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REVIEW PAPER

Nanoparticle-based Sensors

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ABSTRACT

Nanoparticles exhibit several unique properties that can be applied to develop chemical and biosensors possessing desirable features like enhanced sensitivity and lower detection limits. Gold nanoparticles are coated with sugars tailored to recognise different biological substances. When mixed with a weak solution of the sugar-coated nanoparticles, the target substance, e.g., ricin or *E.coli*, attaches to the sugar, thereby altering its properties and changing the colour. Spores of bacterium labeled with carbon dots have been found to glow upon illumination when viewed with a confocal microscope. Enzyme/nanoparticle-based optical sensors for the detection of organophosphate (OP) compounds employ nanoparticle-modified fluorescence of an inhibitor of the enzyme to generate the signal for the OP compound detection. Nanoparticles shaped as nanoprisms, built of silver atoms, appear red on exposure to light. These nanoparticles are used as diagnostic labels that glow when target DNA, e.g., those of anthrax or HIV, are present. Of great importance are tools like gold nanoparticle-enhanced surface-plasmon resonance sensor and silver nanoparticle surface-enhanced portable Raman integrated tunable sensor. Nanoparticle metal oxide chemiresistors using micro electro mechanical system hotplate are very promising devices for toxic gas sensing. Chemiresistors comprising thin films of nanogold particles, encapsulated in monomolecular layers of functionalised alkanethiols, deposited on interdigitated microelectrodes, show resistance changes through reversible absorption of vapours of harmful gases. This paper reviews the state-of-the-art sensors for chemical and biological terror agents, indicates their capabilities and applications, and presents the future scope of these devices.

Keywords: Nanoparticles, nanomaterials, chemical warfare, biological warfare, toxins, sensors, biosensors, quantum dots, chemiresistors

1. INTRODUCTION

Sensors for the detection of hazardous gases and disease-causing pathogens are indispensable for military and homeland security. Chemical and biological warfare, involve the purposeful introduction of toxic gases and deadly germs by combatants in the environment of the opponent territory, through air, water, and soil contamination, malignly aiming at wide-scale destruction of human beings, livestock, and plants. Such warfare has been recorded all through history, and its threat is a growing trepidation. The soaring concern for such warfare is expressed in literature[1-17].

A chemical warfare agent (CWA) is intended for use by armed forces to kill, gravely injure or debilitate people because of its physiological effects. The CWAs (Fig. 1) comprise nerve agents like GA (Tabun), dimethylphosphoramidocyanidic acid, ethyl ester; GB (Sarin), 2-(fluoro-methylphosphoryl) oxypropane; GD (Soman), 3-(fluoro-methylphosphoryl)oxy-2, 2-dimethyl-butane, etc. A biological warfare agent (BWA) is a pathogen (disease-causing microorganism) or a toxin derived from a living organism that is deliberately used to induce disease or death in humans, animals, or plants. Biological warfare agents include bacterial agents (bacillus anthracis; the biodeterrents are anthrax spores), viral agents like smallpox, fungal agents, e.g., Coccidioides immitis. and toxins such as cholera toxin (CT), ricin, etc.

Because methods for detection of these warfare agents are currently inadequate, the development of highly sensitive sensors with detection[18] capability ~ 10 parts per billion (ppb) = 10 nanomole/mole is crucial for early warning of these agents to render the possibility of their neutralisation through appropriate countermeasures. Therefore small, low-power sensors are necessary for hand-held instruments to qualitatively detect whether an attack has been made, without prompting false alarms (referred to as detect-to-protect devices). Sensors are also required to quantitatively estimate the magnitude of the attack for treatment of people (detect-to-treat devices).

Nanotechnology has provided an impetus to the development of high-speed and high-sensitivity devices with small cross-talk[19,20]. A nanoparticle is a particle with at least one dimension < 100 nm. Novel properties that distinguish nanoparticles from the bulk material typically originate from their enormously vast surface area showing a dominance of the surface properties over bulk properties. Also, semiconductor nanostructures called quantum dots in which the motion of conduction band electrons, valence

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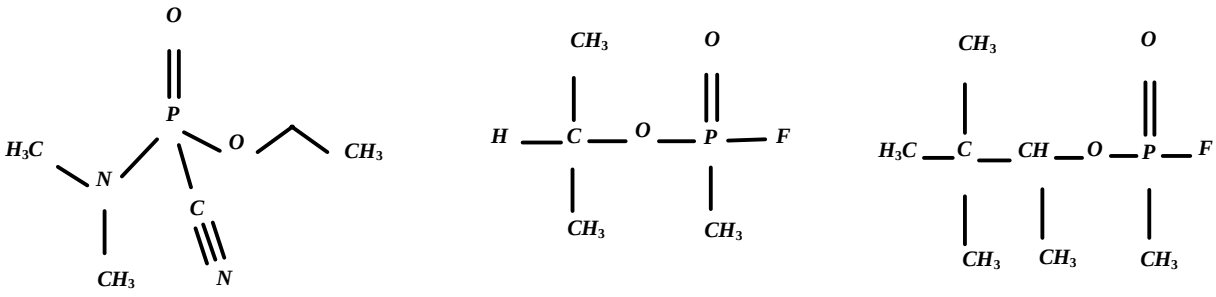

(a) Tabun (b) Sarin (c) Soman

Figure 1. Structural formulae of some chemical warfare agents.

band holes, or excitons is confined in all the three spatial directions[21], have been used for sensing applications. Quantum dots can be as small as 2 nm to 10 nm.

This review paper outlines the important issues with regards to the development of both detect-to-protect and detect-to-treat category of nanoparticle-based sensors for CWAs and BWAs. The current status, advantages and limitations of these devices are presented.

2. OPTICAL SENSORS

2.1 Surface Plasmon-absorption-based Colour-change Sensors

The technique for detection of biological warfare agents being developed by Hone[22], *et al*. is based on the coating of metal nanoparticles with different carbohydrates or sugars that identify particular biological substances. The substance binds to the carbohydrate or sugar, which causes a solution containing the nanoparticles to change its colour (e.g., gold particles were found to change colour from red to blue), revealing the presence of the substance.

As pointed out by Hone[22], *et al.*, the optical characteristics of metal nanoparticles are governed by the coherent oscillations of the conduction band electrons caused by an interacting electromagnetic field. This absorption of light is known as surface plasmon absorption (colour). The surface plasmons are the oscillating plasma waves due to the oscillation of mobile electrons (or plasma) at the surface of the metal film. The term 'plasmon' refers to the collective excitation of electrons in a metal and surface plasmon is one confined to the surface. Plasmonics comprises the study of these particular light-matter interactions. The surface plasmon absorption depends upon the dielectric properties of the metal, the size and shape of the particles, and the surrounding medium. Gold nanoparticles characteristically have a large surface plasmon absorption band centred at 520 nm, and thus aqueous solutions of gold nanoparticles appear red. Upon aggregation, these nanoparticles come closer and coupling interactions cause a shift in the surface plasmon absorption to lower energies.

Vreugdenhil[23], *et al*. reported that on encapsulation of gold nanoparticles in cross-linked sol-gel matrices, the particle size and size distribution were found to increase. Further, a significant red shift in the surface plasmon absorbance band was observed: 520–545 nm at low nanoparticle concentrations and 565 nm at high nanoparticle concentrations**.** They noticed that upon gold nanoparticle encapsulation, a colour change occurred from red to red-purple due to the red shift of the surface plasmon absorption from 525 nm to 565 nm. To establish whether the shift in the surface plasmon absorbance band was dependent on nanoparticle concentration, a series of experiments were carried out by Vreugdenhil[23], *et al*. in which the concentration of the gold nanoparticles was varied between 10 per cent and 100 per cent of the stock solution. The resulting gold nanoparticle solutions were encapsulated in the sol-gel matrix. It was observed that samples in which the nanoparticle concentration was low showed a shift of the surface plasmon between 525 nm to 545 nm. Higher concentrations of gold nanoparticles produced a shift to 565 nm.

A solution of nanoparticles changes colour when the particles cluster. It is also important to ensure that this colour change occurs even in the presence of small amounts of harmful substances enabling the security personnel to deal promptly with dangerous substances and avoid taking unnecessary, time-consuming precautions. Thus, harnessing the ability of coated metal particles to change colour in the presence of toxins, viruses, and bacteria, the above technique seeks to provide a quick affirmative/negative indication of the safety of substances found in the battlefields, at the crime scenes, in luggage or in possession of suspected criminals. This technique has the potential to be incorporated in an easy-to-use, portable, field instrument in contrast to mostly laboratory-based methods of identifying bioterrorist materials. The method could even be adapted to help detect water infected with cholera and other diseases as a result of natural calamities.

2.2 Gold Nanoparticle-enhanced Surface-plasmon Resonance Sensor

If the interface between two transparent media of different refractive indices is coated with a thin layer of noble metal such as gold, and incident light is monochromatic and plane-polarised, then there exists an angle greater than the critical angle at which the loss in intensity of light is greatest and at which the intensity of reflected light reaches a minimum. This angle is called the surface plasmon resonance (SPR) angle. When the wave vector of the incident light matches

with the wavelength of the surface plasmons, the electrons resonate, hence the term 'surface plasmon resonance'.

These resonance conditions are influenced by the material adsorbed onto the thin metal film. A linear relationship is observed between resonance energy and mass concentration of biochemically relevant molecules such as proteins, sugars and DNA. The SPR signal, which is expressed in resonance units, therefore provides a measurement of mass concentration at the sensor chip surface[24].

In practice, SPR-based instruments utilise an optical method to measure the refractive index near (within ~300 nm) a sensor surface. To detect an interaction, one type of molecule (the ligand) is immobilised onto the sensor surface. Its binding partner (the analyte) is injected in aqueous solution. As the analyte binds to the ligand, the accumulation of the binding product on the surface leads to an increase in the refractive index. This change in refractive index is measured in real time, and the result is plotted as response or resonance units (RUs) versus time (a sensorgram)[25].

The miniature SPR sensing chip, described by Soelberg[26], *et al*. and Chinowsky[27, 28], *et al*., is a fully integrated SPR sensor element. Its main components (Fig. 2) are a light emitting diode (LED) source, a gold SPR surface, a reflecting mirror that directs the reflected light to a photodiode array and a temperature sensor. Signal conditioning of the output from the sensor element is performed by a digital signal-processing chip. Then the signal is fed to a computer, which produces and displays both the SPR curves and a plot of refractive index versus real-time. Each sensor element has three separate channels that are individually derivatised with a specific antibody. A cast polydimethylsilane (PDMS) fluidics system is used for this purpose. Parallel derivatisation

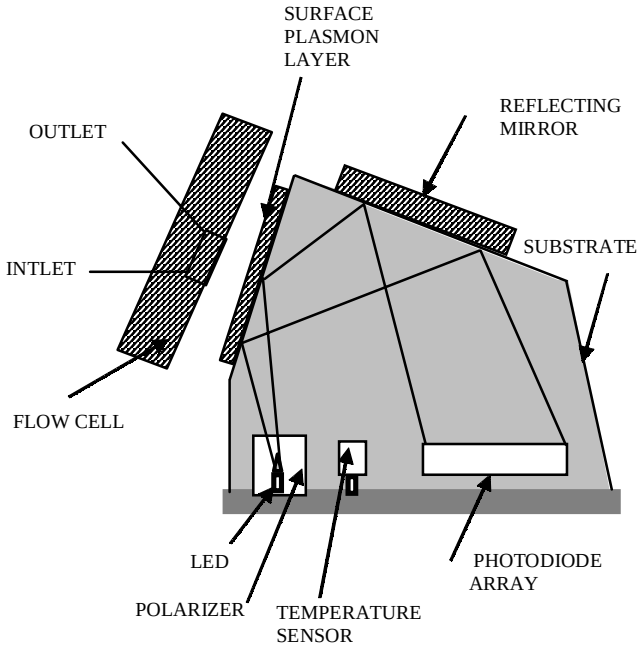

Figure 2. Schematic diagram of surface plasmon resonance sensor[26-28].

of several sensor elements with antibodies is possible. After the conjugation of antibodies to the sensor surface, the sensor elements are fitted into a cast PDMS flow cell. Here, the input flow covers all three channels of one sensor element before flowing to the next element. It is also possible to use flow cells that keep the channels separated.

Antibodies labeled with colloidal gold provide still further amplification. He[29], *et al*. have reported amplification factors as high as 1,000-fold using gold nanoparticles. Soelberg[26], *et al*. reported 20-fold amplification in preliminary experiments using this protocol. Target analytes such as viruses, microbes and spores can be detected.

These low-cost, small, portable systems will find many different applications in detecting the agents used in chemical and biological terrorism activities.

2.3 Fluorescence-quenched Sensors

Kim[30], *et al*. have reported the synthesis of the fluorescent mannose-substituted poly (para phenyleneethynylene) mPPE 5 and its interaction with concanavalin A (ConA), the lectin of the jack bean. They demonstrated that PPE 5 was an excellent fluorescent biosensor for lectins. Concanavalin A (ConA), the lectin of the jack bean, causes fluorescence quenching of a mannose-substituted poly (para phenyleneethynylene) mPPE 5. Fluorescence quenching is the decrease in fluorescence intensity of a substance. Fluorescence or cold light is the phenomenon in which a molecule absorbs light, promoting one or more of the electrons into a higher energy state, which is subsequently lost from these unstable excited electronic states, with emission of light. While ConA is harmless, lectins such as ricin are toxic proteins. The above serves as an effective and sensitive detection method for ConA by fluorescence quenching of the multivalent mannoside 5.

2.4 Fluorescent Polymer-coated Carbon Dot Sensors

Fluorescent semiconductor quantum dots have aroused excitement for a wide variety of applications[31]. Sun[32], *et al*. have developed a new type of quantum dot from carbon. The carbon nanoparticles, due partly to their enormous surface area, are endowed with unusual chemical and physical properties that are different from that of bulk state. Similar to their metallic counterparts, these nano-sized carbon dots glow brightly when exposed to light. The luminescence emission of the carbon dots is stable against photobleaching. Moreover, there is no blinking effect. These strongly emissive carbon dots may find applications like those of silicon or even beyond silicon. In addition, the carbon-based quantum dots show less potential for toxicity and environmental damage. They will be less expensive than metallic quantum dots.

Using nanoparticles produced from graphite, Sun[32], *et al*. demonstrated that when these carbon nanoparticles were covered with special polymers like poly (ethylene glycol) and poly (propionylethyleneimine-co-ethyleneimine), they glowed brightly on exposure to light, behaving like tiny specks of light. The dots glowed continuously as long as

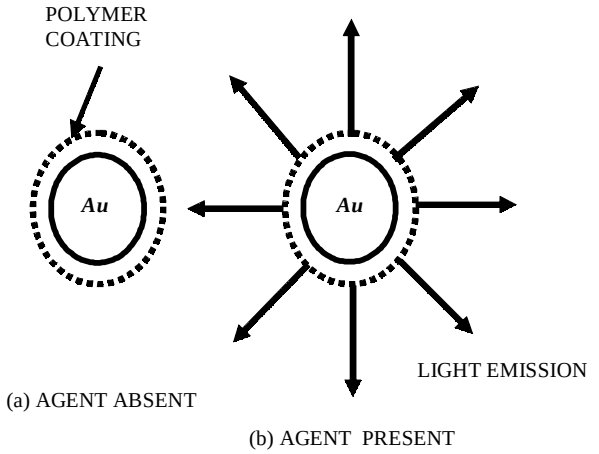

Figure 3. Diagrammatic representation of polymer-coated carbon dot glow sensor.

an optical source was present. These nanosize carbon particles, upon simple surface passivation, were strongly photoluminescent in both solution and in the solid state. Their spectral features and properties were comparable to those of surface-oxidised silicon nanocrystals. The two-sided polymer coating allowed researchers to attach antibodies or other labeling materials to the carbon dot. In laboratory investigations, the researchers successfully labeled anthrax-like spores with luminescent carbon dots. This study confirmed the glow of spores that were easily viewed under a microscope (Fig. 3). This would help in the development of sensors that emit light in the presence of a target, such as anthrax or even food-borne pathogens. Reasonably priced disposable sensors capable of detecting concealed explosives and biological warfare agents such as anthrax are among the possibilities envisaged by the researchers.

2.5 Immunoassays using *CdSe-ZnS* Core-shell Quantum Dot Fluorescent Biosensors

The photophysical properties of quantum dots (QDs) have enabled the creation of a new generation of robust fluorescent biosensors. The advantages offered by QDs over conventional dyes have led to their progressively wide usage in immunoassay detection[33]. Goldman and coworkers[34] have been at the vanguard of small molecule detection using antibody-conjugated QDs, as exemplified by the immuno-detection of the explosive 2,4,6-trinitrotoluene (TNT). Using microtiter well plates functionalised with captured antibodies, Goldman[35], *et al.* developed sandwich immunoassays that were specific for *Staphylococcal enterotoxin B* (SEB) and cholera toxin. These immunoassays were applied for the simultaneous detection of four toxins: cholera toxin, ricin, shiga-like toxin 1 and SEB, in a single microtiter well. Captured antibodies immobilised in a microtiter well plate were exposed to the mixed toxin sample. Later, antibodies specific for each of the toxins coupled to a different colour QD were added to the microtiter well plate. The resultant signal obtained from the mixed toxin samples was deconvoluted employing a simple algorithm.

In another example, QD-antibody bioconjugates were used to identify and differentiate between diphtheria toxin and tetanus toxin proteins. These proteins were non-specifically immobilised onto poly-L-lysine coated cover slips. Detection methods for biotoxins like ricin, SEB and T-2 toxin have been reviewed by Ler[36], *et al.*

2.6 Nanoparticle-modified Fluorescence of Enzyme Inhibitor

The operational principle of an enzyme/nanoparticle-based sensor[37] for the detection of OP compounds is the nanoparticle-modified fluorescence of an inhibitor of the enzyme to generate the signal for the OP compound detection. A gold nanoparticle is covalently bound to an enzyme molecule. A fluorophore decoy, being a feeble competitive inhibitor of OPH with an identical chemical structure to the substrate (i.e., analyte of interest), is introduced to the solution and is bound to the OPH active site. If the gold nanoparticle attached via amino- or sulfhydryl-groups to the OPH is at a certain distance from the decoy, typically between about 10 nm and 40 nm, improvement in fluorescent emission is observed. According as the quantum efficiency of the fluorophore is low or high, the potential enhancement, when the decoy is bound to the enzyme-gold complex, is greater or less. However, if the gold nanoparticle is at a distance > ~ 40 nm from the fluorophore, then fluorescence is unaltered by the presence of the gold. Consequently, the magnitude of the fluorescence signal is reduced. Once the decoy is bound to the OPH active site, it is possible to check for the presence of the analyte of interest (which is a substrate of OPH). If the substrate is present, then the analyte displaces the decoy because of its much stronger affinity for the OPH active site. As a result, there is a change in the fluorescence signal of the sample. For an enhancement-based sensor, the analyte displaces the decoy bound to the enzyme active site. With the shifting away of the decoy from the gold nanoparticle, its fluorescence intensity changes. This variation in fluorescence intensity is correlated with the concentration of analyte present in the solution.

To corroborate the feasibility of this approach, OPH-gold nanoparticle conjugates were prepared[37]. These were incubated with a fluorescent enzyme inhibitor or decoy. The fluorescence intensity of the decoy was sensitive to the proximity of the gold nanoparticle. Therefore it could be used to indicate that the decoy was bound to the OPH. Then different paraoxon concentrations were introduced to the OPH–nanoparticle–conjugate–decoy mixtures and the normalised ratios of fluorescence intensities were measured. Maximum sensitivity to paraoxon was recorded when decoys and OPH–gold nanoparticle conjugates were present at near-equimolar levels. The change in fluorescence intensity was linked to paraoxon concentration in the solution.

2.7 Nanoparticles of Different Shapes and Nanoprism Sensors

Nanoparticles are made in a limited variety of geometric shapes, such as spheres, rods, tetrapods, and dumbbells. Shapes of nanoparticles play an important role in determining

their properties. Willets and Van Duyne[38] have mentioned about the impact of nanoparticle shape and size on both the spectral location of the localised surface plasmon resonance (LSPR) and its sensitivity to changes in the local refractive index. Because the shape and size of a metallic nanoparticle dictates the spectral signature of its plasmon resonance, the ability to fabricate nanoparticles of varying shape, size, and material and study the effect on the LSPR is an experimental challenge of great consequence. It must be clarified that these different shapes are the geometric profiles of nanomaterials and not nanoparticles. These shapes have been a major factor in advancing the understanding and application of LSPR spectroscopy. Lithographic techniques allow the fabrication of periodic arrays with specific particle shape, placement, and orientation. Mention may be made of one particularly useful form of lithography called nanosphere lithography (NSL)[38].

Jin[39], *et al*. have created a nanoparticle with a new shape that could be useful to detect biological threats. The nanoprism, which has a resemblance to a minuscule Dorito, exhibits unusual optical properties. It is helpful in improving biodetectors, allowing testing of a number of biological warfare agents or diseases. The nanoprisms, made up of silver (*Ag*) atoms, showed a rich red colour when exposed to light. These nanoparticles could be used as new diagnostic labels, lighting up when target DNA of anthrax or HIV was present. By developing nanoprisms made of different materials and with varying shapes and sizes, a large number of multicolour diagnostic labels will be available.

Once the technology is optimised, biodetectors incorporating nanoprisms could be used to easily and accurately detect biological weapons such as anthrax, smallpox, and tuberculosis, and a broad assortment of genetic and pathogenic diseases. The applications span over a broad range encompassing from genetic markers for cancer and neurodegenerative diseases to HIV and sexually transmitted diseases[39].

2.8 Raman Integrated Tunable Sensor Coupled with Surface-enhanced Raman Scattering Substrates

Surface-enhanced Raman scattering (SERS) substrates are made of silver nanoparticle island films, silver colloids, silver-oxide thin films, and silver nanoclusters[40]. The field-deployable instrument[40], consisting of an 830 nm diode laser for excitation and an avalanche photodiode (APD) for detection, is a fully integrated, tunable, point-and-shoot Raman device. It is based on solid-state acousto-optic tunable filter (AOTF) technology. To confirm the ability of the instrument to detect low sample concentrations, a series of SERS measurements were performed on various compounds of particular interest for homeland defence applications[40]. This included organophosphorus agents and BWAs that were observable in the low picogram (pg) and ppm ranges using the portable Raman instrument in the SERS mode. The SERS spectra were recorded from methyl parathion (a nerve agent simulant) and dipicolinic acid, which is indicative of *Bacillus endospore* detection. In this assay, 28 ng of methyl parathion or 50 ppm dipicolinic acid was adsorbed on to silver colloids in a plastic vial. The limiting boundary of detection (LOD) for the organophosphorus agent, methyl parathion was ~3 pg.

3. MAGNETIC NANOPARTICLE-BASED BIOSENSORS

The use of magnetic nanoparticles has been reported for the detection of interaction between biotin and streptavidin by Arakaki[41], *et al*. Nikitin[42], *et al*. have described a magnetic nanoparticle-based biosensor. Meyer[43], *et al*. presented a magnetic biosensor for *Yersinia pestis*, which is the causative agent of the plague. It is a non-motile, gram-negative bacterium. The biosensor applies an immunosensoric detection method based on the *Yersinia pestis* YP19 antibody. This antibody binds to the fraction 1 (F1) capsule protein. Magnetic beads are small, chiefly globular, iron oxide containing particles, available at diameter sizes of nm up to hundreds of μm. The sensor works on the detection and quantification of magnetic beads by two frequency-mixing resonant coils. The normal magnetic bead organisation contains an iron oxide (magnetite) core providing the paramagnetic attraction of the particles to a magnet. The beads are detected in a magnetic field, created in a special magnetic measurement head, through their paramagnetic properties. The observed detection limits of 2.5 ng/ml in PBS buffer and human blood serum and the linear detection range of 25–300 ng/ml F1 are comparable with other high sensitivity and fast biosensor methods. The system offers the customer an easy, transportable and highly sensitive measuring system.

4. ZIRCONIA–NANOPARTICLE-BASED ELECTROCHEMICAL SENSORS

Liu and Lin[44] have reported an electrochemical sensor for the detection of organophosphate pesticides and nerve agents. They have used zirconia (ZrO_2) nanoparticles as selective sorbents. The ZrO_2 nanoparticle-based electrochemical sensing protocol entailed electrodynamical deposition of ZrO_2 nanoparticles onto a gold electrode surface by cycling the potential between –1.1 and + 0.7 V (versus *Ag*/*AgCl*) at a scan rate of 20 mV/s for 10 consecutive scans. This was followed by OP adsorption, and electrochemical stripping detection of adsorbed electroactive OPs. The researchers[44] evaluated the electrochemical characterisation and anodic stripping voltammetric performance of bound nitroaromatic OP compounds by cyclic voltammetric and square-wave voltammetric (SWV) analysis. The encouraging stripping voltammetric performances offered novel opportunities for rapid, simple, and sensitive analysis of OPs. A use-and-throw screen-printed gold electrode and portable electrochemical instrument will prove advantageous for the field monitoring of organophosphate pesticides.

5. NANOWIRE OR NANOTUBE-BASED FET SENSORS FOR VIRUS DETECTION

The detection of a single virus has been established by Lieber[45-48], *et al*. using a silicon nanowire field-effect

transistor (FET). Nanowire or nanotube-based FETs have been used by a number of researchers for the detection of protein binding, enzyme activity and even for detecting small molecules such as oxygen. All of these biosensors work on the same underlying principle of a change in resistance through the nanotube or nanowire brought about by the biorecognition event. The Lieber group's contemporary contribution is the first instance of this highly attractive transduction technology being employed for biological agents. Furthermore, the ability of the biosensor to detect viruses has been performed with both pure and unpurified virus solutions with analogous results. Recent work by this group has also shown that these nanowire-based FETs can work in protein samples with no evidence of non-specific binding.

6. CHEMIRESISTOR GAS SENSORS USING METAL OXIDE AND NANOPARTICLES

Chemiresistors or gas-sensing resistors, represent a major category of gas sensors[49]. Their electrical resistance changes in the presence of an oxidising or reducing gas. Apart from metal oxides, which have found widespread application, the use of metal nanoparticles embedded in an organic matrix has proved to be immensely useful. Metal nanoparticle sensors operate at room temperatures while metal oxide nanoparticle devices require elevated temperature platforms (typically 200–500 °C). The former approach is more versatile but is limited by thermal instability.

6.1 Metal Oxide Nanoparticle-based Chemiresistor Sensors

The gas-sensing film, e.g., tin oxide (SnO_2), titanium dioxide (TiO_2), tungsten oxide (WO_3), etc., is deposited over a pair of interdigitated gold or platinum electrodes. The sensor operates through a transference in the equilibrium of the surface oxygen reaction by the presence of the target analyte. A reducing gas increases the conductivity of an *N*-type semiconductor and decreases the same for a *P*-type semiconductor, whereas an oxidising gas behaves conversely. Since the surface oxygen chemisorption reaction determines the sensor response, the use of nanoparticulate metal oxides increases the sensitivity as well as response and recovery times of the sensor as compared to microcrystalline materials by virtue of their larger surface-to-bulk ratio. Xu[50], *et al*. observed that for porous sintered and stabilised SnO_2 sensors, in the nanoparticle size range 5–32 nm, for H_2, *CO* and $i\text{-}C_4H_{10}$, the sensitivity increased sharply with reduction in grain diameter. Furthermore, a smaller film thickness along with larger porosity increased the sensitivity and lowered the response time of the sensor. Doping of the metal oxide with suitable metals provided catalytically active sites for a particular analyte, thereby improving the selectivity for it.

The nanoparticle film is deposited over a microhotplate (μHP) fabricated by microelectromechanical system (MEMS) technology employing microfabrication and micromachining processes[51]. It consists of a polysilicon meander heater over a silicon dioxide-silicon nitride platform (Fig. 4). The heater is capped by another insulating oxide layer upon which a pair of interdigitated platinum electrodes is patterned. The nanostructured SnO_2 film[52-58] lies over this electrode pair. It is deposited by RF sputtering or organo-metallic chemical vapour deposition (OMCVD) techniques. The film thickness[52] is ~100–210 nm. These sensor elements showed high signal-to-noise ratios and reproducibility to CWAs like GA, GB, and HD in the concentration range 5–200 ppb in dry air at heater temperatures (325–475 °C). The 200 ms pulsed temperature-programmed sensing over the temperature range 20–480°C was found to augment analyte selectivity.

6.2 Metal Nanoparticle-based Chemiresistor Sensors

Here, the metal nanoparticles provide electronic conductivity while the organic matrix furnishes the selective binding sites on which the adsorption of analyte molecules takes place. An attractive feature of this approach is the ability to control the sensor properties by molecular design. Wohltjen and Snow[58] demonstrated a chemiresistor consisting of a film of octanethiol-encapsulated gold nanoparticles deposited on interdigitated electrodes. This chemiresistor showed a fast, reversible response towards toluene,

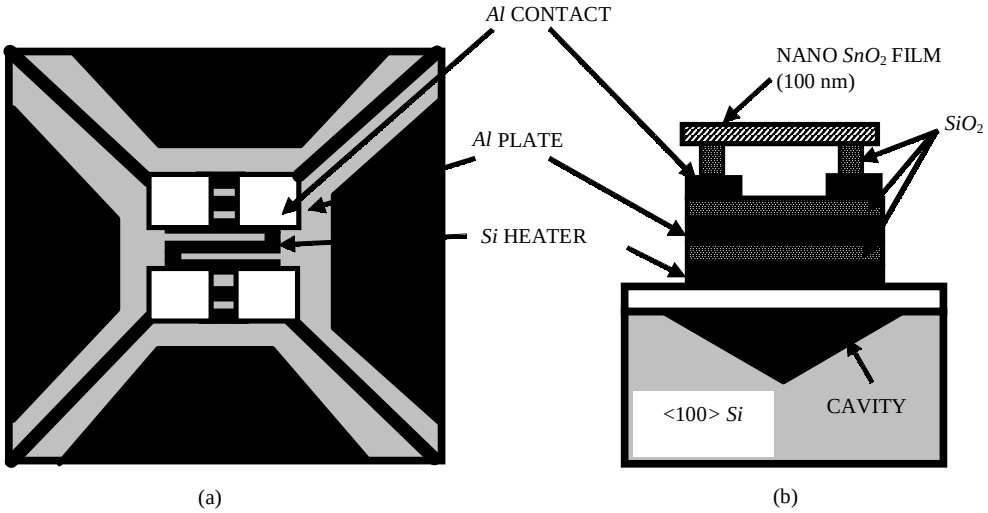

Figure 4. Microhotplate: (a) Top view and (b) cross-section[52].

Table 1. Summary of sensors for warfare agents

Detection mode	Sensor	Tansduction principle	Sensor category
Optical	Carbohydrate-coated metal nanoparticles	Surface plasmon-absorption-based colour change	Biosensor
Optical	*Au* nanoparticle-enhanced surface-plasmon resonance sensor	SPR curves	Biosensor
Optical	Fluorescence-quenched sensors	Fluorescence quenching	Biosensor
Optical	Polymer-coated carbon quantum dots	Fluorescence	Biosensor
Optical	Quantum dot immunoassay using *CdSe-ZnS* core-shell QD biosensors	Fluorescence resonance energy transfer and multiplexed analysis using different colours of quantum dot fluororeagents	Biosensor
Optical	Nanoparticle-modified fluorescence of enzyme inhibitor	Fluorescence intensity change	Biosensor
Optical	Nanoprism	Light emission (Multicolour diagnostic labeling)	Biosensor
Optical	Surface-enhanced Raman scattering (SERS) substrates of silver nanoparticle	SERS spectra	Biosensor
Electrical/ Magnetic	Magnetic nanoparticle- based sensor	Detection of generated frequency mixing components by the differentially wound pickup coil	Biosensor
Electrochemical	Zirconia nanoparticle- based sensor	Voltammetry	Chemical sensor
Electrical	Nanowire- or nanotube-based FETs	Resistance change	Chemical sensor
Electrical	Metal-oxide nanoparticle-based chemiresistor	Resistance change	Chemical sensor
Electrical	Metal nanoparticle-based chemiresistor	Resistance change	Chemical sensor

tetrachloroethene, 1-propanol and water vapours. Later, several other groups[59] reported the tenability of the selectivity of sensor films by introducing chemical functionality into the organic ligand shell. Joseph[60], *et al*. showed the detection of *CO* and NH_3 in the 300 ppb to 5000 ppm range by cross-linking gold and platinum nanoparticles with nonanedithiol.

7. CONCLUSIONS AND FUTURE PERSPECTIVES

In this paper, the overall scenario of the trend in the detection methodologies for various warfare agents using nanoparticle-based sensors was portrayed (Table 1). Optical sensors, especially the optical biosensors hold a great potential in the detection of BWAs. The commonest method of detecting and quantitating biomolecules still remains the use of fluorescence. Nanomaterials such as quantum dots have opened new avenues of research and provide truly inimitable materials for developing new tools in chemical and biological sciences. Apart from these, surface plasmon resonance and Raman scattering have been utilised. Rapid strides have been made in the field of biosensors and efforts have been made to develop portable instruments using these sensors. However, keeping in view the simplicity of electronic instrumentation for signal conditioning, more efforts need to be focused towards electrical sensors.

Further, the use of *Au* nanoparticles as a probe for chemical and biochemical sensing and as a building block for nano-optical devices, currently, remains incompletely understood. It is not known how the surface properties of *Au* nanoparticles ultimately define their optical properties, hindering the progress of rational design of *Au* nanoparticles for biochemical sensing and assembly of nano-optical devices[61]. This is an interesting and promising research area.

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