PHILOSOPHICAL TRANSACTIONS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

Introduction

B. S. Hartley

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Introduction

By B. S. Hartley, F.R.S.
Department of Biochemistry, Imperial College, London SW7 2AZ, U.K.

This meeting is modelled on a previous Discussion Meeting of the Royal Society, 'New horizons in industrial microbiology', held in June 1979 (Brenner *et al.* (eds) 1980). At that time it was apparent to some that the new techniques of genetic engineering would rapidly expand the horizons of biotechnology, but that new applications demanded better communication and closer collaboration between academic and industrial scientists. Hence that meeting included speakers from both sectors, and a panel of leading industrial representatives sought to identify the opportunities and constraints in exploiting the new technology.

Three years later, we have seen that the progress in the technology of genetic engineering has been even more rapid than was predicted and that opportunities for exploitation have been seized, regrettably mostly outside the U.K. The most obvious current dynamic is in the field of new pharmaceuticals such as human hormones, interferons and vaccines, but it is now pertinent to ask whether one can envisage a similar explosion in the field of industrial and diagnostic enzymes.

One must remember that the history of research on enzymes can be measured in a few decades: the 1950s saw the development of techniques for assay and purification, the 1960s was the decade of protein chemistry and the 1970s revealed the tertiary structures of many enzymes. Are the 1980s to herald the age of widespread application of enzymes?

There was considerable optimism during the 1970s that the new knowledge of enzyme structure and mechanism would find widespread industrial application. That optimism has proved rather misplaced, because it became clear that enzymes were relatively expensive and unstable as catalysts for industrial processes. Their applications have been restricted to cases where the enzyme is both cheap and robust or to diagnostic uses where only small amounts are required.

But surely today we must think more broadly? It is clear that genetic engineers can in principle make any enzyme as cheaply as the best current industrial enzyme. Even interferon can be made as more than 5% of the intracellular protein of *Escherichia coli* or in *Bacillus subtilis* which is probably preferable for food technology and can excrete large amounts of foreign proteins. Moreover the range of organisms from which one might seek a useful enzyme has expanded vastly. Thermophilic microorganisms are known that will grow in boiling water: some of their enzymes are as tough as old boots. We probably know only 1% of the world's microorganisms but already these include species that can grow on wood, oil and even rock. Since we no longer have to think of the expense and difficulty of culturing the organisms themselves, could we not steal some useful genes from them? And at the other extreme, could we not use some of our own genes to make useful enzymes? A human enzyme would be unlikely to be antigenic to man.

Moreover we can now think of tailoring enzymes to catalyse a reaction of choice. We know enough about the structure and mechanism of a few enzymes to predict amino acid replacements that would shift their specificity in a desired direction. Such replacements could readily

be made in a cloned gene by the rapidly evolving techniques of site-directed mutagenesis. It is also probable that we could increase the stability of an enzyme by such methods or graft on to it additional properties such as surface adhesion.

Hence I believe that the opportunities are now limited only by our lack of imagination in finding novel uses for the enzymes that we could make, discover or construct. I hope that this meeting will be catalytic in finding these new uses.

Reference

Brenner, S., Hartley, B. S. & Rodgers, P. J. (eds) 1980 *Phil. Trans. R. Soc. Lond.* B **290**, 277–430.

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