Imagine supermarket packaging that could tell instantaneously if the food inside had been exposed to heat or had begun to spoil. Imagine a tiny foolproof automatic indicator that could constantly monitor a home for dangerous chemicals such as gas leaks, carbon monoxide, or ozone. Imagine a simple swab test that would instantly tell whether a patient has strep, diabetes, various genetic diseases, the flu, or an anemia. Imagine a simple wire that could be inserted in the ground to tell a home gardener where the soil is best for planting cucumbers. Imagine a foolproof (and it would need to be) explosives test so that you wouldn't need to remove all your clothes at the airport. All these possibilities are potential applications of nanoscale sensors. Sensors are structures that indicate the presence of particular molecules or biological structures, as well as the amounts that are present. Sensors are already present throughout our society, but the best sensors will be made from nanostructures and, for starters, should revolutionize much of the medical care and the food packaging industries.

Sensors are newer than you might think. Most people's earliest memory of the word is from Mr. Spock in the original *Star Trek* series. In fact, the word isn't much older that that. It was first used in an article in the *New Scientist* magazine in 1958 and is defined by the *Oxford English Dictionary* as "a device giving a signal for the detection or measurement of a physical [or chemical] property to which it responds." Actually, the dictionary definition does not include the information in the brackets, but the application of sensors to the detection of molecular structures is perhaps the most promising and important area of sensing activity.

NATURAL NANOSCALE SENSORS . . . .

As is true with so much of the rest of nanoscience and nanotechnology, examples of sensors at the nanoscale are very widespread in biology. Sensors are crucial to communications, and communication with other organisms is one of the central characteristics of life. Signals come in a variety of formats including molecules, sound, smell, and touch, and they also can come in electroma

and light. The ability to detect th

fragrant perfume, and necessary, as in the detection of mercaptans, which are the nasty-smelling sulfur-containing substances that are added to the natural gas piped into houses.

The exquisite nanosensors in the nasal bulb of some animals, particularly dogs, is crucial to their survival and to some of the ways in which they help people. The fundamental mechanism behind a dog's sense of smell, or behind the sex attractants (pheromones) that are crucial in much of the insect world, is molecular recognition. Complementary shapes within the sensing structure of the dog's nose or the insect's receptors recognize the shape of the signal molecules, and in particular the distribution of electronic charge on their surfaces. The simplest analogy is of a key fitting precisely into a lock, but in this case the key must have not only the right shape but also the right distribution of electrical charges on its surface. In this respect, the magnetic card locks that are common at hotels are better representations of molecular recognition in that they not only detect the key but also flash a green light to show you when they have detected the right key (and are thus true sensors since they both detect the key and give a signal).

In addition to chemical sensing, the biological world relies on sensors for other properties. Many flowers and leaves are attracted to the sun, which is their source of energy. Particular molecular sensors in the structure of the leaf or flower respond to the presence of the sun. These sensors signal the molecular motor structure of the leaf or flower to move in a particular direction, to face the sun and gain more energy from it. We'll talk about this much more in Chapter 9. Animals have ears to sense sounds, and fish have lateral lines to sense sound and pressure variations. All of these are sensing mechanisms and all of them are crucial to life.

Sensors in the synthetic nanoworld will prove to be just as critical and are often built on the same premises as their natural counterparts rather than their current artificial big brothers, macroscale sensors. Those macroscale artificial sensors usually work via physical properties of bulk materials or via complex mechanical or electronic apparatus. For example, thermometers work by measuring the thermal expansion of liquid mercury and accelerometers use microelectromechanical systems to measure the acceleration or deceleration of a car. Neither MEMS nor thermal expansion is an easy process to translate to the nanoscale. Instead, nanoscale sensors will often either mimic those life processes that have already developed in the nanoworld, or use key quantum mechanical or size-dependent physical properties that exist only there. This means not only that nanoscale sensors will be the best and most accurate sensors possible, but also that they will be able to sense things that simply could not be detected by macroscale devices.

Synthetic sensors can be classified according to what they sense—we will discuss sensors for electromagnetic radiation, for small and medium-sized molecules (like the squares we discussed in Chapter 5), and for biological entities.

ELECTROMAGNETIC SENSORS . . . .

The term "electromagnetic" refers to any form of energy that is propagated as a wave. Starting with the lowest energy and going to the highest, some examples are radio waves, infrared light, visible light from the red to the violet, ultraviolet light, and x-rays. Sound is essentially a propagating pressure wave, and therefore slightly different from electromagnetic radiation,.but it is sensed in a very similar fashion.

The simplest electromagnetic sensors respond to a physical condition, like photoelectric cells that are used to turn lights on when the sun goes down. These work by measuring the intensity of light coming from the sun; for example, when a bright light drops below a certain predetermined brightness level, a signal is given for the electricity to be turned on.

To develop a nanoscale photosensor, it is possible to ride on the back of research in solar power generation. In Chapter 5, we discussed the development of the photoelectrochemical cells, such as those developed by Michael Graetzel for capturing sunlight. These cells use molecular dyes that are excited by capturing sunlight. These excited molecules then transfer an electron into a nanoscale quantum dot of a semiconductor like titanium dioxide. Using one of these photoelectric devices as a sensor is straightforward. It is simply necessary to measure that the electron has been transferred, and this is relatively easy to do because the transferred electron moves through an external circuit to lower its energy by recombining with the positive charge left behind on the dye. In other words, if a photocell is producing electricity, we know that it has been exposed to light.

A very much older, and in some senses even more elegant, nanoscale photosensor is behind the science and art of photography. In traditional silver photography, the photons (light energy) cause a chemical reaction among the silver ions that are held in the emulsion on the film surface. The silver ions come together to form nanoscale silver clusters (the simplest is actually just four atoms) that grow large enough to scatter and capture the light, thereby appearing black on the surface. Again, the change in properties with size that is so essential to nanotechnology is at work here.

Making x-ray, ultraviolet, or infrared film requires very similar processes. (Often those films are made by the same companies that make photographic film.) The requirement is simply that the photoactive agent, which is still often silver, must interact with light of the appropriate wavelength. For x-rays, the wavelengths are very much shorter; for infrared, they are very much longer. To tune a Graetzel cell-based photosensor to respond to different colors or types of light, it is only necessary to find an appropriate dye molecule.

The sensors in film are molecular/atomic, and the sensing process consists of an irreversible change in the clustering of the silver atoms. Microphones sense sound or pressure in a very different way. They consist of diaphragms that are set to vibrating when exposed to a pressure or sound wave. This is very much the same principle as a drumhead—when an external source of pressure hits the drumhead, it starts to vibrate. In fact, hair cells in our ears work in this same way: the membrane is set into vibration by the external pressure wave that corresponds to sound, and then a very sophisticated set of chemical signals is activated by the vibrations of the membrane. The ear is a very complex multiscale electromagnetic sensor that is based largely on molecular signals. The energy is changed and propagated (the technical term is *transduced*) from the vibrations in the membrane into electrochemical signals that travel to the brain.

Because most electromagnetic sensors are already designed to deal with nanoscale or near-nanoscale waves, shrinking them tends to be less complicated than it is for other kinds of sensors. It is an interesting part of nanotechnology, but not quite as groundbreaking as nanoscale artificial biosensors, an entirely new field.

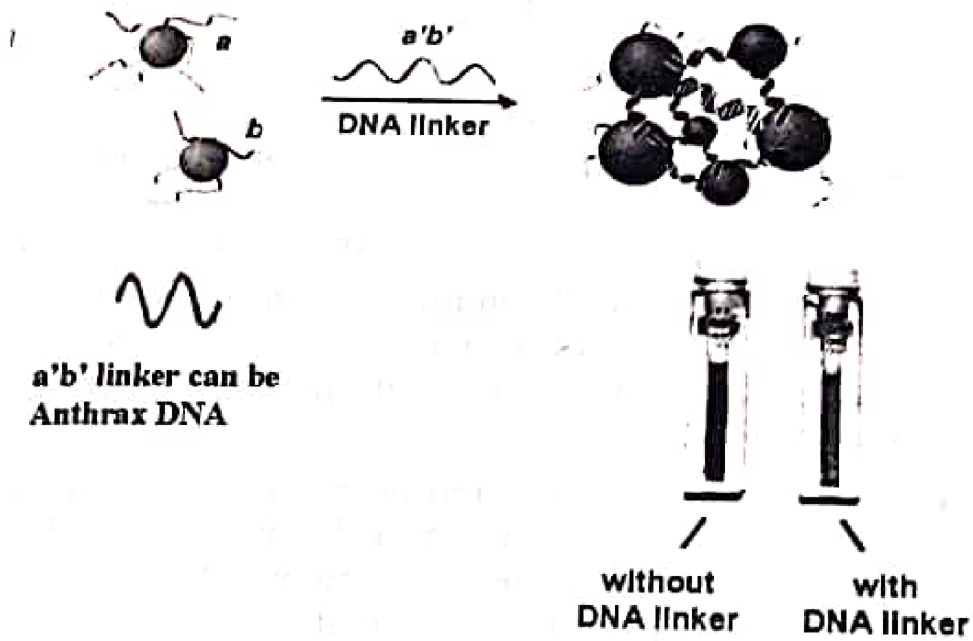

Figure 7.1
The upper schematic shows how the nanodots in a colorimetric sensor are brought together upon binding to the DNA target (in this case anthrax). The clustered dots have a different color than the unclustered ones as is shown in the photograph below them. *Courtesy of the Mirkin Group, Northwestern University.*

ELECTRONIC NOSES

We looked at how biological noses work using molecular recognition to send a neural signal to the brain. In the artificial nose, the most common replacement for the nasal membrane is an electrically conducting polymer. When the polymer is exposed to any given molecule in the vapor phase, its conductivity will change a little bit. In the electronic nose, a random polymer, or mix of polymers, is spread between electrodes. When the molecules to be smelled land on the polymer(s), the conductivity properties in particular regions will change in a particular way that is specific to any given analyte. The nature of the detection is interesting, since it is based on so-called neural nets. The idea is that each sensor will give a particular voltage and current signal, and these are then compared with the list of standard signals that the nose has already smelled. In this sense, it is necessary to "train" the nose, just as we require training. When a child asks what's the funny smell and mom says it's a skunk, the child has learned. By measuring the response of the electronic nose to a series of standard molecular inputs, we can determine the electrical signal caused by particular analytes. Then, when an unknown vapor causes the electrical system to respond in the same way, we can deduce that the analyte is present. Since the electronic properties of the polymer molecules are key to electronic noses, there is some crossover here between sensors and one of our next topics, molecular electronics.

There are already several commercial companies marketing electronic noses (with names like Cyrano) for applications as different as toxic gas detection, disease analysis, air quality monitoring, and food inspection and standardization.

Chad Mirkin, nanoscientist and entrepreneur, envisions a world where doctors will be able to diagnose diseases and conditions in the examination room instantly and accurately not only by analyzing a patient's symptoms but also by actually sensing pathogens in a patient's body or blood. Together with renowned researcher Robert Letsinger, Mirkin founded a startup company Nanosphere, Inc., which has begun commercializing their work on biosensors. Using the same DNA-matching biosensor techniques that we discussed, they have already developed one of the world's quickest and most accurate tests for anthrax and are developing a suite of tests for other diseases including AIDS. If Nanosphere succeeds in developing its planned products (prototypes already exist), medical technicians will be able to administer all common tests right in the office or at the bedside. Additionally, military and law enforcement officials will be able to check for contamination of letters, buildings, and battlefields more easily. By integrating biosensors into a lab-on-a-chip, many tests can be run in parallel and perform a single-step screening for a variety of diseases instead of individual tests for tuberculosis, hepatitis, measles, mumps, and others as is done now. With luck, they will soon create a rabies and tetanus test to eliminate the need to treat these diseases with painful injections just as a precaution. By using these technologies, Nanosphere and other nanotechnology-based sensor companies may be able to make disease screening cheap and easy enough that it could be comprehensive even in low-income countries. This is one part of the dream of nanotechnology that will completely change the way things are done and may be reality as soon as th three years.