through integration of miniaturized nonconventional methods. In order to cope with the diverse contaminants in food and water, future FWS will need to integrate arrays of sensors from optical, mechanical, and chemical platforms. New receptor-less physical sensors will continue to be explored as viable methods for FWS. Success in mitigating the challenges of FWS can also benefit sensing efforts in food science, crop security,[1] agricultural productivity, and quality.[85,86] Due to comparable length scales, future FWS can also be important in characterizing the nanometer-sized components of foods, or "nanofoods".[87] Moreover, while not acute, naturally any established regulation of nanotechnology oversight[26,88] must also be considered in future FWS development, which may impose additional constraints.

Efforts in mimicking human olfaction may lead to the so-called electronic nose.[81,89] Evolved to assess food and water conditions by molecular recognition (presumably by a lock-and-key molecular process or an electron quantum tunneling process[90]), human olfaction can, with varied success, categorize "edible" *versus* "non-edible" material and early detection of food spoilage. Therefore, it is expected that, at the individual consumer level, electronic noses could be used as integrands in other devices, such as refrigerator temperature sensors, infant products, and cellular phones, to detect odors related to food quality.

CONCLUSION

Current sensor development for food and water safety is multifaceted and challenging, with the promise of concomitant benefits in worldwide human health and quality of life. While specificity and sensitivity continue to improve to unprecedented levels in the laboratory, little or no field testing has been reported. Although sensor researchers are keenly aware of the various issues challenging their particular technologies, outsiders may perceive an overestimated level of performance, or in certain cases, the availability of "uber-sensors". It may be argued that new as well as experienced investigators contemplating engaging in sensor development, program managers, and funding sources alike would strongly profit from a better defined status of recognition and transduction technologies that contain the term "sensor", with the expectation that maturation may be many years away from a development level that would permit direct application to field-deployable food and water sensing. However, from current reports, it is expected that field testing of FWS in real environmental conditions will begin to emerge, which would eventually drive the introduction of useful industrial and consumer products for food and water testing.

Acknowledgment. This research was supported by the Department of Homeland Security-sponsored Southeast Region Research Initiative (SERRI) at the Department of Energy's Oak Ridge National Laboratory (ORNL). ORNL, Oak Ridge, Tennessee, is managed by UT-Battelle, LLC, for the Department of Energy under contract number DE-AC05-0096OR22725.

REFERENCES AND NOTES

1. Gebbers, R.; Adamchuk, V. I. Precision Agriculture and Food Security. *Science* **2011**, *327*, 828–831.
2. Fernandez, R. E.; Stolyarova, S.; Chadha, A.; Bhattacharya, E.; Nemirovsky, Y. MEMS Composite Porous Silicon/Polysilicon Cantilever Sensor for Enhanced Triglycerides Biosensing. *IEEE Sens. J.* **2009**, 91660–1666.
3. Koev, S. T.; Fernandes, R.; Bentley, W. E.; Ghodssi, R. A Cantilever Sensor with an Integrated Optical Readout for Detection of Enzymatically Produced Homocysteine. *IEEE Trans. Biomed. Circuits Syst.* **2009**, *3*, 415–423.
4. Kaittanis, C.; Santra, S.; Perez, J. M. Emerging Nanotechnology Based Strategies for the Identification of Microbial Pathogenesis. *Adv. Drug Delivery Rev.* **2010**, *62*, 408–423.
5. Chai, C.; Takhistov, P. Label-Free Toxin Detection by Means of Time-Resolved Electrochemical Impedance Spectroscopy. *Sensors* **2010**, *10*, 655–669.
6. Luo, Y.; Nartker, S.; Miller, H.; Hochhalter, D.; Wiederoder, M.; Wiederoder, S.; Setterington, E.; Drzal, L. T.; Alocilja, E. C. Surface Functionalization of Electrospun Nanofibers for Detecting *E. coli O157:H7* and BVDV Cells in a Direct-Charge Transfer Biosensor. *Biosens. Bioelectron.* **2010**, *26*, 1612–1617.
7. Kilian, K. A.; Böcking, T.; Gaus, K.; Gal, M.; Gooding, J. J. Peptide-Modified Optical Filters for Detecting Protease Activity. *ACS Nano* **2007**, *1*, 355–361.
8. Morelli, I.; Chiono, V.; Vozzi, G.; Ciardelli, G.; Silvestri, D.; Giusti, P. Molecularly Imprinted Submicronspheres for Applications in a Novel Model Biosensor-Film. *Sens. Actuators, B* **2010**, *150*, 394–401.
9. Zhu, Y.; Son, J. I.; Shim, Y.-B. Amplification Strategy Based on Gold Nanoparticle-Decorated Carbon Nanotubes for Neomycin Immunosensors. *Biosens. Bioelectron.* **2010**, *26*, 1002–1008.
10. Arter, J. A.; Taggart, D. K.; McIntire, T. M.; Penner, R. M.; Weiss, G. A. Virus-PEDOT Nanowires for Biosensing. *Nano Lett.* **2010**, *10*, 4858–4862.
11. García-Aljaro, C.; Bangar, M.; Baldrich, E.; Muñoz, F. J.; Mulchandani, A. Conducting Polymer Nanowire-Based Chemiresistive Biosensor for the Detection of Bacterial Spores. *Biosens. Bioelectron.* **2010**, *25*, 2309–2312.
12. Berti, F.; Todros, S.; Lakshmi, D.; Whitcombe, M. J.; Chianella, I.; Ferroni, M.; Piletsky, S. A.; Turner, A. P. F.; Marrazza, G. Quasi-Monodimensional Polyaniline Nanostructures for Enhanced Molecularly Imprinted Polymer-Based Sensing. *Biosens. Bioelectron.* **2010**, *26*, 497–503.
13. Hangarter, C. M.; Bangar, M.; Mulchandani, A.; Myung, N. V. Conducting Polymer Nanowires for Chemiresistive and FET-Based Bio/Chemical Sensors. *J. Mater. Chem.* **2010**, *20*, 3131–3140.
14. Alvarez, M.; Lechuga, L. M. Microcantilever-Based Platforms as Biosensing Tools. *Analyst* **2010**, *135*, 827–836.

15. Chang, Y.-F.; Wang, S. F.; Huang, J. C.; Su, L. C.; Yao, L.; Li, Y. C.; Wu, S. C.; Chen, Y. M.; Hsieh, J. P.; Chou, C. Detection of Swine-Origin Influenza A (H1N1) Viruses Using a Localized Surface Plasmon Coupled Fluorescence Fiber-Optic Biosensor. *Biosens. Bioelectron.* **2010**, *26*, 1068–1073.
16. Li, D.; Li, D.-W.; Fossey, J. S.; Long, Y.-T. Portable Surface-Enhanced Raman Scattering Sensor for Rapid Detection of Aniline and Phenol Derivatives by On-Site Electrostatic Preconcentration. *Anal. Chem.* **2010**, *82*, 9299–9305.
17. Farahi, R. H.; Passian, A.; Ferrell, T. L.; Thundat, T. Microfluidic Manipulation *via* Marangoni Forces. *Appl. Phys. Lett.* **2004**, *85*, 4237–4239.
18. Passian, A.; Zahrai, S.; Lereu, A. L.; Farahi, R. H.; Ferrell, T. L.; Thundat, T. Nonradiative Surface Plasmon Assisted Microscale Marangoni Forces. *Phys. Rev. E* **2006**, *73*, 066311.
19. Tetard, L.; Passian, A.; Farahi, R. H.; Kalluri, U. C.; Davison, B. H.; Thundat, T. Spectroscopy and Atomic Force Microscopy of Biomass. *Ultramicroscopy* **2010**, *110*, 701–707.
20. Passian, A.; Warmack, R. J.; Ferrell, T. L.; Thundat, T. Thermal Transpiration at the Microscale: A Crookes Cantilever. *Phys. Rev. Lett.* **2003**, *90*, 124503.
21. Arshak, K.; Velusamy, V.; Korostynska, O.; Oliwa-Stasiak, K.; Adley, C. Conducting Polymers and Their Applications to Biosensors: Emphasizing on Foodborne Pathogen Detection. *IEEE Sens. J.* **2009**, *9*, 1942–1951.
22. Horgan, A. M.; Moore, J. D.; Noble, J. E.; Worsley, G. J. Polymer- and Colloid-Mediated Bioassays, Sensors and Diagnostics. *Trends Biotechnol.* **2010**, *28*, 485–494.
23. Dadarwal, R.; Namvar, A.; Thomas, D. F.; Hall, J. C.; Warriner, K. Organic Conducting Polymer Electrode Based Sensors for Detection of Salmonella Infecting Bacteriophages. *Mater. Sci. Eng. C* **2009**, *29*, 761–765.
24. Shirale, D. J.; Bangar, M. A.; Park, M.; Yates, M. V.; Chen, W.; Myung, N. V.; Mulchandani, A. Label-Free Chemiresistive Immunosensors for Viruses. *Environ. Sci. Technol.* **2010**, *44*, 9030–9035.
25. Mark, D.; Haeberle, S.; Roth, G.; von Stetten, F.; Zengerie, R. Microfluidic Lab-on-a-Chip Platforms: Requirements, Characteristics and Applications. *Chem. Soc. Rev.* **2010**, *39*, 1153–1182.
26. Yager, P.; Edwards, T.; Fu, E.; Helton, K.; Nelson, K.; Tam, M. R.; Weigl, B. H. Microfluidic Diagnostic Technologies for Global Public Health. *Nature* **2006**, *442*, 412–418.
27. Mairhofer, J.; Roppert, K.; Ertl, P. Microfluidic Systems for Pathogen Sensing: A Review. *Sensors* **2009**, *9*, 4804–4823.
28. Cretich, M.; Sedini, V.; Damin, F.; Di Carlo, G.; Oldani, C.; Chiari, M. Functionalization of Poly(dimethylsiloxane) by Chemisorption of Copolymers: DNA Microarrays for Pathogen Detection. *Sens. Actuators, B* **2008**, *132*, 258–264.
29. Do, J.; Ahn, C. H. A Polymer Lab-on-a-Chip for Magnetic Immunoassay with On-Chip Sampling and Detection Capabilities. *Lab Chip* **2008**, *8*, 542–549.
30. Heinze, B. C.; Gamboa, J. R.; Kim, K.; Song, J. Y.; Yoon., J. Y. Microfluidic Immunosensor with Integrated Liquid Core Waveguides for Sensitive Mie Scattering Detection of Avian Influenza Antigens in a Real Biological Matrix. *Anal. Bioanal. Chem.* **2010**, *398*, 2693–2700.
31. Dykstra, P.; Hao, J.; Koev, S. T.; Payne, G. F.; Yu, L.; Ghodssi, R. An Optical MEMS Sensor Utilizing a Chitosan Film for Catechol Detection. *Sens. Actuators, B* **2009**, *138*, 64–70.
32. Mujika, M.; Arana, S.; Castaño, E.; Tijero, M.; Vilares, R.; Ruano-López, J. M.; Cruz, A.; Sainz, L.; Berganza, J. Magnetoresistive Immunosensor for the Detection of *Escherichia coli* O157:H7 Including a Microfluidic Network. *Biosens. Bioelectron.* **2009**, *24*, 1253–1258.
33. Narakathua, B. B.; Atashbara, M. Z.; Bejcek, B. E. Improved Detection Limits of Toxic Biochemical Species Based on Impedance Measurements in Electrochemical Biosensors. *Biosens. Bioelectron.* **2010**, *26*, 923–926.
34. Peng, Z.; Soper, S. A.; Pingle, M. R.; Barany, F.; Davis, L. M. Ligase Detection Reaction Generation of Reverse Molecular Beacons for near Real-Time Analysis of Bacterial Pathogens Using Single-Pair Fluorescence Resonance Energy Transfer and a Cyclic Olefin Copolymer Microfluidic Chip. *Anal. Chem.* **2010**, *82*, 9727–9735.
35. Piliarik, M.; Párová, L.; Homola, J. High-Throughput SPR Sensor for Food Safety. *Biosens. Bioelectron.* **2009**, *24*, 1399–1404.
36. Ricciardi, C.; Canavese, G.; Castagna, R.; Ferrante, I.; Rici, A.; Marasso, S. L.; Napione, L.; Bussolino, F. Integration of Microfluidic and Cantilever Technology for Biosensing Application in Liquid Environment. *Biosens. Bioelectron.* **2010**, *26*, 1565–1570.
37. Freimund, D. L.; Aflatooni, K.; Batelaan, H. Observation of the Kapitza–Dirac Effect. *Nature* **2001**, *413*, 142–143.
38. Squires, T. M.; Quake, S. R. Microfluidics: Fluid Physics at the Nanoliter Scale. *Rev. Mod. Phys.* **2005**, *77*, 977–1026.
39. Bocquet, L.; Charlaix, E. Nanofluidics, From Bulk to Interfaces. *Chem. Soc. Rev.* **2010**, *39*, 1073–1095.
40. Chemburu, S.; Wilkins, E.; Abdel-Hamid, I. Detection of Pathogenic Bacteria in Food Samples Using Highly-Dispersed Carbon Particles. *Biosens. Bioelectron.* **2005**, *21*, 491–499.
41. Leach, K. M.; Stroot, J. M.; Lim, D. V. Same-Day Detection of *Escherichia coli* O157:H7 from Spinach by Using Electrochemiluminescent and Cytometric Bead Array Biosensors. *Appl. Environ. Microbiol.* **2010**, *76*, 8044–8052.
42. Zelada-Guillén, G. A.; Bhosale, S. V.; Riu, J.; Rius, F. X. Real-Time Potentiometric Detection of Bacteria in Complex Samples. *Anal. Chem.* **2010**, *82*, 9254–9260.
43. Banerjee, P.; Bhunia, A. K. Cell-Based Biosensor for Rapid Screening of Pathogens and Toxins. *Biosens. Bioelectron.* **2010**, *26*, 99–106.
44. Salam, F.; Tothill, I. E. Detection of *Salmonella typhimurium* Using an Electrochemical Immunosensor. *Biosens. Bioelectron.* **2009**, *24*, 2630–2636.
45. Tsai, W.; Li, I. SPR-Based Immunosensor for Determining Staphylococcal Enterotoxin A. *Sens. Actuators, B* **2009**, *136*, 8–12.
46. Sharma, S.; Sachdeva, P.; Virdi, J. S. Emerging Water-Borne Pathogens. *Appl. Microbiol. Biotechnol.* **2003**, *61*, 5.
47. Gummow, B. Challenges Posed by New and Re-emerging Infectious Diseases in Livestock Production, Wildlife and Humans. *Livestock Sci.* **2010**, *130*, 41–46.
48. Actis, P.; Jejelowo, O.; Pourmand, N. Ultrasensitive Mycotoxin Detection by STING Sensors. *Biosens. Bioelectron.* **2010**, *26*, 333–337.
49. Tetard, L.; Passian, A.; Farahi, R. H.; Davison, B. H.; Thundat, T. Optomechanical Spectroscopy with Broadband Interferometric and Quantum Cascade Laser Sources. *Opt. Lett.* **2011**, *36*, 3251–3253.
50. Zhu, S.; Du, C.; Fu, Y. Localized Surface Plasmon Resonance-Based Hybrid Au–Ag Nanoparticles for Detection of Staphylococcus aureus Enterotoxin B. *Opt. Mater.* **2009**, *31*, 1608–1613.
51. Ben Rejeb, I.; Arduini, F.; Arvinte, A.; Amine, A.; Gargouri, M.; Micheli, L.; Bala, C.; Moscone, D.; Palleschi, G. Development of a Bio-Electrochemical Assay for AFB1 Detection in Olive Oil. *Biosens. Bioelectron.* **2009**, *24*, 1962–1968.
52. Cozzini, P.; Ingletto, G.; Singh, R.; Dall-Asta, C. Mycotoxin Detection Plays "Cops and Robbers": Cyclodextrin Chemosensors as Specialized Police. *Int. J. Mol. Sci.* **2008**, *9*, 2474–2494.
53. *Foodborne Pathogens: Microbiology and Molecular Biology*; Fratamico, P. M., Bhunia, A. K., Smith, J. L, Eds.; Caister Academic Press: Norfolk, UK, 2008.
54. Schep, L. J.; Temple, W. A.; Butt, G. A.; Beasley, M. D. Ricin as a Weapon of Mass Terror — Separating Fact from Fiction. *Environ. Int.* **2009**, *35*, 1267–1271.
55. Bevilacqua, V. L. H.; Nilles, J. M.; Rice, J. S.; Connell, T. R.; Schenning, A. M.; Reilly, L. M.; Durst, H. D. Ricin Activity Assay by Direct Analysis in Real Time

Mass Spectrometry Detection of Adenine Release. *Anal. Chem.* **2010**, *82*, 798–800.
56. Melchior, W. B., Jr.; Tolleson, W. H. A Functional Quantitative Polymerase Chain Reaction Assay for Ricin, Shiga Toxin, and Related Ribosome-Inactivating Proteins. *Anal. Biochem.* **2010**, *396*, 204–211.
57. Suresh, S.; Gupta, A. K.; Rao, V. K.; Kumar, O.; Vijayaraghavan, R. Amperometric Immunosensor for Ricin by Using on Graphite and Carbon Nanotube Paste Electrodes. *Talanta* **2010**, *81*, 703–708.
58. Zhuang, J.; Cheng, T.; Gao, L.; Luo, Y.; Ren, Q.; Lu, D.; Tang, F.; Ren, X.; Yang, D.; Feng, J.; *et al.* Silica Coating Magnetic Nanoparticle-Based Silver Enhancement Immunoassay for Rapid Electrical Detection of Ricin Toxin. *Toxicon* **2010**, *55*, 142–152.
59. Marinov, I.; Ivanov, Y.; Gabroska, K.; Godjevargova, T. Amperometric Acetylthiocholine Sensor Based on Acetylcholinesterase Immobilized on Nanostructured Polymer Membrane Containing Gold Nanoparticles. *J. Mol. Catal. B* **2010**, *62*, 67–75.
60. Jiang, X.; Li, D.; Xu, X.; Ying, Y.; Li, Y.; Ye, Z.; Wang, J. Immunosensors for Detection of Pesticide Residues. *Biosens. Bioelectron.* **2008**, *23*, 1577–1587.
61. Mandal, P. K.; Biswas, A. K.; CHoi, K.; Paul, U K. Methods for Rapid Detection of Foodborne Pathogens: An Overview. *Am. J. Food Technol.* **2011**, *6*, 87–102.
62. Van Neste, C. W.; Senesac, L. R.; Thundat, T. Standoff Spectroscopy of Surface Adsorbed Chemicals. *Anal. Chem.* **2009**, *81*, 1952–1956.
63. Farahi, R. H.; Passian, A.; Tetard, L.; Thundat, T. Pump-Probe Photothermal Spectroscopy Using Quantum Cascade Lasers. *J. Phys. D* **2012**, *45*, 125101.
64. Gan, N.; Yang, X.; Xie, D.; Wu, Y.; Wen, W. A Disposable Organophosphorus Pesticides Enzyme Biosensor Based on Magnetic Composite Nano-Particles Modified Screen Printed Carbon Electrode. *Sensors* **2010**, *10*, 625–638.
65. Mahmoud, K. A.; Hrapovic, S.; Luong, J, H, T. Picomolar Detection of Protease Using Peptide/Single Walled Carbon Nanotube/Gold Nanoparticle-Modified Electrode. *ACS Nano* **2008**, *2*, 1051–1057.
66. Doorneweerd, D. D.; Henne, W. A.; Reifenberger, R. G.; Low, P. S. Selective Capture and Identification of Pathogenic Bacteria Using an Immobilized Siderophore. *Langmuir* **2010**, *26*, 15424–15429.
67. Xu, S.; Mutharasan, R. Detection of *Cryptosporidium parvum* in Buffer and in Complex Matrix Using PEMC Sensors at 5 Oocysts mL^{-1}. *Anal. Chim. Acta* **2010**, *669*, 81–86.
68. Banerjee, P.; Bhunia, A. K. Mammalian Cell-Based Biosensors for Pathogens and Toxins. *Trends Biotechnol.* **2009**, *27*, 179–188.
69. Mao, C.; Liu, A.; Cao, B. Virus-Based Chemical and Biological Sensing. *Angew. Chem., Int. Ed.* **2009**, *48*, 6790–6810.
70. Li, S.; Li, Y.; Chen, H.; Horikawa, S.; Shen, W.; Simonian, A.; Chin, B. A. Direct Detection of *Salmonella typhimurium* on Fresh Produce Using Phage-Based Magnetoelastic Biosensors. *Biosens. Bioelectron.* **2010**, *26*, 1313–1319.
71. Tombelli, S.; Minunni, M.; Mascini, M. Analytical Applications of Aptamers. *Biosens. Bioelectron.* **2005**, *20*, 2424–2434.
72. Ding, S.; Gao, C.; Gu, L.-Q. Capturing Single Molecules of Immunoglobulin and Ricin with an Aptamer-Encoded Glass Nanopore. *Anal. Chem.* **2009**, *81*, 6649–6655.
73. Wig, A.; Arakawa, E. T.; Passian, A.; Ferrell, T. L.; Thundat, T. Photothermal Spectroscopy of *Bacillus anthracis* and *Bacillus cereus* with Microcantilevers. *Sens. Actuators, B* **2006**, *114*, 206–211.
74. Meier, D. C.; Taylor, C. J.; Cavichi, R. E.; V, E. W.; Ellzy, M. W.; Sumpter, K. B.; Semancik, S. Chemical Warfare Agent Detection Using MEMS-Compatible Microsensor Arrays. *IEEE Sens. J.* **2005**, *5*, 712–725.
75. Senesac, L. R.; Yi, D.; Greve, A.; Hales, J. H.; Davis, Z. J.; Nicholson, D. M.; Boisen, A.; Thundat, T. Micro-Differential Thermal Analysis Detection of Adsorbed Explosive Molecules Using Microfabricated Bridges. *Rev. Sci. Instrum.* **2009**, *80*, 035102.
76. Greve, A.; Olsen, J.; Privorotskaya, N.; Senesac, L.; Thundat, T.; King, W. P.; Boisen, A. Micro-Calorimetric Sensor for Vapor Phase Explosive Detection with Optimized Heat Profile. *Microelectron. Eng.* **2010**, *87*, 696–698.
77. Tetard, L.; Passian, A.; Eslami, S.; Jalili, N.; Farahi, R. H.; Thundat, T. Virtual Resonance and Frequency Difference Generation by van der Waals Interaction. *Phys. Rev. Lett.* **2011**, *106*, 180801.
78. Tetard, L.; Passian, A.; Farahi, R. H.; Thundat, T. Atomic Force Microscopy of Silica Nanoparticles and Carbon Nanohorns in Macrophages and Red Blood Cells. *Ultramicroscopy* **2010**, *110*, 586–591.
79. Kim, S.; Yi, D.; Passian, A.; Thundat, T. Observation of an Anomalous Mass Effect in Microcantilever-Based Biosensing Caused by Adsorbed DNA. *Appl. Phys. Lett.* **2010**, *96*, 153703.
80. Velusamy, V.; Arshak, K.; Korostynska, O.; Oliwa, K.; Adley, C. An Overview of Foodborne Pathogen Detection: In the Perspective of Biosensors. *Biotechnol. Adv.* **2010**, *28*, 232–254.
81. Concina, I.; Falasconi, M.; Gobbi, E.; Bianchi, F.; Musci, M.; Mattarozzi, M.; Pardo, M.; Mangia, A.; Careri, M.; Sberbeglieri, G. Early Detection of Microbial Contamination in Processed Tomatoes by Electronic Nose. *Food Control* **2009**, *20*, 873–880.
82. Suárez, G.; Jin, Y.-H.; Auerswald, J.; Bershtold, S.; Knapp, H. F.; Diserens, J.-M.; Leterrier, Y.; Månson, J.-A. E.; Voirin, G. Lab-on-a-Chip for Multiplexed Biosensing of Residual Antibiotics in Milk. *Lab Chip* **2009**, *9*, 1625–1630.
83. Varshney, M.; Li, Y.; Srinivasan, B.; Tung, S. A Label-Free, Microfluidics and Interdigitated Array Microelectrode-Based Impedance Biosensor in Combination with Nanoparticles Immunoseparation for Detection of *Escherichia coli* O157:H7 in Food Samples. *Sens. Actuators, B* **2007**, *128*, 99–107.
84. Fiegel, F.; Buhl, A.; Jaekel, H.-P.; Werle, E.; Schmolke, M.; Ollert, M.; Luppa, P. B. Autoantibodies to Double-Stranded DNA-Intermethod Comparison between Four Commercial Immunoassays and a Research Biosensor-Based Device. *Lupus* **2010**, *19*, 957–964.
85. Ruiz-Altisent, M.; Ruiz-Garcia, L.; Moreda, G. P.; Lu, R.; Hernandez-Sanchez, N.; Correa, E. C.; Diezma, B.; Nicolaï, B.; García-Ramos, J. Sensors for Product Characterization and Quality of Specialty Crops—A Review. *Comput. Electron. Agric.* **2010**, *74*, 176–194.
86. Lee, W. S.; Alchanatis, V.; Yang, C.; Hirafuji, M.; Moshou, D.; Li, C. Sensing Technologies for Precision Specialty Crop Production. *Comput. Electron. Agric.* **2010**, *74*, 2–33.
87. Chun, A. L. Will the Public Swallow Nanofood? *Nat. Nanotechnol.* **2009**, *4*, 790–791.
88. Morris, J.; Willis, J.; De Martinis, D.; Hansen, B.; Laursen, H.; Sintes, J. R.; Kearns, P.; Gonzalez, M. Science Policy Considerations for Responsible Nanotechnology Decisions. *Nat. Nanotechnol.* **2011**, 73–77.
89. Kelly, T. L.; Garcia Sega, A.; Sailor, M. J. Identification and Quantification of Organic Vapors by Time-Resolved Diffusion in Stacked Mesoporous Photonic Crystals. *Nano Lett.* **2011**, *11*, 3169–3173.
90. Brookes, J. C.; Hartoutsiou, F.; Horsfield, A. P.; Stoneham, A. M. Could Humans Recognize Odor by Phonon Assisted Tunneling? *Phys. Rev. Lett.* **2007**, *98*, 038101.