

## picture story

## Nice guys needn't finish last

"Nice guys finish last?" It ain't necessarily so. Within the past few weeks David Blow and David Davies, two of the leaders in protein crystallography, were honoured, not just for their scientific accomplishments but because they are widely admired as two of the all-round nice guys of structural biology.

David Davies is, perhaps, best known for his contributions to our understanding of the structure and function of antibodies. His early studies of a human G-myeloma protein, in which he combined X-ray crystallography and electron microscopy, provided the first visualization of the overall architecture of an immunoglobulin molecule<sup>1,2</sup>. This analysis, which, for technical reasons, was at low resolution, was soon complemented by elegant high-resolution studies of a phosphorylcholine-binding Fab<sup>3</sup>. This provided the first known structure of an antibody recognition site in complex with a known hapten. These results, together with parallel studies from other laboratories, led to the now standard view of antibody-antigen recognition being achieved through a set of hypervariable loops on the antibody molecule.

Among many other contributions one less well known is Davies' demonstration of a relationship between the amino acid composition and the amount of  $\alpha$ -helix in a protein<sup>4</sup>. His 1965 paper was the forerunner of a myriad of proposed methods for predicting the secondary structures of proteins from their amino acid sequences.

The highlight of a recent symposium

'Structural thinking in molecular biology' held at the United States National Institutes of Health on April 25, 1997, in Davies' honour was, without a doubt, Max Perutz's explanation of 'How the structure of proteins was not solved'. One could only won-

der the determination of the structure of  $\alpha$ -chymotrypsin by David Blow and his colleagues — submitted to *Nature* on May 3, 1967, and published a mere 10 days later<sup>6</sup>. The occasion was celebrated in Cambridge on April 11, 1997. The reunion included



**Fig. 1** In the days before political correctness. David Blow and the  $\alpha$ -chymotrypsin group, Cambridge, May 1966. From left to right: Jill Dawes, Di Watson (previously Singleton), Paul Sigler, David Blow (front), the author, Sue Simpson and Sue Wickham. At the left can be seen part of the Joyce-Loebl densitometer used to scan the X-ray films. At the right is the top of a stack of boxes of IBM punched cards used to record the individual X-ray intensities.

not only the scientific protagonists, colleagues and 'competitors', but also the superbly talented support group that made it possible: Jill Dawes, Di Watson (Singleton), Sue Simpson, Sue Wickham and Pat Hutchins (Masters), among others. Included in this group, and in the days before political correctness, were the so-called 'computer girls' (job description: computer). They were the ones who, with remarkably good spirit, scanned the endless films and filled rooms with IBM punched cards in the process.

Blow's determination of the structure of  $\alpha$ -chymotrypsin<sup>6</sup>, and introduction of the 'charge relay system'<sup>7</sup> were important not just because chymotrypsin was the first known serine protease structure, but because of the wealth of bio-

chemical data against which the structural data could be evaluated, and *vice versa*. It was the beginning of a new era in enzymology.

A handful of individuals led by Max Perutz and Dorothy Hodgkin established protein crystallography and have shown how it should be practiced. David Blow and David Davies are among that select group.

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der at the drudgery of measuring by hand a three-dimensional X-ray data set from haemoglobin crystals and the calculation of a three-dimensional Patterson function, driven by the fervent hope that the amount of labour required would have to provide information that would be rewarding in proportion to the effort invested. Perutz poignantly noted that when the task was finished he actually wrote to his father-in-law stating that the structure of haemoglobin was solved. As is now well known, success would have to wait, but Perutz's enthusiasm for the task remained undiminished.

It was David Blow who provided one of the key pieces in the puzzle that did lead to the first successful protein structure determinations. Blow joined Perutz as a PhD student at a time when isomorphous replacement had been shown to be effective in determining the phase angles of the 'centrosymmetric' X-ray reflections, but the more formidable analysis of the non-centrosymmetric data was yet to be solved. Blow and Francis Crick's elegant solution<sup>5</sup> to the problem remains as one of the most influential papers in the history of protein crystallography.

It is also 30 years this Spring since

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