Nobel prize

Merrifield wins in chemistry

THOSE who have followed the growth of peptide research over the past twenty years will have received with delight and no surprise the news of Bruce Merrifield's Nobel Prize for Chemistry. The simple solid phase technique for the chemical synthesis of peptides which bears his name has been adopted in scores, possibly hundreds, of research laboratories worldwide. The concept has been widely applied in other areas of research, notably in oligonucleotide synthesis, with important consequences for genetic engineering, and in structural studies including protein sequencing.

To understand the impact that Merrifield's technique has made upon the development of peptide synthesis itself, it is necessary first to sketch in the situation in the 1950s and earlier. Peptide chemistry was then in an expansive mood. Natural peptides with powerful and important biological action, such as the pituitary hormone oxytocin, were being isolated. These natural peptides were soon shown to consist of short chains of the same building blocks (the α amino acids) as constitute the proteins. The sequence of amino acids in these linear chains was soon determined and the stage was set for the understanding of biological activity in terms of these relatively simple sequences. The techniques of peptide synthesis — the chemical union of α amino acids into chains of defined sequence — had been growing steadily during this period but were slow and labour-intensive. They could barely meet the explosive demand from pharmacologists and others for synthetic natural peptides and their structural variants which could be used to correlate chemical structure and biological activity.

It was just at this time that Merrifield introduced the simplifying step in peptide synthesis which rapidly transformed the situation. Much of the labour in contemporary peptide synthesis was involved in the isolation, purification and characterization of reaction products after each chain extension. Merrifield reasoned that by attaching the first amino acid to an insoluble polymeric support, these isolation steps could be much simplified and speeded up. There were other chemical advantages which might also increase the efficiency of synthesis — a necessary concomitant since the polymeric system did not allow separation of the products of incomplete reactions. Most importantly, the process became amenable to mechanization.

Merrifield demonstrated these advantages convincingly in 1964 with a synthesis of the nonapeptide hormone bradykinin. The hormone was prepared singlehandedly in eight days, evidently in a highly pure form. By contemporary conventional methods, it could have occupied several skilled chemists for weeks or months.

The new technique of solid phase peptide synthesis was adopted with enthusiasm by biologists, sometimes beyond its immediate capabilities at this early stage in development. Organic chemists were slower to accept its advantages, some finding it in conflict with their rigorous classical training. Within the decade, the limitations and advantages were well recognized and solid phase peptide synthesis found and established a secure place alongside more conventional methods. The number of synthetic peptides prepared with its aid must now be counted in thousands.

By the mid-1970s, improved understanding of the solid phase system and numerous technical improvements allowed successful application to oligonucleotide synthesis. This was a timely development in view of the rapid strides in genetic engineering around this time. Again, synthetic DNA fragments became much more accessible using solid phase techniques. On the structure side, solid phase methods were developed for protein sequence analysis. Throughout organic chemistry, the concept of polymer-supported reagents and reactions has become commonplace. Although Merrifield confined his own activities to the peptide field in which he has continued to make massive contributions, many of these later developments must be attributed to his inspiration. The dream of automated synthesis of artificial proteins remains to be realized, but the impact of Merrifield's work is without question.

Robert C. Sheppard

DR Carlo Rubbia, who shares this year's Nobel Prize for Physics (see p.701).

Animal welfare

Berkeley again in trouble

Washington

THE University of California at Berkeley is awaiting with more than the usual apprehension the result of an investigation by the US Department of Agriculture (USDA) into new allegations of animal welfare abuses. The reason: $41 million of state funds earmarked for a new life sciences building cannot be spent until the university is able to satisfy the state legislature that there will be no future violations of the Animal Welfare Act. The building is already well behind schedule, and a decision by USDA to prosecute would further delay construction until the case had been decided.

Last July, the university was fined $12,000 and ordered to correct long-standing deficiences in its treatment of laboratory animals at the Berkeley campus (see *Nature* 2 August, p.356). The university was still under an order to "cease and desist" from future violations when the latest allegations were made on 10 September. Complaints were made to USDA by animal welfare groups, which entered animal houses "surreptitiously" and photographed a monkey with a tumour on its face and rabbits with local infections around cranial implants. The USDA investigation started after a surprise inspection on 12 September.

The complaint about the monkey has been dropped because USDA found no evidence of lapses in veterinary care. The care given to the rabbits is now being scrutinized, and a decision on whether to prosecute is expected before the end of the month.

Both the university and the researcher involved, Dr Walter Freeman, maintain that the animals were at all times under adequate veterinary care and that there were no violations. A university spokesman, Mr Debley, said the university "had been told" that the second complaint would also be dropped.

The requirement that the university must demonstrate compliance with the Animal Welfare Act before using state funds for the new building was written into California's 1984 Budget Act. A report by the university on the steps taken to improve animal care since the court case this summer is now being reviewed by the state legislature. Ironically, the building that may now be delayed is needed partly to improve the Berkeley campus's animal facilities. On 28 September, the university postponed an appearance before the state public works board where it was to have pressed its case for the new building. The university says the decision to postpone the appearance was due to "administrative delays" that had nothing to do with the latest allegations.

Tim Beardsley