COMMENTARY/

by Bernard Dixon

ADVENT OF THE BIOSENSORS

A paradox. At what the organisers billed as the First World Conference and Exhibition on the commercial applications and implications of biotechnology, held recently in London, a major talking point was something many participants believed to be exceedingly remote from the marketplace and stock market: the so-called biochip. Not even listed on the agenda for Biotech '83, this futuristic prospect certainly loomed large in technical gossip around the convention bars and lounges.

The topic was first raised in the plenary address by an unquestionably realistic man, Charles Reece, ICI's director of research, who confessed great admiration for biochip researchers and wished them well. Thereafter, while the formal sessions got down to such immediately or imminently profitable pursuits as polyhydroxybutyrate production and biological pest control, several coffee break chats drifted towards the tantalising goal of bringing together those two paramount arms of modern science: microelectronics and molecular biology. It's not hard to see why. The idea of, for example, programming bacteria to build up computers from molecules, rather than using lithographic techniques to engrave more densely packed information on fragments of silicon, is one of those rare, uniquely exciting proposals which challenge our imagination and technical ingenuity alike.

Yet, as many of those conference conversations concluded, the formidable obstacles to such heady concepts were realised. Above all, there is no real analogy between man-devised electronic gadgets and their natural counterparts. Nerve impulses in animals are transmitted not by electrons but by comparatively heavier, slower ions. Even photosynthesis and respiration, which *are* based on electrons, seem tardy when compared with the events inside your typical pocket calculator.

At the same time, tempting similarities and possibilities do exist. The electron switches that form the very basis of modern computers have their parallel in the gated ion channels that regulate the flow of nerve impulses. And while proteins produced by bacteria do not conduct electrons, such organisms could be directed with exquisite precision to yield amino acid sequences which would then serve as templates for the grafting of electronic elements. The biological computer may not be an impossible dream.

But over what time scale can we expect to see the considerable technical barriers broken down, and the dream realised? I have no infallible forecasting technique at my disposal—electronic, biological or metaphysical. What I *would* urge interested parties to do is to consider the staggering progress already achieved in another field founded upon a marriage between biology and electronics. The field I have in mind, which certainly was a highlight of Biotech '83, is that of biosensors.

While biosensor development owes much to a decade of research by Professor Shuichi Suzuki's group at Tokyo Institute of Technology, the real explosion in applications has occurred over the past two or three years—and what we have seen so far is undoubtedly only the beginning. In concept, every biosensor is identical; it consists of a bacterial cell, enzyme or other biological component immobilised in close proximity to a transducing element such as an ion-selective electrode, thermister, or even an optoelectronic device. Exposed to its relevant substrate, the organic component responds, and its response is in turn converted by the transducer into a measurable electrical signal.

One strikingly elegant application, reported by Dr. Christopher Lowe and his team from the University of Southampton, is a sensor employed to assay substances such as penicillin, glucose, and urea. For penicillin measurement, Dr. Lowe uses an enzyme, penicillinase from *Bacillus cereus,* which he co-immobilises along with a pH-sensitive dye, bromocresol green, to a transparent cellophane membrane. The membrane is sandwiched between a light source and a detector. When exposed to penicillin, the enzyme hydrolyses its beta lactam ring and thus generates protons. This alters the colour of the indicator from blue/green to yellow and thereby raises the output voltage from the detector. Even vanishingly tiny concentrations (0.3–50 mm) of antibiotic can thus be measured. In his preliminary work Lowe found that the sensor's response did not deteriorate over 12 weeks at room temperature, and that at least 80 percent of the initial activity remained after one year.

One of the most appealing features of the biosensors devised so far is their versatility. If penicillinase is replaced by glucose oxidase from *Aspergillus niger,* for example, the Southampton version can be adapted to monitor glucose levels. It also responds to reactions which consume protons, such as the one catalysed by jack bean urease, permitting it to be harnessed for the quite different task of measuring urea. At a time when clinicians are seeking tests capable of revealing metabolites and other substances in ultra-small quantities, the significance of these developments is enormous. Continuous *in vivo* monitoring of blood metabolites is particularly valuable in intensive care facilities, and here biosensors offer obvious advantages over immunoassays conducted on the laboratory bench.

Environmental analysis and fermenter regulation are two other areas offering unlimited scope for biosensors. Professor Suzuki himself described gluma-

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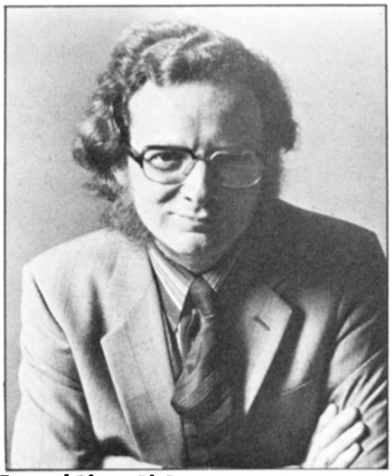

Bernard Dixon, Ph.D.

Bernard Dixon, Ph.D., is a microbiologist and regular columnist for BIO/TECHNOLOGY. He is a former editor of New Scientist.

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encouraged.

As biotechnology's commercialization becomes increasingly linked to public scrutiny, it is in the self-interest of researchers to actively promote direct public education in biotechnology: a public with technological savvy is more likely to support innovative research. As citizens, researchers may feel compelled to participate because improved education in science and engineering is necessary for an effective modern democracy. To borrow a term from science educator Mary Budd Rowe, fate control—the sense that people can know about and influence the direction of society as it affects their lives—is essential for participatory democracy. The current tendency for students (and future citizens) to believe or disbelieve the textbook or verbal scientific instruction—based upon the authority of Science—works against fate control. As new technologies play an increasingly important part in rapidly transforming occupational and personal roles, scientists and engineers must accept the burden of informing future citizens directly to ensure the effectiveness of participatory government. **—Christopher Edwards**

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tic acid, acetic acid, ammonia, ethyl alcohol, and biochemical oxygen demand probes used for these purposes in Japan. The commercially promising models listed by Dr. Anthony Turner of Cranfield Institute of Technology detect substances ranging from lactic acid (for use in sports medicine) to TNT (for use in anti-terrorist work). My guess is that an equal dividend from this burgeoning technology could be the insight it provides into organic–inorganic interrelations. This is essential groundwork if the dizzy goal of true bioelectronics is to be achieved.

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monplace to observe the inbreeding depression of time serving "cover your rear" bureaucracies and of gridlocked administrators who unwittingly shield the "deleterious recessives" from too much exposure to selection pressure. While this was the Lysenko story, private organizations can suffer similar fates.

Building a polity in the biotechnology community, at any level, means keeping the heterogeneous nature of the culture in a healthy balance. A culture of collective sameness (which usually develops mimicry into its principal survival skill) creates little that is new. The trick is to keep our heterogeneous community from flying apart or disemboweling itself. Just think of all the short sighted investors, greedy brokers, closet Marxists, threatened hacks, over-reaching egotists, cheap-shot competitors, ambitious politicians, and idiotic fantasy mongers swimming in the pond. (This is the short list). But after all, it is in part the chaotic nature of capitalism that is responsible for its creative vigor. Personally, I think it's coming together beautifully.

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