Air Pollution Science for the 21st Century
J. Austin, P. Brimblecombe and W. Sturges, editors

Chapter 22

Future Directions: Could transgenic mice hear pollution?

J.G.T. Hill
Department of Chemistry, University of Cambridge, Lensfield Road, Cambridge, CB2 1EW, UK
Matthew Lythe
Department of Civil Engineering, University of Surrey, Guildford, Surrey, GU2 7XH, UK

In this world of Genetically Modified food that gives cheap tomato puree, cloned pigs that are going to guarantee us all immortality and biological weapons that scare us all witless, will we soon see GM instrumentation that will cost us all our jobs? With a near infinite supply of inexpensive and accurate biosensors on the horizon there will soon be a sonde for everything. Whereas currently we search for an organism that could be a biosensor, we are proposing to engineer them. This will allow sensors to be built for the task rather than found and then employed, eliminating much fruitless work as well as creating a new field of instrumentation.

Biosensors can be defined as any sensing device that employs a biological system, be it a "simple" enzyme through to a miners' canary. Currently many different systeris are used, moss and lichen, enzymes, bacteria and devices using antibodies. All based on naturally occurring organisms, these can be split into two rough groups, those where the pollutant acts as a messenger triggering further reactions and those where it is stored in the sensor ready for later analysis.

In moss and lichen the skill lies in selecting the size and species of the sampler for a specific target material (Gailey, Lloyd, Environ. Pollut. Ser. B, Vol. 12 (1986) pp. 41–59). Enzymes, however, are typically used in potentiometric devices such as sulphite biosensors in the wine industry (Situmorang et al., Analyst, Vol. 124 (1999) pp. 1775–1779). There has been suggestion of using antibodies to alter the physical properties of an optical system, allowing *in situ* measurements to be made. Measuring the toxic effect of the pollutant on bacteria growth rates is another useful method, though bacteria also act as enzymatic biosensors. This however only touches on the potential of biological systems to be used for detecting pollution.

The intrinsic specificity of biosensors drives work in this field, as it enables the sensors to differentiate between related compounds, or even enantiomers. For repetitive analyses this offers significant advantages over current laboratory methods, both in speed and cost. Biological sensors can also benefit from an increased sensitivity due to chemical amplification. This comes about from the pollution acting as a messenger, causing large changes in the chemistry across a membrane. Sensitivity can also be enhanced for enzymatic systems by paying careful attention to the medium (e.g. controlling pH or ionic strength). Because of the nature of the chemistry involved it is possible to get an absolute measurement of the "pollution messenger". Further gains in sensitivity can be made by the stabilising of reactive compounds by binding to fats and proteins, or storing in a less hostile environment. The technology has the potential to reduce costs by removing the regular need for expensive machine time. Since bacteriological systems can be self-replicating, it would make large networks of instrumentation cheaper to produce. All this will lead to a less expensive, more sensitive, accurate system of pollution detection.

Moss and lichen work primarily by storing the pollutant in the cells – this means in order to get the data they are rendered down and the contents of their cells analysed. This is true of other systems such as bio-accumulation in estuarine fish. The enzymatic systems work by using the messenger to activate or inhibit the enzymes catalytic activity. What is measured in these systems is usually the product of enzyme reaction or (if NAD^+/NADH is required by the reaction (Stryer, Biochemistry, Freeman, 1995) the optical absorbance. The same can be said for antibody systems where binding of the pollutant molecule will cause a conformational change which will either drive an enzyme catalysed chemical response, or a change in the physical properties (e.g. the optics of a wave guide on gold leaf). The bacterial systems can work either as bioaccumulators or similarly to enzymatic systems.

The potential for using genetic manipulation to engineer sensors brings about many intriguing possibilities. Initially these manipulations could be used to understand and fine tune existing sensors to improve their functionality. There is also tie potential for creating entirely new sensors and families of sensors. As a starting point for this we should turn to bacteria.

The reason for starting off with bacteria is that the genetics of the host can be easily and well defined (Alberts et al., The Cell, Garland, 1994). The host itself does not have to be "genetically engineered" as such, what is used is a designed plasmid that will encode for the receptor. This receptor should use an already present signal transduction method, such as regulating an ion channel. If we choose a host so that the response can be something that can be measured (such as pumping protons), then the binding of a pollutant to the receptor can be measured as a change in pH of the growth medium. The skill is then in designing the receptor to bind the molecule of interest. Once this is done then the building of plasmid libraries will be a relatively simple task allowing the mass production of a sensor for any molecule that is in the library.

The recognition of hydrocarbon pollutants may well be a matter of finding relevant receptors or attempting protein engineering to alter parts of the receptor protein. The latter process is more desirable, though much harder as secondary and tertiary interactions are difficult to model (Smith, Regan, Science, Vol. 270 (1995) pp. 980–982).

Once a sensor has been designed then how it is implemented is then an issue. For bacteria there is the problem of how the cellular signal is resolved and what form an instrument will take. An associated problem is deployment, how do we get the bacteria to where we want the measurement? The most obvious extension is to move on to "higher lifeforms", and to some extent this happens already. The correlation between traffic noise and carbon monoxide emissions have been investigated by Tirabassi in an article "Listening out for Urban Air Pollution (Atmospheric Environment 33 (1999) pp. 4219–4220). Effectively a redesign of the miners' canary is needed. Although this would represent a movement from an enzymatic assay style sensor to a bioaccumulation sensor, the organism would still have to be altered to preferentially retain the pollutant. "Higher lifeforms" could well be self-deploying and then have their pollutant levels measured when recaptured. Releasing tagged, sterile transgenic mice could well be the future for monitoring environmental pollution in air conditioning vents or similar confined areas.