29 Chemosensors and Chemical Privacy

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This chapter discusses a part of "21st century science," the work we are doing at Sensors for Medicine and Science, and some future policy implications related to chemical privacy.

21st Century Science

"Chemosensors" are an example of this new science. A sensor is any device that allows you to determine the presence of energy or matter using one of your senses. The home fire sensor is one example. When it detects heat or something combustible, it sets off an audible signal. It translates either energy or matter into a sound that you can perceive and act on.

To the military, a sensor is more likely to be a device like radar or a laser. A sensor can be used to signal spectroscopically either bulk items or chemical substances at a distance. Most of the energy you shine at it is either reflected or absorbed, but some of it comes back to you. You can then measure the change between what you sent off and what you got back.

Chemosensors, on the other hand, are quite different. Imagine wanting to sense the chemical components in a human being. A living organism has tens of thousands of individual small molecules, and the vast majority of them play an essential role in the maintenance of health or in other activities that are essential to that organism. There are reasons why one might like to follow the concentrations of those species in a living organism. But you cannot do it by shining radar or a laser at a

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living organism and then discerning changes in the energy of that beam. The reason is quite simple: The absorbencies and fluorescent properties of the molecules in a living organism are too similar spectrally to resolve them. For example, if you shine a red light onto your hand, you can see most of it coming out of your hand because your hand does not absorb red light. By comparison, the change in intensity of blue light between the time it goes in and the time it comes out tells you almost nothing useful about what was in your hand because hundreds of species in your hand can absorb blue light.

Many chemical systems, including living systems, are far too complicated to analyze using the kinds of sensor tools that people are accustomed to thinking about in the world of sensors. It is becoming increasingly clear that ascertaining chemical concentrations is going to require not the contact of energy with the analyte but the contact of a chemical species (some form of receptor) with the analyte.

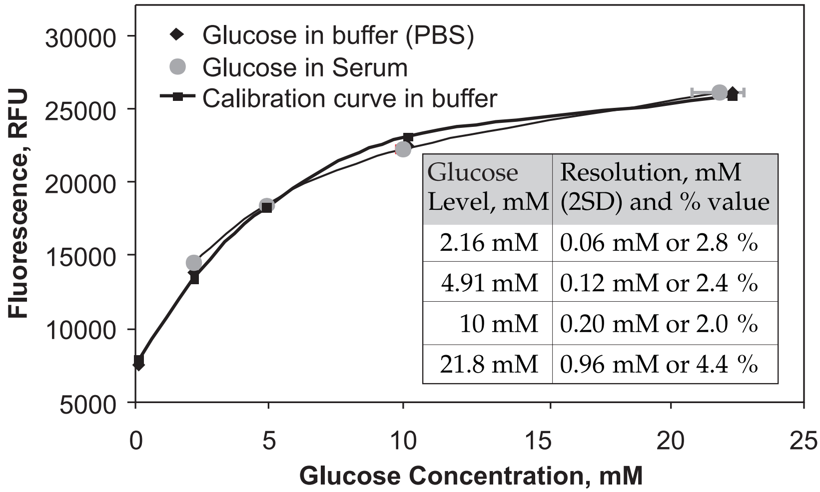
A chemosensor can be something you can hold in your hand. Or it can be something the size of a single molecule that can bind to an analyte of interest and then send a discernible signal back to the experimenter, who will be able to tell if that species was there and, if so, how much was there.

Current Work at Sensors for Medicine and Science, Inc.

The company I work at, Sensors for Medicine and Science, is focused on enabling diabetics to monitor their glucose levels in ways that are simpler and less painful than exist today. To measure glucose in blood today, you need to draw a sample of blood and do an enzymatic reaction that generates a color. A machine reads that color and tells you how much glucose is there. This is not really a sensor. It is an indicator (a dosimeter) because the measurement is not a reversible process. You cannot take the test strip, wash it off, and use it a second time. From a scientific standpoint, the reactions do not lend themselves to this. From a business standpoint, nobody wants people reusing those little strips.

A sensor, on the other hand, is nondestructive, gives continuous realtime information, and is completely reversible with the analyte of interest. Figure 1 shows the measurement of glucose by a fluorescent chemosensor. The curve demonstrates a change in fluorescence with a change in glucose concentration ranging from zero millimolar to approximately 24 millimolar.

Figure 1
Measurement of Glucose in Serum



Glucose Level, mM	Resolution, mM (2SD) and % value
2.16 mM	0.06 mM or 2.8 %
4.91 mM	0.12 mM or 2.4 %
10 mM	0.20 mM or 2.0 %
21.8 mM	0.96 mM or 4.4 %

Source: Sensors for Medicine and Science, Inc.

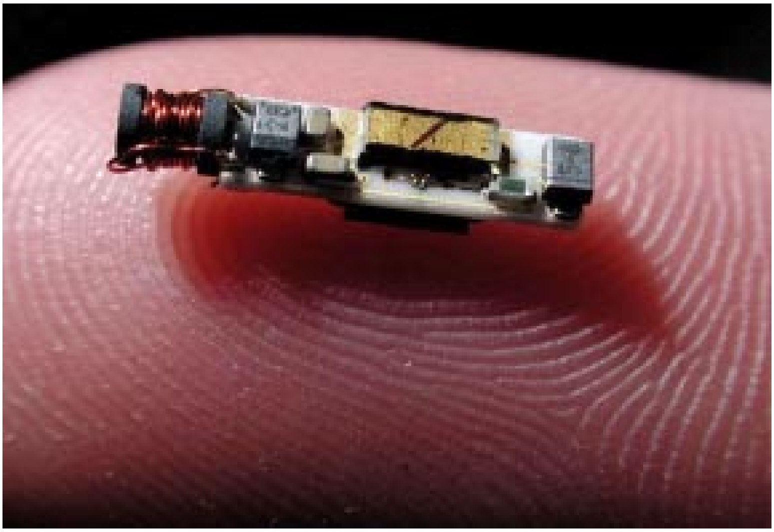
In humans, the relevant range of glucose concentration is about 2 to 20 millimolar, so this simple molecular device is capable of discerning the concentration range of interest in the human animal.

What is most remarkable about this data is that they were obtained without ever touching the animal. No blood is drawn; in fact the skin is not punctured. The device is held over the skin and the concentration of glucose is read.

This is going to work not because we have learned to read the unreadable; it is going to work because we are going to be able to implant minuscule sensors throughout the body. Each of those sensors will be capable of measuring a single analyte. Glucose is just the first analyte for which we are going to be able to measure changes in concentrations of chemical species in real time, in a completely noninvasive procedure.

Figure 2 shows an implanted sensor. Instead of taking a drop of blood and bringing it to the fluorimeter (a device like a spectrophotometer that can measure changes in light), we have reduced the fluorimeter to the size of a grain of rice, and we implant the whole fluorimeter in the person or organism. (I want to emphasize that we are currently working in animal models. Plans for human studies are currently being finalized.)

Figure 2
Implanted Sensor Prototype



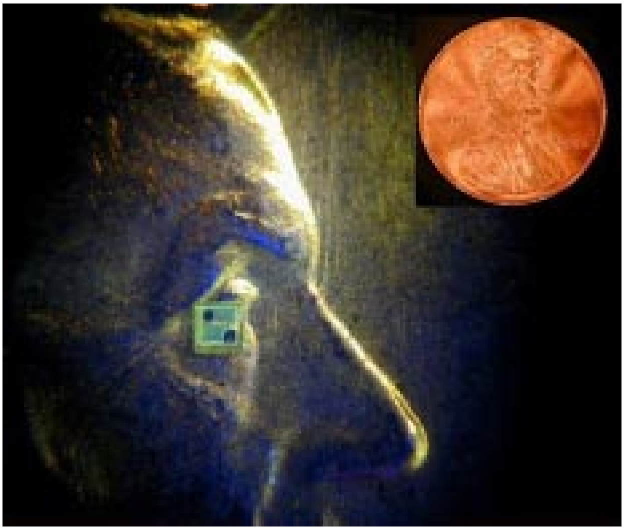
Source: Sensors for Medicine and Science, Inc.

By reducing the size of the fluorimeter to something exquisitely small, we can apply the right indicator molecule to this fluorimeter and have an integrated device. This is a chemical optoelectronic device that we call a chemosensor.

The concept behind miniaturizing the fluorimeter comes from my colleague at Sensors, Skip Colvin. He realized that if you want to make a fluorimeter really small, you have to do a couple of things. First, you have to bring the light source, the indicator, the filter, and the photodetector very close together. Rather than stringing them out along an optical fiber, for example, we stick them all together.

The second thing you have to do is make the system very, very efficient. Because you can not deliver a lot of power through the skin, this whole thing needs to be functional with microwatts of power. This fluorimeter is 50 percent efficient, which is remarkably efficient for a device, and it allows us to use microwatts of power. Once you have decided that you can use microwatts of power, you can go to very inexpensive, very small light sources. Instead of using a laser to do the analysis, we use a light-emitting diode of the same type used in cheap Christmas tree light bulbs.

Figure 3
LED Comparative Size



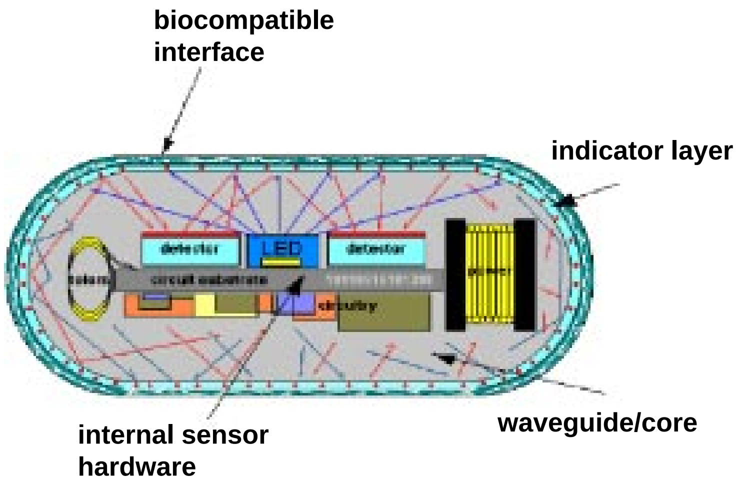
Source: Sensors for Medicine and Science, Inc.

Figure 3 gives you a sense of scale. The light-emitting diodes can easily be made so they do not even cover Lincoln's eye on a penny. That will give you a good indication of how small the actual device can be made.

The range of light-emitting diodes available until recently was limited. But over the last ten years, light-emitting diodes (LEDs) have been invented for a generation of blue and ultraviolet light. It is the creation of those new LEDs that enables a lot of this sensor work. The reason for that is because the molecules that you need for sensing are often excited in the blue or the ultraviolet part of the spectrum.

Skip is the scientist/engineer who invented the device. He realized that the device was only half of the problem. The other half was chemistry. To make this work, we were going to need stable indicator molecules that would sense the presence or absence of a specific analyte with light. That is exactly what I had been doing at Ohio State University for six years (supported, by the way, by the National Science Foundation when the National Institutes of Health would not support the work). The glucose indicator that I have discussed is based entirely on the chemistry that I described back in 1992, at Ohio State University, while doing fundamental research on sensors. We even reported glucose sensing as one example of how this could be used.

Figure 4
Integrated Sensor Implant



Source: Sensors for Medicine and Science, Inc.

The integrated device can be something considerably smaller than the size of a grain of rice. Figure 4 shows the inside, with a circuit board, a light-emitting diode, and detectors.

This device is powered inductively. Consider the devices that you can put on the windshield of your car so that instead of stopping at a tollbooth, you can drive underneath a detector. The detector senses this item on your car, knows who you are, and charges your credit card. This device was invented by Texas Instruments in the early 1970s, specifically for this application. The device on your windshield has no power. The power comes from the alternating magnetic field in the detector above you. It powers up the device, reads your code, and sends that code back to the reading device, which is entirely inductively powered and monitored telemetrically.

That is exactly the technology that we are using for our chemosensors, except that instead of the unit sending back a number that says who you are, this unit sends back the reading of the fluorimeter. The chemistry required to generate that reading is simply coded on the exterior surface of this small, rice-sized device. And it is small enough for the diabetic application. We anticipate that it can be administered with a large-gauge syringe needle.

Chemical Privacy

From a unique policy perspective, we need to begin thinking about the implications for personal privacy that this kind of research may generate in the future. Tiny sensors like these, each selected for a different analyte, are going to be implanted. We will have compelling reasons to do this. What this means, is that you no longer need to give up a sample of yourself to be analyzed. It means that you can be analyzed simply by letting someone get close enough to you with a magnetic field to take your readings. We may find that the standard for privacy no longer becomes whether or not you are compelled to hand over a sample, but rather how close to a detector you can be compelled to stand.

It is interesting to think about human beings essentially being networked entities by way of these devices. You may find someday that when you type a certain URL into a computer, you are not accessing a machine someplace, but a person. You will be able to know a lot about that person based on the amount of information that these kinds of sensors send out.

Conclusion

In the near future, diabetics will be able to know their glucose levels simply by looking at their watch. Later, the same will be true for sodium, potassium, and many other species. Chemical sensing will be simple, and therefore chemical privacy will become a public policy issue.