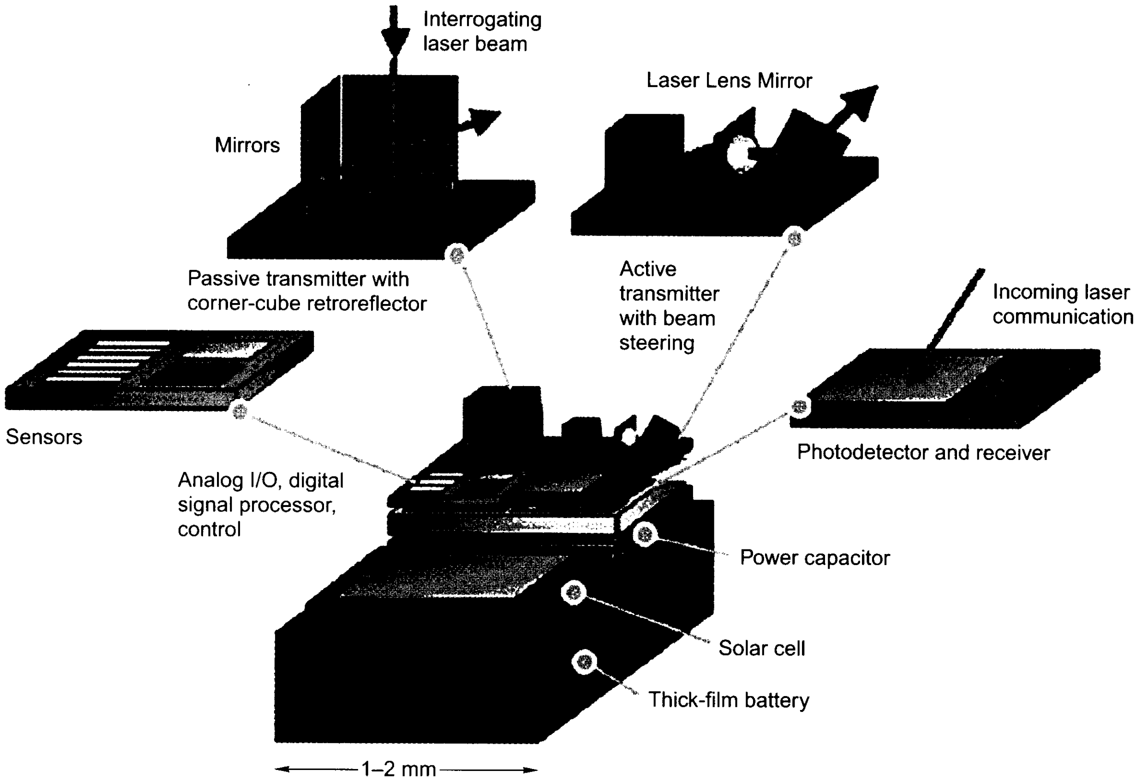


Scheme 12.9: *Proposed structure of a smart dust multifunctional sensor. From the Webpage, http://www.bsac.eecs.berkeley.edu/archive/users/warneke-brett/SmartDust/index.html. Used with permission.*

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

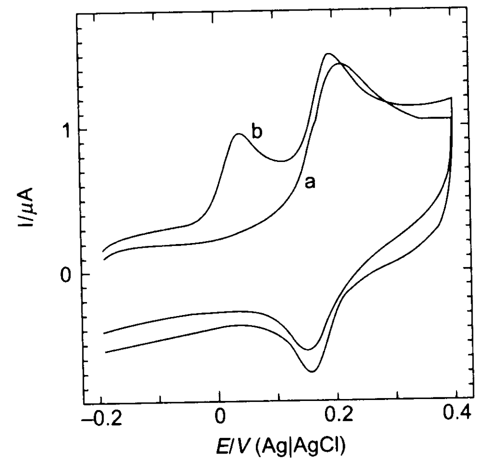


Fig. 12.1: *Cyclic voltammograms of a binary mixture containing equimolar concentrations (50 mM each) of AA and DA at the bare Au (a) and nano-Au (b) electrodes in 0.1 M PBS (pH 7.2). Scan rate: 100 m Vs^{-1}. Reprinted from Raj, et al. (Ref. 10). Copyright (2003), with permission from Elsevier.*

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.

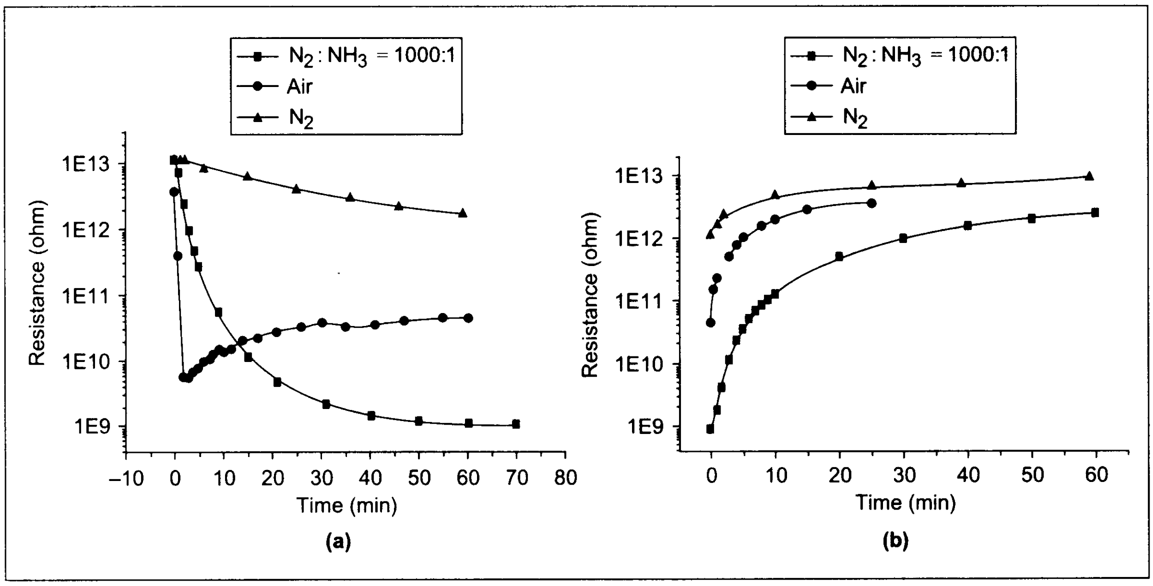
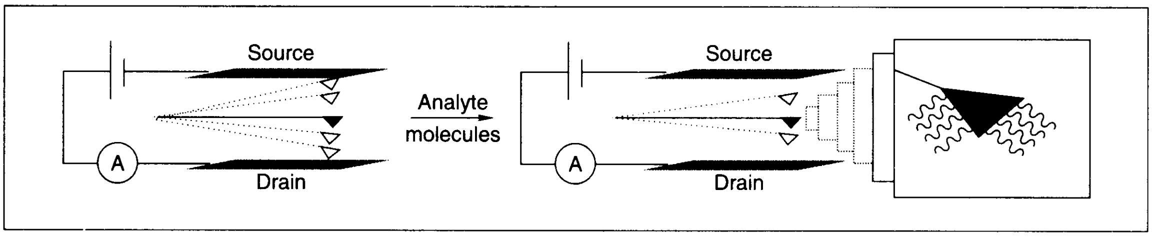


Fig. 12.2: *Electrical responses of the Si nanowire bundle to N_2, a mixture of N_2, NH_3 (NH_3 concentration: 1000 ppm), and air with a relative humidity of 60%; (a) When the gases were introduced into the chamber, and (b) when the gases were pumped away. Reprinted from Zhou, et al. (Ref. 11). Copyright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

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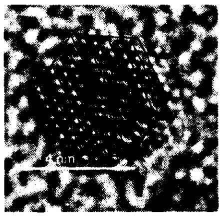
Chapter 13



NANOMEDICINES

Nanomaterials are finding their way into biology in the form of drug carriers. This is probably the most important application of nanomaterials right now. The property utilizes the large surface area available to load materials. Due to their small size, nanomaterials can be transported into cells and nuclei. Specificity to the target can be achieved by appropriate labeling. The materials put in can be subjected to magnetic fields, photons, etc. and can respond to all these situations. The diagnostic and therapeutic applications of such systems are being suggested. Here we present an overview of this area.

Learning Objectives

- Why should nanomaterials be used in medicine?
- How do we apply them?
- What are the materials currently used in this area?
- What are the medical applications currently being investigated?
- What is the future of nanomedicine?

13.1 Introduction

The objective of nanotechnology is to gain atomic and molecular control over matter. It involves the creation of functional materials with control over their physical sizes, which exhibit novel physical and chemical properties that are drastically different from the corresponding bulk forms. The physical sizes of these materials create a strong possibility for their interactions with biological systems (see Chapter 11). Biological systems themselves contain various components which are essentially in the nanometer dimensions (proteins, nucleic acids, membranes); a fact implying possible synergies between nanosystems and biological components. This can have implications for the understanding of biology. Such an understanding can be achieved through the use of nanosensors or probes for disease detection, all of which will ultimately offer robust solutions for the well-being of all.

The concept of the effective use of nanotechnology in disease treatment was suggested as early as 1959 by Nobel Laureate Richard Feynman in his famous talk on, "Plenty of room at the bottom" (Ref. 1).

Feynman provided insights into how nanomedicines could be developed as effective solutions for heart disease: "A friend of mine (Albert R. Hibbs) suggests a very interesting possibility for relatively small machines. He says that, although it is a very wild idea, it would be interesting in surgery if you could swallow the surgeon.You put the mechanical surgeon inside the blood vessel and it goes into the heart and looks around (of course the information has to be fed out). It finds out which valve is the faulty one and takes a little knife and slices it out. Other small machines might be permanently incorporated in the body to assist some inadequately functioning organ."

Today nanomedicines are being developed to have accurate, controllable, reliable, economic and rapid responsive diagnostic and treatment solutions for various kinds of diseases. With advancements in drug discovery processes, stress is on effective drug delivery to the affected organ. It is well-known that many therapeutic agents have intracellular compartments as their site of action. For example, the nucleus is the site of action for anti-cancer intercalating agents whereas cytoplasm is the centre for a number of steroids. Accordingly, the efficacy of drug depends on its sustained availability at the targeted point of delivery. As such, drug administration is affected by the inability of the drug molecule to effectively escape the endosomal/lysosomal pathways, get transported across the membranes and reach the intended location of delivery inside the cell. Even though liposomes have been tried as potential drug carriers because of their unique abilities to avoid drug degradation, reduction in side effects and targeted delivery, their effective usage has been limited due to their low encapsulation efficiency, rapid leakage of water-soluble drugs in the presence of blood components and poor storage stability (Ref. 2). This fact emphasizes the desired attributes of an effective drug carrier system.The use of nanoparticles for drug delivery purposes becomes important because of their high surface-to-volume ratio, enhanced detection features, easier transport across the membrane and possible protection of drug molecules. A high proportion of the atoms in small metal nanoparticles will be present at the surface.The surface-to-bulk ratio bears a strong inverse dependence on particle size. A high surface-to-bulk ratio ensures strong interaction between nanoparticles and the reacting species. Additionally, there is a need to develop a molecular tool for disease detection and treatment because of the uniqueness of each individual's response to therapeutic intervention. This uniqueness is the result of differences in the interaction of therapeutic tools and biological processes, which means that an individualized approach to this problem can lead to a dramatic improvement in results.

Various studies confirm the fact that particle size should be sufficiently small for it to get transported across the membrane and this transport occurs more readily for nanoparticles rather than for micro-particles (Refs 3, 4, 5).

Here we discuss the various approaches that are currently being researched for developing nanomedicines. Additionally, we also discuss various nanomaterials which are strong candidates for use in nanomedicines.

13.2 Approach to Developing Nanomedicines

Depending on the method of preparation and the capping agent present, nanoparticles vary in size from 10 to 1000 nm. Drugs can be associated with the nanoparticles in entrapped, encapsulated or attached form. Nanodrugs are being synthesized in various forms such as nanospheres (drug present on the nanoparticle as the capping agent), nanocapsules (drug confined in a cavity surrounded by a polymeric layer, see Chapter 10 on nanoshells) (Refs 6, 7, 8), nanopores (nanoparticle surface perforated with holes, holes contain drug molecules) (Refs 9, 10), dendrimers (Refs 11, 12), etc. The purpose of encapsulation or entrapment is to gain a better degree of control over the drug release process. This approach finds favor for effective and steady drug delivery over conventional drug due to kinetic behavior observed during drug release. Encapsulated nano-system based drugs are observed to show nearly zero-order kinetic profile whereas conventional oral drugs follow first-order kinetics leading to unsteady drug release at the location of drug delivery (Ref. 13).

Recently, attempts have also been made towards developing biodegradable polymeric nanoparticles as potential drug delivery devices. In addition to the inherent property of reduced cytotoxicity, biodegradable polymeric nanoparticles have been found to be extremely effective in controlled and targeted drug release, even through administration is oral (Refs 8, 14). The phenomenon of zero-order kinetics has been observed predominantly for polymeric nanoparticles. Additionally, various research groups have also established the use of polymeric nanoparticles for nasal (Ref. 15) and ophthalmic delivery of drugs (Refs 16, 17). This group of nanoparticles has also shown prominence for use in neuro-disorders, in which case a large number of other drugs fail (Refs 18, 19). Furthermore, nanosize carriers of vitamin molecules such as vitamin A and E, have potential applications in dermatology and cosmetics (Refs 20, 21).

Various kinds of approaches can be used to attach drugs to nanosystems. There can be electrostatic interaction or covalent binding between the nanoparticle and the drug. The nanoparicle surface can be made electrically neutral or charged, depending on the functional group present on the surface. The surface properties can be tuned depending on the drug-nanoparticle interaction required.

13.3 Various Kinds of Nanosystems in Use

Metal nanoparticles themselves are used as drug delivery vehicles (see Chapter 8). However, there are several other systems for this application which are briefly reviewed here.

13.3.1 Nanoshells

Nanoshells (Chapter 10) represent a unique class of medically prominent nanoparticles. These are made of drug-coated metal nanospheres/dielectric metal nanospheres (e.g. gold-coated silica nanoparticle). Typical metals include gold, silver, platinum and palladium. It is quite evident that the response of these nanoshells is a function of the thickness of the shell/capping agent. When these nanoshells are irradiated with a laser of known intensity, it causes release of the drug coat present on the nanoparticle surface. The release process can be accomplished with the use of an alternating magnetic field as well (Ref. 11).

This approach to the release of capping agent can have implications in cancer treatment. A high surface-to-volume ratio for nanoparticles enables large quantity of drugs to be transported into the affected region.

Attempts have also been made to coat nanoparticle surfaces with antibody molecules, specific to a particular protein present in the human body. This can have profound implications in cancer detection, protein immunoassay and biosensing (Ref. 22).

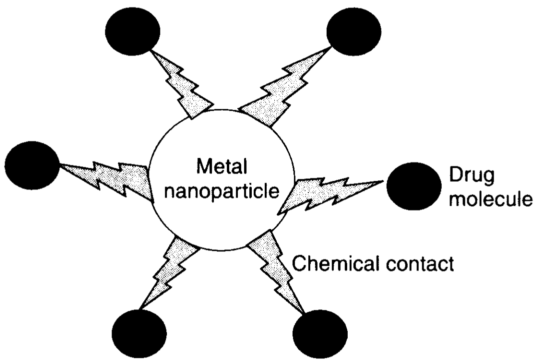


Fig. 13.1: *Drug molecule attached to metal nanoparticle via covalent/ionic interaction.*

13.3.2 Nanopores

Nanopores are essentially nanoparticles whose surface contains pores, which can be used for containing drugs. Uniformly spaced holes are created on the surface in which a drug molecule is contained. The pore size imposes a restriction on the size of the biomolecules present. This means that small molecules like oxygen, glucose, insulin, neurotransmitters, etc. can move across the pore surface while large immune system molecules like immunoglobulin cannot. The released molecule can therefore be used in disease treatment, e.g. the use of insulin in diabetes treatment, use of neurotransmitters in neural disorders, etc. (Refs 9, 10).

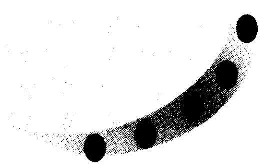


Fig. 13.2: *Cross section of nanopore with drug molecule contained inside the pore.*

Attempts are also being made to control the flow of the molecules across the pore for highly specific molecular transport capabilities, by the use of voltage gating (Ref. 23) and immobilized biochemical molecular-recognition agents (Ref. 24). The first attempt to create a voltage gated nanopore involved an array of cylindrical gold nanotubules with inside diameters as small as 1.6 nm. On developing a positive charge on the tubule, positive ions were not transported inside the nanopore to undergo a reaction with the drug molecule trapped inside. Similarly, only positive ions could pass on applying a negative voltage. The aim is to gain a significant improvement in isolating the targeted molecule with which drug molecules have to interact, by the use of combinatory tools such as voltage gating, pore size and shape.

13.3.3 Tectodendrimers

Dendrimers are branched tree-shaped nanoparticles, which have an immense potential for use in clinical diagnostics and therapeutics. Various research groups (Refs 11, 12) have also synthesized multi-component nanodevices called 'tectodendrimers' which are formed by attaching different types of dendrimers with each other through their branches. These smart nanodevices have been synthesized for applications ranging from the detection to treatment of diseases.

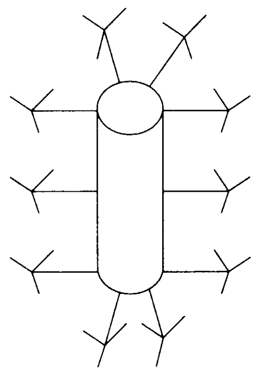


Fig. 13.3: *Dendrimer (tree-shaped nanoparticle), nanometers in dimension with branches projecting out.*

13.4 Protocols for Nanodrug Administration

13.4.1 Nanoparticle-drug System for Oral Administration

Various kinds of approaches are being attempted for the delivery of nanoparticle–drug complex to target particular locations in the human body. An analysis of conventional oral administration indicates that the basic requirements for the successful delivery of a nanoparticle-drug system via oral administration are:

1. The complex should be stable in the gastrointestinal tract.
2. Digestive system enzymes should act on the complex and digest it, and the product should subsequently get transported across the intestinal epithelium.
3. Products from the digestion of nanoparticle system complex should not be cytotoxic for the human body.

In order to avoid the disintegration of the complex before the digestive enzymes start interacting with it, a hybrid system of hydrophobic core–hydrophilic shell has been designed which acts as a carrier for drug molecules (Ref. 25). The core is made of hydrophobic material such as oils or lipids whereas the shell is hydrophilic in nature and composed of polyethylene glycol (PEG which protects against protein adsorption) or chitosan (a known permeability enhancer). Chitosan is a naturally occurring substance (shown in Fig. 13.4, chemically similar to cellulose, $-NH_2$ group in chitosan is replaced by $-OH$ group in glucose) with the ability to significantly bind fat without itself being digested. The various reported applications for chitosan are that it:

1. Absorbs and binds fat/promotes weight loss.
2. Promotes healing of ulcers and lesions.
3. Is used as an anti-bacterial agent and antacid.
4. Inhibits the formation of plaque/tooth decay.
5. Helps control blood pressure and prevent constipation.
6. Has an anti-tumor action.

The drug molecules present inside the core of the nanoshell are protected against degradation by the shell. This system is created by forcing the orientation of the PEG segment towards the surface and concentrating the hydrophobic polymer to core (Fig. 13.4). This nanosystem proved its efficacy in drug delivery when it safely transported the tetanus toxoid protein to the blood stream. Similar successful results were reported for salmon calcitonin peptide-nanoparticle complex when used in rats (Ref. 26). It has also been proved that nanocapsules made of poly alkylcyanoacrylate are able to increase the absorption of insulin when administered orally (Ref. 27).

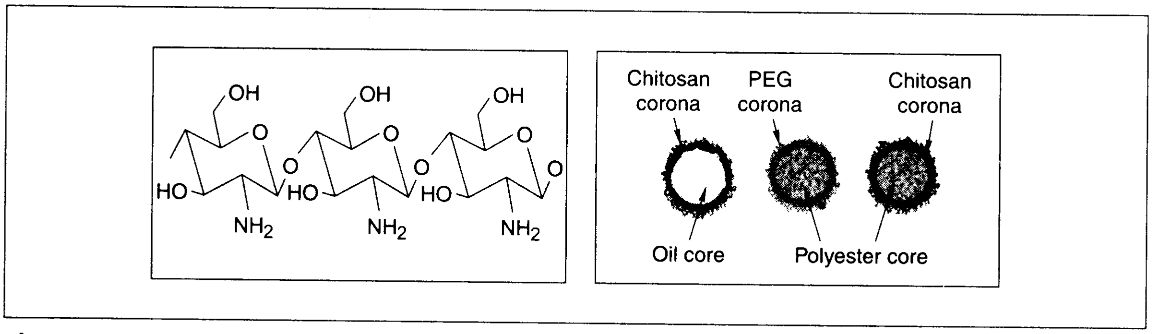


Fig. 13.4: *Structure of chitosan and various kinds of core-corona (core-shell) nanosystems.*

13.4.2 Nanoparticle-drug System for Nasal Administration

It has been established that the nasal route of drug delivery is more effective (especially for small peptides) due to a better transport process and lower enzymatic activity for nasal mucosa. Studies show that the nanoparticle–drug system is capable of crossing the nasal epithelium with the strong influence of nanoparticle surface composition on transport rates (Ref. 28). Bare nanoparticles aggregated on the mucus layer and hence were not transported with the model protein tetanus toxoid whereas a significant increase in the absorption was observed when PEG was used as a surface cover on the bare nanoparticle. PEG-covered nanoparticles were observed to be circulating in the blood stream and the associated protein was delivered at an appropriate location. Similar results have also been observed for various other kinds of vaccines (Ref. 29).

Chitosan-coated nanoparticles have also been observed to respond in a similar way. When they were tested for the nasal absorption of insulin in rabbits, it was observed that the absorption of the drug was significantly higher (Ref. 30). Similarly, improved nasal transport of the tetanus toxoid protein was observed when it was encapsulated in a chitosan-coated nanoparticle. This is because of the facilitated interaction and internalization of these nanosystems in the nasal epithelium.

13.4.3 Nanoparticle-drug System for Ocular Administration

It was observed that polyalkylcyanoacrylate nanoparticles were able to enter the well-organized corneal epithelium though it caused a slight damage to the epithelial cells. Due to better organization of cells in the corneal epithelium, the dimension of the carrier must be in the sub-micron region. It has also been established that the coating present on the surface of the nanoparticle has an important effect on drug transport through the corneal epithelium. When the experiments were conducted with ^{14}C-indomethacin-chitosan-coated nanosystems, it was observed that the complex penetrated to the superficial layers of the epithelium through a trans-cellular pathway and chitosan-coated systems had a good ocular tolerance (low ocular lesion index). This nanoparticle complex was also able to provide a selective and prolonged delivery of cyclosporine A to the ocular mucosa without compromising the inner ocular tissues by avoiding systemic absorption. This prolonged delivery was attributed to the ocular retention of chitosan nanoparticles (Refs 31, 32).

13.5 Nanotechnology in Diagnostic Applications

Research efforts are also being driven in the direction of using nanotechnology for molecular diagnostic purposes such as biological research, clinical diagnostics, detection of biomolecules and drug discovery. The focus of this section is on understanding the use of nanosystems for clinical diagnostics, especially in the early diagnosis of various forms of cancer.

The main drawback of the laboratory tests currently used for the detection of cancer is that they try to identify visible changes in cell morphology through microscopy. Evidently, this practice cannot state with 100 per cent specificity and sensitivity the true cases of disorder (identified by the clinical criterion) in the malignancy stage of cells. Unfortunately, detection of many cancers at the microscopic level often takes place when it is too late for successful intervention and these techniques suffer from intra-observational subjectivity (Ref. 34).

The development of tumors is a complex process, requiring the co-ordinated interactions of numerous proteins, signal pathways and cell types. As a result of extensive studies of the molecular pathogenesis of cancer, several novel regulatory pathways and networks have been identified. The delineation of these pathways has revealed several unique events, marked by morphological and histological changes of cells, and the expression of genes and proteins that accompany oncogenic transformation. Thus, the cell signature changes during cancer development. If these changes are read accurately, there is a strong likelihood of improving the early detection and diagnosis capabilities for various forms of cancer. These early changes in cell signature are reflected in the state of biomarkers. Biomarkers are measurable phenotypic parameters that characterize an organism's state of health or disease, or its response to a particular therapeutic intervention (Ref. 35).

Various approaches are being followed for improving clinical diagnostic capabilities. Essentially these approaches have to be molecular in nature. Here we discuss two approaches to develop molecular-based diagnostic tools, which can detect cancer in the very early stages.

Several groups have reported intra- as well as extra-cellular synthesis of metal nanoparticles using bacteria, fungi and viruses. This process involves the reduction of metal ions added to cells under suitable conditions, and the resultant appearance of nanoparticles or their aggregates, both inside as well as outside the cell boundary (Refs 36, 37).

Recent attempts to synthesize gold nanoparticles using human cells indicate that the cellular response towards the reduction of chloroaurate ions is different for normal and malignant cells. The growth of gold nanoparticles is confirmed by TEM images presented in Fig. 13.5. The cells shown here are HEK

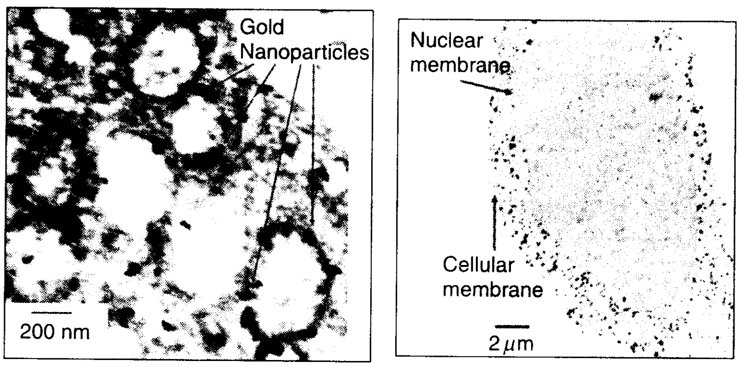


Fig. 13.5: *Electron micrographs of the growth of gold nanoparticles in HEK 293 (left) and SiHa (right) cells after incubation with 1 mM chloroaurate ions for 96 h. The left side image shows nanoparticles around cell bodies (From the author's work).*

(normal cell) and SiHa (cervical cancer) cells. The images show the presence of Au nanoparticles as black dots. The particles are in the size range of 20–100 nm and are distributed throughout the cytoplasm. Particles are found in the nucleus too, which are much smaller in diameter. The ability with which nanoparticles are synthesized by cells in different stages of infection can be quantified and may be used to pinpoint the level of infection in various kinds of cancer. The results indicate that there is a significant difference between the responses of cancer cells and those of non-cancer cells towards the bio-reduction process, which may be attributed to differences in the metabolism and kinetics of nanoparticle formation in the cells being investigated.

When the growth of gold nanoparticles was observed over a duration of 96 hours after incubating various cell lines with 1 mM chloroaurate ion solution, it was found that there existed a difference in the UV-visible feature for the cancer and non-cancer cells (Fig. 13.6). What one observes is that as a function of incubation time, the peak at 560 nm, corresponding to the plasmon excitation of gold nanoparticles, increases in intensity. Further, the curves for cancerous cells broadened after the cells were lysed, which suggests that the nature of the nanoparticles present inside and outside the cells was different. Lysing releases the nanoparticles into the solution, as a result of the breaking of the cell membrane. During the course of incubation, the supernatant solution above the cell line shows the gradual evolution of nanoparticle signature as mentioned before, because part of the nanoparticles can be leached of the cell. However, it is important to note that since most of the particles grown are large, they cannot diffuse out of the cell membrane and are seen in the absorption spectrum only after lysing. The quantification of the cellular response towards the nanoparticle synthesis of cells during various stages of cancer can then be utilized to develop a protocol for the early diagnosis of cancer.

In the second approach, research attempts are being made to read the state of various kinds of biomarkers for different types of cancer. The known biomarkers which can be utilized for this purpose are changes in protein concentration, genetic mutations, etc. For example, the concentration of protein p16, which is known to over-express itself during the Human Papilloma Virus (HPV) infection, can be used as a biomarker for cervical cancer detection. Hence, when the antibody specific to protein p16 is bound to nanoparticles and used for reading the p16 concentrations, the absolute concentration level can be ascertained. When this level is quantified for various stages of cervical cancer it can help in early diagnosis. The use of nanosystems for reading the state of biomarkers becomes important because of the high surface area offered by the nanoparticle surface (which facilitates the reading of even small changes in the biomarker state) and the ease with which nanosystems can interact with biomolecules. The feasibility of reading the state of biomarker (though without the use of nanosystems) has been demonstrated by the use of a molecular-based tool developed by Digene Corporation, The Hybrid Capture System. It is a signal amplification assay that uses antibody captures and signal detection for cervical cancer diagnosis. This protocol involves releasing the target DNA of HPV and combining it with an RNA probe. The resultant DNA–RNA hybrid is captured by using the antibody specific to the hybrid. The antibodies are bound to alkaline phosphatase which assists in the detection by the use of a luminometer (Ref. 38).

Various kinds of nanoparticles have been used for diagnostic applications. These include gold nanoparticles, quantum dots and magnetic nanoparticles, which are described in detail below.

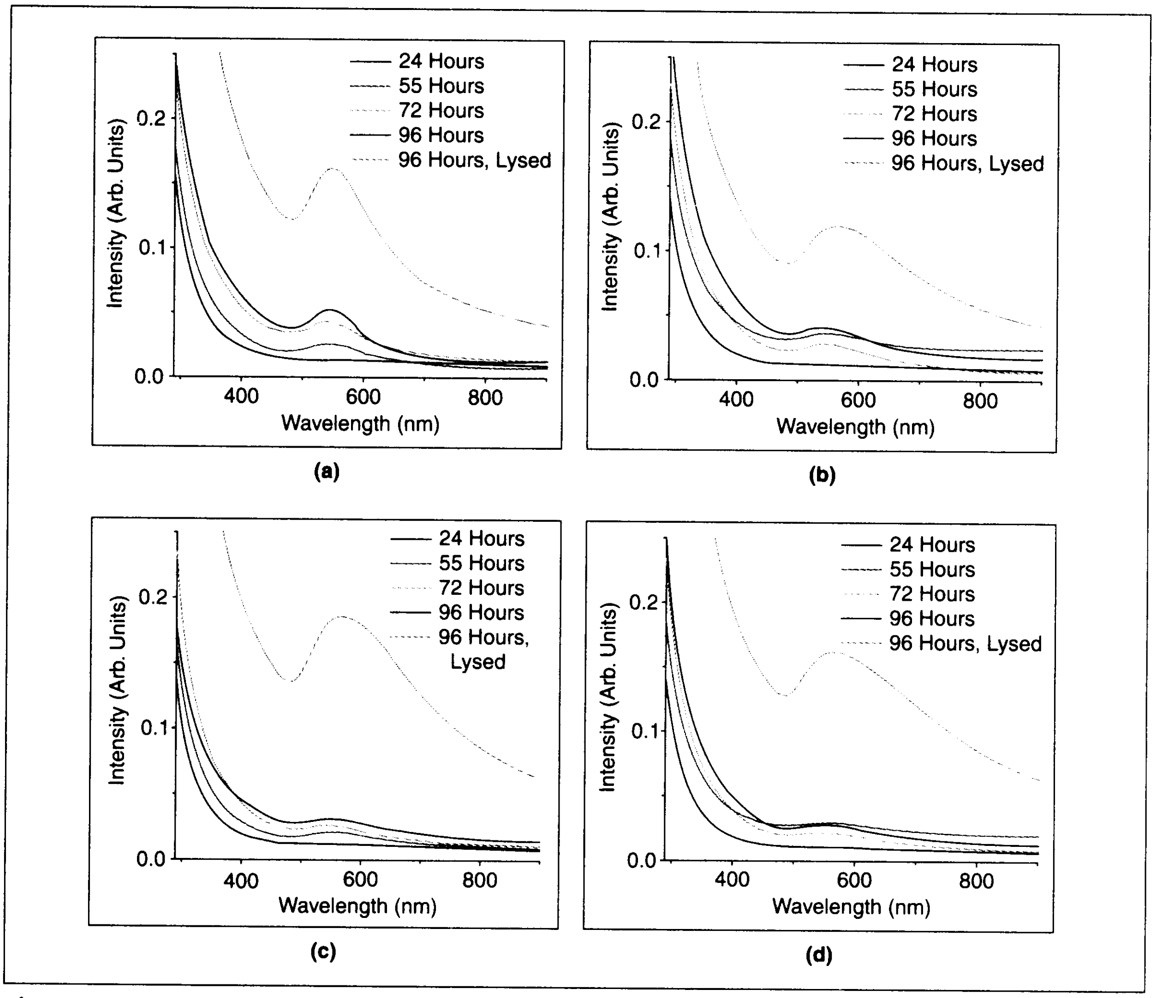


Fig. 13.6: *UV-vis spectrum for: (a) HEK 293 cells with 1 mM chloroaurate ion solution. (b) HeLa cells with 1 mM chloroaurate ion solution. (c) SiHa cells with 1 mM chloroaurate ion solution. (d) SKNSH cells with 1 mM chloroaurate ion solution. Except HEK 293, all others are cancer cells. Note the increase in width of the lyseel sample in b, c and d. All other measurements correspond to the supernatant solution in the cell culture well (From the author's work).*

13.6 Materials for Use in Diagnostic and Therapeutic Applications

13.6.1 Gold Nanoparticles

Gold nanoparticles are extraordinarily efficient for clinical diagnostic purposes as they give strong signatures in optical absorption and fluorescence spectroscopy, X-ray diffraction and electrical conductivity.

Additionally, gold nanoparticles interact strongly with biomolecules containing thiol or amine groups and can be suitably modified with a number of small molecules, proteins, DNA and polymers. Various biomolecules bound to the gold nanoparticle surface can be detected by using various analytical measurement tools such as MALDI-TOF MS and confocal Raman spectroscopy. Gold can be synthesized routinely in sizes varying continuously from 0.8 to 200 nm with <10 per cent size dispersity.

Gold nanoparticle characterization can be done by UV-vis spectroscopy in which a surface plasmon band appears at 500–700 nm. This happens because of electronic oscillations in the conduction band of metals, on exposure to electromagnetic waves (see Chapter 9, for a detailed description). The surface plasmon resonance phenomenon occurs due to a matching of the frequency of the oscillation of the electron cloud and that of the incident light. For gold nanoparticles, the frequency is in the visible region which imparts intense color to the nanoparticle solution.

13.6.2 Quantum Dots

Quantum dots (QDs) are nanoscale crystals synthesized with semiconductor materials (see Chapter 7). QDs are generating strong research interests in biology due to their fluorescence property seen when they are excited by a laser. Their fluorescence intensity is also significantly higher and are more stable as compared to conventional fluorescent markers. QDs have fairly broad excitation spectra which can be tuned by varying the physical size and composition. Additionally, QDs have narrow emission spectra, which means that it is possible to resolve the emissions of different nanoparticles simultaneously and with minimal overlap. Finally, QDs are highly resistant to degradation.

QD technology holds special promise for use with biomolecules. QDs can be specifically attached to molecules like proteins and nucleic acids. Some of the value additions that QDs can bring are:

1. It is easy to excite QDs which means that the possibility of drug degradation due to a high intensity excitation beam is discounted.
2. Whole blood assay can be done with the use of QDs because they can emit light throughout the electromagnetic spectrum.
3. This technology has high sensitivity and is easy to use.
4. Photobleaching does not occur with QDs which is a serious limitation in the case of fluorescent dyes.

The difficulty encountered with QDs is that their surface is hydrophobic in nature which makes its interaction with water-friendly molecules like proteins and DNAs extremely difficult. Research is being carried out to modify the surface of QDs so as to make them more biocompatible. For example, short size peptides have been used to coat QD surfaces and make them interact with cells. A unique new coating has been developed for inorganic particles at the nanoscale that may be able to disguise QDs as proteins—a process that allows particles to function as probes which can penetrate the cell and light up individual proteins inside, thereby creating the potential for a wide range of applications including cell imaging and clinical diagnostics (Ref. 39). Highly luminescent and stable QD bioconjugates are constantly being evaluated for use in cell imaging, which will help in developing better tools for clinical diagnostics. QDs, coated with a polyacrylate cap and covalently linked to antibodies or to streptavidin, have been used for the immunofluorescent labeling of breast cancer biomarker HER2 (human epidermal growth factor receptor 2). The advantages of using QD are that it facilitates highly specific labeling and makes the label brighter and more stable than that obtained with the use of conventional fluorescent markers.

13.6.3 Magnetic Nanoparticles

Another special class of nanoparticles, which is being intensively researched for use in biological systems is magnetic nanoparticles. These particles are superparamagnetic, i.e. they do not possess any magnetism in the absence of an applied field. They are being used for the detection of various kinds of biomolecules. Research efforts have proven the potential of cellular organisms to synthesize various magnetic nanoparticles. Like gold nanoparticles, they can also be used for cancer diagnostics through two approaches discussed in Section 13.5. Magnetic immunoassay techniques have been developed in which the magnetic field generated by the magnetically labeled targets is detected directly with a sensitive magnetometer. The binding of the antibody to the target molecules or to the disease-causing organism forms the basis of several tests. Antibodies labeled with magnetic nanoparticles emit magnetic signals on exposure to a magnetic field. Antibodies bound to targets can thus be identified as unbound antibodies are dispersed in all directions and produce no net magnetic signal. Another challenge in cancer diagnosis is the detection of circulating cancer cells in the blood. Magnetic nanoparticle-based tests are being developed to screen, diagnose, stage and monitor cancer on the basis of the circulating cancer cells in the blood.

13.7 Future Directions

Nanosize materials have found practical implementation in the field of medical diagnoses with the proper and efficient delivery of pharmaceuticals. While on the one hand, attempts are being made to develop accurate and versatile biomarkers for various kinds of diseases, on the other hand, research is constantly being driven to develop new protocols for creating synergies between bio- and nano-systems. However, there are several other intriguing proposals for the practical applications of nanomechanical tools into the fields of medical research and clinical practice. Such nanotools still await construction, but they may become a reality in the near future.

Newer avenues are being developed for using nanodevices in the field of clinical diagnostics and therapeutic applications. Currently, research efforts are being directed to develop suitable nano-bio-systems which can successfully replace defective/incorrectly functioning cells in various parts of the body. Attempts are being made to create artificial red blood cells which will provide oxygen more effectively as compared to the natural ones, deliver them into the human body and monitor their flow by using onboard nanosensors (Ref. 40). An onboard nanocomputer and numerous chemical and pressure sensors would facilitate complex device behaviors that will be remotely reprogrammable by the physician via externally applied acoustic signals. The ultimate aim is to develop a robust mechanism whereby the therapeutic intervention is able to locate the site of infection/disorder, diagnose the level of infection, deliver the drug in case therapeutic treatment is required (or kill the cells if necessary) and in the meantime, provide metabolic support in the event of impaired functioning. Attempts are being made to develop a feedback system integrated to therapeutic intervention which will constantly update the physician about the action of the drug and possibly make it feasible for the physician to change the guidelines for drug delivery as he/she may deem it better for more precise treatment. Such devices would have a small computer for information analysis, several binding sites to determine the concentration of specific molecules, drug molecules for treatment, and a supply of some 'poison' that could be released selectively. Similar machines equipped with specific 'weapons' could be used to remove obstructions in the circulatory system, or to identify and kill cancer cells. The use of such nanorobots would enable medical specialists to ascertain the level of infection after examination of the tissue location and variations in its biochemistry and biomechanics. Accordingly, a programmable algorithm would initiate therapeutic intervention for accurate and reliable drug delivery (Refs 41, 42).

These steps for reaching the ultimate objective of gaining control over various kinds of diseases that humans suffer from, will involve a three-dimensional approach, i.e. development of a better understanding of biological systems, creation of nanosystems and integration of nano-bio systems. It may seem impossible to develop a kind of nanomachine which when injected into the human body, will itself do the job of finding the location of the disease, treating/killing it and providing transitory support for the metabolic processes but a step-by-step approach to nano-bio integration could make this possibility real in the distant future.

Review Questions

1. Will nanomedicines be used in nanoscale? How do we apply them?
2. What are the systems used and how nano-properties are useful?
3. What are the properties useful for diagnostic applications?
4. What are the advantages of magnetic nanoparticles in nanomedicine?
5. What are the properties of nanoparticles themselves (as opposed to the molecules anchored on them) useful for therapeutic applications?

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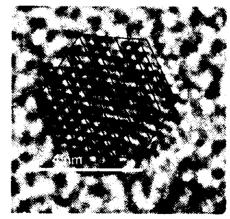
Chapter 14

Molecular Nanomachines



The designing of molecules performing mechanical functions is one of the larger goals of nanoscience. The development of such molecular systems would lead to the creation of integrated nanodevices. Several molecular systems have been designed to perform translations and rotations. These have also been used as switches and logic gates. In this chapter, we provide an introduction to this area, purely from the point of view of synthetic molecular machines, while focusing on one class of chemical systems, namely rotaxanes. We also highlight the problems that occur in this area when such systems are used as device components.

Learning Objectives

- What are molecular machines?
- What are the various functions achieved by these systems?
- What are rotaxanes and catenanes?
- How do we construct molecular shuttles with them?
- What are the difficulties in developing molecular devices?

14.1 Introduction

Nanoscience and technology are concerned with the manipulation of objects of nanometer dimensions. This entails playing with atoms and molecules in a programmed fashion. The motion of objects as per instructions (or stimuli) can be used to store and retrieve information, construct switches, and deliver materials of molecular dimensions among other things. This branch of science, which is concerned with the motion of molecules and atoms as a result of external stimuli, is called 'molecular nanomachines'. In brief, it deals with molecular objects performing mechanical functions. All these functions are similar to those being performed by biology in a highly precise manner for millions of years. The current interest in such processes stems from the fact that device dimensions are shrinking, and it is necessary to rely on to the molecular regime ultimately to perform functions which have hitherto been undertaken with macroscopic objects. Obviously in this size regime, systems have to obey the rules of atoms and molecules, namely quantum mechanics. Newton's equations of motion have to be satisfied by a macroscopic object in motion, and the former give the position at every stage of motion. In the case of molecular objects, the forces and quantum states of the system are related by the Schrödinger equation of motion. Due to the abstractness of the wave equation, the macroscopic analogies of motion may not be accurate enough to describe molecular processes. In this chapter, we shall examine some of the examples of molecular nanomachines constructed in the laboratory so that the reader can appreciate the challenges and prospects related to these machines. The discussion will not include the theoretical aspects of molecular motion for which the reader may consult the additional reading material listed at the end of the chapter.

14.2 Covalent and Non-covalent Approaches

As mentioned in the Introduction, Feynman postulated the possibility of atomically manipulated matter in 1959. He said, "The principles of physics do not speak against the possibility of maneuvering things atom by atom." However, the manipulation of atoms is difficult as isolated atoms are extremely reactive and form bonds instantaneously. The construction of an architecture arranged by atoms, one by one, therefore, may be possible in an inert atmosphere, but it is practically impossible in the laboratory ambience, unless, of course, it is used in synthesis in condensed media as in the case of nanoparticles. However, such approaches are important even for devices and we have outlined atomic manipulations in vacuum in Chapter 2 of this book. Thus the 'bottom-up' methodology is unlikely to be realized by starting with atomic building blocks.

The manipulation of molecules and implementation of their functions requires the use of synthetic chemistry. In the covalent approach of synthesis or routine chemistry, covalent bonds are added in a series to assemble larger structures. These approaches have yielded phenomenal successes in the past such as advances in pharmaceuticals, in which complex structures with structural and steriochemical specificity are synthesized in large quantities. However, this approach necessitates precise control of synthetic parameters to assemble units one after another. There can be minor errors in the construction and the synthesized structure can have a smaller fraction of the unwanted structures. This requires purification, which involves additional effort. Thus a typical covalent synthesis requires precise control of parameters, longer time and more effort.

The alternate approach used for making larger structures is non-covalent self-assembly. In this case, smaller building blocks are added together to form larger structures that utilize weak non-covalent interactions between the molecular units. These interactions ultimately create a structure which is thermodynamically stable. This process makes the assembly reversible, implying that dismantling and reconstruction are possible. In biology, all the structures are made by self-assembly, and the DNA double helix is a classic example wherein non-covalent interactions make and reform structures. This branch of chemistry, called 'supramolecular chemistry', was recognized with a Nobel prize awarded to C.J. Pedersen, D.J. Cram and J.-M. Lehn in 1987.

The approaches of supramolecular chemistry are better for making bottom-up architectures, especially those intended to function as machines. This is because molecular building blocks have definite shapes, sizes and properties. Developments in areas such as scanning probe microscopy have made it possible to manipulate molecules effectively. These modified structures can be studied at the single molecule level by advanced spectroscopic techniques such as single molecule spectroscopy. Today, it is possible to make electrical contacts with single molecules so that single molecule conductivity can be investigated. All these advances have propelled device structures at the single molecule level to the forefront of research.

We must also remember that self-assembly can also occur with covalent modifications. Here, a self-assembled superstructure goes through a covalent modification. As a result of this change, the system, as a whole, achieves functional competence. Several of the structures discussed in this chapter are formed as a result of this process. Here kinetic control of the process makes the system.

Numerous kinds of structures can be made by using the above approaches. All of them are directed towards making 'functional structures'. In the context of a molecular system, a functional assembly constitutes chemical architecture in which responsive modules can be made to perform specific functions by activation by external stimulus including photons, electrons, ions, heat, etc. Such structures can be used for a variety of functions such as chemical switching, logic gates, molecular shuttles, etc. In the following sections, we shall study some functional entities. It is important to realize that a functional system will have several components and all those components have to be linked in a co-ordinated manner in order to form a working machine.

14.3 Molecular Motors and Machines

Terms such as 'molecular motors' and 'molecular machines' are commonly used in literature. Before discussing specific examples, it is important to understand what their macroscopic analogues are. A macroscopic motor is a device which converts energy into mechanical work, often in the form of displacement. A machine is an assembly of devices designed to perform functions by consuming energy. Thus machine is a larger entity in comparison to a motor in its complexity. Molecular analogues of motors and machines facilitate the displacement of molecular co-ordinates by external energy stimulus. Although a single bond allows free rotation resulting in atomic displacements in most molecules in the gaseous and liquid phases, they are not referred to as molecular motors because designed molecular motion is not possible. In a molecular motor or machine, displacement can be controlled by a chemical or physical stimulus. A physical stimulus is far better than a chemical one as a chemical reaction leads to by-products which may hinder the performance of the motor or machine on a larger scale. The displacements themselves will be only of the order of molecular dimensions, but when scaled to the size of macroscopic objects, the distances involved become very large.

Molecular machines are characterized by the same kind of parameters that characterize macroscopic motors. They could involve: (i) a type of energy stimulus (chemical reactions, photons), (ii) a type of mechanical transformation (which could be translational or rotational), (iii) repeatability of the event as and when required (controllability) and (iv) time scale needed for the process to occur (as all these machines depend on a change in the nuclear co-ordinates of atoms). Ultimately, the motor results in a function which can also be used to categorize it. The resultant motions should be monitored, which makes it mandatory to bring about changes in the spectroscopic/molecular properties of the system while the change occurs. The changes should be monitored with the help of experimental techniques which become the readout when the device is used for a read-write operation. Obviously, the reading and writing mechanism should be able to pick the molecular scale objects. Ultimately, the molecular motion devices made should be usable somewhere. While the functions of macroscopic analogues are performed in day-to-day life, the functions that molecular motors are likely to perform are still being discussed. In several cases, such operations can be used to construct logic gates and transistors, and may be useful in molecular computing. These ideas have been proven in the simplest cases, but no functional architectures have been made. For a recent review of the topic, see Ref. 1.

The molecular machines discussed here are distinctly different from the molecular motors investigated in biology. Biological systems work through the co-operation of several molecules with different functions. Here, the motor proteins bind to a cytoskeletal filament and move along its length by repeated adenosine triphosphate (ATP) hydrolysis. Several kinds of motor proteins co-exist in the cell and they differ in various aspects such as the binding filament, direction of motion and the cargo carried. The protein contains a head region which binds and hydrolyses ATP, and a tail region which recognizes the cargo. The protein motion occurs in steps wherein the protein is bound and unbound to the filament, and in between the steps, conformational changes occur, which trigger motion. There are broadly three kinds of motor protein families: myosin, kinesin and dynein. While the myosin proteins move on actin filaments, the kinesin and dynein proteins move on microtubules. Within a family, the motor head is shared and can be attached to a variety of tails, as a result of which they perform different functions. Myosin and kinesin walk along different tracks but they share a structural core suggesting that they have common ancestry. A discussion of molecular motors of biology can be found in Ref. 2. The motion of single actin filaments supported on myosin heads, which in turn, are adsorbed on nitrocellulose-coated glass cover slips, has been imaged. The filaments are fluorescent-labeled in this kind of study, which is carried out by optical microscopy. Although the filament has a ~9 nm diameter, the fluorescence technique suffers from the diffraction limit and the single filaments appear much larger in the optical images. In contrast, the molecular motors of chemists, are single molecules in which one part undergoes motion upon excitation by a stimulus.

14.4 Molecular Devices

The most important aspect of nanoscale devices is the incorporation of molecular building blocks. As we have seen in several chapters (Chapters 4, 5, 7 and 8) in order to make architectures efficiently, it is necessary to use the approaches of self-assembly as the serial arrangement of units will be practically impossible (to make structures on a large scale). The approaches must be similar to those used in biology. In such structures, the molecular systems used are functional in nature. This functionality is triggered by activation involving photons, electrons and ions. Any form of effect seen in a material made of molecular components is caused by an external trigger, as very few systems change without any stimulus. An exception would be phenomena such as radioactivity. In a molecular system, there can be many responses to a stimulus. However, here we will consider only molecular level changes, which are easier to probe by using the techniques of spectroscopy. Properties such as magnetism or conductivity are also observed when an assembly of molecules is considered, though there are also molecular analogues of such phenomena. As a result of the stimulus, several processes can occur, including changes in the volume or shape (photoresponsive polymers, actuators), in color (photochromic), in molecular order (liquid crystal), in sensing (molecular recognition), in movement (molecular machines), etc. The nanosystem or device can be categorized as being photoactive, redoxative or ionactive depending on the nature of the stimulus, namely photons, redox chemistry or ions, respectively.

14.5 Single Molecule Devices

14.5.1 Switches

The most important aspect of a switch is that it has the ability to exist in two states, which can be interconverted. This property is called 'bistability'. The manner in which the change is brought about is referred to as 'writing' and the process through which these states are identified constitutes 'reading'. Thus the switch can be used as a memory element in binary logic (Fig. 14.1).

Several molecular systems are used as switches (Ref. 3). These conform to several broad categories, namely conformational change, configurational change and constitutional change. In conformational change, the conformational property of the system is altered when the stimulus is applied. In configurational change, the typical approach is to change *cis-trans* isomerization resulting in a system which has different properties from the earlier one. In configurational change, the chemical entity formed as a result of external stimulus is different as in the case of photoinduced cyclization. Here, we shall discuss one example from each of these categories. The objective is not to discuss the entire literature, but to present the concepts.

	Stimulus 1	
State A	$\rightleftharpoons$	**State B**
State 0	Stimulus 2	State 1

Fig. 14.1: *Concept of bistability. The system is stable in two states and they can be interconverted by the action of external stimulus.*

Conformational change The process shown in Fig. 14.2 can be illustrated with the example of a reversible molecular brake. Here, the triptycene unit undergoes free rotation around the single bond which connects it to the bipyridine unit. This occurs in solution. Upon the addition of the Hg salt, a conformational change occurs and the free rotation around the single bond is hindered. In this process, the bipyridine unit acts as a brake. The removal of the Hg^{2+} ion by the addition of EDTA restores free rotation. Thus the system is reversible. A motion of this kind is observable in terms of the NMR signatures of the system (Ref. 4).

Configurational change Azobenzenes exist in two forms (*E* and *Z*) and these are interconvertible by light irradiation. The state in which azobenzenes exist can be probed by absorption spectroscopy. When incorporated in matrices such as polymeric liquid crystals, such systems induce observable changes.

Constitutional change The photochromic behavior of syropyrans is one example of a light-induced structural change. Here the closed colorless form (spiropyran) gets converted into an open colored form (merocyanine) upon light irradiation. The open form goes back to the closed form photochemically or thermally. The lifetime of the zwitterionic form can be increased by the introduction of substituents that have an electron withdrawing character. The incorporation of these units into materials can result in observable changes.

14.5.1.1 Supramolecular systems

Supramolecular structures can also be effective in switching. In fact, it is possible to make switches easily with weak non-covalent interactions as they are reversible. Numerous kinds of such systems are known. The following case is an example of such systems. The incorporation of azobenzene unit into a crown ether can make the complexation ability of the latter photoswitchable (Ref. 5). The (*E*)-isomer of the azacrown molecule does not have space to accommodate the alkali metal cations, but the (*Z*)-isomer shows a high affinity. The (*E*) to (*Z*) conversion is both photoswitchable and reversible. Thermal re-isomerization, as it occurs in azobenzenes, is inhibited due to the formation of the complex. The switching is complete as the (*E*)-isomer does not bind at all. The examples listed above are presented in Fig. 14.2.

There are several other ways in which supramolecular structures can show switching behavior. The switching on and off of fluorescence is a common approach. Changes in the ionic concentration and pH can be used to effect this change. The switching of ligands and the resultant change in the properties of a metal containing system is another method used to bring about switching. The photoswichable complexation of metalloporphyrins is another example of such switching. The spectroscopic signature of the complexed and uncomplexed states will be different which can be used for identification.

14.5.2 Molecular Ratchet

Ratchets allow motion in one direction only. The simplest devices of this kind would have a toothed ratchet wheel, a pawl that prevents rotation in the unintended direction and a spring to hold the pawl in position, as shown schematically in Fig. 14.3. One can think of designing a ratchet with these components in a molecular sense. A candidate for the same is shown in Fig. 14.3, which has a [4]helicene unit. Helicenes are polycyclic aromatic compounds which possess a helical structure as a consequence of the steric repulsion of the aromatic nuclei at the ends. The structure has a helicity, which is evident from Fig. 14.3. Rotation of the triptycene unit will make the helicene more aplanar so that an energy maximum is reached. This rotation in the clockwise direction is preferred over the anti-clockwise rotation. The NMR investigations of this system have indicated that the rotation is possible in both the directions and has no specificity (Ref. 6). This is because the molecular system obeys the principle of microscopic reversibility, i.e. in a system at equilibrium, the reverse process is equally probable as the forward process. What this means is that every position of the molecular conformation is possible and the system has an equal probability of yield a rod with stoppers and not a rod with the bead in the middle and stoppers at the end. This is a matter of probability. However, if the interacting units can be self-organized to some smart reacting system forming a pre-assembly, the reaction may become more feasible. It can be seen that a rod and bead can pre-assemble and the stopper is added later. The routes used for the synthesis are listed in Fig. 14.5,

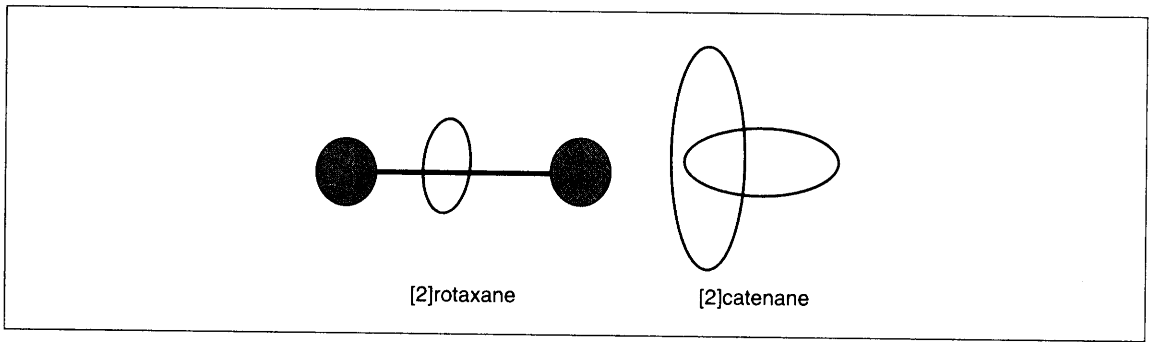


Fig. 14.4: *Schematic representations of a rotaxane and a catenane. There are two interconnected units in both and that makes the prefix [2].*

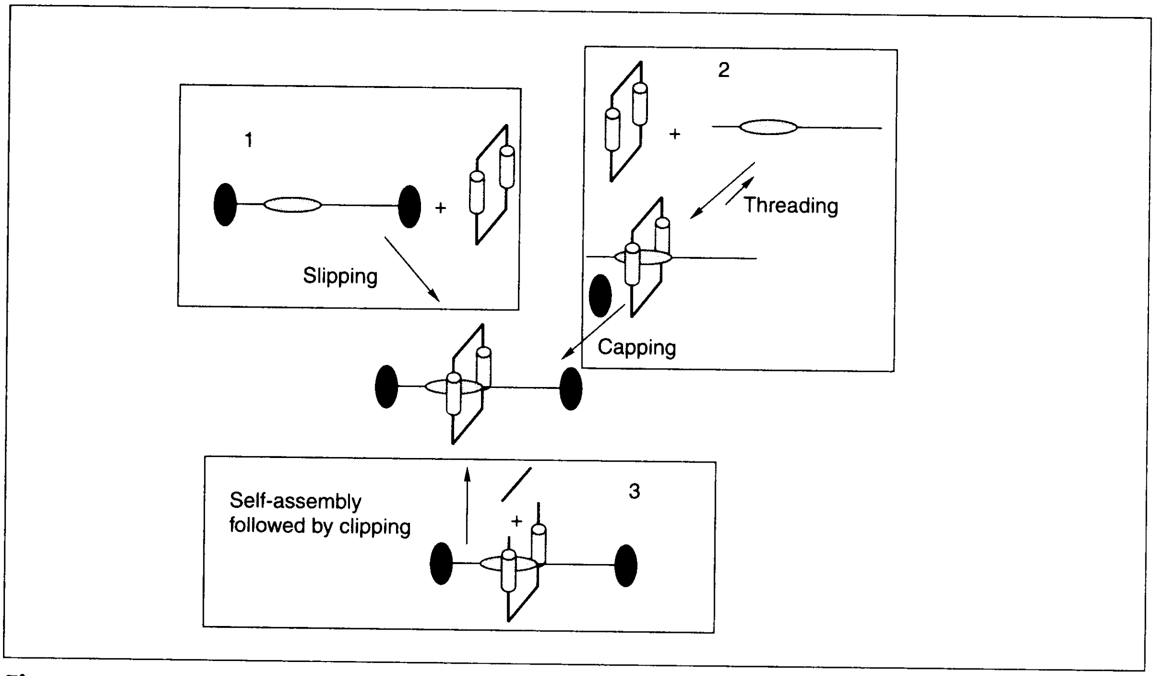


Fig. 14.5: *Synthetic approaches used for rotaxanes. In step 2, the de-threaded state exists in equilibrium with the threaded state. Three strategies are shown of which 3 involves proper design of components so that the starting material is assembled to some extent.*

while specific chemical examples are not given. Each of the specific methods is named and the process is self-explanatory. In the case of clipping, part of the structure is self-assembled utilizing preferred interactions and the last unit is integrated to the assembled structure.

There are several ways whereby mechanical motions can be introduced in this kind of systems. In the case of psueodorotaxanes, wherein the molecules are not physically restricted, two kinds of processes, namely 'threading' and 'de-threading', can occur without external stimulus. The two states are, in fact, in dynamic equilibrium. In rotaxanes and catenanes, two (or more) possible arrangements can also occur as a result of thermal activation. In Fig. 14.6, we show the schematic of a [2]rotaxane in which two states are possible. These correspond to the residence of the bead at the two possible stations. If the energy difference between the states is not large, and is within thermal energy, the states can co-exist and interconvert at room temperature. The equilibrium between various structures can be shifted by temperature. However, in the case of a molecular machine, we are interested in programmed conversion between structures by a stimulus. Ideally only one state should exist (corresponding to occupancy of station 1), which will get converted completely to the other (corresponding to occupancy of station 2) as a result of the stimulus. The state 1 will convert back to 2 and this process is reversible.

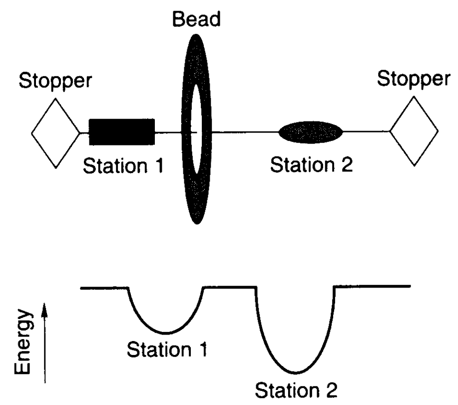


Fig. 14.6: *Schematic illustration of a [2]rotaxane structure in which two stations are incorporated on the rod. The bead can slide over the thread and can be held at station 1 or station 2, depending upon the strength of the interaction as shown in the potential energy diagram. Deeper potential well at station 2 makes that isomer to form preferentially. When the potential is unfavorable at that position, due to repulsive interaction between the station and the bead (as in the case of an electrochemical oxidation), the potential energy surface gets modified and the minimum becomes a maximum. As a result the bead slides over to the other station. When the oxidized state is reduced, the original situation returns and the bead returns.*

The first molecular shuttle (Ref. 7) was reported in 1991. It has a rod with two hydroquinone rings separated by a polyether chain and two stoppers at the end. The bead is the cyclobis(paraquat-*p*-phynylene) tetracation. The bead shuttles between the two degenerate positions approximately 500 times a second in solution, at room temperature. The movement of this kind of a unit shows no switching properties. In order to incorporate switching properties, the bead has to preferentially reside at one place and has to move to another location by the use of an external stimulus which may be chemical, photochemical or electrochemical. The effect of the stimulus has to be reversible so that the system can work as a switch.

One of the systems (Ref. 8) in which such a switching bahavior is manifested is shown in Fig. 14.7. The stations consist of benzidine and biphenol units. The bead preferentially lies on the π-electron rich benzidine unit. This is inferred from the proton NMR spectrum measured in CD_3CN. The two possibilities, namely occupancy of station 1 (benzidine) is 84 per cent in comparison to station 2 (biphenol). However, upon electrochemical oxidation of the benzidine unit to the radical cation, the cyclophane faces repulsion and moves to the neutral biphenol unit. When the benzidine unit is reduced back to the neutral form, the system comes back to the original situation. The same switching behavior is produced by protonating the bezidine unit by treatment with trifluoroacetic acid (TFA) and subsequent treatment with pyridine to get back the neutral form. Therefore, this reversible character makes it possible to form a binary molecular switch.

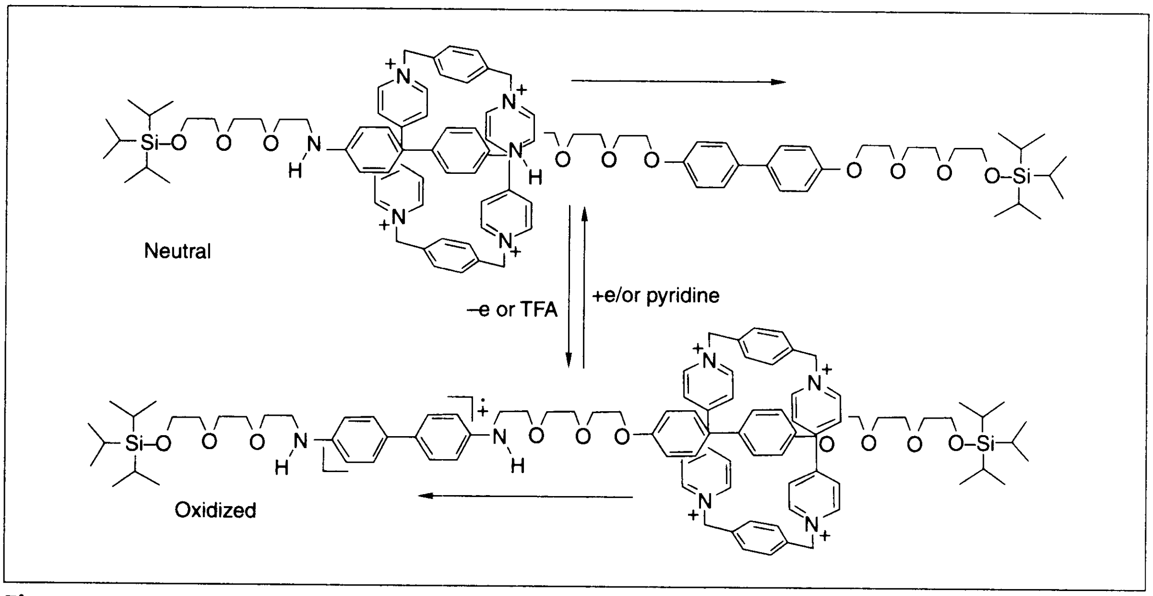


Fig. 14.7: *A rotaxane in which molecular motion has been demonstrated. The neutral molecule predominantly exists in the structure shown (86 per cent occupancy) and when the benzidine unit is oxidized either electrochemically or chemically, the bead shifts to the other station.*

The two isomeric structures have their characteristic charge-transfer bands. The differences are quite distinct and the color changes can be observed even by the naked eye. The charge transfer of benzidine occurs at 690 nm whereas that of biphenol occurs at 480 nm. As a result of the different charge transfer bands, the color changes from deep green to light red when acid is added, and the green color is regenerated by the addition of base. Thus the read-write property of the system can be demonstrated.

The principal advantage of the rotaxane- or catenane-based system is the confinement of the moving part within the molecule. It is possible to have a system in which the electron acceptor is in equilibrium with the two possible donor molecules. The binding with one of the donors can be stronger than that of the other but a complete switching from one to the other donor is not possible as the trimolecular system will always be in thermodynamic equilibrium between the various possibilities. It is important to recall that complete reversible switching is required for the system to be used as a device. The co-existence of other structures would lead to information scrambling in a storage device.

Similar kinds of molecular switches have been made with stimuli such as pH and light. In the case of light, photoisomerization is often utilized. The light-induced structural change of the rod makes the bead move in one direction. This process is reversed by a photon of another frequency thereby effecting recovery of the initial state. The binding of ions at specific locations and reversible electrochemistry of such systems can lead to interesting changes such as color (light absorption) or emission.

14.6 Practical Problems with Molecular Devices

It would be interesting to use any device of this kind for technological applications only if it has specific advantages. These advantages should pertain to device density, switching speed and device stability. A brief discussion of the important parameters is given below. The switching rate between the two states is an important parameter. In the specific case of the rotaxane discussed earlier, the measured shuttling time is of the order of milliseconds (Ref. 9). This means that one can have 1000 operations per second. In a semiconductor device such as MOSFET, the switching speed is of the order of 10 MHz, while the switching time is in the range of nanoseconds. What is the best time that can be achieved in a rotaxane? In the most simplistic model, the motion of the bead along the thread can be treated as a random walk in the absence of any interaction. The displacement, d after a time t is characterized by a diffusion coefficient, D. One can write $d = \sqrt{(2Dt)}$. In the case discussed above, d is 16 Å and if one takes the typical diffusion coefficient of 10^{-5} cm^2/s in condensed media, the shuttling time is of the order of nanoseconds. However, this is not achieved experimentally. This indicates that the interaction of the bead with the thread and the station limits its motion. Faster shuttling motion will be difficult to attain in these molecular systems and it is not possible to achieve the motion as fast as electrons or holes. This is because it will be practically impossible to eliminate interactions.

However, it may be possible to increase storage density by using rotaxanes. Substantially smaller number of atoms are needed to store per bit of information in rotaxanes in comparison to silicon. In the case discussed, one bit of information is stored with 274 atoms while typical electronic circuits require about 10^6 atoms to do the same job, though this number is shrinking. In real devices, it may not be possible to pack the molecules close together to get larger storage densities as intermolecular interactions would cause scrambling. In a device using the rotaxane discussed, the information is written in terms of the oxidized or neutral form. The oxidized form has to be stable for the period of storage for the information to be safe. This would necessitate the inclusion of spacers in order to avoid intermolecular electron transfer processes, which would reduce storage density.

When the device dimension shrinks, it is important to address single molecules with electrical connections. Although molecular wires have been developed, facilitating single molecule electrical contacts is a problem, which is yet to be solved. It may be necessary to develop devices with scanning probe microscopies to read and write the information. In a recent demonstration, a L-B film of rotaxane was made on a conducting glass surface and a potential was applied to it by using a scanning tunneling microscope. The potential switches the position of the bead to another area of the thread, changing the conformation and part of the molecule stick out from the surface by a small distance. This makes it possible to record information. However, erasing the information has not been possible (Ref. 10). The stability of such devices for repeated usage is an important issue to be considered.

Review Questions

1. What are the differences between molecular machines and macroscopic machines?
2. What are molecular switches?
3. What are the molecular properties used to achieve mechanical functions?
4. What are the functions achieved by rotaxanes and catenanes?
5. How fast molecular shuttles are?
6. What are the limitations of molecular devices?
7. What are the possible device applications?
8. What are molecular logic gates?

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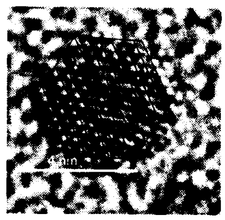
Chapter 15

NANOTRIBOLOGY



Nanotribology is concerned with the interactions of objects at the nanoscale. These interactions are important as device structures are shrinking in size and information is compressed in space. Reducing friction of interacting surfaces will be very important in the area of micro and nano electromechanical devices. As one studies these interactions at nanometer precision, we see that they have a molecular basis. Thus the study of nanotribology is to do with understanding macroscopic processes such as friction at the molecular level. This is possible with the application of modern techniques to engineering problems.

Learning Objectives

- What is nanotribology?
- Why are interfacial problems important at nanodimensions?
- How do we study interfacial properties with atomic precision?
- What are the typical applications of nanotribology?

15.1 Introduction

Tribology is one of the oldest sciences, but is still not well understood. 'Tribology', like many other technical terms, has a Greek origin. The two Greek words 'tribo' and 'logy' refer to 'rubbing' and 'knowledge', respectively, defining tribology as 'the knowledge of rubbing'. The Greeks applied it to understand the motion of large stones across the earth's surface. However, today tribology plays a crucial role in a number of technological areas with the main ones being polishing and lubrication of substrates for electronic applications (MEMS/NEMS) and in increasing the lifespan of mechanical components.

With advances in technology, the size of mechanical, electrical and optical components is reducing rapidly. Today, we require rapid actuation, which requires fast moving interacting surfaces. Extraordinary advances in MEMS/NEMS, data storage devices and micro-machines have been observed in recent times. Aerospace and automotive industries require materials with low friction and adhesion. Lubrication has served as a solution to face these needs, but the development of lubricants in the automobile industry depends on the adhesion of monolayers (see Chapter 5) to the material surface and hence a need to study tribology at a proportionate scale is being felt.

Technically nanotribology can be defined as the investigations of interfacial processes, on molecular length scales, occurring during adhesion, friction, wear, nanoindentation and thin-film lubrication at sliding interfaces. Nanotribology studies reveal behavior that can be quite different from that observed at macroscopic levels. A study of tribological behaviors can help us manipulate matter at the nanoscale. We can take advantage of the new electronic and atomic interactions as well as the new mechanical and magnetic properties observed at the nano levels to understand the synthesis, assembling and processing of nanoscale building blocks, composites, coatings, and smart materials with reduced and controlled friction, wear and corrosion. Ultimately these interactions will decide the applicability of nanomaterials in emerging areas (Refs 1, 2, 3).

15.2 Studying Tribology at the Nanoscale

Several instruments are being used nowadays to study tribology at this length scale. Some of them have been described below. Some of these techniques are discussed in detail in Refs 4–8.

15.2.1 Nanotribometer

In nano-tribometer (Fig. 15.1) a flat, a pin or a sphere is pressed onto the test sample with a precisely known force. These are mounted on a stiff lever, which acts as a transducer to measure the friction force. The friction coefficient is determined by measuring the normal and lateral forces as the pin moves by

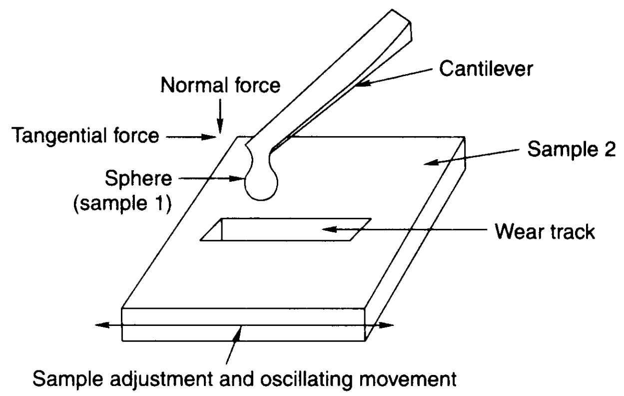


Fig. 15.1: *A nanotribometer being used to study the wear of sample 2 by sample 1, spherical in shape. The tangential force causes a deflection in the cantilever (attached to the ball), which gives the measure of the friction force (by using a traducer). By studying the wear tracks, wear coefficients are obtained.*

keeping track of the deflection in the cantilever. Wear coefficients for the pin, disc, sphere or plate are calculated from the amount of material lost during the test. The method facilitates the study of friction and wear behavior of almost every solid combination with or without the presence of a lubricant in between.

15.2.2 Surface Force Apparatus (SFA)

SFA or the surface force apparatus was developed in the 1960s and has been commonly used to study the static and dynamic properties of molecularly thin films sandwiched between two molecularly smooth surfaces. The SFA has a pair of atomically smooth surfaces (mica sheets) mounted on crossed cylinders (cylinder axis 90° to each other). This pair of crossed cylinders of the same radius of curvature, is the geometrical equivalent of a sphere in interaction with a flat surface. Molecules of our interest can be attached to these mica surfaces, and then surfaces may be immersed completely within a liquid, or maintained in a controlled environment. Actuators attached to either or both of the surfaces' supports are used to apply a load or shear force and used to control the distance of separation between them. Load and friction forces are measured with the help of the sensors. The contact area and relative separation of the surfaces can be measured with optical (as shown in Fig. 15.2) or capacitance measurements. The separation distances can be measured and controlled to the angstrom levels.

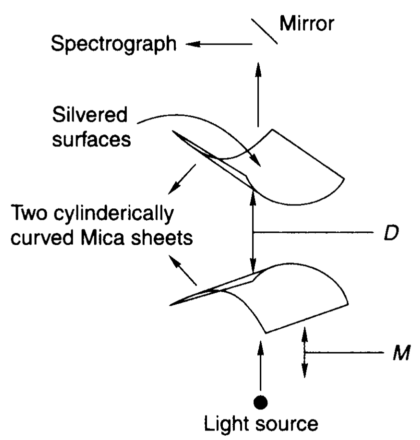


Fig. 15.2: *Schematic of a SFA (top view).*

The distance D between the surfaces is varied by using a piezoelectric actuator (which moves by a distance M). When the two surfaces are sufficiently far apart, the motion of the actuator will result in an equal change in the surface distance. But when the surfaces are close to each other, due to the interactions, the actuator motion will not be equal to the distance between the surfaces. Hence, by calculating the actual distance between the sheets by interferometry, we can learn about the forces of interaction. The difference in the actual distance and that detected by the device is positive if there is repulsion between the sheets and vice versa.

The lateral resolution is limited to the range of several micrometers. The instrument is thus a model contact wherein the contacting geometry is known. Therefore, by varying the material between the surfaces, the interaction forces can be controlled and measured. The drawbacks of the instrument are that the lateral resolution is limited, molecular smoothness is required to obtain meaningful results, and so usually, the substrate is restricted to mica.

15.2.3 Quartz Crystal Microbalance (QCM)

QCM is used for monitoring thin film growth with sub-monolayer sensitivity, since the shift in resonance frequency (of the sensing surface) is proportional to the mass of the absorbed film. It is nothing but an ultra-sensitive mass sensor. It consists of a quartz crystal sandwiched between two electrodes, as shown in Fig. 15.3. These electrodes are further connected to an oscillator, which make the quartz crystal oscillate with a stable frequency of f_o. If a rigid layer is evenly deposited on one or both of the electrodes (sensing surface), the resonant frequency will decrease proportionally to the mass of the adsorbed layer according to the Sauerbrey equation:

$$D_f = -[2f_o^2 D_m]/[A(r_q m_q)^{1/2}],$$

where

D_f = measured frequency shift,

f_o = resonant frequency of the fundamental mode of the crystal,

D_m = mass change per unit area (g/cm^2),

A = piezo-electrically active area,

r_q = density of quartz, 2.648 g/cm^3,

m_q = shear modulus of quartz, 2.947×10^{11} g/cm. s^2.

The typical surface used for QCM studies is a thin film gold coated over a quartz crystal (Fig. 15.3). The electrode surfaces are deposited by using vapor deposition.

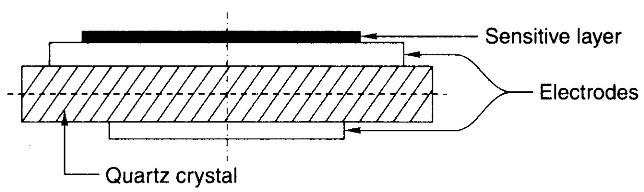


Fig. 15.3: *Schematic of a quartz resonator working in shear mode. The standard quartz crystal has a gold sensor surface. Other surfaces are available such as metals, polymers and chemically modified surfaces.*

In other words,

$$D_f = C \times D_m/A,$$

where C directly depends on the quartz crystal properties. C is typically around 10^8 and hence even a slight change in mass during the tribological action can be detected easily by keeping note of the QCM frequency. Thus a quartz crystal microbalance can be helpful in studying tribology at the nano-level.

15.2.4 Atomic Force Microscope

For friction force calculations, we slide the cantilever orthogonal to the long axis of the cantilever (in the contact mode). Here the changes in the intensities in the right and left halves of the four quadrant photodiode (because of twisting of the cantilever due to friction) help us calculate the friction parameters. Please see Chapter 2 for a discussion of the principle of AFM.

Figure 15.4 gives the images after scanning on the surface along the long axis of the cantilever, (a), and perpendicular to it, (b). Note how different the two scans are. Actually, Bhushan (Refs 6, 7) has shown that the friction force scan images are found to be more similar to the 3D plot of slope of the roughness scan, (a), versus distance. For example, the initial peak in (b) is similar to the sudden increase in slope of the roughness scan in (a) at the same location.

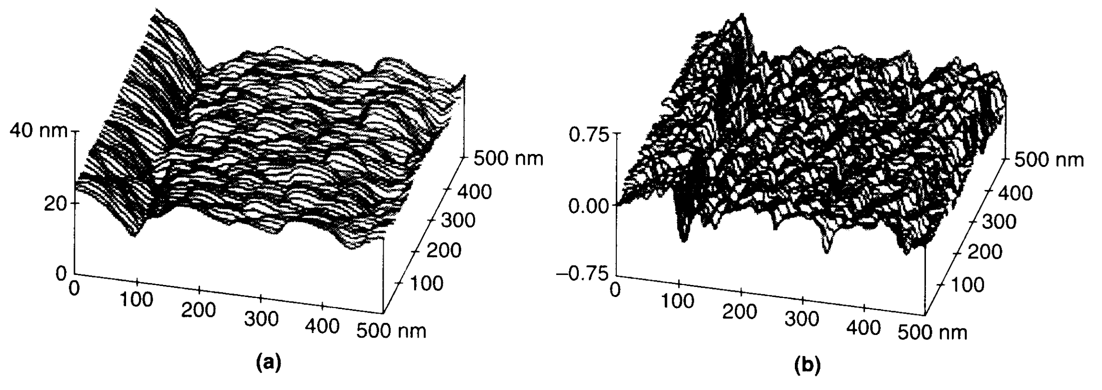


Fig. 15.4: *Comparison between the roughness and friction force scan. (a) Roughness scans of a surface, (b) friction force scan of the same surface. Reprinted from Bhushan, (Ref. 7). Copyright (1999), with permission from Elsevier.*

For studying the adhesive properties of one material with another, a tip of one material (generally a micropsphere on the usual tip) and the sample of another are used. The tip is brought closer and closer to the sample till it comes into contact with it. It is then pulled back. However, due to adhesive forces, it stays stuck to the surface beyond the point it came into contact with it. The extra displacement given to the piezo drive to loose contact is noted. Multiplying this value with the cantilever stiffness directly gives the adhesion force value. For example, consider the deflection *Vs* distance (moved by the piezoelectric) in Fig. 15.5. While bringing the tip closer to the surface (marked 'extending' in the figure) the contact occurs at *B*. From *A* to *B*, attractive van der Walls forces come into play. After contact, the cantilever movement is directly proportional to the distance that the piezoelectric drive moves. However, in retracting, the contact is lost at *C*, way beyond point *B* due to the presence of adhesive forces from *B* to *C*.

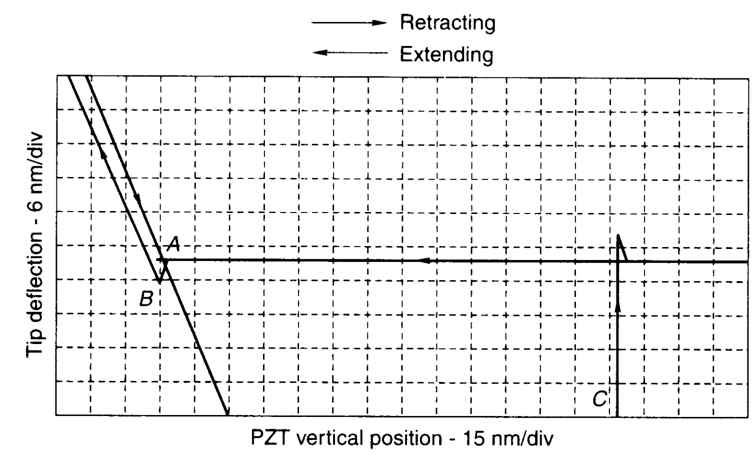


Fig. 15.5: *A deflection vs distance curve obtained to measure the adhesive force. Reprinted from Bhushan, (Ref. 7). Copyright (1999), with permission from Elsevier.*

The adhesive Force, $F = BC \times k$,

where, BC is the distance from the graph = the extra distance that the piezoelectric tube had to travel to loose contact and k is the stiffness of the cantilever.

For scratching and wear, a single crystal diamond (of high hardness) tip is used in the contact mode. After scratching, the surface around the scratch is scanned to study the effects more elaborately. Nanofabrication and nanomachining refer to scratching and wearing the surface at intended locations and in an intended fashion, with the mechanism being the same.

Nanoindentation is another important measurement in nanotribology. It can help us get the hardness and elasticity moduli values of a localized point. It is done in the normal mode of AFM, by indenting the surface with the tip after setting the scan size to zero. After indenting, a finite size scan is done around the indent to calculate the projected area of indent. The hardness (H) is then given by,

H = (load applied)/(projected area of indent),

where the projected area of indent is the area of the indent projected on to a plane perpendicular to the tip (Fig. 15.6(b)).

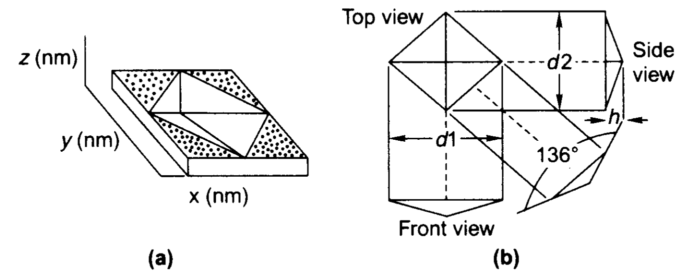


Fig. 15.6: *(a) A schematic showing an indent made by the pyramidal (136°) AFM tip. (b) The projected area of the indent.*

Young's modulus is obtained from the slope of the force-displacement curve while unloading. Using the AFM technique, we can investigate surfaces of interest at the atomic scale. The AFM relies on a scanning technique to produce three-dimensional images of sample surfaces of high resolution. AFM can be used to measure ultra small forces (<1 nN) present between the cantilever tip and a sample surface. These small forces are measured by tracking the motion of a highly flexible nano-sized cantilever (having a very small mass), by various measurement techniques like optical deflection, optical interference, capacitance and tunneling current. The deflection can be measured to the very low limits of 0.02 nm. For a typical cantilever having a force constant of 10 N/m, a force as low as 0.2 nN can be detected. In the operation of high-resolution AFM, it is the sample that is moved rather than the cantilever, as the movement of the cantilever may cause vibrations thereby affecting the measurements. AFMs are now available for large samples too, wherein the tip is scanned and the sample is stationary. In order to obtain good atomic resolution, the spring constant of the cantilever should be less than the equivalent spring constant between the atoms. As per the experimental results, a cantilever beam with a spring constant of about 1 N/m or lower is desirable. Tips have to be as sharp as possible. Tips with a radius ranging from 10 to 100 nm are commonly available.

Surfaces in contact will generally have a thin layer of liquid (and sometimes a solid) lubricant at the interface. Tribological studies under such environments can lead to completely different results. John Pethica and co-workers have made useful contributions to the study of nanoindentation of liquid environments (Ref. 9), comparing these data to the conventional results reported. The same group has also reported useful results based on the mechanical deformation of nanocontacts due to the size and structure of the asperities at the point of contact (Ref. 10).

15.2.5 Friction Force Microscope

Subsequent modifications to AFM led to the development of the friction force microscope or the lateral force microscope (LFM), designed for atomic-scale and micro-scale studies of friction and lubrication. This instrument measures the lateral or frictional forces (in the plane of sample surface and in the direction of sliding). By using a standard or a sharp diamond tip mounted on a stiff cantilever beam, AFM is also used in the investigations of scratching and wear, indentation, and fabrication/machining. Surface roughness, including atomic-scale imaging, is routinely measured by using the AFM. Adhesion, friction, wear and boundary lubrication at the interface between two solids with and without liquid films have been studied by the using AFM and FFM. Nanomechanical properties are also measured by using an AFM.

15.3 Nanotribology Applications

When the devices scale down from 1mm to 1nm, the surface area decreases by a factor of 10^{12}. At the same time, the volume decreases by a factor of 10^{18}. Therefore, the surface-to-volume ratio of the device increases a billion times. This results in an increase in the surface forces (proportional to the surface area) like friction, adhesion, meniscus forces and surface tension, by the same factor. However, studying tribology at a proportionate scale has helped us overcome this problem to a great extent, as described by the following applications.

15.3.1 Superlubricity

Hirano and Shinjo (Ref. 11) in 1990 showed the origin of the ultra low friction of graphite between two incommensurable (having an incommensurate contact geometry, which prevents collective slip-stick motion of all atoms in that contact) graphite layers rotated with respect to each other. Since then, many research groups have used the Frictional Force Microscope to study this further. Recently, Martin Dienwiebel, *et al.* (Refs 12, 13) have revealed that when two parallel surfaces slide over each other in an incommensurate contact, superlubricity has been observed in certain orientations. Superlubricity is defined as a phenomenon wherein when two parallel surfaces slide over each other in incommensurate contact, they experience non-existent or negligible friction. In such geometry, the lattice mismatch prevents a collective slip-stick motion of all atoms in the contact together, and hence the kinetic friction force can be vanishingly small. The atoms in graphite are oriented like an egg crate, forming an atomic hill and valley pattern. When the two graphite surfaces are in registry (every 60°), the friction force is high. When rotated out of registry, the friction is largely reduced, just like two egg crates can slide over each other easily when twisted with respect to each other. In order to understand this better, consider Fig. 15.7. The maximum friction force is observed when the tungsten tip-surface orientation angle is 60° (in registry) and decreases as the graphite surface is rotated about an axis perpendicular to the surface and parallel to the tip (out of registry). Although the superlubricity phenomenon was discovered during the 1990s, it has received little attention even though it drastically reduced friction in between dry, unlubricated surfaces, making it relevant to various applications.

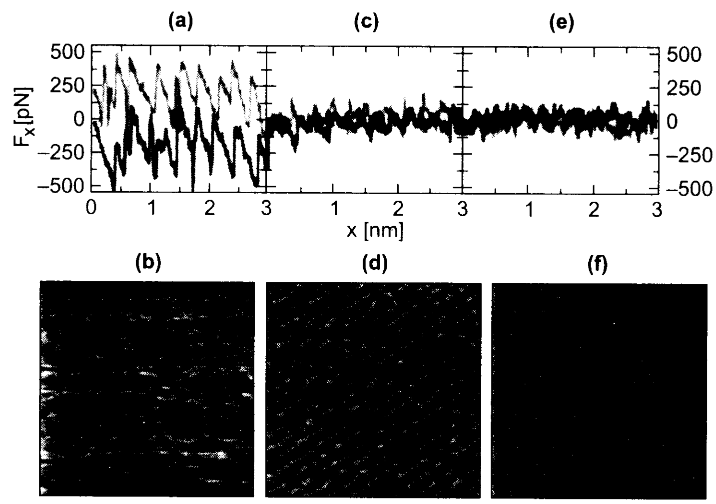


Fig. 15.7: *Friction loops (black, forward and grey reverse) and lateral force images (forward) measured along scanning direction at tip-surface orientation angles of: (a), (b) 60°; (c), (d) 72°; (e), (f) 38°. Reprinted with permission from Dienwiebel, et al. (Ref. 13). Copyright (2004) by the American Physical Society.*

15.3.2 Head Disk Capacity

Technology today demands ultra low flying head-disks. The aerial densities of these head disks strongly depend on the distance maintained between the slider and the hard disks. This distance (known as the flying height) is generally kept in the nanometer range and hence the probability of contact is high. In order to decrease the chances of contact, the roughness values of the slider and disk surfaces are kept within molecular dimensions (see Fig. 15.8). However, at such low flying heights between the molecularly smooth surfaces, the surface forces (adhesion) are very strong. Due to this reason, modern hard disks are found to have a fly height of about 20–30 nm. A fly height of around 15 nm is known to give an aerial density of about 10 Gbit/in^2. However, technically it is desired to have an aerial density of about 100 Gbit/in^2, for which the head disks are required to operate at a flying height of 6–7 nm.

Fly heights of this order require the roughness of the disk to be of the order of 1nm peak to valley. Such smooth disk surfaces are undesirable because of elevated stiction. Also, at such low heights, the potential for discontinuous contacts between the slider and disk cause vibrations in slider that may lead to track mis-registration. The use of textured sliders (Fig. 15.9) has helped in reducing stiction at the head/disk interface for low flying heights with super smooth disk surfaces. The use of textured sliders is also helpful in reducing in-plane and out-of-plane vibrations at low flying heights. Also, textured sliders show less lubricant depletion on disk surface as compared to the untextured sliders.

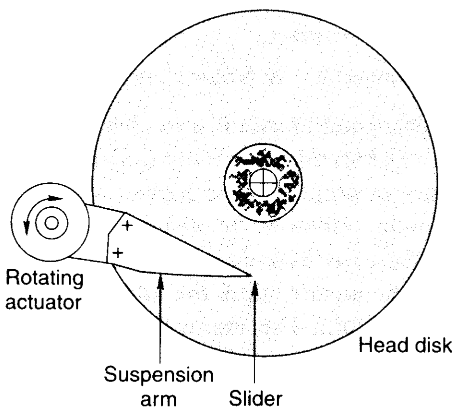


Fig. 15.8: *The image of a typical PC hard disk. The head (slider) and the disk can be clearly seen.*

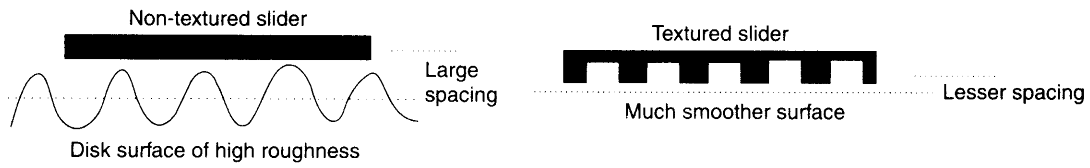


Fig. 15.9: *Reducing stiction by texturing slider rather than compromising for rough disk surface.*

The slider and the magnetic recording layer on the disks are generally given a carbon overcoat. This facilitates sliding between the two surfaces without any cohesive failure in the magnetic layer. The addition of a carbon overcoat also improves the slider wear durability. These coatings also prevent damage to the magnetic layers in corrosive environments. These carbon overcoats are lubricated by perfloropolyethers (PFPE) with polar end groups that enhance their attachment to the surface and limits spin-off. The commonly used PFPE has two –OH functional groups at the ends of the molecules. The film is deposited by dip coating and the thickness is generally kept to 1 ± 0.1 nm (Refs 14, 15).

15.3.3 Nanolubrication

One of the major aspects of tribology is lubrication. It is the most common way to prevent wear. The idea is to maintain a liquid or grease layer between the two solids and the compressive stresses generated in this layer keep the two solids from coming in contact. Theoretically, a good lubricant is supposed to:

1. Generate fluid pressures to keep the two surfaces separate.

2. Sacrificially wear off to protect the surface.
3. Redistribute the stresses at the contact.
4. Increase the contact area (lowering the contact pressure).

Another important property of a good lubricant is its ability to produce boundary lubricating films when needed—in situations when the film thickness is not sufficient to avoid contact (if the film thickness is lesser than the roughness of the surface), then the highest asperities of the two surfaces come into contact with each other. As the pressure increases, the deformation of these asperities becomes more and more plastic. This situation is referred to as 'boundary lubrication'. However, in this situation (under the conditions of high temperature of the asperity tips), the lubricant and its additives react with the solid surface forming a protective chemical film. This film is sheered away, thus protecting the surface from any damage.

The effectiveness of a film depends on several factors like its adhesive and cohesive strength, density, its thickness, etc. Most of these properties can be measured by using the techniques mentioned above to study nanotribology. It is desirable to use a film that is thicker than the surface roughness which is capable of generating fluid pressures to avoid contact and which also has good adhesion and cohesion properties.

However, most of the time at the nanoscale, there is only a limited supply of lubricant and only one or two monolayers are available to do the job. In such a situation, even a small damage to the film (by shear or oxidation, which is why the lubricating film should be oxidation-resistant and non-volatile) can continue to get aggravated, exposing the surface to contact and hence strong frictional forces. This is very common with the Langmuir-Blodgett films. Therefore, it is highly essential for these films to have self-repairing properties. This is possible only if the molecules from another location can move in to cover the exposed surface. Thus, the molecules should be free to move around on the surface, and should not be chemically absorbed on the surface, which would result in low bonding strength. In order to overcome these two contradicting problems, we use mixed molecular films, wherein one species bonds to the surface, while the other is free to move. Thus a carefully designed molecular assembly, wherein each molecule improves a certain property of the film, is required (Refs 1, 3, 16).

15.3.4 Micro-electro Mechanical Systems (MEMS)

Micro-Electro-Mechanical Systems (MEMS) signify the integration of mechanical elements, sensors, actuators and electronics on a common silicon substrate through microfabrication technology. While the electronics are fabricated by using integrated circuit (IC) process sequences, the micromechanical components are fabricated by using compatible 'micro-machining' processes that selectively etch away parts of the silicon wafer or add new structural layers to form the mechanical and electromechanical devices.

Most MEMS are made by using single crystalline silicon (generally doped). But bare silicon exhibits an inadequate tribological performance and needs to be coated with a solid and/or liquid overcoat to lower the coefficient of friction and wear factor at the interface. However, due to their dimensions, normal lubricants cannot be used. Instead ultrathin liquid films are deposited at the interfaces. These are generally the Langmuir-Blodgett (L-B) films or the self-assembled monolayers (SAMs). The L-B films are bonded to the substrate by weak van der Waals forces while the SAMs are bonded covalently. Therefore, SAMS exhibit better wear and hence better durability than the L-B films, thus proving a better choice for lubrication.

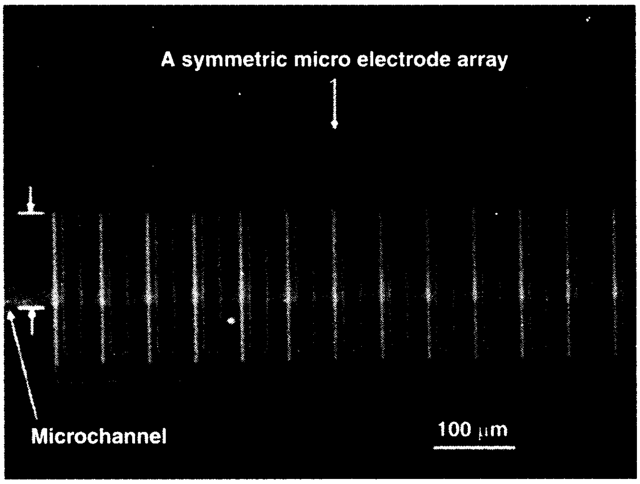


Fig. 15.10: *A microscopic picture of fabricated micro-fluidic devices (a micro-electro mechanical system) showing a 100 mm width channel and asymmetric micro-electrode array. Reprinted from Dhayal, et al. (Ref. 17). Copyright (2005), with permission from Elsevier.*

15.4 Outstanding Issues

Although progressive research has been conducted in the field of nanotribology since the 1970s, it is still a new field with a lot yet to be discovered. Some interesting work has been done and there is a lot more to do. The atomic-scale understanding of complex phenomena will help us design better engineering products with greater efficiency and durability. Several such efforts have been made and the interested reader may consult Ref. 5. Following are some of the important outstanding issues, which need to be addressed to facilitate progress in the sphere of nanotribology.

- Bridging the gap between macroscopic tribology and nanotribology. Atomic scale stick-slip behavior must be examined in more detail.
- Modifying the existing theories or proposing new continuum theories to accommodate nanoscopic experimental observations.

- Selective lubrication of the lubricant as it determines the effectiveness of lubricant films to protect the materials in contact. Molecular basis of lubrication: concept, design and principle of nanolubrication.
- Investigation of friction in low speed and moderate load conditions.
- Electronic and photonic contribution to friction.
- Modeling on the atomic-scale related to dissipation force microscopy and tunneling microscopy.
- Wear prediction and wear process must be considered in detail. The wear prediction of ceramics requires immediate attention in view of the extensive use of ceramics in industry.
- Applying what we understand to frictional processes in biology and medicine.

It is important to mention that several of the nanomaterials such as C_{60} are shown to have applications in lubrication. Studies (Ref. 18) have shown that the inorganic fullerenes of WS_2 are potential solid state lubricants.

Review Questions

1. What is the molecular basis of friction?
2. What are the methodologies to study interfacial properties at nano dimensions?
3. Where do we apply such molecular understanding?
4. State a few examples where nanotribology is important.

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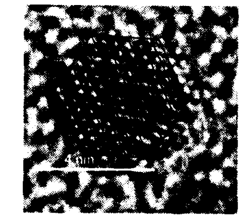
PART

FIVE

Society and Nano

Contents:

Chapter 16



Societal Implications of Nanoscience and Nanotechnology (in Developing Countries)

The phenomenal expansion and growth of nanoscience and nanotechnology has been historically unprecedented. Further the convergence of these two with the growth of information science and molecular biology has heralded new challenges for society and natural environment. Technological revolutions have shown that pioneering scientific discoveries have the potential to pave the way for radically innovative and integrated approaches and for providing new solutions to the international community's most pressing problems. In order to enable decision-makers to devise policies in keeping with the needs of the society, communities and nations, it is important to understand the societal implications of these newly emerging fields. Nanotechnology, unlike any other technology, can find application in virtually all areas of human life. Because of its distinctiveness and pervasiveness it has the potential to revolutionize the way we live, think, behave and act. In spite of the fact that it is an infant in terms of its evolution, some of the issues related to nanotech indicate a wide spectrum of potential societal impacts. These need to be studied further, especially in the context of the developing countries, where nano commodities, devices and services have the potential to make a significant difference, especially with regard to economic and social development. The current public nano-discourse offers sociology a unique opportunity to switch from a merely passive, observational role to an active participating one, especially wherein the key players involved meet to find joint and concerted solutions for the development of advanced sciences and technologies. Nanotechnology's unique and distinct features have the potential to bridge the technological gap between the developed and the developing worlds, if designed and implemented to serve the needs of people who were left out of the ambit of previous technological evolutionary processes. This larger objective necessitates the fusion of several ideas and experiences, from abstract science to the realities of the downtrodden, from sociology to materials science; nevertheless the realm of nano appears to possess the necessary ingredients to attain these goals.

Learning Objectives

- Are there specific implications for society when nanotechnologies are applied?
- What is unique to nanotechnology in comparison to the recently pioneered areas such as biotechnology?
- What are the parallels between nano and other technologies?
- How did technology impact society? How will its impact be different in the case of nano?

- Are we spending enough on nano and are we gaining enough from it?
- Does the use of nanotechnology signify specific areas of economic benefit for the developing world?
- How can we harness these benefits?

16.1 Introduction

The objective of this chapter is to address and outline the wider societal implications of nanosciences and its deriving technologies on society within the context of the developing world. In order to prepare the reader for the novel scientific and technological terrain, we begin with an introductory historical retrospective of the scientific and technological evolution, from the first Industrial Revolution to the third and onwards to the newly emerging technologies of the 21st Century to illustrate the influence of technological progress on the evolution of the society. The rapid pace of discoveries and development in the realm of nano indicates that this newly emerging field is different from others which gives rise to specific questions, even though the problems encountered in this field are common to other advanced technologies. The aim of exploring the world of nano is to discover new properties and to translate the new knowledge into the manufacturing process for obtaining enhanced structures and components with novel chemical, physical or biological properties. This futuristic manufacturing method can virtually invade and pervade all areas of human life, since it modifies the identity of all matter, animate and inanimate. It will definitely revolutionize human society in an ever unprecedented way. This new scientific branch and associated technology will doubtless have both desirable and undesirable repercussions, which will impact the society at large and change its structure, organization and functioning in the longer term. Since different aspects related to nanoscience and nanotechnologies need to be woven into the nano-discourse, we are examining these specific aspects with a special focus on the developing world. We try to provide a comprehensive framework on the issues relevant to nanoscience and technology, and map the social, economic, political, legal and ethical aspects, which are applicable to both the developed as well as the developing worlds, with particular attention to the latter. With nanoscience and nanotechnology being hailed as the science of the future and the technology of the next generation, respectively, along with their infinite market potential, the key focus lies on the control, manipulation and construction of matter at the atomic and molecular level. Recent studies have revealed the significance of nanotech for fostering economic growth, human health and increasing wealth in the developing world. The possible application of nanotech in the fight against poverty will be addressed and illustrated with practical examples. In the past, we have experienced the consequences of technology and society drifting apart. In order to prevent a further gap—the nano-divide—cross-cutting ties, and institutional linkages along with innovative, integrated and original solutions are needed.

16.2 From the First Industrial Revolution to the Nano Revolution

16.2.1 A Historical Retrospective

When James Watt invented the steam engine in 1765, little could he have imagined that his invention would unleash the first Industrial Revolution and transform society in a way only the invention of the wheel did in 3500 BC.The steam engine entered the history of technological evolution as a symbol of the era of mechanization. Watt's invention of steam-powered machinery revolutionized the manufacturing process and almost all areas related to human and social life in the course of the 18th and 19th Centuries in a massive and irreversible way. A new era for science, technology, economy, society and culture had just begun—called the "Modern Times".That period is characterized by the transformation of the transportation sector, the advent of capitalism and rapid urbanization, and the gradual rise of the modern industrial society.The rapid expansion of the industrial sector, successive inventions and technological breakthroughs enabled the extension of the factories to technology parks leading to increased production. All these developments laid the ground for the next revolution. Industrial Automation, also known as the second Industrial Revolution, started around the year 1870. Industrial robotics transformed the technological manufacturing process since it enabled automated large-scale production at reduced costs.The introduction of the assembly line on the verge of the 20th Century changed the entire organization of the manufacturing process and labour. Improved and more efficient production methods facilitated mass production at a global scale. Mass production at an ever-increasing productivity rate and speed became a must imperative in order to satisfy the rising demands of post-modern and upcoming consumer society.The invention of the transistor and the gradually growing semiconductor industry paved the way for the third revolution, the Digital Revolution. Computerization, starting in the early 1960s led to large-scale production and higher cost-efficiency all over the world and fostered flexibility in the manufacturing process.The era of post-modernism had just begun when in 1959, Richard Feynman gave his speech, "There is Plenty of Room at the Bottom". Most likely, he had imagined that his prognostics would lead to further transformations of the manufacturing process but he could not have thought that a new nano-revolution, would manifest itself at the threshold of the new millennium.The technologies of the late 20th Century and newly emerging technologies of the 21st Century, namely information and communication technologies, and biotechnology, have notably altered the industrial and service sectors, the production methods and society.They heralded the information age and the biotech era, and have ushered in a new kind of society, the knowledge society. Since nano-science and technology as well as manufacturing of nanomaterials are no longer futuristic fantasies but reality, we should assess how the 'disenchantment of the atomic world' will change our present societies.What comes next, the nano-society?

16.2.2 The Milestones on the Trajectory of Nanotech

The cornerstone of nanoscale science, engineering and technology was laid when in 1959, Richard Feynman envisaged the possibility of arranging atoms to create new matter at the atomic and molecular level. In 1964, the Nobel Laureate in Chemistry, Glenn T. Seaborg patented two of the elements he had synthesized—Americium and Curium. This was the beginning of patenting atomically and molecularly engineered matter. The term 'nanotechnology' was coined in 1974 by Norio Tanigutchi, professor at Tokyo Science University who pointed out the trend of precision manufacturing at the scale of nanometres. In his MIT doctoral thesis of 1981, Eric Drexler extended the term to a wider area and studied the subject in depth. During the same year, Gerhard Binning and Heinrich Rohrer, who were awarded the Nobel Prize in Physics in 1986, invented the scanning tunnelling microscope, a novel measurement tool facilitating the sensing of matter at the nanometre scale. This was a significant technological breakthrough and had a great impact on the future development of nanoscale science because every new science requires new instruments and equipment. In the early 90s, Warren Robinett of the University of North Carolina and R. Stanley Williams of the University of California established a virtual reality system and linked it with the aforementioned scanning tunnelling microscope to see and touch atoms. When D.M. Eigler placed xenon atoms to a shape, reflecting the logo of IBM in 1990, he showed the possibility and feasibility of atomic-scale manipulation, which marked a further pioneering breakthrough in this newly emerging field (Ref. 1). In 1993 the first academic research centre dedicated to nanotechnology was institutionalized in the USA, namely at the Rice University. Only five years later, Zyvex, the first molecular nanotechnology company, was established in the USA, which marked the beginning of nanotechnology private venture capital companies. In 2000, another step forward was taken, when Lucent and Bell Labs, along with Oxford University, created the first DNA motor, the first nano-biotechnological artefact. Since the beginning of the 21st Century, discoveries and new technological facilities, molecularly precise manufacturing, nanofactories, public and corporate investments in nano-research and public-private venture partnerships are rapidly expanding and increasing. The development in this newly emerging area suggests that the time span between milestones on nanotech's trajectory is reducing considerably, as we move further on. It is obvious that nano has gathered momentum and the nano-revolution has just begun.

16.2.3 The Distinctness of Nanoscience, Engineering and Technology

We have seen how the scientific discoveries and technological inventions of the past three centuries have revolutionized the manufacturing sector and society. The common traits of the new technologies that transformed human and social life in-between the first Industrial Revolution and the Digital Revolution are that they were designed for large-scale production which was capital- and energy-intensive in consonance with the needs of large manufacturing infrastructures, and were designed to compete in the global markets. Big became beautiful and the manufacturing process and methods were aligned along the macro-principle. However, the transistor and semiconductor industry ushered in a change in that trend and small became beautiful, as a result of which manufacturing began to focus on micro and then on nano. Nanoscience and technology require nanomaterials. The manufacturing of nanomaterial is not just another step in the growth ladder but is also about using the knowledge of the atomic realm to produce novel artefacts in a cheaper and cleaner way, with reduced capital and energy inputs, and with more precision. The unparalleled development of nanotech and the dissimilar preconditions for nano show that nanoscale science, engineering and technology are different from other newly emerging sciences and technologies. Here we highlight a few of the most salient peculiarities that explain the distinctness of nanoscience and manufacturing of nanomaterials. Firstly, at the nanometre scale, sciences and technologies converge and therefore go beyond the traditional boundaries of disciplines. Nanoscience is of a trans-disciplinary nature since it involves chemistry, physics, biology, mathematics, cognitive science and life sciences, in particular genomics and proteomics. Nanotechnology fuses with other recent technologies like information and communication technologies, and biotechnology. Secondly, control and manipulation of the very elementary building blocks of all objects of the living and non-living world—atoms and molecules—enable modifications of the same, which can influence each and every area of life. In other words, the core novelty in science and technology on the scale of the nanometre is that scientists and technologists do not invent the world *ex novo*, as in past, but *de novo* since the new artefacts are made of components which have no natural analogues. Thirdly, the term 'nano' refers to measurement, the nanometre, as it indicates the size of the matter being observed and manipulated and the term does not refer to any object *per se*. This explains the unlimited spectrum of nano since all physical matter, irrespective of its nature, can be measured, and the only condition is that measurement facilities for that size regime should exist. Fourthly, the manufacturing of nanomaterials does not entail enormous initial capital outlays for industrial infrastructure that other technologies require. This has made gigantic technological parks obsolete, at least in cases wherein controlling the shape of the nano object is not a stringent condition. There are factual examples substantiating the assumption that production can be cost-effective and tailored to local needs—either large or small. These examples include the production of nanomaterials through biology. We will come back to this argument later. A further novel aspect with regard to nanotechnology that gives a practical expression to the pace of technological change, is the reduction in time from the scientific discovery to the application of the new knowledge.

16.3 Implications of Nanoscience and Nanotechnology on Society

16.3.1 Science and Technology Change Society

In order to better understand the nexus between nanoscience, nanotechnology and society in the context of social change, a few preliminary concepts relevant to both nanotechnology and other technologies are briefly outlined here. Science, technology and society are intrinsically interlinked and characterized by mutual interdependency. Since technology is firmly imbedded in society, it cannot be looked at in isolation. The application of scientific knowledge and associated developments are two of the major factors determining social progress and prosperity. Social change is as dynamic and complex as social systems and is both an essential ingredient and the driving force of social evolution. A myriad other factors determine, shape and characterize the technological, social and cultural evolutionary processes of society. Advances achieved in scientific and technological knowledge in any discipline or branch inevitably lead to changes in social relations, meanings and societal patterns. Earlier, we have seen how scientific discoveries and technological inventions had literally revolutionized societies with time. Considering the time factor, technological and social changes may not occur contemporaneously since the social system takes its own time to respond to changes and to find its new equilibrium. The coexistence of several forms of societies and the analogous coexistence of technologies in the world today, from pre-industrial to state-of-the-art technologies, illustrates the above.

Progressive technological and social changes do not necessarily eradicate previous societal structures and historically, science and technology have been used by all kinds of societies, irrespective of their stage of development, instead of just being restricted to the most advanced societies. As regards social and technological change, as far as nanoscience and its deriving technologies are concerned, it is highly likely that their potential impacts will be stronger, because nano has the incomparable force to pervade all societies and economies, from the pre-industrial to knowledge societies, from ancestral to highly industrialized economies, and is not necessarily subjected to a nation's current development stage and/or geographical location. Nanotechnology can also bridge yesterday's missing technological link between the developed and the developing worlds.

16.3.2 Society and the Scientific and Technological Innovation Process

Protecting, improving and preserving life by using new scientific knowledge and technical findings is intrinsic to scientific and technological research since the very premise of science is to serve humanity. Society is reacting to technological change with new forms of institutions and develops its own responses to technological innovation, which is valid for nanoscience and technology as well. As in all other cybernetic systems, a change in one of the systems will generate changes in the others because these complex organic systems are linked by multiple feedback loops and therefore the social world always responds to scientific and technological innovations. Discoveries in nanoscale science and innovations in molecular manufacturing will certainly have an impact on society because technology has never been and will never be neutral, as knowledge itself is not neutral. The scientific and technological innovation process shapes the evolution of society, and therefore it is essential to understand the societal implications of nanoscale science, engineering and technology in order to understand the direction in which society is advancing. The current infant stage of this technology limits reliable or accurate prognostics but in spite of these limitations, a historical retrospective on how technologies of the previous centuries revolutionized the social organization, structure and value systems can help understand and predict the potential impacts of nanoscience and nanotechnology.

16.3.3 Forecasting the Nanofuture

How will society respond to the distribution and diffusion of engineered nanomaterials, including commodities, instrument facilities and services and how will these change society? The advancements in nanoscience and nanotechnology, necessitate these questions. It is commonly believed that the social implications in the developed as well as in the developing worlds will be similar to the other newly emerging technologies of the 21st Century like biotechnology and information and communication technologies. This assumption, however, ignores two facts: first, nanotechnology is a fusion technology and therefore incorporates, for instance, bio and information technologies. The synergy effects, resulting from the interface of two or more systems, will amplify the complexity and inevitably exceed the hypothetical consequences of one single technology and secondly, the world is entering the sphere of nano, even where information and communication technologies have not yet pervaded society at large. In the developing countries, where pre-industrialized and post-modern technologies coexist with the newly emerging technologies, nano-engineered commodities and services can be designed for the needs of people belonging to pre-industrialized, post-modern or knowledge societies since no preclusions apply. As far as the predictions of nano's future are concerned, global trends suggest that nano is gathering momentum. Expansion in scientific research and development, public and corporate investments, public-private partnerships, media coverage, patents, services and devices clearly indicate that nanotechnology is growing rapidly. From these positive projections, one can conclude that nano has the potential to become the flagship of the new millennium's industrial production methods in the developed as well as in the developing worlds. Nanotech will certainly not replace all other technologies, but will coexist with and borrow from the technological inventions of the past. It is thus unlikely that the nano era will replace the digital. Instead, the digital age will converge with the nano, and their synergy effects will lead to fundamental and irreversible alterations in the existing, cultures and institutions of society, societal organization, and various mechanisms and patterns, including the demographic structure of society. Its all pervasiveness and the magnitude of this new technology will exceed those of the precedent technologies because the intensity of the impact of any phenomenon's is positively correlated with its pervasiveness. The circumstances indicate that the possible impacts of nanotech will exceed even those of the first Industrial Revolution.

16.4 Issues—An Outlook

16.4.1 Artificial Evolution—How Green is Green Nanotechnology?

The term 'Green Nanotechnology' apparently seems a paradox *per se*, as it challenges both nature and the ecosystem, because the control and manipulation of matter at its very elementary level leads to the creation of new matter not present in the realm of nature. Since the concept 'green' refers primarily to environmental protection and not to the evolutionary process, nanoscience and technology are not inconsistent with 'green'. 'Green Nanotechnology', in fact, has the potential to play a pivotal role in the struggle against the world's most pressing environmental problems. Bio-nanotechnology, for instance, offers a wide spectrum of possibilities for mitigating the adverse effects of environmental degradation, regardless of its causes and sources. In particular, bio-nanotech can provide viable solutions to soil, air and water pollution, and the unsustainable exploitation of natural ressources. These solutions include the support of cleaner production methods, provision of alternative and renewable energy sources, reduction of input into the manufacturing process and purification of water. The interface of bio and nanotech, however, does not only generate positive results. The potential risks inherent in the convergence of life sciences and nanoscience and its deriving technologies need to be addressed and understood. Threats may arise from the increased chemical reactivity of materials at the nanoscale, the toxicity of nanoparticles and the yet unknown side effects of the atomic and molecular engineered materials. The release of atomic and molecular engineered matter into the biosphere poses additional problems to human beings and nature, since test results obtained in the laboratory may differ from those carried out in an open environment. It is still unknown how humans and the environment will respond with regard to the distribution and accumulation of novel materials. The lifecycle of products containing nanoparticles is difficult to establish since the degradation process of nanomaterials and components can only be estimated. The hazards identified with regard to health are chiefly related to the absorption of nanoparticles by the human body and their distribution as well as the risk of accumulation in organs. It is also unknown, as to how the human (and animal) metabolism will react to the intake of nano-engineered food and nanoparticles, which once introduced in the ecosystem, will enter the food chain. This necessitates research into the possible negative impacts of bio-nanotech, and transparency in the results in view of the credibility and plausibility of green nanotechnology. However, recent results obtained suggest that the benefits far outweigh the risks (e.g., applied nanotech techniques for water purification systems).

16.4.2 Crossing Land—Melting of the Traditional Boundaries of Natural and Human Sciences

The realization of the possibility to explore and control the world at the nanometre scale has given life to new scientific fields, and blurred the traditional boundaries of disciplines, and even led to fusion and convergence amongst natural sciences. These new circumstances present a unique chance for the sciences, both hard and soft, to meet and to overcome C.P. Snow's paradigm of the two cultures, dividing the scientific from the human sciences (Ref. 2). Despite the scientific tradition of hard and soft sciences using different methodologies and jargons, at the nanoscale there seems to be a trend of convergence of the two apparently opposing scientific cultures. Scientists belonging to the first category have recognized that at the atomic and sub-atomic level, an organic world view becomes extremely useful since the observation, control and manipulation of matter in realms inaccessible to human's ordinary senses demand not only new instrumental facilities but also novel approaches (Ref. 3). This revolutionary shift in the scientific mentality of natural scientists has the potential to overcome both the two-culture paradigm postulated by Snow and the long-lasting *Methodenstreit* (disputes about methodologies) between the natural and human (cultural) sciences. This new situation frees the various disciplines from their life in isolation, and offers natural and human scientists a common meeting ground. This, of course, does not mean that a physicist becomes an ethicist or vice versa, but that both are needed for finding solutions that contribute to the qualitative enhancement of human life and responsible scientific development. Recent conferences held on nanoscience and technology bear witness to the paradigm shift and have revealed that the scientific fraternity has recognized the importance of bridging the cultural gap. Today's scientists seem to be prepared and willing to cross the borders of their own disciplines.

16.4.3 Education and Training in Nanoscale Science and Technology

Frontier sciences and technologies represent a true opportunity to enhance a country's qualitative and quantitative level of human capital since new ways of manufacturing require the development of new capabilities and skills, which creates new job opportunities. Enhanced human capital strengthens a country's competitiveness, spurs economic growth and prosperity, all of which are essential ingredients for a more sustainable economic, human and social development. These factors are of paramount importance to developing countries since the latter are rich in human capital. In recent years, the academic world has begun to react to the upsurge of the nano-phenomenon and started preparing the future workforce for the emerging opportunities arising in the nano realm by offering multi-disciplinary curricula that complement basic natural science education with specialized courses in nanoscience, materials science and molecular biology as well as by sponsoring continuing education and training. Since the socio-economic situation of a country conditions its public expenditure in education, research and training, most educational and scientific activities in the nanoscale science, engineering and technology are offered in highly industrialized countries. Since nano-manufacturing is also possible in developing countries, it is vital to develop the necessary human intellectual resources for nano-manufacturing in the developing world. The development of educational, research and training programmes in nanoscience and its related fields of application, analogous to those of highly industrialized economies, has become a necessity. That this is possible in the developing world as well, can be the illustrated by existing strategic partnerships between government agencies, industries and businesses established for starting nanotech research centres of excellence. It is widely believed that scientific education, training and research have the potential to narrow the gap between the developed and the developing world, even if not within the society itself. It is a matter of fact that if the developing world does not catch up with the scientific progress of the industrialized world, the risk of being further marginalized becomes real and it would make real the public fear of a new gap between the haves and have-nots: the nano divide.

16.4.4 The Nano Economy

Technology has always played a central role in wealth generation and the emerging nanotech market has the potential to transform and reshape all economic sectors, from the primary to the tertiary, and this applies to nano as well. The often-advocated assumption that nanoscience and its deriving technologies will change the world must stem from a basic premise: namely that novel findings and innovations on the nanometre scale will have a visible and significant impact on productivity. The projected consequences of rapidly advancing technologies on the nanometer scale will see the rise of new industries and the fall of those stuck to the conventional or sustaining technologies of the past (Ref. 4). The marketing of scientific discoveries at the frontiers of science and technological innovations in the nano realm will become the driving force of the nanomarket. We can assume that in the years to come, this relatively new economic phenomenon will contribute to an increase in the global Gross Domestic Product (GDP) as projected by reliable global economic institutions like the World Bank (WB) and the International Monetary Fund (IMF). A comparison of the economic performance of the nano industry and business with the development of the national and global GDP could reveal possible correlations between the two and provide an answer to the question as to whether nanotech truly contributes to economic growth in quantitative terms.

16.4.5 The Nanobusiness and Finance

Since nanobusiness is still in its infancy even in the developed world, it is difficult to assess the possible economic impact it will have in the developing world. In highly industrialized economies, like the USA, the commercial spin-offs of nanoscientific research, start-ups and venture capital enterprises, together with multinational companies reaching out for nanotechnology and competing for market shares of the newly emerging nanotech market, will shape the national and world economies. Nanobusiness, which is still in its nascent phase but growing rapidly, encompasses a wide spectrum of well-established and solid manufacturing branches, from biotech, materials, electronics, energy, healthcare, textiles, sensors and many others, and does not preclude any business sector. The ongoing globalization process tends to amplify the importance of nanotech use, since the manufacturing of nanomaterials provides the link with international capital markets and global technology, and production networks. Not only is the future nano-market impressive in size, but so also is the potential clientele of nanotech derivates, products, devices and services. Since all forms of matter are ultimately composed of atoms and elements, theoretically all people could become exposed to the nearly unlimited nanomarket and become its benefactors. To put this into perspective, the US National Science Foundation (NSF) estimates the total global market for nanotechnology-related products and services to reach US$ 1 trillion by 2015 (Ref. 5). Based on these projections, the Nanobusiness Alliance forecasts the global nanotechnology market to reach US$ 225 billion by 2005 and expects it to touch US$ 700 billion by 2008 (Ref. 6). When these figures are seen in consonance with the projected world GDP, the share of the nanomarket can be expected to exceed one per cent by 2008 (Ref. 7). The ever-increasing number of private nanotechnology companies and the sharp rise in patent filings from public and private institutions testify the upward trend in the commercial innovations made in the field of nano-manufacturing and the run into nanobusinesses. To illustrate what is stated before, the US Patent and Trademark Office issued, until the first half of 2005, 3,818 patents with reference to nano and 1,777 patent applications were handed in and were waiting to be transformed into lucrative licences (Ref. 8).

Private nanobusiness was born only in 1997, when nano pioneers started the first venture capital company in the USA. While large and well-established trans-national companies (TNCs) followed Zyvex and started diversifying and integrating attributes of nanotech techniques into their manufacturing activities, small and medium-sized enterprises (SMEs) too entered the arena of the upcoming nanobusiness. The preliminary findings of business experts suggest that the latter have already conquered niche markets and by consolidating their positioning at the global level, they are challenging the big market leaders. A look at the companies and sponsors present at the Eighth Nanotech Conference and Trade Show in May 2005 in Anaheim, California reveals who the contenders in the newly emerging market are. More than 100 corporate companies, both TNCs and SMEs, are in some way or other involved in nanomaterial manufacturing (Ref. 9). As far as the capital market is concerned, nano-stocks are already traded at the world's major stock exchanges and financial institutions as well as insurance companies nurture high interest in this novel technology and its derivates. As regards private investments and risk management, they already play a significant role. At the micro-economic level, it is still difficult to express the prognostics because of two major reasons, namely, the absence of hard data about the cost structure of nano-engineered products, devices and services, and secondly, the fact that nanotech commodities are still not an integral part of everyday life in any part of the world (primarily because there are only a few commodities for mass consumption).

16.4.6 Public and Private Investments in Nano Research and Development

Public and private research funding in nanoscale science and technology has progressively increased over the past years in both the developed and the developing worlds. Research and development activities are generally segregated in relatively large industrial, government and academic laboratories but the latest trend suggests, to a smaller but not less remarkable extent, that the private sector, and in particular SMEs, are investing into the nanometer scale technology. The public sector still holds the lion's share of research and has been growing at an unprecedented rate during the last few years. The global public spending in nanoscience and technology exceeded US$ 3 billion in 2003 and it will increase further since more countries, including the developing countries, are planning to or have already launched national nano-initiatives (Refs 5, 10). A look at the government funding of the next five years of the USA confirms the progressive trend in public investments into nanoresearch and development. For the year 2005, a sum of US$ 809.8 million has been approved and the figure for 2008 exceeds an annual spending of US$ one billion (Ref. 11). The developing as well as the newly emerging economies have started realizing the inherent opportunities of nanoscience and nanotechnologies, and the importance to compete in these areas from the beginning and not, unlike in the case with information and communication technologies, wherein they could afford, to wait for these to be transplanted from the developed world at a later stage. For a good performance in the global research and development arena, public and private investments into nano are a precondition. The trend of increasing public spending into nano in the developing world is parallel to that seen in the highly industrialized world. However, investments in the development world in nano are lower than those of the developed world, in terms of their respective GDPs.

16.4.7 Reliability, Safety and Risks: Assessment and Management

Systematic identification and assessment of the risks posed by any new technology are essential. The idea of a system getting out of control is the nightmare of every conscientious scientist and technologist and not only of technophobes and those predicting a cataclysmic end to humanity because of the release of toxic nano-engineered artefacts from the laboratory into the environment. The potential risks might arise as a result of the characteristics of the nanoparticles themselves, as also of the properties of products manufactured with nanoparticles along with the manufacturing process itself. Systematic research into the flip side of this new technology, especially the risks that it entails, is essential, chiefly because of two reasons. Firstly, because if unintended consequences, including negative side effects and counter intuited results are known, it is possible to calculate the risk and to take precautions. The presentation of worst-case scenarios, which include the necessary mechanism and measures for managing such striking situations, serves to limit or mitigate the adverse effects on society and its natural habitat. Several existing instruments and methods used in technology management, like the Environmental Impact Assessment (EIA) help in analyzing, assessing and evaluating the reliability, safety and risks of new products, services and devices using atomic or molecular engineered matter. Secondly, the fear of derailing nanoscale science and technology, because it is evolving faster than the researchers' ability to keep pace with its development, is undermining the research and development process and gives rise to anti-nanotechnology feelings and attitudes. Therefore, it is imperative to foster methodical research in the fields of safety, reliability and risk management of nanocommodities, devices and services. The fantasy apocalyptical worst-case scenario involving nanotechnology, named by Eric Drexler as the "Grey Goo", has contributed little towards broadening our societal understanding and knowledge of the potential risks of molecular engineered artefacts (Ref. 12). Since people are receptive to fictional representations as they shape their imaginaries, the "nanomania" has rather alienated the entertainment and leisure industry, and given rise to misconceptions, misunderstandings and distorted views regarding this particular technology rather than contributed to a rational and genuine discussion.

16.5 Nano Policies and Institutions

When we look at the nano-phenomenon from the political perspective, in general, we look principally at issues relating to long-term strategic technology policies, including intellectual property reforms, international co-operation, monitoring and the regulation of research and development. Because of its unlimited potential, nanoscale science, engineering and technology necessitates the adoption of national and international nano policies. The management of research and development in nanoscience and technology, in terms of administration and control by the public authorities, has to guarantee the responsible use of the potentials that both offer. The claim for formalizing a regulatory regime over nanoscience and technology indicates that a minimum level of coercive intervention is needed by the state, especially vis-à-vis responsible nanotech. Scientists, politicians, the private sector and representatives of the civil society have opposing views as far as the intensity of the public interference into scientific and technological research and development is concerned and even within these groups, their views do not converge. The opponents, i.e. the nano sceptics, a heterogeneous flock, call for a regulatory and institutional framework that limits the scope of scientific activities, and of atomically and molecularly engineered commodities and services. Despite the clash of interests and opinions, the two blocks agree on three central issues in the public nano discourse, namely the non-interference into privacy, preservation of human dignity, and the protection of the society and natural environment from hazards. The first two, since they have strong ethical connotations, will be addressed separately while the third has already been addressed. In order to counter misuse, including activities and actions that are in contradiction with the universally shared ethics and principles, a minimum regulatory framework has become a necessity to guarantee the responsible use of nanoscale science and its deriving technologies. The current scenario suggests that the institutionalization of a supranational body with a standing committee exercising minimum international control, monitoring the technological development in the atomic realm and providing a legal framework to which the countries doing nano research and development conform their activities, make sense. Despite their differing value systems, political and legal traditions and systems, all members of the international community should agree at least on a minimum political control and administration in order to ensure that nanoscale research and development is consistent with the ethical principles present in all universal value systems. Defining the perceived benefits and risks of nanoscale science applications, as perceived by the scientific community, industry and business and public, is necessary while policy-makers decide what is best for their community and the nation.

16.5.1 Nano Rules and Regulations

The *laissez-faire* approach of the past has led to a lack of rules and regulations regarding research, development and the deployment of atomically and molecularly engineered produces, services and devices. The absence of appropriate norms at both the international and national levels, reflect what W.F. Ogburn described as the cultural lag (Ref. 13). According to his theory of technological evolutionism there is a gap between the technical development of a society and its moral and legal institutions. It is a social fact that while scientific and technological development in nanomaterials manufacturing is leaping ahead, legal regulations lag behind and leave a gap in terms of trust between the people and public authorities. The present situation has the potential to generate social tensions and problems since the misuse of nanotech for destruction purposes cannot be ruled out explicitly. There is a need for new forms of regulations and international standards to direct the research, development, manufacturing and commercialization of nanotech. However, the mere establishment of a legal framework or standards is not enough since the laws and regulations need to be enforced. A better understanding of the legal implications of nanotech would help the policy-makers in the establishment of a regulatory framework and standards that are consistent with the dominant value system of their society. This is particularly valid and important for developing countries, where new laws and institutions have been introduced, after their independence from colonial rule, without taking into consideration the local culture, institutions and traditions. Since the control and manipulation of the genetic signature imprinted in the DNA of each human being and manipulation of human cells has become possible, including the use of stem cells used in laboratories, a regulatory framework for setting limits to the exploration of human nature has become a necessity. However, none of the regulations should delay or inhibit the growth of knowledge aimed toward the betterment of humankind.

16.5.2 Nano Ethics—A Deontological Code for the Nano Community

Not all that can be done should be done: This is the nucleus of the ethical dimension with regard to research and the technological innovation process, in general, and it applies to nano, in particular. Since science and technology on the scale of the nanometre are not restricted to the domain of materials science but reach out to life sciences, it is important to understand the ethical implications of this new branch. The formalization of a deontological code is needed to prevent nanoscience and technology from derailing and heading into the wrong direction. Ethical guidelines related to research procedures and activities in the realm of atoms and molecules are, in fact, needed to bridge the present gap between science and ethics. One of the core tenets of such a deontological code is the observation, respect and protection of human dignity and non-invasion of the privacy of individuals. From a purely scientific point of view, humans do not enjoy a higher status than other living creatures but from the ethical perspective, humans have a different status because of their highly complex nature resulting from their genetic endowment which equips them with faculties that other living beings do not have. This is where ethics and science clash. Little systematic research into the ethical consequences of nanotech has been undertaken so far. The ethical community needs to be actively involved in the nano debate because the expertise of ethicists is required for softening the confrontation between the two blocks. The big ethical controversies will not focus on the threats to the dignity of the average grown-up adult, but will be concerned with foetuses, children, the terminally sick, elderly and disabled, all of whom belong to the most vulnerable groups of society.

16.6 Nanotech and War—Nano Arms Race

The military apparatus plays a crucial role in the scientific and technological innovation process, and applies to discoveries and development in the nanometer scale as well. In the developed as well as in the developing worlds, large investments are made in national security and defence. In the current international political scenario, the effort to acquire more powerful instruments to secure national integrity and interests, is a common phenomenon throughout the world, regardless of a country's economic status. The use of nano-engineered materials for weaponry and the potential use of atomically manufactured matter and devices for weapons of mass destruction is no longer science fiction and has today become a reality. In view of the increased political instability and feeling of uncertainty in the world today, the need to safeguard a nation's interests has gained importance. It is therefore possible that weapons equipped with nanotech will be deployed in present and future armed conflicts since there is as yet no international or national ban on weapons using nanoparticles and nanotechniques. The direct link between nanotechnology and ballistic studies scares people as also the potential abuse of nano-engineered weaponry (Ref. 12). However, we must state here that research for military use results in innovations that could later be utilized for civil purposes as well. It is still too early to speculate about the possible technological fallout of nano commodities designed for defence but one cannot preclude this possibility.

16.7 Public Perception and Public Involvement in the Nano Discourse

One of the most pressing issues in science is the involvement of the public. The Triple Helix, i.e. academia, government and industry, needs to be extended to a fourth dimension, the civil society, because of the latter's role and relevance in today's world. The public plus the print and electronic media need to be involved from the beginning, since news and information regarding nanoscale science and technology will shape public perception and determine to a large extent, people's knowledge, attitude and behavior toward this new technology. Consumer acceptance is the key when it comes to commercially-developed nanotech products, services and devices because ultimately it is the end-users who will influence the trajectory of nanotech. Therefore, it is of paramount importance to communicate with the public from the very beginning so that people understand rather than misunderstand the novelty of atomically and molecularly engineered products and services. The under-estimation of consumer acceptance and consumer resentment with regard to biotechnologically engineered organisms in the past has revealed the importance of social acceptance since knowledge and perception finally direct people's attitudes *vis-à-vis* new technologies. Studies conducted in the USA have already shown that artificially created matter having the attributes of living creatures, namely the ability to adapt, co-operate, learn and adjust to change occurring in them, or another system scares people (Ref. 12). It is therefore important for such studies to be conducted in the developing world as well, especially in areas where nanoengineered products have to be used. People's apocalyptical predictions with regard to nanotechnology do not find any foundation in rational reasoning. Uncertainty and unpredictability are, however, effective instruments for manipulating the public opinion and for undermining their trust in the development of science and technology.

16.7.1 Nanotech and the Media

In the age of information and an emerging knowledge society in many parts of the world, including the developing countries, mass media play a crucial role and hence should not be neglected. With regard to nano it is even more important to envisage the social function of mass communication tools. The printed and electronic media, including the Internet, known respectively as the fourth and fifth estates, are among the most influential instruments used to shape public perception and people's understanding of nano. Scientific and technological breakthroughs generally reach the public through the media, which is why it is important to inform people in a way they understand. Two possible avenues can be used to assess the trend of nano's presence in the media. If we use the number of scientific publications about nano as a variable indicator over a certain time span, we can assess the trend and trace its development over the past years and forecast future trends. The same can be done with publications in popular science, business media and entertainment. The rapid increase in publications in scientific literature during the past ten years is striking (Fig. 16.1). To put it in perspective, in 1995, 4,372 nano* references were recorded in English scientific publications, while in 2000, there were 11,447 and in the first five months of 2005, alone there were 16,518 titles. These figures, made available by the Institute of Scientific Information (ISI) web of knowledge, do not leave any doubt about the rise in number of scientific publications and this trend will certainly grow progressively. As the analysis here refers only to English language publications traced by ISI, it does not reflect the global scenario. It also includes titles that may not be purely nano-specific but include hybrids.

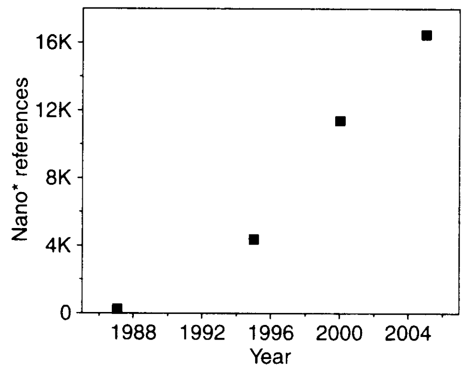


Fig. 16.1: *Increase in nano-related publications in English journals.*

With regard to the popular science literature, business media and entertainment, a similar trend stands out, though it could not be quantified here. Broadcasting, television and film industries as also the computer game industry have already developed a great interest in nano for increasing their clientele and turnovers. Science fiction literature about nano is fascinating not only adults but even the youth, and video games have already paved the way for nano to the children's room. The media hype about new discoveries in the atomic and sub-atomic world gives rise to distortions and reflects the commercial exploitation of an event rather than the aim to popularize the potentials of nanotech or to inform the public of the latest discoveries and achievements in this field. Without any doubt, the media has become an important platform wherein scientists, government officials, pressure and advocacy groups and social activists can voice their opinions and influence the minds of the uninitiated audience.

16.7.2 The Public Eye on Nanotechnology

The exclusion of the civil society in the dialogue on the potential positive and negative implications of nanotechnology and the course on which academia, public and private research funding agencies, and the industry are navigating, will have disturbing consequences and cause a backlash among public opinion. Therefore, the Triple Helix must become aware of the role that the public plays in the advances in science and technology. The participation of the civil society in the current public debate on nano is doubtless a sensitive issue. Public fears, possible negative social response or even rejection of nanotechnology, indicate that the involvement of the civil society, i.e. social movements, non-governmental organizations (NGOs) and community-based organizations (CBOs), is no longer just an option, but a necessity. Resentments and social discontent about nanotechnology have been openly voiced by the call for a moratorium on the deployment of nanomaterials and the opinions of nano-critics and nano-sceptics can no longer be ignored. The mobilization against nanotech by certain social activist groups constitutes a first, but alarming sign that public acceptance cannot be taken for granted. The primary intention of the anti-nano community is to heighten public awareness on the possible negative impacts of nano and to influence the policy-makers to jeopardize technological advancement. These groups are less likely to be influential since in the developing world where the democratic instruments to challenge national policies are limited. Further, social acceptability is more likely where people are willing to accept the risk of new technologies and generally have a positive view of science.

16.8 Harnessing Nanotechnology for Economic and Social Development

16.8.1 Nanotechnology and the Developing World

The manner in which industrialization advanced in the developing world has no parallels in the highly industrialized countries. In the former, various kinds of technologies—from indigenous to state-of-the-art technologies—co-exist and a plurality of different kind of societies live together, ranging from pre-industrial to emerging knowledge societies. The ongoing industrialization and modernization trend in the developing world has generated a range of problems that have culminated in the global phenomena of environmental pollution, widespread diseases and urbanization (Ref. 14). The situation in the developing world has not significantly improved and in certain countries, the condition of the people has deteriorated further. The world's most pressing problems are manifold and relate to a variety of issues. Extreme poverty, lack of education, high rates of mortality and morbidity, widespread epidemics and environmental problems are rampant. Innovative and holistic approaches and strategies thus need to be developed and implemented while addressing these highly complex and intertwined problems, and no technology should be considered irrelevant in this effort. We stated earlier that nanotech techniques can find applications in societies and economies, irrespective of their development or status and that at least theoretically, everyone can benefit from their potential applications. Nanoscale techniques have the potential to be in harmony with both traditions and technological development, which makes them a valid tool in the struggle against poverty. They can indeed make a significant difference in the current scenario and contribute to a more sustainable economic and social development. Several developing countries have recognized nanotech as a catalyst for economic, human, social, technological and environmental development and launched national nanotechnology initiatives. Worldwide, more than one-third of all the nations are promoting research and development, including education and training of nanoscientists and nanotechnologists, and more than seven of these countries belong to the developing world (Ref. 15). To put it in the right perspective, in India for instance, the Department of Science and Technology, has allocated $ 20 million in the present Five-Year Plan for the national Nanomaterials Science and Technology Initiative. Several academic institutions in India already possess the necessary ingredients to compete at a global level and to become research centres of excellence, with highly educated and trained workforce, state-of-the-art research infrastructure and well established links with industry and business. Figure 16.2, shows the investment in nano research in a number of countries, grouped separately. It is clear that the investment in India is still very low in comparison to other countries in the region.

Developing countries are rich in human capital and their brainpower will, in the medium and long-term, reshape the imbalance between the North and South. Nanotech offers a new opportunity to the manufacturing industry in the developing world. The wide range of possible applications of nanoscale technologies suggests that if the industrial sector of developing countries enters the field of manufacturing of nanomaterials, it can enhance its competitiveness in manufacturing at the global level.

16.8.2 Harnessing Nanotechnology for Sustainable Development

For the development and application of technology to be successful, it needs to be designed in consonance with the needs of the target group and to be suited to the socio-economic context. Nanoscale science and its deriving technologies can virtually enhance the lives of nearly every human being, be he rich or poor, because of its pervasive benefits and its suitability in resource-limited settings (Ref. 16). It has the potential to provide the most innovative tools and strategies for fighting poverty-related issues. Five billion people live in the developing world, and their lives and living conditions can be enhanced by the diffusion of applications of discoveries made in this area. In order to substantiate our optimistic views with concrete examples, we have identified seven core areas, wherein nanotechnology can make a significant difference in the developing world. These are detailed below.

1. Economic Development Nanobiotechnology, involving the biological production and utilisation of nanomaterials, is a promising new field, especially in the developing world with its unparalleled biodiversity. This natural asset of the developing world can be harnessed through nanomaterials synthesis using micro-organisms, including bacteria, viruses, fungi as well as plant and animal-based products. Several examples

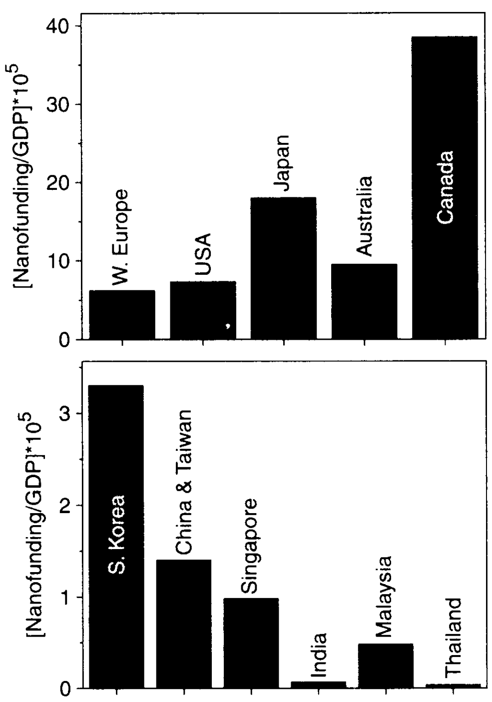


Fig. 16.2: *Investment in nano research for the year 2003 in several countries, given as a fraction of their GDP. Data from http://www.nano.gov/html/res/IntlFundingRoco.htm, www.imf.org/external/pubs/ft/weo/2004/01/pdf/, www.ics.trieste.it/Documents/Downloads/df2625.ppt.*

of nanomaterials synthesis using biology have been reported (Ref. 17). Techniques related to nanobiotechnology do not require large investments and infrastructure, and can therefore be developed on the site of application itself. The green and cost-effective solution to nanomaterials manufacturing is one example which proves that with the requisite knowledge and skills, nanotech can be developed and utilized in the developing world. This approach has been applied to the synthesis of nanoparticles and nanotriangles of gold as well as various other inorganic nanoparticles such as those of CdS and $CaCO_3$. These methodologies can be suitably adapted to facilitate the large-scale synthesis of materials which can be used for applications such as cancer therapy, IR absorbing coatings, etc. The synthesis of nanoparticles in human cells has added a new dimension to this research (Ref. 18). It is also likely that an understanding of the underlying processes may permit us to alter the chemistry to facilitate control of the shape and size of nanomaterials. The biochemical events may be transplanted to other organisms so that processes similar to the bulk production of enzymes become feasible. All these developments could take place in the foreseeable future with an investment that would be much lower than that necessary for chemical or physical routes.

2. Safe Drinking Water Among the numerous possible applications of nanotechnology, the most widespread impact as far as the developing world is concerned may be in the area of water purification. Access to safe drinking water is one of the major concerns in the developing world since almost half of the world population has no access to safe drinking water and basic sanitation. Water purification systems, equipped with nanomaterials and using new kinds of membrane technologies with variable pore sizes as filters, could provide people in any area with safe drinking water. These are easy in application and maintenance, and are already available in the market; the forward-osmosis membrane technology of Hydration Technologies (Ref. 19) is one technique utilising nanotechnology. Thus a combination of nanotechnologies will be useful in providing safe drinking water through cost-effective measures, which will be less dependent on energy resources. Although the product is currently marketed only to provide emergency water supply, large-scale water purification is indeed feasible in the future. To substantiate the validity of these suggestions, we mention the following. Carbon nanotube-based filters can be developed for water purification. The development of a filter which can separate petroleum hydrocarbons from crude oil has been demonstrated (Ref. 20). The filters also remove bacteria from water. With nanotubes, smart sensors can be incorporated into the filter as several nanotube-based sensors are already known. Nanoparticles have been shown to degrade pesticides and pollutants (Ref. 21). Several nanomaterials are known to be anti-bacterial and can be incorporated on various kinds of substrates (Ref. 22). It may be mentioned that we have not listed numerous other discoveries in the area related to this application.

3. Improving Food Security Nutrient deficiency is a widespread phenomenon throughout the developing world, which challenges the physical and mental health of over one billion people. Food starvation can be, but is not always, related to crop failure. Novel techniques using nanotechnology can be applied in agriculture for breeding crops with higher levels of micro-nutrients, enhancing pest detection and control, and improving food processing techniques. The lack of adequate storage facilities besides crop failure is one of the major reasons causing food shortage in the developing world, particularly in the remote areas. In India alone, millions of tons of wheat and rice are rotting in the open because of lack of storage facilities. Food spoils easily, especially in the tropical belt because increased temperatures here favour the growth of micro-organisms in food, which reduce its quality or even render it inedible. Oxygen accelerates the degeneration process because it enables the growth of micro-organisms. It is known that carbon dioxide inhibits the growth of microbes. Carbon nanotubes can be used in food processing and preservation as an oxygen scavenger and can prevent packaged food from deteriorating (Ref. 23). Another application of one of the recent nanoscale innovations involves the use of atomically modified food, which marks the beginning of a radically new paradigm for food production. It has the potential to sidestep the controversial genetically modified food and to increase the yield of agricultural produce. In Thailand, researchers at Chiang Mai University have modified local rice varieties to develop a variant of rice that grows throughout the year by applying nanotechnology (Ref. 24). This particular nanotech technique involves the perforation of the wall of a rice cell through a particle beam for introducing one nitrogen atom into the cell, which triggers the re-arrangement of the rice's DNA. Novel techniques applying nanotechnology could thus contribute towards improving the current food situation, which in several part of the globes, is quite alarming.

4. Health Diagnosis, Monitoring and Screening Nanoscale techniques have the potential to revolutionize the health sector, particularly in the fields of diagnosis, screening and monitoring of diseases and health conditions (Ref. 25). A large spectrum of novel applications using nanoscale techniques in healthcare is possible and this is the beginning of a new paradigm for healthcare. Lack of accurate, affordable and accessible diagnostic tests impedes global health efforts, especially in the remote and inaccessible regions of the world. Many communicable diseases like HIV/AIDS, malaria, tuberculosis and others can be diagnosed with the help of screening devices using nanotechnology. The standard diagnostic tests for these diseases in the developing world are costly, complex, and poorly suited to resource-limited settings. A radically new approach to health diagnosis has been developed in India by the Central Scientific Instruments Organisation (CSIO). Theoretical simulation and design parameters for a micro-diagnostic kit using nano-sized biosensors were completed in 2004 and are ready for clinical trials (Ref. 26). The techniques are based on highly selective and specific biosensors and receptors like antibodies, antigens and DNA, which enable an early and precise diagnosis of various diseases. The diagnostic kit "Bio-MEMS" (micro-electro-mechanical-system) has a size of about 1 cm × 1 cm, costs around Rs 30 per piece is easy to apply. The testing time in this is very fast and only requires a tiny amount of blood. This novel diagnostic tool could also find application in the detection of other diseases and pollutants in the environment, including water and food (Ref. 27). In order to develop therapeutics to combat malaria caused by the parasite plasmodium falciparum, a common disease in many parts of the developing world, Subra Suresh and his team at MIT are using nanotechnology to systematically measure the mechanical properties of biological systems in response to the onset and progression of the disease (Ref. 28). Innovative drug delivery systems, using nanotechnology constitute another area wherein nanotechnology can find application. Cancer is widely prevalent in the developing world as elsewhere and poses a big challenge to human health. The latest results obtained in cancer detection and treatment with nanoscale techniques give the hope that nanotechnology could be heading for a breakthrough in defeating this disease. One way of detecting cancer early, safely and economically, is by the injection of 'molecular beacons' into the body. Britton Chance and his colleagues at the University of Pennsylvania have developed tiny capsules that use the specific biochemical activity associated with a tumor to detect breast cancer (quoted in Ref. 29). As far as cancer treatment is concerned, Jennifer L. West and her team at Rice University, Houston, Texas have developed gold 'nano bullets' that can destroy inoperable human cancers. The nanoshells consist of tiny silica particles plated with gold, which when heated with infrared light, cause the cancer cells to die (Ref. 30). Carbon nanotubes have been transported into the cell nucleus and continuous near infrared radiation absorption of nanotubes causes cell death. This methodology has been used for cancer cell destruction (Ref. 31).

5. Environmental Pollution Environmental degradation due to unsustainable production techniques and other human activities has exposed the entire world's population to increased risks. Innovative techniques, using nanoengineered materials and devices, can be deployed for the removal of polluting molecules in air, water and soil. Cleaner manufacturing processes and methods, by applying nanoscale techniques, can also contribute to a reduced level of environmental pollution, especially in the developing world where international standards are often not adhered to. For instance the high levels of arsenic in soil and water are posing a major environmental problem in several regions of the developing world. A simple and cheap but effective nanoscale technique to remove arsenic involves the use of TiO_2 nanoparticles (Ref. 32). Nanomaterials have further proved to be very effective in removing metal ion contamination. A wider application of such technologies, which are harnessing discoveries made in nanoscience, could have a positive and wider impact on the health conditions and natural habitat of millions of people.

6. *Energy Storage, Production and Conversion* Chronic power shortages and increased need for energy resources because of the rapidly growing population and economies of the developing world, are posing challenges to the energy market. Since almost all sources of energy are not renewable, the world will soon face a global energy supply problem. Solar energy is an interesting and valid alternative, especially in the tropical sunny South. Scientific studies have demonstrated that nanoscale techniques involving nanotubes and nanoparticles lead to increased conversion efficiencies. Semiconducting particles of titanium dioxide, coated with light-absorbing dyes bathed in an electrolyte and embedded in plastic films, are cheap and easy to manufacture and offer a viable alternative to conventional energy production and storage. Because of their low cost-structure, photovoltaics using nanotech constitute a valid alternative for overcoming the problem of power shortage, especially in the developing world. Researchers at Nanosolar, a venture capital start-up based in Palo Alto, California, are developing cheaper methods for producing photovoltaic solar cells by using nanotechnology (Ref. 33). The objective is to boost the power output of nano solar cells and make them easier to deploy by spraying them directly on surfaces. This approach is simple and can be easily replicated in the developing world. These highly efficient solar cells can be made of a mix of alcohol surfactants and titanium compounds sprayed on a metal foil. Within 30 seconds, a block of titanium oxide perforated with holes of nano-meter size rises from the foil. The solar cells form when the holes are filled with conductive polymer and electrodes are added and then covered with a transparent plastic. These are concrete examples wherein nanotechnology can be used for energy storage, production and conversion in the developing world.

7. *Global Partnerships* The inclusion of the South in the nano-dialogue has created new platforms and alliances between the North and South and strengthens their ties. The allocation of some of the large public scientific funding of nanoscience and technology could be directed to developing countries in order to foster the development, diffusion and dissemination of nanoscience, engineering and technology in the developing world. Global research networks of excellence create more value for the international scientific community. It is certainly important to encourage international partnerships between the North and South, similar to the first North–South expert group meeting of nanoscientists and nanotechnologists in Trieste (Italy) in February 2005, but there is also a growing need for scientific exchange and alliances among countries of the developing world in view of the ongoing regionalization trends in politics and economics (Ref. 34). Global research networks, including scientific co-operation and collaboration, are needed to find joint solutions for the most pressing problems of the world community. Since partnerships at the regional level are likely to gain importance in the long term, the establishment of South-South nano-networks must be envisaged.

16.8.3 Unexplored Biodiversity of the South—Opportunities for Bio-nanotechnology

The development of nanocomponents that imitate or emulate natural processes can find many applications in many sectors. The protection and preservation of species in the tropical belt has acquired a new dimension because of bio-nanotechnology and its potential applications. The scientific exploration of the nano-bio interface becomes very interesting in view of the developing synthetic life-forms, manufactured organs and bio-nanodevices. Since they have the requisite research infrastructure, developing countries enjoy a strategic advantage vis-à-vis the industrialized world. This is also true because the biodiversity is much larger in the tropical and sub-tropical belt as in other geographical and climatic zones. It is thus up to the developing countries to make use of this distinctive asset and to discover the secrets of this unexplored biodiversity and the particular physical properties of its living organisms. The 'Lotus Effect', discovered by Wilhelm Barthlott and his student Christoph Neinhuis of the University of Bonn, illustrates how knowledge of what happens at the bio-nano interface can be made fruitful. Lotusan, a dirt repellent paint is the commercialized form of the scientific discovery of the Lotus Effect. The developing countries need to discover the richness of their flora and fauna, which will help them optimise the use of bio-nanotechnology. Their rich cultural heritage, including the millennia old traditional knowledge in the areas of homeopathic, Ayurvedic and herbal medicine, along with their large biodiversity provide developing countries with a strategic advantage that the developed countries do not have. It lies in the hands of these countries, especially those that have already adopted nanotechnology initiatives within the bounds of their national technology development policies, to utilize their unique assets for moving ahead in the emerging global nano world.

16.9 Conclusions

The potential societal implications of the scientific and technological innovation in the realm of nano and the future applications of discoveries at the frontiers of science are only partially understood and therefore need to be further explored. The uniqueness and distinctiveness of nanoscience and nanotechnology, especially with regard to its pervasiveness into virtually all spheres of human life, explain why their potential impacts will exceed those of all other conventional technologies hitherto developed. The convergence of the newly emerging technologies of the 21st Century have the potential to revolutionize social and economic development and may offer innovative and viable solutions for the most pressing problems of the world community and its habitat. A better understanding of the potential benefits and hazards of nanoscale science and technology is essential because it will provide policy-makers with better tools to take responsible choices. Nanoscience and its deriving technologies have the potential to improve the state of the developing world, if the applications are designed and tailored to best fit the needs of the people. Unlike other technologies, nanotechnology offer a unique chance to bridge the technological gap between the industrialized and the developing world. But a favourable terrain for the growth of these sprouts needs to be prepared and therefore joint and concerted efforts by all concerned are needed to rule out future factions and new divides.

Review Questions

1. What are the specific implications to society when advanced technologies are implemented?
2. Contrast nanotechnology from other emerging technologies.

3. Summarize the landmarks in nano research.
4. List the specific areas of economic benefit to the developing world particularly from the perspective of biodiversity.
5. How can nanotechnology be used for sustainable development?
6. How can nano research lead to a new political divide?

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Additional Reading

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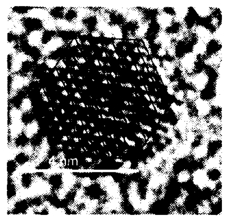
Appendix

HISTORY OF NANOSCIENCE AND TECHNOLOGY*



- **December 29, 1959: *Plenty of Room at the Bottom***
  The lecture of Richard Feynman at the California Institute of Technology. It was titled, "There's Plenty of Room at the Bottom." Here, he proposed the "possibility of maneuvering things atom by atom."
- **Mid-1970s: *Nanotechnology***
  Idea of molecular nanotechnology, originated in the mind of Eric Drexler, MIT undergraduate. He realized that the biological 'machinery' could be adapted to build non-living products upon command.
- **1974: *Molecular Devices***
  The first molecular electronic device was patented by Aviram and Seiden of IBM. Professor Norio Taniguchi of Tokyo Science University invented the term *nanotechnology*.
- **1980: *Molecular Nanotechnology***
  K. Eric Drexler, an MIT student, writes the first paper on advanced nanotechnology.
- **1980s: *Chemical Synthesis of Nanoparticles***
  Various kinds of nanoparticle systems were made. These include stable, dispersible materials of almost every element and common binary oxides and sulphides.
- **1981: *Scanning Tunneling Microscopy***
  Binning and Rohrer (IBM) build the scanning probe microscope making it possible to work with atoms and molecules.
  "Surface Studies by Scanning Tunneling Microscopy," Binning G., H. Rohrer, Ch. Gerber and E. Weibel, *Phys. Rev. Lett.*, **49** (1982), p. 57.
- **1983: *Self-assembled Monolayers***
  Self-assembled monolayers (molecularly thin films) of thiols on gold surfaces were made. These are used for various nanopatterning applications now.

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* The author is aware of the fact that a selection of this sort reflects personal preferences. As a result, several noteworthy contributions are not listed although the author has no intention to undermine the significance of those works. A brief summary of the work with original reference citation is given so that the reader can explore specific topics further. Such a selection may be useful for classroom presentations.

"Adsorption of Bifunctional Organic Disulfides on Gold Surfaces," Nuzzo, R.G. and D.L. Allara, *J. Am. Chem. Soc.*, **105** (1983), p. 4481.

- **1985: *Scientists Richard Smalley, Robert Curl, Jr., and Harold Kroto discover spherical cages of 60 carbon atoms called "buckminsterfullerene".***

  "C_{60}: Buckminsterfullerene", Kroto, H.W., J.R. Heath, S.C. O'Brion, R.C. Curl and R.E. Smalley, *Nature*, **318** (1985), p. 162.

- **1986: *Atomic Force Microscopy***

  Atomic force microscope (AFM) invented.

  "Atomic Force Microscope", Binning, G., C.F. Quate and Ch. Gerber, *Phys. Rev. Lett.*, **56** (1986), p. 930.

- **1986: *Engines of Creation***

  During the same time period, K. Eric Drexler publishes "Engines of Creation." Drexler presented his provocative ideas on molecular nanotechnology to a general audience.

- **November 9, 1989: *Writing with Atoms***

  Don Eigler at IBM's Zurich Research Laboratory arranges 35 xenon atoms to write "IBM" using the tip of a scanning tunneling microscope (STM), achieved at temperatures close to absolute zero.

  "Positioning Single Atoms with a Scanning Tunneling Microscope", Eigler, D.M., and E.K. Schweizer, *Nature*, **344** (1990), p. 524.

- **1991: *Nanotubes Arrive***

  Discovery of carbon nanotubes by Sumio Iijima.

  "Helical Microtubules of Graphitic Carbon", Iijima, S., *Nature*, **354** (1991), p. 56.

- **1992: *Nanosystems***

  Drexler published *Nanosystems*, a technical work outlining a way to manufacture extremely high-performance machines out of molecular carbon lattice ('diamondoid').

  Drexler, K.E., *Nanosystems: Molecular Machinery, Manufacturing and Computation*, (1992), Wiley/Interscience, New York.

- **1994: *Gold Particles***

  Stable gold nanoparticles with molecular protection were made in solution.

  "Synthesis of Thiol-Derivatised Gold Nanoparticles in a Two-Phase Liquid–Liquid System", Brust, M., M. Walker, D. Bethell, D.J. Schiffrin and R. Whyman, *J. Chem. Soc., Chem. Commun.*, (1994), pp. 801–802.

- **January 1996: *Assembling Molecules***

  Scientists at IBM succeed in moving and precisely positioning individual molecules at room temperature.

- **August 1998: *Aligned Nanotubes***

  Aligned nanotube bundles have been grown on surfaces by the pyrolysis route.

"Large Aligned-Nanotube Bundles from Ferrocene Pyrolysis", Rao C.N.R., R. Sen, B.C. Satishkumar and A. Govindaraj, *Chem. Commn.*, (1998), pp. 1525–1526.

- **July 1999:** ***Molecular Logic Gate***

  A team at UCLA and Hewlett-Packard create a molecular 'logic gate'.

  "Electronically Configurable Molecular-Based Logic Gates", Collier, C.P., E.W. Wong, M. Belohradský, F.M. Raymo, J.F. Stoddart, P.J. Kuekes, R.S. Williams and J.R. Heath, *Science*, **285** (1999), p. 391.

- **1999, 2000:** ***Y-Junction Nanotubes***

  Using Y-shapes nanochannel alumina, Y-jucntion nanotubes have been synthesized.

  "Y-Junction Carbon Nanotubes and Controlled Growth", Li, J., C. Papadopoulos and J. Xu, *Nature* **402** (1999), p. 253.

  Pyrolysis of a metallocene and thiophene has been used to make such junctions.

  "Y-Junction Carbon Nanotubes", Satishkumar, B.C., P.J. Thomas, A. Govindaraj and C.N.R. Rao, *Appl. Phys. Lett.*, **77** (2000), p. 2530.

- **2001:** ***Moore's Law Surpassed***

  In June 2001, Intel Corporation researchers announced that they had created the technology needed to produce the world's smallest and fastest silicon transistor on a mass scale. These switch on and off 1.5 trillion times a second.

- **April 2002:** ***Optical Microscopy at Nanometer Scale***

  Scientists used conventional optics to image clumps of bacteria, just 33 nanometres across—much smaller than the wavelength of light used to illuminate them. The study shows that 'far-field' optical microscopes can operate well beyond the diffraction limit ($\sim \lambda/2$). A new kind of optical microscopy is born to look at nano objects.

  "Focal Spots of Size $\lambda/23$ Open Up Far-Field Florescence Microscopy at 33 nm Axial Resolution", Dyba M. and S. Hell, *Phys. Rev. Lett.*, **88** (2002), p. 163901.

- **May 2002:** ***Photons can Move Molecules***

  The first conversion of light to mechanical energy by a single-molecule device has been demonstrated.

  "Single-Molecule Optomechanical Cycle", Hugel, T., N.B. Holland, A. Cattani, L. Moroder, M. Seitz and H.E. Gaub, *Science*, **296**, 1103.

- **May 2002:** ***Molecular Shuttling Leads to Nanoconstruction***

  Receptor-lipid molecules disperse and regroup across an artificial cell membrane by adding and removing free-floating ligands.

  "Crown Ether Functionalized Lipid Membranes: Lead Ion Recognition and Molecular Reorganization", Sasaki, D.Y., T.A. Waggoner, J.A. Last and T.M. Alam, *Langmuir*, **18** (2002), p. 3714.

- **June 2002:** ***Nanofilter-based Chirality Separation***

  A bionanotube membrane that can separate out the left- and right-handed forms of chiral drug molecules has been developed. An antibody which binds preferentially to one mirror image form (or enantiomer) of the chemical is used in this approach.

"Antibody-Based Bio-Nanotube Membranes for Enantiomeric Drug Separations", Lee, S.B., D.T. Mitchell, L. Trofin, T.K. Nevanen, H. Söderlund and C.R. Martin, *Science*, **296** (2002), p. 2198.

- **June 2002: *Magnetic Spins Store Quantum Information***

  Spins of clusters of atoms in a magnetic compound became aligned when a magnetic field was applied. This coherence persisted for up to ten seconds, and the clusters could have information stored on them.

  "Coherent Spin Oscillations in a Disordered Magnet", Ghosh, S., R. Parthasarathy, T.F. Rosenbaum and G. Aeppli, *Science*, **296** (2002), p. 2195.

- **June 2002: *Diffraction Limit and Light Transport***

  A large amount of light can pass through a sub-wavelength aperture in a patterned metal film without being diffracted. The diffraction limit could be overcome this way.

  "Beaming Light from a Sub-Wavelength Aperture", Lezec, H.J., A. Degiron, E. Devaux, R.A. Linke, L. Martin-Moreno, F.J. Garcia-Vidal and T.W. Ebbesen, *Science*, **297** (2002), p. 820.

- **June 2002: *Laser Lithography for Cheaper Chips***

  Silicon chips could be made more quickly and cheaply by using a new technique which would make it possible to go on with silicon for some more time than previously anticipated.

  "Ultrafast and Direct Imprint of Nanostructures in Silicon", Chou, S.Y., C. Keimel and J. Gu, *Nature*, **417** (2002), p. 835.

- **June 2002: *Magnets Make Logic***

  A ferromagnetic NOT gate, a new class of device has been made. It is believed that a full set of logic gates could be developed by using this technique.

  "Sub-Micrometer Ferromagnetic NOT Gate and Shift Register", Allwood, D.A., G. Xiong, M.D. Cooke, C.C. Faulkner, D. Atkinson, N. Vernier and R.P. Cowburn, *Science*, **296** (2002), p. 2003.

- **June 2002: *Nanorod Devices for Photovoltaics***

  The plastic solar cells with semiconducting nanorods have been made.

  "Hybrid Nanorod-Polymer Solar Cells, Huynh, Wendy U., Janke J. Dittmer and A.P. Alivisatos", *Science*, **295** (2002), p. 2425.

- **June 2002: *Dip-pen Nanolithography with Biomolecules***

  Dip-pen nanolithography has been used to create nanoscale patterns.

  "Direct Patterning of Modified Oligonucleotides on Metals and Insulators by Dip-Pen Nanolithography", Demers, L.M., D.S. Ginger, S.J. Park, Z. Li, S.W. Chung, and C.A. Mirkin, *Science*, **296** (2002), p. 1836.

- **July 2002: *Carbon Nanotube-based Imaging***

  Carbon nanotubes have been used as the basis of a cold-cathode X-ray device. It has been used to image a fish and a human hand.

"Generation of Continuous and Pulsed Diagnostic Imaging X-Ray Radiation Using a Carbon-Nanotube-Based Field-Emission Cathode",Yue, G.Z., Q. Qiu, B. Gao,Y. Cheng, J. Zhang, H. Shimoda, S. Chang, J.P. Lu and O. Zhou, *Appl. Phys. Lett.*, **81** (2002), p. 355.

- **August 2002: *Tagged Nanoparticles for Detection***

  Nanoparticle probes have been developed for detecting DNA with unique "fingerprints".

  "Nanoparticles with Raman Spectroscopic Fingerprints for DNA and RNA Detection", Cao,Y.W.C., R. Jin and C. A. Mirkin, *Science* **297** (2002), p. 1536.

- **August 2002: *Converting Alcohol into Carbon Nanofibres***

  Carbon Nanofibres have been made from methyl alcohol.

  "Carbon nanofibers Synthesized by Decomposition of Alcohol at Atmospheric Pressure", Jiang, N., R. Koie, T. Inaoka, Y. Shintani, K. Nishimura and A. Hiraki, *Appl. Phys. Lett.*, **81** (2002), p. 526.

- **August 2002: *Liquids Driven by Light***

  Liquids have been driven without using mechanical parts. The technique involves shining a light on the surface of the tube and transporting the fluid by a process known as photocapillarity.

  "Photon-Modulated Wettability Changes on Spiropyran-Coated Surfaces", Rosario, R., D. Gust, M. Hayes, F. Jahnke, J. Springer and A.A. Garcia, *Langmuir*, **18** (2002), p. 8062.

- **August 2002: *Nanoscale Patterns to Boost Magnetic Density***

  A film-patterning technique that could overcome the problems associated with high-density magnetic recording has been developed.

  "Nanoscale Patterning of Magnetic Islands by Imprint Lithography Using a Flexible mold", McClelland, G.M., M.W. Hart, C.T. Rettner, M.E. Best, K.R. Carter and B.D. Terris, *Appl. Phys. Lett.*, **81** (2002), p. 1483.

- **August 2002: *Nanoparticles to Destroy Bacteria***

  Magnesium oxide nanoparticles kill bacteria.

  "Metal Oxide Nanoparticles as Bactericidal Agents", Stoimenov, P.K., R.L. Klinger, G.L. Marchin and K.J. Klabunde, *Langmuir*, **18** (2002), p. 6679.

- **August 2002: *Single Molecule Light Emission***

  Electroluminescence from individual molecules of silver has been demonstrated.

  "Strongly Enhanced Field-Dependent Single-Molecule Electroluminescence", Lee, Tae-Hee, J.I. Gonzalez and R.M. Dickson, *Proc. Natl. Acad. Sci.*, **99** (2002), p. 10272.

- **September 2002: *Molecular Electronics Breakthrough***

  The highest density electronically addressable memory to date has been developed. The 64-bit memory uses molecular switches. The total area is less than one square micron, giving it a bit density that is more than ten times that of current silicon memory chips.

  http://nanotechweb.org/articles/news/1/9/8/1.

- **September 2002:** ***Nanografting Makes Tiny DNA Patterns***

  DNA patterns that are one-thousandth the size of those in commercially available microarrays have been developed. This method could help create faster, more powerful devices for DNA sequencing, biological sensors and disease diagnosis.

  "Production of Nanostructures of DNA on Surfaces", Liu, M., N.A. Amro, C.S. Chow and Gang-yu Liu, *Nano Letters*, **2** (2002), p. 863.

- **September 2002:** ***GaN Nanowire Laser Emits Light***

  The first GaN nanowire laser has been made.

  "Single Gallium Nitride Nanowire Lasers", Johnson, J.C., Heon-Jin Choi1, K.P. Knutsen, R.D. Schaller, P. Yang and R.J. Saykally, *Nature Materials*, **1** (2002), p. 106.

- **October 2002:** ***Atom Lithography for the Future***

  The resolution of 'atom lithography' need not be limited by the wavelength of light.

  "Demonstration of Frequency Encoding in Neutral Atom Lithography", Thywissen, J.H. and M. Prentiss, *New J. Phys.*, **7** (2005), p. 47.

- **October 2002:** ***Optical Thermometer with Molecules***

  A common luminescent organic semiconductor based thermometer has been developed. This can possibly do thermal imaging of nanometre-sized devices.

  "A Molecular Thermometer based on Long-Lived Emission from Platinum Octaethyl Porphyrin", Lupton, J.M., *Appl. Phys. Lett.*, **81** (2002), p. 2478.

- **October 2002:** ***Molecules to Power Nanoscale Computers***

  A new kind of computing that relies on the motion of molecules rather than the flow of electrons has been demonstrated. Logic gates use cascades of carbon monoxide molecules to transfer data. Devices made in this way have dimensions on the scale of nanometres, which are several orders of magnitude smaller than existing components.

  "Molecule Cascades", Heinrich, A.J., C.P. Lutz, J.A. Gupta and D.M. Eigler, *Science*, **298** (2002), p. 1381.

- **November 2002:** ***Carbon Nanotube Makes Transistors Better than Silicon***

  It is claimed that a carbon nanotube transistor has better properties than silicon transistors of an equivalent size.

  "High-κ Dielectrics for Advanced Carbon-Nanotube Transistors and Logic Gates", Javey, A., H. Kim, M. Brink, Q. Wang, A. Ural, J. Guo, P. Mcintyre, P. Mceuen, M. Lundstrom and H. Dai, *Nature Materials*, **1** (2002), p. 241.

- **November 2002:** ***Conductance of Hydrogen Molecules***

  The conductance of a single hydrogen molecule has been measured. A single hydrogen molecule has been trapped between two platinum electrodes and its conductance measured. This is a simple test system in which fundamental properties of single-molecule devices can be explored.

"Measurement of the Conductance of a Hydrogen Molecule", Smit, R.H.M., Y. Noat, C. Untiedt, N.D. Lang, M.C. van Hemert and J.M. van Ruitenbeek, *Nature*, **419** (2002), p. 906.

- **December 2002:** ***Artificial Nanopores Detect DNA Molecules***

  An artificial nanopore has been made by micro-moulding poly (dimethylsiloxane)—(PDMS)—elastomer. The on-chip electronic sensor detected single DNA molecules.

  "An Artificial Nanopore for Molecular Sensing", Saleh, O.A. and L.L. Sohn, *Nano Letters*, **3** (2003), p. 37.

- **January 2003:** ***Nanoelectronic Devices are Made from Nanowires***

  One-dimensional heterostructure electronic devices based on nanowires have been made. Resonant tunnelling diodes by bottom-up assembly of different III/V semiconductor materials have also been made.

  "Luminescence Polarization of Ordered GaInP/InP Islands", Håkanson, U., V. Zwiller, M.K.J. Johansson, T. Sass and L. Samuelson, *Appl. Phys. Lett.*, **82** (2003), p. 627.

- **January 2003:** ***Functional Devices for Drug Delivery***

  A nanoporous material that opens or closes its pores under the influence of light has been created. This hexagonal mesoporous silica may have applications in the controlled release of chemicals such as drugs.

  "Photocontrolled Reversible Release of Guest Molecules from Coumarin-Modified Mesoporous Silica", Mal, N.K., M. Fujiwara and Y. Tanaka, *Nature*, **421** (2003), p. 350.

- **January 2003:** ***Molecules have been Shown to Store Data***

  Data storage devices using rotaxane molecules have been made. The films made by using these molecules have been scanned with an atomic force microscope (AFM) to create a pattern of dots to store the information.

  "Information Storage Using Supramolecular Surface Patterns", Cavallini, M., F. Biscarini, S. Léon, F. Zerbetto, G. Bottari and D.A. Leigh, *Science*, **299** (2003), p. 531.

- **January 2003:** ***Single Molecule Detection Using Nanoshells***

  Single molecules have been detected with the help of surface-enhanced Raman scattering (SERS) by using nanoshells.

  "Controlling the Surface-Enhanced Raman Effect via the Nanoshell Geometry", Jackson, J.B., S.L. Westcott, L.R. Hirsch, J.L. West and N.J. Halas, *Appl. Phys. Lett.*, **82** (2003), p. 257.

- **February 2003:** ***DNA Computing Device Makes Its Own Energy***

  A DNA computing device that provides its own energy has been made. The device uses DNA molecules as both input data and as a fuel source.

  "DNA Molecule Provides a Computing Machine with Both Data and Fuel", Benenson, Y., R. Adar, T. Paz-Elizur, Z. Livneh and E. Shapiro, *PNAS*, **100** (2003), p. 2191.

- **February 2003:** ***Record-breaking Superconductor Transistor***

  A superconducting amplifier has been built with the highest current and power gains till date. The device can be used in low-temperature applications in the form of read-out elements for quantum computers.

  "Low-Noise Current Amplifier Based on Mesoscopic Josephson Junction", Delahaye, J., J. Hassel, R. Lindell, M. Sillanpää, M. Paalanen, H. Seppä and P. Hakonen, *Science*, **299** (2003), p. 1045.

- **February 2003:** ***Nanofibre 'Bandage' to Heal Wounds***

  A nanofibre mat from fibrinogen, a soluble protein that is present in the blood, has been made which can be used as a wound dressing or tissue-engineering scaffold.

  "Electrospinning of Nanofiber Fibrinogen Structures", Wnek, G.E., M.E. Carr, D.G. Simpson and G.L. Bowlin, *Nano Letters*, **3** (2003), p. 213.

- **February 2003:** ***Carbon Nanotube Device to Detect Gas Molecules***

  An array of detectors containing single-walled carbon nanotubes, which can sense gases, has been made.

  "Efficient Formation of Iron Nanoparticle Catalysts on Silicon Oxide by Hydroxylamine for Carbon Nanotube Synthesis and Electronics", Choi, H.C., S. Kundaria, D. Wang, A. Javey, Q. Wang, M. Rolandi and H. Dai, *Nano Letters*, **3** (2003), p. 157.

- **February 2003:** ***Expanding and Contracting DNA Nanomotor***

  A DNA nanomotor that expands and contracts by up to 5 nm has been made.

  "DNA Duplex-Quadruplex Exchange as the Basis for a Nanomolecular Machine", Alberti, P., and J.L. Mergny, *PNAS*, **100** (2003), p. 1569.

- **February 2003:** ***Carbon Nanotube Flow Sensors***

  Carbon nanotubes generate a potential when a liquid flows over it. The potential is sensitive to the flow parameters.

  "Carbon Nanotube Flow Sensors", Ghosh, S., A.K. Sood and N. Kumar, *Science*, **299** (2003), pp. 1042–1044.

- **March 2003:** ***Sensing Polymers are Now Nanocrystalline***

  Porous silicon has been used for making nanocrystalline polymer structures. The resulting structures may have applications as sensing devices inside the body.

  "Polymer Replicas of Photonic Porous Silicon for Sensing and Drug Delivery Applications", Li, Y.Y., F. Cunin, J.R. Link, T. Gao, R.E. Betts, S.H. Reiver, V. Chin, S.N. Bhatia and M.J. Sailor, *Science*, **299** (2003), pp. 2045.

- **March 2003:** ***Highest Resolution Optical Microscopy***

  'Near-field Raman microscopy' has been used to look at carbon nanotubes revealing 30 nm features.

  "High-Resolution Near-Field Raman Microscopy of Single-Walled Carbon Nanotubes", Hartschuh, A., E.J. Sánchez, X.S. Xie and L. Novotny, *Phys. Rev. Lett.*, **90** (2003), p. 095503.

- **March 2003: *Carbon Nanotubes Linked Up by Amino Acids***

  Sidewalls of single-walled carbon nanotubes have been functionalized with amino acids.

  "Sidewall Amino-Functionalization of Single-Walled Carbon Nanotubes through Fluorination and Subsequent Reactions with Terminal Diamines", Stevens, J.L., A.Y. Huang, H. Peng, I.W. Chiang, V.N. Khabashesku and J.L. Margrave, *Nano Letters*, **3** (2003), p. 331.

- **April 2003: *Biomolecular Electronic Devices Show Higher Gain***

  A prototype field-effect transistor using a deoxyguanosine derivative, has been made. The device has a maximum voltage gain of 0.76, which is higher than that reported for other molecular devices.

  "Field-Effect Transistor Based on a Modified DNA Base", Maruccio, G., P. Visconti, V. Arima, S. D'Amico, A. Biasco, E. D'Amone, R. Cingolani R. Rinaldi, S. Masiero, T. Giorgi and G. Gottarelli, *Nano Letters*, **3** (2003), p. 479.

- **April 2003: *Hydrogen Storage by Nanostructured Graphite***

  Nanostructured graphite has been shown to absorb hydrogen to the tune of 0.20–0.25 per cent by weight.

  "Dense Hydrogen Adsorption on Carbon Sub-Nanopores at 77 K", Kadono, K., H. Kajiura and M. Shiraishi, *Appl. Phys. Lett.*, **83** (2003), p. 3392.

- **April 2003: *Nanowires Made with Protein Templates***

  On a yeast protein template metallic nanowires have been made by using nanoparticles.

  Scheibel, T., R. Parthasarathy, G. Sawicki, Xiao-Min Lin, H. Jaeger and S. L. Lindquist, *PNAS*, **100** (2003), p. 4527.

- **May 2003: *DNA Detection by Using Nanotubes***

  A nanotube-based DNA detection method has been developed which uses fluorescence detection.

  "Carbon Nanotube Nanoelectrode Array for Ultrasensitive DNA Detection", Li, J., H.T. Ng, A. Cassell, W. Fan, H. Chen, Q. Ye, J. Koehne, J. Han and M. Meyyappan, *Nano Letters*, **3** (2003), p. 597.

- **May 2003: *Genes Inserted into Cells by Using Nanotubes***

  Carbon nanofibres have been used to insert plasmid DNA into cells.

  "Intracellular Iintegration of Synthetic Nanostructures with Viable Cells for Controlled Biochemical Manipulation", McKnight, T.E., A.V. Melechko, G.D. Griffin, M.A. Guillorn, V.I. Merkulov, F. Serna, D.K. Hensley, M.J. Doktycz, D.H. Lowndes and M.L. Simpson, *Nanotechnology*, **14** (2003), p. 551.

- **May 2003: *Large Magnetic Anisotropy***

  Large magnetic anisotropy energy (MAE) of over 9 milli-electron-volts has been found in cobalt atoms placed on a platinum substrates. It is suggested that this discovery would help in the design of new magnetic materials that may be used for data storage.

  "Giant Magnetic Anisotropy of Single Cobalt Atoms and Nanoparticles", Gambardella, P., S. Rusponi, M. Veronese, S.S. Dhesi, C. Grazioli, A. Dallmeyer, I. Cabria, R. Zeller, P.H. Dederichs, K. Kern, C. Carbone and H. Brune, *Science*, **300** (2003), p. 1130.

- **May 2003:** ***Enhanced Superconductivity***

  Superconductivity has been shown to be enhanced in a nanoengineered magnetic field.

  "Nanoengineered Magnetic-Field-Induced Superconductivity", Lange, M., M.J.V. Bael, Y. Bruynseraede and V.V. Moshchalkov, *Phys. Rev. Lett.*, **90** (2003), p. 197006.

- **June 2003:** ***Nanoparticles Destroy Halocarbons***

  A solution of gold and silver nanoparticles carries out the catalytic destruction of halocarbons in water. The authors claim that this may be used for the removal of halocarbons from drinking water.

  "Halocarbon Mineralization and Catalytic Destruction by Metal Nanoparticles", Nair A.S. and T. Pradeep, *Current Science*, **84** (2003), p. 1560.

- **June 2003:** ***Bar-codes with DNA***

  DNA self-assembly around a DNA scaffold has been used to create a bar-code pattern containing information.

  "Directed Nucleation Assembly of DNA Tile Complexes for Bar-Code-Patterned Lattices", Yan, H., T.H. LaBean, L. Feng and J.H. Reif, *PNAS*, **100** (2003), p. 8103.

- **June 2003:** ***Gold Nanoparticles Synthesized by Biology***

  A micro-organism, *Rhodococcus* sp., which normally grows on fig trees, has been used to synthesize gold nanoparticles.

  "Intracellular Synthesis of Gold Nanoparticles by a Novel Alkalotolerant Actinomycete, *Rhodococcus* Species", Ahmad, A., S. Senapati, M.I. Khan, R. Kumar, R. Ramani, V. Srinivas and M. Sastry, *Nanotechnology*, **14** (2003), p. 824.

- **July 2003:** ***Precision Sensors to Detect Quantum Movement***

  A nanoelectromechanical bridge and a single-electron transistor have been used to detect ultra small displacements.

  "Nanometre-Scale Displacement Sensing Using a Single Electron Transistor", Knobel, R.G., and A.N. Cleland, *Nature*, **424** (2003), p. 291.

- **August 2003:** ***Quantum Circuits, Freated and Erased***

  Devices and circuits can be created and changed at the atomic level by using erasable electrostatic lithography.

  "Erasable Electrostatic Lithography for Quantum Components", Crook, R., A.C. Graham, C.G. Smith, I. Farrer, H.E. Beere and D.A. Ritchie, *Nature*, **424** (2003), p. 751.

- **August 2003:** ***Wet Nanoparticles Change Structure***

  Certain nanoparticles change their structure by the addition of water.

  "Water-Driven Structure Transformation in Nanoparticles at Room Temperature", Zhang, H., B. Gilbert, F. Huang and J.F. Banfield, *Nature*, **424** (2003), p. 1025.

- **September 2003:** ***Nanotubes Sense Helium***

  Multi-walled carbon nanotubes under a positive bias field-ionize passing gas atoms.

"Helium Detection Via Field Ionization from Carbon Nanotubes", Riley, D.J., M. Mann, D.A. MacLaren, P.C. Dastoor, W. Allison, K.B.K. Teo, G.A.J. Amaratunga and W. Milne, *Nano Letters*, **3** (2003), p. 1455.

- **September 2003:** ***Biological Cells Imaged with Nanoparticles***

  Proteins have been imaged efficiently and non-destructively by using gold nanoparticles.

  "Single Metallic Nanoparticle Imaging for Protein Detection in Cells", Cognet, L., C. Tardin, D. Boyer, D. Choquet, P. Tamarat and B. Lounis, *PNAS*, **100** (2003), p. 11350.

- **September 2003:** ***Nanopores Analyze DNA***

  The properties of single DNA molecules have been studied by using a solid-state nanopore membrane. The technique may be ultimately used for rapid DNA sequencing.

  "DNA Molecules and Configurations in a Solid-State Nanopore Microscope", Li, J., M. Gershow, D. Stein, E. Brandin and J.A. Golovchenko, *Nature Materials*, **2** (2003), p. 611.

- **November 2003:** ***Nerve Agent Detector Using Nanotubes***

  A nerve agent detector using single-walled carbon nanotubes has been developed.

  "Nerve Agent Detection Using Networks of Single-Walled Carbon Nanotubes", Novak, J.P., E.S. Snow, E.J. Houser, D. Park, J.L. Stepnowski and R.A. McGill, *Appl. Phys. Lett.*, **83** (2003), p. 4026.

- **December 2003:** ***Nanotube Sorter Using DNA***

  Self-assembly of DNA has been used to sort carbon nanotubes according to their diameter and electronic properties.

  "Structure-Based Carbon Nanotube Sorting by Sequence-Dependent DNA Assembly", Zheng, M., A. Jagota, M.S. Strano, A.P. Santos, P. Barone, S.G. Chou, B.A. Diner, M.S. Dresselhaus, R.S. Mclean, G.B. Onoa, G.G. Samsonidze, E.D. Semke, M. Usrey and D.J. Walls, *Science*, **302** (2003), p. 1545.

- **2003:** ***Assorted Discoveries***
  - A nanowire has the potential to detect the gene for cystic fibrosis (CF) more efficiently than conventional tests carried out for the disease. CF is the most common fatal genetic disease among people of European origin.
  - A 'nanosensor' that only works when noise is added has been developed. The device uses 'Stochastic Resonance' to enhance sub-threshold signals. In a noise-free environment, the detectors will not receive a signal. If a moderate amount of noise is present, the signal will, as it were, float on top of the noise, while triggering the detectors.
  - Nanoscale fibers that are thinner than the wavelengths of light have been developed.
  - Nanoshells can act as anti-cancer drugs. The light used is near-infrared light which gets absorbed by the shells, thereby heating and destroying the cells which are injected with the shells. Detection of the cancer cells is also done by the shells.
  - Prostate specific antigen (PSA) at extremely low levels in a blood sample has been detected with nanoparticles. This heralds the use of new kinds of detection methods for proteins.
  - Multi-photon microscopy of the blood vessels has been carried out with quantum dots.
  - Nano bones have been implanted in patients.

- A new type of protein chip has been developed on the basis of protein-binding silica-nanoparticles. Chips are analyzed by using MALDI-TOF mass spectrometry.
- It has been shown that an injection of magnetic nanoparticles into the bloodstream can reveal where harmful viruses are located. The particles are coated with antibodies to fight a particular virus, so that they will form clumps that would be visible on conventional body scans.

- **January 2004:** ***World's First Nanotechnology College***

  The world's first college of nanotechnology is established at Suny Albany, USA.

- **February 2004:** ***Transition from Quantum to Classical through Decoherence***

  Decoherence—The transition from quantum to classical behavior, caused by the thermal emission of radiation was observed in the case of C_{70} molecules at higher temperatures.

  "Decoherence of Matter Waves by Thermal Emission of Radiation", Hackermüller, L., K. Hornberger, B. Brezger, A. Zeilinger and M. Arndt, *Nature*, **427** (2004), p. 711.

- **March 2004:** ***Controlling the Rotation of a Molecule***

  Simple electron transfer processes and photoexcitation have been used to control the rotary motion of a metallacarborane, resulting in the possible applications for nanovalves and in the modification of surface properties.

  "Electrical or Photocontrol of the Rotary Motion of a Metallacarborane", Hawthorne, M.F., J.I. Zink, J.M. Skelton, M.J. Bayer, C. Liu, E. Livshits, R. Baer and D. Neuhauser, *Science*, **303** (2004), p. 1849.

- **April 2004:** ***Nanomehanical Resonator Approaching Quantum Limit***

  A tiny nanoelectromechanical arm's vibrations have been measured to probe the limits at which classical physics takes over from quantum behavior.

  "Approaching the Quantum Limit of a Nanomechanical Resonator", LaHaye, M.D., O. Buu, B. Camarota and K.C. Schwab, *Science*, **304** (2004), p. 74.

- **April 2004:** ***New Nanocrystal Mesophase Produced by Self-assembly of Nanocrystal Micelles***

  The self-assembly of water-soluble nanocrystal micelles leads to the formation of a new nanocrystal mesophase, which is suitable for integration into devices that use standard techniques of microelectronic processing.

  "Self-Assembly of Ordered, Robust, Three-Dimensional Gold Nanocrystal/Silica Arrays", Fan, H., K. Yang, D.M. Boye, T. Sigmon, K.J. Malloy, H. Xu, G.P. López and C.J. Brinker, *Science*, **304** (2004), p. 567.

- **May 2004:** ***Single-electron Transistor***

  A single-electron transistor has been made which operates by using a nanometer-scale vibrating arm. It was built by using a simple two-step process and unlike previous devices of the kind, it does not require cryogenic temperatures to be operational.

  "Silicon Nanopillars for Mechanical Single-Electron Transport", Scheible, D.V. and R.H. Blick, *Appl. Phys. Lett.*, **84** (2004), p. 4632.

- **May 2004: *Carbon Nanotubes Respond to Magnetic Fields***

  Carbon nanotubes have been found to respond to magnetic fields. In the presence of a magnetic field, semiconducting nanotubes can be made metallic and vice versa.

  "Optical Signatures of the Aharonov-Bohm Phase in Single-Walled Carbon Nanotubes", Zaric, S., G.N. Ostojic, J. Kono, J. Shaver, V.C. Moore, M.S. Strano, R.H. Hauge, R.E. Smalley and X. Wei, *Science*, **304** (2004), p. 1129.

  "*h/e* Magnetic Flux Modulation of the Energy Gap in Nanotube Quantum Dots", Coskun, U.C., Tzu-Chieh Wei, S.Vishveshwara, P.M. Goldbart and A. Bezryadin, *Science*, **304** (2004), p. 1132.

- **May 2004: *Nanotube Mixture***

  Rolled-up nanotubes of InAs/GaAs with tube walls containing alternating layers of crystalline and non-crystalline materials have been made. The structure of these radial superlattices was altered by using a laser, which resulted in the production of small regions of β-Ga_2O_3.

  "Radial Superlattices and Single Nanoreactors", Deneke, Ch., N.Y. Jin-Phillipp, I. Loa and O.G. Schmidt, *Appl. Phys. Lett.*, **84** (2004), p. 4475.

- **May 2004: *DNA Detection Using Bio-bar-code-based Technique***

  DNA detection using the bio-bar-code-based technique achieves a sensitivity similar to the generally used polymerase chain reaction (PCR) method. This technique involves the use of both gold nanoparticles attached to the bar-code DNA as well as the magnetic nanoparticles.

  "Bio-Bar-Code-Based DNA Detection with PCR-Like Sensitivity", Nam, Jwa-Min, S.I. Stoeva and C.A. Mirkin, *J. Am. Chem. Soc.*, **126** (2004), p. 5932.

- **May 2004: *Nanoscale Conveyors for Nanoassembly***

  An important tool for nanoassembly has been developed, wherein the indium atoms are carried to a precise location by using a multi-walled carbon nanotube.

  "Carbon Nanotubes as Nanoscale Mass Conveyors", Regan, B.C., S. Aloni, R.O. Ritchie, U. Dahmen and A. Zettl, *Nature*, **428** (2004), p. 924.

- **May 2004: *Solid-state C_{50} Molecules***

  For the first time, solid-state carbon-50 molecules have been prepared by using an arc-discharge technique involving chlorine.

  "Capturing the Labile Fullerene[50] as $C_{50}Cl_{10}$", Xie, Su-Yuan, F. Gao, X. Lu, Rong-Bin Huang, Chun-Ru Wang, X. Zhang, Mai-Li Liu, Shun-Liu Deng and Lan-Sun Zheng, *Science*, **304** (2004), p. 699.

- **June 2004: *Nanoprticles to Clean Tumours***

  Tumors in mice have been eradicated by photothermal ablation using near infrared-absorbing nanoparticles without affecting the healthy tissues.

  "Photothermal Tumor Ablation in Mice Using Near Infrared-Absorbing Nanoparticles", O'Neal, D.P., L.R. Hirsch, N.J. Halas, J.D. Payne and J.L. West, *Cancer Letters*, **209** (2004), p. 171.

- **June 2004: *Inkjet Printing at Nanometer Scale***

  Thin layers of molecules have been deposited on cantilever beams using the inkjet-printing technique, which enables the beams to act as chemical or biochemical sensors.

  "Rapid Functionalization of Cantilever Array Sensors by Inkjet Printing", Bietsch, A., J. Zhang, M. Hegner, H.P. Lang and C. Gerber, *Nanotechnology*, **15** (2004), p. 873.

- **June 2004: *Water Molecules Confined in Nanotube***

  Water molecules confined inside an open-ended single-walled carbon nanotube were studied using neutron-scattering measurements and molecular-dynamics simulations.

  "Anomalously Soft Dynamics of Water in a Nanotube: A Revelation of Nanoscale Confinement", Kolesnikov, A.I., Jean-Marc Zanotti, Chun-Keung Loong, P. Thiyagarajan, A.P. Moravsky, R.O. Loutfy and C.J. Burnham, *Phys. Rev. Lett.*, **93** (2004), p. 035503.

- **June 2004: *Quantum Dot Infrared Photodetectors***

  Semiconductor nanocrystals (quantum dots) have been used for making infrared detection devices, finding applications in night-vision googles, environmental monitors and military target tracking systems.

  "High Detectivity InAs Quantum Dot Infrared Photodetectors", Kim, Eui-Tae, A. Madhukar, Z. Ye and J.C. Campbell, *Appl. Phys. Lett.*, **84** (2004), p. 3277.

- **June 2004: *AFM Imaging Less than 1Å Resolution***

  A new higher-harmonic force microscope using a single carbon atom as a probe has been developed, which has a resolution close to three times better than that of the traditional STM.

  "Force Microscopy with Light-Atom Probes", Hembacher, S., F.J. Giessibl and J. Mannhar, *Science*, **305** (2004), p. 380.

- **June 2004: *Nanoconnections Using Photolithography***

  Interconnects to nanowire devices have been developed by using the photolithography technique which ensures that higher proportions of the nanowires connect to the electrodes.

  "Scalable Interconnection and Integration of Nanowire Devices without Registration", Jin, S., D. Whang, M.C. McAlpine, R.S. Friedman, Y. Wu and C.M. Lieber, *Nano Letters*, **4** (2004), p. 915.

- **June 2004: *Carbon Nanotubes for Bulb Filaments***

  A light bulb with carbon nanotubes as the filament has been designed, and it is found to have several advantages over the conventional tungsten filament.

  "Carbon Nanotube Filaments in Household Light Bulbs", Wei, J., H. Zhu, D. Wu, B. Wei, *Appl. Phys. Lett.*, **84** (2004), p. 4869.

- **June 2004: *Exothermic Nanocomposites***

  A nanocompsoite of aluminium and iron oxide that reacts exothermically on igniting has been made. This could have possible applications in explosives, as an energy source in MEMS devices, etc.

"Controlling the Dynamics of a Single Atom in Lateral Atom Manipulation", Stroscio, J.A. and R.J. Celotta, *Science*, **306** (2004), p. 242.

- **September 2004: *Imaging on sub-Angstrom Scales***

  A crystal was imaged on sub-Angstrom scales by using a technique developed for correcting the aberrations in a scanning transmission electron microscope.

  "Direct Sub-Angstrom Imaging of a Crystal Lattice", Nellist, P.D., M.F. Chisholm, N. Dellby, O.L. Krivanek, M.F. Murfitt, Z.S. Szilagyi, A.R. Lupini, A. Borisevich, W.H. Sides, Jr. and S.J. Pennycook, *Science*, **305** (2004), p. 1741.

- **September 2004: *Carbon Nanotubes of Record Length***

  A single-walled carbon nanotube, which is four centimeters long, has been prepared and it is believed to be the world's longest one.

  "Ultralong Single-Wall Carbon Nanotubes", Zheng, L.X., M.J. O'connell, S.K. Doorn, X.Z. Liao, Y.H. Zhao, E.A. Akhadov, M.A. Hoffbauer, B.J. Roop, Q.X. Jia, R.C. Dye, D.E. Peterson, S.M. Huang, J. Liu and Y.T. Zhu, *Nature Materials*, **3** (2004), p. 673.

- **September 2004: *Diamond Films for Biosensor Applications***

  Nanocrystalline diamond has been modified with protein molecules such that the molecules still remain active. Also the enzyme catalase was attached to a diamond film for creating a biosensor for the detection of H_2O_2.

  "Protein-Modified Nanocrystalline Diamond Thin Films for Biosensor Applications", Härtl, A., E. Schmich, J.A. Garrido, J. Hernando, S.C.R. Catharino, S. Walter, P. Feulner, A. Kromka, D. Steinmüller and M. Stutzmann, *Nature Materials*, **3** (2004), p. 736.

- **September 2004: *Superhard Carbon Phase***

  By cold compression of carbon nanotubes, a quenchable superhard high-pressure carbon phase was synthesized. Its hardness is comparable to that of cubic diamond and it also retained its properties at room temperature.

  "A Quenchable Superhard Carbon Phase Synthesized by Cold Compression of Carbon Nanotubes", Wang, Z., Y. Zhao, K. Tait, X. Liao, D. Schiferl, C. Zha, R.T. Downs, J. Qian, Y. Zhu and T. Shen, *PNAS*, **101** (2004), p. 13699.

- **September 2004: *Surface Modification of C_{60} Molecules Linked to its Toxicity***

  It has been found that the toxicity of C_{60} molecules to human cells is highly dependent on the molecules attached to the C_{60} molecules surface.

  "The Differential Cytotoxicity of Water-Soluble Fullerenes", Sayes, C.M., J.D. Fortner, W. Guo, D. Lyon, A.M. Boyd, K.D. Ausman, Y.J. Tao, B. Sitharaman, L.J. Wilson, J.B. Hughes, J.L. West and V.L. Colvin, *Nano Letters*, **4** (2004), p. 1881.

- **September 2004: *Self-assembled Biocidal Nanotubes***

  Biocidal nanotubes have been created which can also self-assemble into a nanocarpet structure. These tubes changed color in the presence of bacteria apart from killing it.

"Self-Assembly of Biocidal Nanotubes from a Single-Chain Diacetylene Amine Salt", Lee, S.B., R. Koepsel, D.B. Stolz, H.E. Warriner and A.J. Russell, *J. Am. Chem. Soc.*, **126** (2004), p. 13400.

- **September 2004: *Carbon Nanotube Filters***

  Multi-functional filters using carbon nanotubes have been developed. These can filter bacteria and viruses from water as well as separate petroleum into its molecular components.

  "Carbon nanotube filters", Srivastava, A., O.N. Srivastava, S. Talapatra, R. Vajtai and P.M. Ajayan, *Nature Materials*, **3** (2004), p. 610–614.

- **October 2004: *Molecular Switches Stabilized by Self-assembled Monolayer***

  The electrical switching of single molecules has been stabilized by altering their environment. A self-assembled monolayer has been used for surrounding oligo (phenylene-ethynylene) (OPE) molecules.

  "Mediating Stochastic Switching of Single Molecules Using Chemical Functionality", Lewis, P.A., C.E. Inman, Y. Yao, J.M. Tour, J.E. Hutchison and P.S. Weiss, *J. Am. Chem. Soc.*, **126** (2004), p. 12214.

- **October 2004: *Anti-bacterial Agents to be Released by Silica Nanoparticles***

  Mesoporous silica nanoparticles have been produced from room-temperature ionic liquids (RTILs) by using them as a template. For the anti-bacterial ionic liquids, these nanoparticles act as controlled release agents.

  "Morphological Control of Room-Temperature Ionic Liquid Templated Mesoporous Silica Nanoparticles for Controlled Release of Antibacterial Agents", Trewyn, B.G., C.M. Whitman and V.S.Y. Lin, *Nano Letters*, **4** (2004), p. 2139.

- **October 2004: *Nanoparticles for Rapid Bioassay of Food Samples***

  A single bacterial cell has been detected within 20 minutes by using bioconjugated nanoparticle-based bioassay. In the case of ground beef samples, this technique has been used to identify *Escherischia coli* bacteria.

  "A Rapid Bioassay for Single Bacterial Cell Quantitation Using Bioconjugated Nanoparticles", Zhao, X., L.R. Hilliard, S.J. Mechery, Y. Wang, R.P. Bagwe, S. Jin and W. Tan, *PNAS*, **101** (2004), p. 15027.

- **October 2004: *Novel Optoelectronic Fibres***

  Novel optoelectronic fibres containing metal, insulator and semiconductor layers have been created. These fibres could find applications in photodetectors by weaving them into a spectrometric fabric.

  "Metal-Insulator-Semiconductor Optoelectronic Fibres", Bayindir, M., F. Sorin, A.F. Abouraddy, J. Viens, S.D. Hart, J.D. Joannopoulos and Y. Fink, *Nature*, **431** (2004), p. 826.

- **October 2004: *Dip-pen Nanolithography Boosted by Surfactant***

  Using dip-pen nanolithography, it has been found that the surfactant added ink patterned maleimide-linked biotin onto the mercaptosilanized glass. Now the range of ink-substrate combinations used for patterning biotin and other biomolecules such as proteins can be expanded by the use of this technique.

  "Surfactant Activated Dip-Pen Nanolithography", Jung, H., C.K. Dalal, S. Kuntz, R. Shah and C.P. Collier, *Nano Letters*, **4** (2004), p. 2171.

"Water-Assisted Highly Efficient Synthesis of Impurity-Free Single-Walled Carbon Nanotubes", Hata, K., D.N. Futaba, K. Mizuno, T. Namai, M. Yumura and S. Iijima, *Science*, **306** (2004), p. 1362.

- **November 2004: *Nanoscale Test Tube to Carry Out Reaction***

  Fullerene epoxide polymer $(C_{60}O)_n$ has been been prepared by polymerization using single-walled carbon nanotubes as a nano test tube. This polymer that is usually seen in a tangled and branched three-dimensional form, was surprisingly found to be linear with unbranched topology.

  "Selective Host–guest Interaction of Single-Walled Carbon Nanotubes with Functionalized Fullerenes", Britz, D.A., A.N. Khlobystov, J. Wang, A.S. O'Neil, M. Poliakoff, A. Ardavan and G.A.D. Briggs, *Chemical Communications*, **2** (2004), p. 176.

- **December 2004: *STM Probes Lock-and-key Effect in Surface Diffusion***

  The diffusion of some large organic molecules on to a Cu(110) surface was found to depend on their orientation. Here the surface diffusion was observed to follow a lock-and-key model as probed by STM.

  "Lock-and-Key Effect in the Surface Diffusion of Large Organic Molecules Probed by STM", Otero, R., F. Hümmelink, F. Sato, S.B. Legoas, P. Thostrup, E. Lægsgaard, I. Stensgaard, D.S. Galvão and F. Besenbacher, *Nature Materials*, **3** (2004), p. 779.

- **December 2004: *Nanotube Transistor of sub-20 nm Size***

  A field-effect carbon nanotube transistor device having a channel length of just 18 nm has been created, which is the world's smallest nanotube transistor.

  "Sub-20 nm Short Channel Carbon Nanotube Transistors, Seidel, R.V., A.P. Graham, J. Kretz, B. Rajasekharan, G.S. Duesberg, M. Liebau, E. Unger, F. Kreupl and W. Hoenlein, *Nano Letters*, **5** (2004), p. 147.

- **December 2004: *Biosensing using Peptide Nanotubes***

  Self-assembled peptide nanotubes have been used for creating a novel electrochemical biosensor. The sensitivity of the biosensor was found to improve several folds in the presence of these nanotubes.

  "Novel Electrochemical Biosensing Platform Using Self-Assembled Peptide Nanotubes", Yemini, M., M. Reches, J. Rishpon and E. Gazit, *Nano Letters*, **5** (2005), p. 183.

- **December 2004: *Superconductivity Related to Film Thickness***

  It has been found that the superconducting transition temperature for ultrathin lead films varied with the number of atomic layers present in it.

  "Superconductivity Modulated by Quantum Size Effects", Guo, Y., Yan-Feng Zhang, Xin-Yu Bao, Tie-Zhu Han, Z. Tang, Li-Xin Zhang, Wen-Guang Zhu, E.G. Wang, Q. Niu, Z.Q. Qiu, Jin-Feng Jia, Zhong-Xian Zhao and Qi-Kun Xue, *Science*, **306** (2004), p. 1915.

- **December 2004: *Micro-machined Fountain Pen to Etch Nanopatterns***

  An AFM-based micromachined fountain pen with molecular ink has been used for etching nanopatterns on a surface.