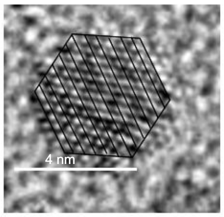
Chapter 12



NANOSENSORS

Sensors can be developed by using the properties of matter at nano dimensions. In such devices, the functional units will be nano entities though the material itself may not be nano in dimension. The properties of nanomaterials such as the large surface to volume ratio and photophysical properties will be used in generating a signal when analyte molecules interact with it. Several such sensors have been developed. Our objective here is to categorize these systems and put them in the perspective of materials discussed so far.

Learning Objectives

- What are nanosensors?
- What are the typical things one can sense with nanodevices?
- What are the properties used for sensing?
- What is the status of current research in this area?
- How useful can a smart dust be?

12.1 Introduction

One unifying property for all life forms is their ability to sense, perceive and react to situations. This characteristic is exhibited, albeit to different extents, by the most developed living organisms down to the lowest organisms. What is surprising, however, is that man, having proclaimed himself as the most advanced and developed of all species, looks at other 'lower' species for their exceptional ability to sense and react to their surroundings. They provide him with ideas and inspirations on how to develop and acquire an improved sense of perception. Since science has still not allowed man to tamper with and modify his own self to the extent he would like to, he attempts to develop external sensors and devices to obtain a better knowledge of his surroundings. This understanding equips him with the ability to react and eventually assume better control of his surroundings. Therefore, in his never-ending quest for controlling his locality, he tries to constantly innovate and invent devices equipped with better sensory perceptions than what has been bestowed on him naturally.

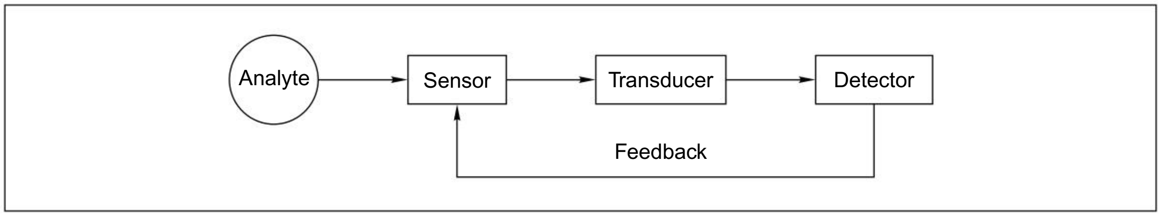
A careful analysis would reveal that the development of sensory devices has been vital for ushering in various technological advancements that have revolutionized civilizations. After all, every experiment, entails a measurement, which involves sensing something. In the modern day world, our ability to point to the exact location of a person owes its existence to a satellite that can sense the time delay between the signals it receives from various other satellites and translate it into distance on a three-dimensional space. Perhaps, it would be difficult to believe that this complex concept is also employed by a bat to sense its environment!

12.2 What is a Sensor?

In the context of this book, the term 'sensor' can be referred to any device that uses an active chemical species or component that generates a signal in presence of an analyte molecule. The signal, in turn, is used either directly or after suitable amplification to trigger a suitable detector.

Thus, the three essential components of a sensor device are:

1. *The responding element*, which recognizes the presence of the analyte species and generates a signal. This is the principal component which 'sees' the molecule, ion or process. In general, a sensor element has to satisfy certain requirements like:
    (a) It should be capable of detailing the analyte in a qualitative and quantitative manner.
    (b) It should be able to detect even very small amounts of the analyte.
    (c) The signal it generates should be reproducible. This implies that the sensor should not have a strong affinity for the analyte, in which case the sensor will be passivated with the analyte after some time, leading to an irreproducible response. The affinity should be optimal so that the analyte is disengaged from the sensor after a short interaction time period, during which the sensor transfers its response to the next stage.
    (d) The sensor should be very selective and specific in its response towards a target molecule.
2. *An amplifier*, which receives the signal of the sensor as an input and amplifies it to a level that is acceptable for processing by the detector, and
3. *A detector*, which receives the output of the amplifier as an input and converts it, in a pre-programmed manner, to a parameter which represents either the analyte species or its concentration or both. In most cases, the detector is equipped with a feedback control through which it signals to the sensor that the input has been received and processed. This acts as a trigger for the sensor to release the analyte molecule. This process causes an induction time period during which the sensor is not available for response. Therefore, the induction period should be as small as possible. An overall schematic of a sensor device is represented in Scheme 12.1.



Scheme 12.1: *Schematic of the design of a sensor.*

12.3 Nanosensors—What Makes Them Possible?

So where do nanomaterials, and the properties that arise thereof, stand in the realm of things? As has been discussed in all the previous chapters, the size regime of nanomaterials gives rise to an entire gamut of physical and chemical properties, which are being currently explored by numerous research groups worldwide. The main properties of nanomaterials that are utilized for conceiving and designing a viable sensor are as follows:

1. Properties derived from the high surface to volume ratio
2. Optical properties
3. Electrical and electrochemical properties
4. Physical properties.

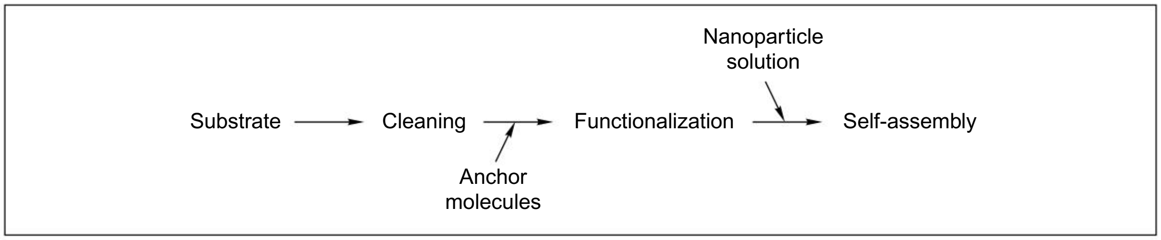
Apart from these broadly classified attributes, some specific properties also find application in the development of sensors. Such properties will be briefly discussed as and when required.

12.4 Order from Chaos—Nanoscale Organization for Sensors

A translation of liquid state properties to solid state is of utmost importance in the development of sensors and devices. One of the major hurdles in achieving this is that this transfer has to be done without altering the liquid-phase properties. In this process, assembling of the particles and an enhanced ordering have to be achieved to enable uniform and isotropic detection protocol. A variety of substrates are employed for carrying the nanoparticles, with the most common among them being metals like Au, Pt, etc. and conducting glass substrates. Metallic surfaces are utilized for the spectroscopic probing of the molecules using Surface Enhanced Raman Spectroscopy (SERS) that gives information about the alignment and the nature of interaction existing between the molecule and metal. On the other hand, transparent conducting glass substrates lend themselves to a variety of electrical and microscopic (as well as spectroscopic) probing, besides being technologically more attractive. Many methods are used to achieve the assembly and further ordering of the nanoparticles. The most important and relevant techniques are discussed here, with examples.

12.4.1 Self-assembly

This is one of the most widely used and simplest methods of organizing nanoparticles onto substrates. Normally, this method is adopted for attaching the nanoparticles (usually metallic) on surfaces like conducting glass or metal films. The substrate is first cleaned and activated suitably, with the process depending on the nature of the substrate and the nanoparticles. The surface is made either hydrophobic or hydrophilic as is necessitated by the type of the nanoparticle. In the case of metallic substrates, the cleaned surface might be sufficiently active for the attachment of the nanoparticles. Otherwise, the activated surface is functionalized with anchor molecules to facilitate the binding of the nanoparticles. These anchor molecules are characterized by the presence of certain functional groups to which the nanoparticles will adhere. A silane containing thiol (Ref. 1) or an amino functional group, capable of forming a covalent link, is best suited for the adhesion of gold nanoparticles. The type and extent of functionalization is controlled by the nature of application for which it is fabricated. For example, for electrochemical studies, a thick polymeric layer of alkoxysilane will hinder the transport of ions and electrons between the nanoparticles and the substrate. A representative schematic of the procedure is shown in Scheme 12.2.



Scheme 12.2: *Schematic representation of self-assembly.*

The assembly thus achieved is referred to as a 'self-assembled layer' (SAL). More specifically, if a single monolayer adsorption is achieved, it is known as a 'self-assembled monolayer' (SAM). This is more relevant with respect to the organization of molecules on a metal or nanoparticle surface. It is thus known as there is no external driving force other than the mutual affinity between the nanoparticles and the functional groups on the substrate. This plays a crucial role in deciding the specificity of the nanoparticles that goes on to form the SAL or SAM. To know more about self-assembled monolayers, see Chapter 5.

12.4.2 Template Method

One of the main disadvantages of the self-assembly method is its sensitivity in terms of external parameters. It is almost impossible to obtain two similarly arranged surfaces, with the adhesion and the organization depending on various factors like solvent, concentration, temperature, type of substrate, and so on. In fact, even on a given surface, there is a high possibility of the existence of a coverage gradient, leading to inconsistency in results.

One way to overcome this is to fabricate a template with regions wherein the possibility of the adsorption of a nanoparticle is artificially enhanced. The most common example is the use of polymethylmethacrylate (PMMA) (Ref. 2) to create the necessary patterns on the substrate. On activating the plate, the portions containing the PMMA remain passive and hence the nanoparticles are not able to bind to the substrates at those places. Conversely, if a suitably charged microstructured polymer is chosen, instead of PMMA, the nanoparticles adhere on the substrate to the regions containing the polymer. An example in this case would be the patterning of Pd nanoparticles using a polydimethylsiloxane (PDMS) template.

An advancement of this technique is the use of light to create the patterns on a functionalized surface. The silanization is done with a suitable group such as amine or thiol in the case of gold nanoparticles. The substrate is then exposed to light in certain areas leading to oxidation of the groups. Exposure to nanoparticles makes the light-exposed regions passive. A schematic overview of the various methods is given below.

Although only a few of the template-based techniques have been discussed here, the possibilities with this methodology are innumerable, with creativity being the only limitation. See also Chapter 5 on self-assembled monolayers.

12.4.3 Biological Assembling

With assembling constituting the *raison d'etre* for the existence of life, it is hard not to think of strategies based on biological entities for assembling and patterning nanoparticles. Accordingly, many approaches have been developed by combining these two areas. Since an exhaustive discussion on this has already been provided in Chapter 5, a more detailed picture is beyond the scope of this book. Thus only a few of the interesting approaches utilizing biological entities for assembling and patterning are discussed here, see Scheme 12.3 (Plate 10).

Complimentary DNA strands can be used to self-assemble nanoparticles in the form of wires and helical structures (Ref. 3). Going further, the recent trend has been to immobilize DNA, either as oligonucleotides or as duplex strands, on substrates. This is followed by the deposition of nanoparticles to create specific patterns. These patterns arise due to the enhanced affinity of the nanoparticles towards certain residues of DNA. For example, it has been established that DNA strands can act as stabilizers for CdS nanoparticles and that the content of adenine influences its morphology and photophysical properties (Ref. 4). Accordingly, duplex DNA are immobilized on substrates and Cd^{2+} ions are assembled on it, with high degree of specificity. Following exposure to H_2S, these are converted into CdS nanoparticles. These methodologies offer a high degree of flexibility in generating various patterns of arrangement.

The recognition-based organizational ability of biomolecules has led to their qualification as ideal candidates for organizing and patterning nanoparticles. One of the strategies adopted for generating nanoparticle arrangements is through the interaction between antigens and antibody. Besides their high specificity, these interactions are chemically stable and offer a wide range of equilibrium constants, thereby allowing fine control over the organizational behavior and pattern. The most commonly exploited biomolecule for achieving this is the biotin-sav (See Box 12.1) combination. Nanoparticles are configured by tagging them to one of the biomolecules and arranged by using the other molecule. An extrapolation of this approach allows one the flexibility to order different types of nanoparticles. This can be achieved by capping each type of nanoparticles to one specific type of biomolecule, and then bringing about regularity by utilizing the recognition between the biomolecules involved in the capping.

Box 12.1
Biotin-Sav

The interaction between biotin, a member of the Vitamin B family, and streptavidin (sav), a tetrameric protein, is of great interest due to many significant reasons. Biotin, besides playing a part in the synthesis of fatty acids (like L-leucine and L-valine), is also believed to take part in gene expression and DNA replication. The binding constant between biotin and sav is exceptionally high and is stable over a wide range of pH and temperature. These aspects have made this system the focus of a number of studies with particular focus on drug designing and targeted drug delivery.

12.4.4 Lithographic Techniques

Lithography, which has its origin in the Greek words—*lithos* meaning stone and *graphy* meaning writing, has developed into one of the most sophisticated and accurate techniques for creating molecular and nano-architectures. Lithography can be classified into various types based on the type of probe used for accomplishing the arrangement. Some of these important classifications are Atomic Force Microscopy (AFM), Scanning Probe Microscopy (SPM), Focused Ion Beam (FIB) lithography and e-beam lithography. Besides providing lithographic resolution to a few nanometers, these techniques are also used in the characterization of surfaces. These procedures have been used for various advanced accomplishments such as creating a nanopen with a molecular 'ink' to develop patterns on surfaces. This device works by making the ink flow through micro-fluidic channels to an AFM tip, which then 'writes' on a suitable substrate. The basis and the use of these techniques are best discussed separately as an in-depth discussion is beyond the scope of this chapter. While these techniques hold the promise of taking nanoscience to a new level, their only drawback is their limited affordability and high sensitivity to handling. Some of the lithographic techniques along with their working principles are summarized in Table 12.1. The interested reader is urged to look up the relevant literature for further details (See Chapter 2 for references).

12.5 Characterization—To Know What has been Put In

The surface coverage and its uniformity are decisive factors in the functioning and reliability of the sensor or device. These, along with other information about the surface, can be measured with the help of a Quartz Crystal Microbalance (QCM) or investigated with various microscopic techniques like AFM and SPM. Other methods of analysis are discussed in the following sections, as and when the relevant properties are being used for detection and quantification.

Table 12.1: *Summary of some of the lithographic techniques and their working principles*

Technique	Working Principle
Atomic Force Microscopy	Oscillating tip which contacts the surface at the atomic level resulting in variation of the oscillation characteristics.
Scanning Tunneling Microscopy	A bias voltage is applied between the tip and the substrate and the variation in tunneling current is used to study surface morphology.
Dip Pen Nanolithography	An AFM tip which delivers molecules with atomic precision, onto a surface through a solvent meniscus.
Electron Beam Lithography	Electron beam exposes the resist causing physical or chemical changes at the exposed position, modifying the surface at those positions.
Focused Ion Beam Lithography	Lenses focus the metal ion beam resulting in deposition, etching or imaging of the surface.

After digressing to discuss a few existing procedures for the realization of nanoscale order and architectures, we will proceed with the main focus of this chapter—the development of sensors based on nanosystems. An attempt has been made here to classify the nanosensors according to the properties of the nanomaterials being utilized in the sensing process.

12.6 Perception—Nanosensors Based on Optical Properties

One of the most easily noticeable features, common to almost all types of nanoparticles, is their color. This intense, characteristic quality arises because of the excitation of the electron cloud present at the surface, in the case of metal nanoparticles. This feature in the Ultraviolet–Visible absorption spectroscopy (UV–Vis) is known as 'Surface Plasmon Resonance' (SPR). For semiconductor nanocrystals, quantum size effects operate resulting in an enhanced overlap of the electron and hole wave functions.

The occurrence of SPR provides information about the size of the nanoparticles. This is truer in the case of semiconductor nanoparticles, wherein there is a non-linear increase in the band gap with sizes approaching the Bohr exciton radius of the materials (See Box 12.2). Apart from this, it also provides information about the local environment of the nanoparticle. The position of SPR in UV-Vis is known to be a reflection of the local environment of the particle. Even a small chemical change in its surroundings (typically about a few hundred square nanometers) causes a monitorable shift in the occurrence of SPR. This property is exploited to track chemical changes taking place in the vicinity of the nanoparticles. If monitored in the liquid state, it might lead to: (a) a perceivable shift in SPR, (b) complete disappearance of the SPR band, sometimes accompanied by a simultaneous appearance of another band, or (c) change in the structure or intensity of SPR. Inter-particle interaction leads to a coupling of the SPR resulting in the emergence of another band, which is usually red-shifted as compared to the original feature. These types of interactions arise in solid-state immobilization of the particles, or due to analyte-mediated agglomeration. An analysis of the coupled plasmon band, which belongs to the latter category, has been used for sensing biomolecules like DNA (Ref. 5). Here, single strands of DNA act as capping agents for the nanoparticles. Recognition between the bases of one nanoparticle, to the complimentary bases on another particle, leads to duplex formation in suitable conditions. This draws the nanoparticles together, thereby inducing an aggregated state. This is reversed by altering the conditions (like temperature, pH, etc.), which causes the duplex DNA to unwind, leading to a disaggregated state of the nanoparticles. Sometimes, a metal ion can chelate with the functional groups on the nanoparticle surface, thereby bringing the nanoparticles within the interaction range (Ref. 6). This causes changes in the SPR of the nanoparticles; the effect can be reversed by adding a more powerful chelating agent of the metal ion, whereby the metal–ion bound nanoparticles are released back into the solution.

The sensing protocol involves the binding of one component of a recognition pair on the surface of a nanoparticle, which is present either in the solution or immobilized on a surface, and allowing the other component to interact with it. The recognition, interaction and binding events give rise to a change in the chemical environment of the nanoparticle. The nanoparticle responds to this modification, either by altering its SPR feature to a different frequency or by losing its resonant frequency altogether. Both these actions can be detected through UV-Vis spectroscopy. A knowledge of the kind and amount of change produced in the SPR helps in making an accurate qualitative and quantitative estimate of the analyte.

An alternative means of following these changes is through Surface Plasmon Resonance Spectroscopy (SPRS). This is widely used for opaque substrates, wherein the absorbance cannot be monitored. In such cases, light of a known intensity is shone on the substrate containing the nanoparticles and the intensity of the reflected light is monitored. The angle of incidence is varied and at a specific angle, the intensity of the reflected light falls to a minimum. This is because at a specific angle, which is greater than the total internal reflection angle, the electron oscillations of the nanoparticles resonate with the frequency of the incident light. The plasmon oscillations create an electric field which pervades to about 100 nm around the particle.

Box 12.2
Exciton Radius

An exciton, in the context of semiconductors, refers to the combination of an excited electron in the conduction band and the corresponding hole thus produced in the valence band. The electron and the hole constituting the exciton, always possess a mean separation distance, dependent on the nature and the size of the material. In the nanoscale size regime, the size of the semiconductor becomes small enough to be comparable to the exciton radius. At this limit, the electron energy levels can no longer be treated as a continuum, but are discrete. As a result of this discretization of the energy levels of the band gap of the semiconductor material, minor variations in the number of atoms constituting the semiconductor or its local environment have immediate consequences in the absorption and emission characteristics.

Any change in the environment of the particles within this boundary results in shifting of the angle at which maximum absorbance occurs. In a physical sense, the incident angle at which the maximum absorbance occurs is mainly controlled on the refractive index of the medium surrounding the nanoparticles. Thus SPRS is a powerful and sensitive analytical tool for comprehending binding events occurring at the nanoparticle surface. A schematic representation of the working of the SPRS is shown in Scheme 12.4 (Plate 10).

Nanoparticles cast either separately as free standing films or incorporated into film-forming polymeric matrices and gels, are being developed as sensors for gas molecules. Depending on the size of the gas molecules, they are either physisorbed or chemisorbed in the voids between the nanoparticles. This causes changes in the interparticle distance, which results in the decoupling of the interparticle plasmon. An alternative approach is to form films or gels of materials that are sensitive to the analyte molecules of interest, and then incorporate nanoparticles in them. The interaction between the analyte and the film/gel forming materials leads to a change in its physical structure, which is picked up by the nanoparticle. This gives rise to changes in the SPR features, sometimes leading to a complete disappearance of the interparticle interaction feature. The advantage of such systems lies in their high sensitivity and reproducibility. Efforts are on to optimize the residence time of the gas molecules in the matrix, which will result in increased efficiency of detection and also reusability of the material.

12.7 Nanosensors Based on Quantum Size Effects

The electrical, and consequently electrochemical, properties of materials in nanosize are entirely different from those exhibited by the bulk state of the corresponding substances. These variations stem from the fact that the electronic state of nanomaterials lies somewhere in between that of the bulk and atomic states. In bulk materials, there are distinct continua of valence and conduction bands. On the other hand, the electronic states in atoms and molecules are distinct with discrete energy levels. In comparison to these two, nanosystems possess a quasi-continuum state, wherein the bands are distinct, but with discrete energy levels. They exhibit size- and material-dependent spacing of the energy levels. This offers us a great handle to tune the electronic properties, by regulating the size of the particles.

The most unique property that arises in nanoscale materials, which is currently being developed further, is known as 'Coulomb Blockade' (CB). In the nanoregime, due to high surface/volume ratio, charge and energy quantization become the dominant forces in deciding electron transport. The charge quantization dictates the capacitance of the material and restricts it to the nanodimension. This implies that the energy that has to be supplied to add an electron to an uncharged nanoparticle varies inversely with the dimension of the particle and so far exceeds the thermal energy available at room temperature. This provides us with a handle to regulate and manipulate charges flowing through nanosystems. This phenomenon is known as Coulomb Blockade and has been detailed in both theory and experiments. Coulomb Blockade is discussed in more detail in Chapter 7.

Of late, sensor devices called electron turnstiles (Ref. 7) have been developed on the basis of this concept. These are being tried out for their applicability to count electrons. It consists of a number of islands interconnected by insulting barriers, through which charges can tunnel. By controlling the gating voltage of individual islands, one can regulate the number of electrons fed into the system.

With the rapid advancement of lithographic techniques and achievement of maneuverability of a single nanoparticle, research in single electron tunneling in nanoparticles has also gained prominence in recent years. Conventional electronics relies on the transport of charge carriers. In nanodevices, the transfer of the charges has to take place in a controlled manner. This is realized by tunneling of the charges. The set-up consists of two electrodes separated by a mesoscopic island of nanoparticles. The transfer of charges in such islands is largely governed by a minimum capacitance of the island. If that is the case, then the creation of a very small charge excess in the island affects its potential significantly. This acts as a feedback system and prevents further charging of the island, until the excess charge is dissipated to the other electrode. Essentially, this methodology enables us to control the transport of a small but definite amount of charge carriers. As is evident, these single electron tunneling events are greatly dependent on the capacitance of the island. If the nanoparticle comprising the islands has imbibed some of the analyte species present either in gaseous or liquid state, then the capacitance of the island is modified. This is reflected on its step value of the coulomb staircase in the I–V characteristics. If the affinity of the analyte to the nanoparticles is low, then the I–V characteristics would be similar to the nascent case. Thus, all it takes for a signal variation is a few atoms of the analyte. The unprecedented detection capability and sensitivity of single electron sensors (SES) make them very advantageous in specialized applications wherein detection is of utmost importance.

Semiconducting metal oxide nanoparticles are being widely researched as chemoresistive gas sensors (Ref. 8). Single gas detection, leakage detectors, and fire detectors, and humidity sensors fall under the category of gas sensors. The operating principle of these electronic noses is that of variation in the resistance of these materials, when exposed to certain gases. When the gas comes into contact with the semiconducting metal oxide nanoparticles, it results in structural variations of the particles. These variations might occur either at the surface or in the bulk of these particles. As a consequence, electrical conductivity of the material varies. The variation in the conductivity can be monitored and tabulated for a series of gases over a range of partial pressures. This is then analyzed to provide information about the best sensor for a particular gas over a given range of partial pressures. The important considerations to be taken into account while designing the sensor are its cross-sensitivity and detection capability.

The commercial production of some materials has also been started and they are more commonly known as electronic noses (Ref. 9). Essentially, an electronic nose functions just like a human nose and hence its name. These consist of an array of varying nano-metal oxides, each of which has a selective and specific response to certain gas molecules. While the changes in conductivity in a single type of nanoparticle film might not be sufficient to identify an analyte, the varied changes in the array of films produce a distinctive, identifiable pattern. Together, they are able to respond to mixtures of gases, providing both quantitative and qualitative information about them. The working is better shown as a schematic in Scheme 12.5 (Plate 11).

12.8 Electrochemical Sensors

A discussion of sensors based on their electrical properties will not be complete without detailing some of the aspects of electrochemical sensors. Normally, multi-layers of metal nanoparticles find extensive use as electrodes, since they are known to retain the electrochemical activity of the analyte species. The electrodes also mediate charge transfer between the bulk electrode and the analyte molecules. The single electron events discussed earlier induce changes in the double layer charging of the nanoparticle, which, in turn, modifies the redox potential of the system. This gives us an opportunity to quantify the charge transfer occurring at the electrode surface. The deviation from the peak voltages of the nascent electrode helps us to qualitatively arrive at the chemical nature of the analyte. The sensitivity of the electrode can be tuned by controlling the number of layers fabricated on it. The use of nanoelectrodes has fuelled an enormous increase in the surface area which causes a multifold increase in the sensitivity to the analyte molecules. As in the previously discussed techniques, a similar strategy of binding suitable receptor molecules on the surface of the nanoparticle is followed. On coming into contact with the analyte molecules, a host–guest interaction occurs, which is manifested in the I–V characteristics of the electrode. The specificity is best illustrated in the detection of dopamine (DA) in the presence of ascorbic acid (AA), using a cysteine-capped gold nanoparticle electrode (Ref. 10, Fig. 12.1). This drives home the point of specificity, since dopamine and ascorbic acid are not distinguishable through their I–V characteristics using a normal bulk electrode.

The enhanced sensitivity in this case arises because of the preferential catalytic oxidation of ascorbic acid at the surface of the nanoelectrode, which shifts the anodic current for oxidation of ascorbic acid to

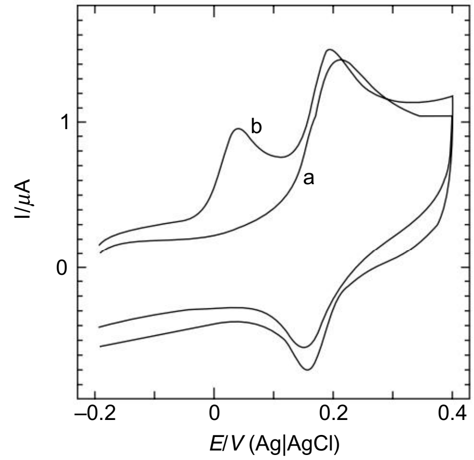


Fig. 12.1: *Cyclic voltammograms of a binary mixture containing equimolar concentrations (50 mM each) of AA and DA at the bare Au (a) and nano-Au (b) electrodes in 0.1 M PBS (pH 7.2). Scan rate: 100 m Vs^{-1}. Reprinted from Raj, et al. (Ref. 10). Copyright (2003), with permission from Elsevier.*

less positive values. Thus the oxidation of ascorbic acid is finished well before the onset of oxidation of dopamine.

In summary, an ordered nanoparticle array shows environment–dependent electrical properties (such as conductivity). These properties are modified by the chemical species present in its vicinity. The conductivity of nanoparticles is believed to occur due to:

1. Tunneling of electrons through the metal core.
2. Hopping of the electrons along the atoms constituting the chain of the ligand molecule encapsulating the nanoparticle.

By changing the parameters of the nanoparticle-modified electrode such as its particle diameter, space between the particles and the number of layers, the conductivity of the system can be altered. The analyte can be made to interfere with any one of the processes and hence can help vary the conductivity. This could lead to a sensing of the analyte.

The use of silicon nanowires (SiNWs) as gas sensors has been reported (Ref. 11). The I–V characteristics of bundles of SiNWs have been investigated as a function of exposure for a range of concentrations of various gas analytes (Fig. 12.2). They are found to possess high sensitivity to humidity and can act as water vapor sensors. The sensitivity is shown up in the form of resistance changes upon exposure to water vapors. Interestingly, the process is found to be perfectly reversible, with the resistivity reaching the original value on removing the gas analyte.

12.9 Sensors Based on Physical Properties

A new field of research has been emerging due to the utilization of physical properties at the nanoscale. This field is known as 'Nano-electro-mechanical-systems' (NEMS). This comprises a class of devices that relies on the mechanical properties at the nanoscale to power them. The fabrication of such devices is attracting heavy attention with newer strategies being developed everyday.

Under this category, cantilevers fabricated in the nanodimension are gaining prominence for use in sensor gadgets. The discussion on this subject will first focus of some of the known methods to fabricate these nanocantilevers followed by their applications and advantages.

The usual methods of nanolithography like AFM, STM and electron beam lithography can reach up to tens of micrometer dimensions, but are not economically viable for large-scale production. Therefore, FIB is a more compatible technique. Here a Ga ion beam is used to physically scoop out nanodimensional cantilevers from silicon substrates. Going a step further, FIB can be complemented with wet etching, wherein the FIB is used not to etch the surface but rather to dope the wet-etched surface selectively. The primary requirement for these techniques is that one has to start with a single crystal. Although widely done on a silicon substrate, it can also be extended to other surfaces.

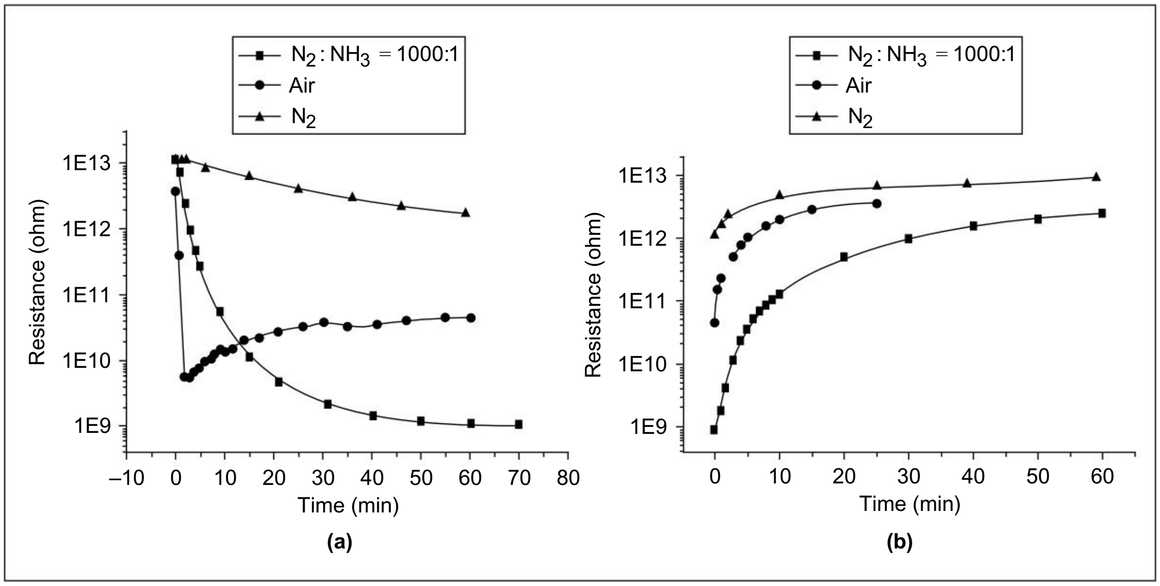
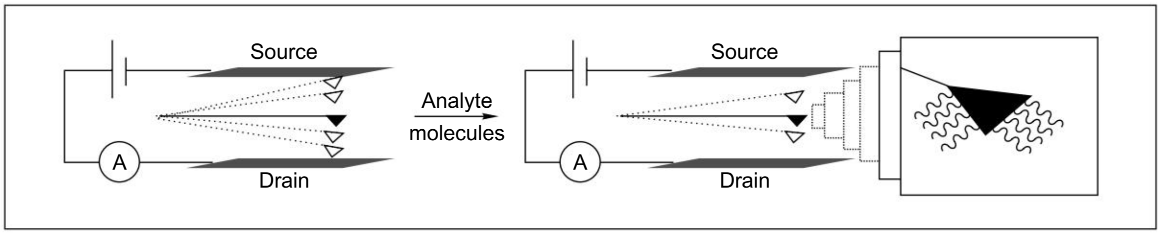


Fig. 12.2: *Electrical responses of the Si nanowire bundle to N_2, a mixture of N_2, NH_3 (NH_3 concentration: 1000 ppm), and air with a relative humidity of 60%; (a) When the gases were introduced into the chamber, and (b) when the gases were pumped away. Reprinted from Zhou, et al. (Ref. 11). Copyright (2003), with permission from Elsevier.*

The normal techniques of detecting cantilever motion, such as piezoelectricity and optical beam, are not useful in the case of nanosize cantilevers (Ref. 12). This is because the nanosize causes greater scattering of the light beam, thus making it difficult to exactly fix the resonant frequency. Therefore, techniques like electron tunneling or shuttling which are compatible with the dimension of the cantilever, are used for their detection. A preliminary set-up consists of two micro-machined electrodes, between which a nanocantilever is fixed. At the resonant frequency of the cantilever, one of the electrodes is made to act as a source with the other functioning as the drain. As the cantilever oscillates, it makes electrical contact with either of the electrodes and thus acts a gate for the flow of charges. This is determined by monitoring the current generated, which is typically of the order of pico amperes, for a bias voltage of few millivolts.

When the cantilever is exposed to analyte gas vapors, its resonant frequency is bound to vary, with the oscillations becoming more damped (Scheme 12.6). This will be discernible in the plot of bias voltage versus current. By comparing the voltage at which the peak current is obtained in both the damped and undamped cases, the effective mass of the cantilever before and after exposure can be calculated. The difference between the two readings will point to the quantity and nature of the gas to which the cantilever was exposed. Phenomenal mass sensitivity of a few femtograms has been achieved with the use of nanocantilevers. This corresponds to a multifold increase in sensitivity of nanocantilevers as compared to normal cantilever sensors. At the masses of these ranges, it can be safely assumed that the detected mass is proportional to the original mass of the molecule. Therefore, a very efficient way of calculating the mass, which is a characteristic property of every matter, is developed.

Moreover, recent research has been concentrating on developing techniques to capture the phase changes and the amplitude of vibration of the nanocantilever sensors. Achieving this would only result in unprecedented ability to image and view, as though through a microscope, the analyte molecules. One main limitation of this sensor is its inability to function in environments wherein a leakage current is possible, since this will obscure the actual current from the oscillating cantilever. Its use in biological areas is also restricted due to the increased presence of particulate matter. Liquid state applications are also constrained due to large-scale damping. However, research is underway to overcome these shortcomings, mainly inspired by its increased sensitivity.



Scheme 12.6: *Graphical representation of the working of a nanocantilever sensor. The damping of oscillations after exposure to analyte molecules is observed. The cantilever tip is enlarged to show the presence of the analyte (indicated by curved lines).*

Another detection protocol, utilizing the weight of the nanoparticles as amplifying agents for the detection of complementary DNA pairs and misfits, is Quartz Crystal Microbalance (QCM). The inverse piezoelectric effect is the key to the operation of the QCM. The application of an electric field to the quartz crystal causes a shear deformation of the order of few nanometers. Initially, the gold electrode is modified with single stranded DNA. When complementary-DNA functionalized gold nanoparticles are allowed to interact on the electrode, the vibrating frequency of the quartz crystal varies and therefore, the mass change can be detected. When the same process is carried out without the complementary DNA functionalizing the nanoparticles, the weight change is not significant enough for the QCM to register. Therefore, in this case the nanoparticles do not influence or participate in the detection process, but are merely involved in amplifying the signal.

12.10 Nanobiosensors—A Step towards Real-time Imaging and Understanding of Biological Events

The evolution of nanoscience and that of biology have complemented each other beautifully. There is widespread interest in combining both the fields, so much so a new field known has nanobiotechnology is one of the frontier areas of research. In keeping with the time at which this book is being written, an attempt has been made to emphasize the role of nanomaterials in developing sensors for biological applications. Any of the protocols detailed in the previous sections can be extended to biosensors. Besides those techniques, a few techniques specific for following bio-related events have been developed, which will be the focus of this section. In this section also, like in other parts of the book, there will be greater focus on the current research directions, with a pointer to the future prospects.

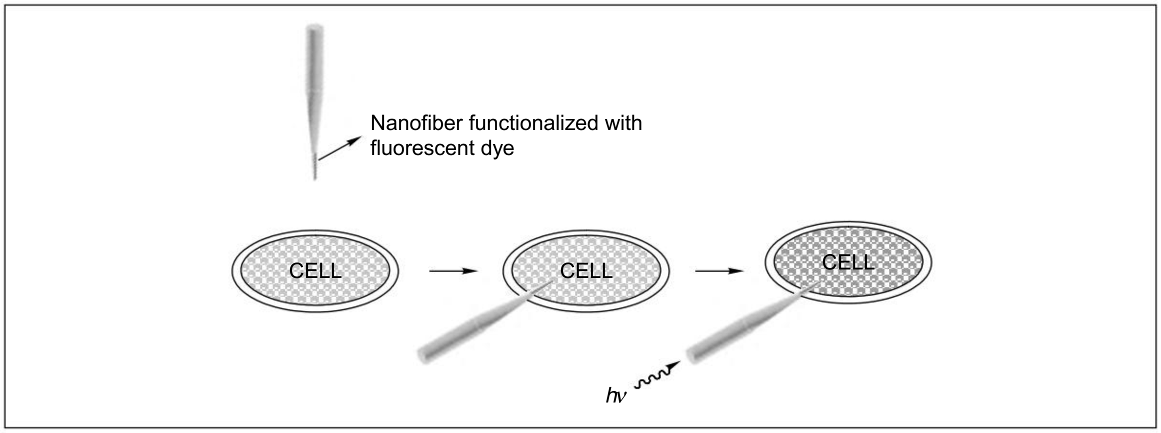
A nano-biosensor concept has to contain a biological recognition component, which is involved in interacting with the analyte molecule. This interaction causes reversible changes in both the bioreceptor and the analyte. These chemical changes have to be transformed into recordable signals. In most of the cases, the transducer has to convert the chemical modification into an electrical signal. The signal from the transducer is analyzed and interpreted to provide details about the analyte. Therefore, the bioreceptor controls the selectivity and specificity while the transducer determines the sensitivity of the sensor.

The nature of the bioreceptor depends on the type of analyte molecule. Since the binding and recognition events in biology are highly specific, the choosing of the bioreceptor should be done keeping in mind the kind of application the device is going to be used for. Since the biological medium is mostly aqueous, Surface Enhanced Raman Spectroscopy (SERS) is a widely used tool to bring out the maximum information from biological sensing events. However, due to limited low spatial resolution, near field spectroscopy and associated microscopy have been receiving attention. With near field SERS (NF-SERS), single molecule detection is now a reality.

Two main approaches are widely followed for the fabrication of nanofiber probes, and are needed to sense the plethora of processes occurring inside individual cells. The first approach is known as the 'heat and pull' method (Ref. 13). A glass fiber is spot-heated by using a focused heating source such as a laser. In the hot condition, the fiber is pulled apart, yielding probes the morphology of which depends heavily on the experimental parameters. The second, more systematic procedure is known as 'Turner's method' and entails chemical etching of the surface to yield nanoscale probes (Ref. 14). The etching, in case of glass probes is done with HF. A fiber with a silica core and an organic shielding material is exposed to HF. The slow etching of the inner silica core by HF takes place. This is followed by the controlled emergence of the silica core, during which HF rises up the fiber due to capillary action. On complete emergence, the HF drains of the glass fiber, etching a nanotip in the process. A schematic procedure of the etching process is shown in Scheme 12.7 (Plate 11).

The nanofiber tip thus fabricated is functionalized with an appropriate bioreceptor. The functionalization is carried out by suitably activating the nanofiber tip and coating silver over it. The silver coating is done by evaporating the metal under a rotating tip, which results in a uniform layer of silver on the tip. The tip is used for immobilization of the bioreceptor, which can be anything ranging from antigens to biomimetic molecules.

The use of this functionalized nanotip is clearly demonstrated by its capability to penetrate the cells and thus study the actual locations inside a cell wherein the analyte molecules are accumulated or processed. Benz[a]pyrene (BaP) is a chemically generated carcinogenic compound and there has been a keen interest in tracking its chemistry inside the cells. Benzopyrenetetrol (BPT) has been used as an antibody probe for this chemical and to study its metabolic pathway inside the cells and the mechanism by which it causes mutations. After penetrating the cell with a bioreceptor bound nanotip, the BaP and BPT form a receptor-ligand complex. The fluorescent signal form this complex is monitored for detailing the concentration of BaP and its mechanism of action (Ref. 13).



Scheme 12.8: *Diagrammatic representation of in-situ detection and imaging of cellular components.*

Another interesting protocol involves incorporation of the dye molecules inside the cells. Then a nanotip is carefully inserted inside the cell. Light of suitable frequency is passed through this fiber optic nanotip to cause fluorescent emission from the dye molecules. This makes possible a chemical photograph of the cell, indicating the regions where the dye molecules are present (Scheme 12.8).

Sönnichsen and Alivisatos, have utilized the light scattering property of gold nanorods (and metallic nanorods in general) as a means of sensing its motion (Ref. 15). A similar protocol can be extended to detect orientation changes and track the movement of large biomolecules. The strategy adopted is to attach gold nanorods loosely on the surface of a glass flow cell. On this surface, under the influence of a small flow current, the rotational behavior of the nanorods can be mapped. The detection protocol consists of a dark field set-up, with an illumination source and an objective to collect the scattered light. Due to their anisotropy, nanorods are the best suited candidates for observing rotational dynamics, the resolution of which can be brought down to as far as 20 nm.

12.11 Smart Dust—Sensors of the Future

In the constant urge to innovate and improvise, man has been breaking many barriers. This trend has been observed, in the field of nanosensors also, giving rise to fierce competition for developing detection capabilities and sensor characteristics. Towards this end, 'stand-off detection' has been undertaken in a big way. This pertains to the detection of harmful and toxic chemicals which cannot be analyzed under laboratory conditions. Paradoxically, the detection of these chemicals is much more important and relevant as compared to the detection of normal chemicals. This is achieved by the 'smart dust' approach, wherein small particles resembling dust are carried by air currents to the area under investigation. In one such study, porous silicon was etched out from crystalline silicon by a combination of anodic and galvanic currents. These were ground or ultrasonicated to form the materials for smart dust. Porous silicon used here exhibits visible photoluminescence. When it comes into contact with explosive chemicals like dinitrotoluene (DNT) or trinitrotoluene (TNT), its photoluminescence is quenched due to NO_2 produced by catalytic oxidation. The signal can be monitored from a safe distance and provides information about the nature and quantity of the chemical present in the ambience. Detection capabilities of parts per billion (ppb) have been achieved using this system.

Taking this development further, researchers at UC, Berkeley have embarked on an ambitious project, the outlay of which is shown in Scheme 12.9 (Plate 12) (Ref. 16). It entails building an integrated sensor array, complete with power supply, receivers and transmitters. Each little sensor has the capability of analyzing a multitude of parameters ranging from humidity to explosives. Every 'dust' particle can communicate with another through a distance of about thousand feet, thus enabling three-dimensional concentration profiling. Although questions are being raised about the environmental and health safety aspects of these systems, it is likely that these problems will be solved in the coming years.

Review Questions

1. What are sensors?
2. What is the ultimate size of a sensor? What decides it?
3. What is the requirement of a nanosensor?
4. What are the current nanotemplating methods?
5. If the sensor is nano in dimension, how can one measure the property, as the magnitude of which will be reduced by that order?
6. What properties of the sensor are modified during sensing?
7. What are the physical properties used for sensing?

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