Book Reviews

Genetic Manipulation of Streptomyces: a laboratory manual By D. A. HOPWOOD, M. J. BIBB, K. F. CHATER, T. KIESER, C. J. BRUTON, H. M. KIESER, D. J. LYDIATE, C. P. SMITH, J. M. WARD and H. SCHREMPF. Norwich: The John Innes Foundation, Paperback. ISBN 0 7084 0036 0.

Streptomyces species form one of the most important groups of industrial microorganisms, in view of the great variety of antibiotics and other promising secondary metabolites which they produce; but they have been remarkably slow in achieving status as fashionable organisms for the microbial geneticist. Genetic recombination in *Streptomyces* was described thirty years ago, and successful methods of forming protoplasts, fusing them and growing recombinant strains from the products have been developed during the last ten years. The more recent development of efficient gene cloning techniques in *Streptomyces* finally makes this organism excellent material for the molecular microbiologist, and we might expect it shortly to supplant *E. coli* at the head of the list of fashionable prokeryotic organisms for the molecular microbiologist.

If this forecast is correct, it will be mainly attributable to the long and uphill efforts of the John Innes Streptomyces group, who gathered at the John Innes Institute after it had finished its leisurely progress from London to Hertfordshire to Norwich and had acquired David Hopwood. There are, of course, problems with *Streptomyces*, e.g. its greater genetic complexity than that of *E. coli* (a genome size three times as large), a variable and varying amount of reiterated DNA sequences (reported as 5–40% of the total DNA and not confined to plasmids), a tendency to show phenotypic instability – perhaps associated with DNA repeats, and, of course, the variety of strains producing different secondary metabolites. But these factors should all be grist to the genetic mill, and raise questions of evolutionary interest as well as biotechnological questions.

The John Innes group has now lightened the task of the *Streptomyces* student by producing the manual under review. This is designed for microbiologists of all types, coming from taxonomy, ecology, biochemistry, classical bacterial genetics, etc. and is based on courses given for visitors to the Institute in 1983 and 1985, under EMBO sponsorship. Its eight chapters cover (1) preparation of organisms and phages, (2) in vivo *Streptomyces* genetics, (3) preparation of chromosomal, plasmid and phage DNA, (4) transformation and transfection, (5) In vitro manipulation of DNA, (6) Cloning of DNA: choice of vectors and strategies, (7) techniques using radiolabelled DNA, (8) techniques for handling RNA. There is also an appendix on media and maps, and references and an index.

Each chapter gives the protocols for a series of specific procedures, presented in numbered steps with helpful comments which should make them easy to follow successfully. These protocols are in routine use at the John Innes Institute, and therefore can be assumed to work well – if not, no doubt one of the authors of the book would put the novice right. Many of the molecular techniques are, of course, in standard use in other laboratories and will be found in many of the numerous textbooks of 'genetic engineering' on the market. However, this manual is nicely tuned for use with *Streptomyces* and includes a great deal of essential background information for that organism. The book seems to me excellently written and organized, and, if it were left about in microbiological laboratories, I suspect that it would cause many research workers to write off (or search the soil for) strains of *Streptomyces*. There is obviously plenty of scope for studying, modifying and improving the yield of a variety of secondary metabolites in this group of organisms.

One mystery is that Cold Spring Harbor Laboratory sent me a review copy of the book with a leaflet leaving me to infer that they had published the book. However, they offer it for $25 (post free?), whereas an English bookseller (Haigh & Hochland, Manchester) quotes £20·50. The book is actually published by the John Innes Foundation, Norwich, and shows no obvious connection inside with Cold Spring Harbor; and both suppliers referred to above quote a different ISBN number from the one given in the manual. So my advice is: the book is very good value and deserves

to be widely available, but shop around between GB and the USA!

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Current Communications in Molecular Biology: *Computer Graphics and Molecular Modeling*. Edited by MARK ZOLLER and ROBERT FLETTERICK. Cold Spring Harbor Laboratory. 1986. 150 pages. $29. ISBN 0 87969 193 X.

Many current problems in Molecular Biology require an understanding of the three-dimensional nature of macromolecules. The dynamics of macromolecules adds yet another dimension, time, as another layer of complexity. The use of computers in the analysis of biomolecular data is already widespread: as a non-graphics worker in this area, I was very interested in this collection of extended abstracts from a meeting on Computer Graphics and Molecular Modeling held in December 1985 at the Banbury Center of Cold Spring Harbor Laboratory.

The book concentrates almost entirely on proteins: indeed a better title might have been 'Computer Graphics and Molecular Modeling of Proteins'. This area of research involves many fields: Molecular Biology, X-Ray Crystallography, Peptide Synthesis, Computer Science, and Protein Dynamics. This volume is an attempt to bring these diverse fields together. The problems discussed are: protein sequence homology, three-dimensional structure homology in proteins, molecular design of functional macromolecules, X-ray crystallography, and software for the analysis of the energetics and dynamics of proteins.

The development of powerful hardware and software for computer graphics in the last ten years has brought about a new era: structural models can now be fitted to X-ray data and 3-D models can now be accurately described, displayed and compared. The computer transforms the 3-D structure to a 2-D representation that is displayed on the VDU screen. The success of this representation depends on the resolution of this display, and on the quality of the techniques (e.g. shading, removal of hidden lines, range of colours) used to bring out the 3-D nature of the molecule. It is possible to view the 3-D structure from different angles and to zoom in and out at will. This requires considerable computer memory. At present these requirements restrict the use of computer graphics to mini-computers (although already a simple molecular graphics program is available for the IBM-PC and Apple II). Using present knowledge of protein structure and protein dynamics, some researchers, are attempting to predict structure and function, and are even considering designer molecules.

This slim volume contains two abstracts on Graphics Software, three on Computer Hardware, five on Structural Principles in Proteins, six on Protein Modelling, and three on Molecular Dynamics of Proteins. They range in length from just over a page to seven pages long. A smaller collection of articles would seem preferable to many extended abstracts. There is also a 27-page appendix listing Molecular Graphics Installations, including information on hardware and software.

The Graphics Software section gives an outline of two of the many graphics packages, although in effect others are mentioned in later abstracts. Most Graphics systems are running on Vax machines. I found two of the abstracts in the Computer Hardware section fascinating, especially M. E. Pique's 'Technical Trends in Molecular Graphics'. This is an excellent review of Molecular Graphics and of the current state of graphics technology. Pique also makes 'some tame predictions for the period 1986–1990'. It is clear that WIMP technology (Windows, Icons, Mice, and Pull-down menus) will become available for Molecular Graphics. Among many other interesting thoughts, Pique also feels that 'the one-dimensional pattern-matchers and the three-dimensional energy-modellers...' will keep on '... running separate horse races'. Ferrin and Langridge's contribution on 'The UCSF Computer Graphics Laboratory' was an interesting account of the development of their Graphics system over the last decade, including the MIDAS package (which models proteins and DNA). The third Computer Hardware article was on the future use of parallel computers in Molecular Graphics: possibly a little early to discuss this developing technology.

The next two sections (Structural Principles in Proteins, Protein Modelling) are essentially applications of Computer Graphics to the elucidation of protein structure. Eleven abstracts cover a wide range of approaches. The last section, on Molecular Dynamics of Proteins, contains three abstracts: These are essentially simulations. Karplus *et al.* apply a simple molecular dynamical model to active sites. Struthers *et al.* apply 'modern theoretical techniques to the development of improved antagonists of gonadotropin-releasing hormone'. I found it hard to envisage the use of computer graphics in such complex areas, especially in Levitt and Stern's abstract entitled 'Normal-mode Dynamics: Energy Calculations, Interactive Graphics, and Movies': – a 200-word and 2-tables abstract discussing a 16 mm film shown at the meeting!

Besides the sections quoted in the contents table and a one page introduction, there are no other attempts to bring together the nineteen abstracts: I would have liked to have seen an overview of each of the sections. In a book on computer graphics, there are only four colour photographs and only some relatively simple diagrams in the abstracts: it is, not surprisingly, a little difficult to grasp the power of this technology from (almost) words alone. It is a pity that