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Book Reviews

DNA and Chromosomes: Cold Spring Harbor Symposia on Quantitative Biology, Volume LVIII. Cold Spring Harbor Laboratory Press. 1994. 861 pages, illustrated, with colour plates. Prices: Cloth $210, ISBN 0 87969 065 8. Paper $95. ISBN 0 87969 066 6.

This is the report of the 1993 meeting, which celebrates both the 40th anniversary of the discovery of the structure of the double helix by James Watson and Francis Crick and also Jim Watson's 25th year as Director of the Cold Spring Harbor Laboratory. So the subject of the symposium is very appropriate. The book contains 86 papers distributed under the following headings: Genome expression; transcription of DNA and chromatin; genome structure; replication of the genome; recombination, repair and genome stability; centromeres and telomeres; nuclear structure; and, as the Foreword puts it 'The week of exciting science was capped by a masterful summary presented by Hal Weintraub, who is one of the leading innovators in the field of DNA and chromosomes'. The title of this summary, 'Genetic tinkering – local problems, local solutions' will encourage many readers to turn to it first.

The inaugural lectures by Francois Jacob and Sydney Brenner, which 'blended science and highly personal experiences with Jim Watson', are not included in the book, which is a disappointment. Brenner talked about his new work with the puffer fish, which has the advantage that it is very economical with DNA, and is no doubt fed on a rich diet of surplus members of the Cambridge population of *Caenorhabditis elegans*. Weintraub quotes Sydney as complaining about God 'who publishes in unrefereed journals and whose experiment has not yet been repeated', but this assumes that all the 50000 Americans who believe in little green men must be wrong.

Dr Weintraub will not, I hope, accuse me of plagiarism if I quote another passage from his summary. He writes: 'Thus, I thought it might be worth while to summarise this year's Symposium in the context of some of the highlights of our collective progress since the last meeting on DNA and Chromosomes in 1973:

1. The emergence of *trans*-acting factors as key regulators in eukaryotes
2. The discovery of long-range control of transcription
3. The genetic documentation of chromatin as an important factor in gene repression and derepression
4. The enormous number of new protein sequences, structures, and motifs and the realization that at one extreme many proteins function in the context of a complex machine, and at the other extreme protein parts can often be readily mixed or swapped
5. The large number of instances where the genome is modified, imprinted, silenced, or marked in some other way
6. The great progress being made in identifying the genes and mechanisms involved in generating positional and temporal information during development'

Weintraub's summary goes on to discuss in some depth *Trans*-acting factors; long-range control: enhancers and silencers, LCRs and insulators; repression by chromatin; nucleosomes and activators, histone III; positive effect of histones; protein motifs; proteins machines; the dynamic genome: epigenic tinkering, which includes marking DNA, imprinting and surveying genetic instability; development: transcription factors and combinatorial logic; and finally the future.

I hesitate to pick out any among the 86 articles, but, under the section headed 'Genome Structure' I noted 'Mapping and sequencing the nuclear genome of the yeast *Saccharomyces cerevisiae* strategies and results of the European enterprise' by B. Dujon, 'The genome of the nematode *Caenorhabditis elegans*' by (I think) 42 authors, and 'Integrated mapping across the whole human genome' by the French team of Chumakov *et al.* There is likely to be another 5 yr of concentrated work to be done on even the *C. Elegans* genome before the sequence is complete, and that, of course, will be far from the end of the story. *Arabidopsis thaliana*, the 'Botanical Drosophila' as it is nicknamed, only makes a very brief appearance in pages 123–126 in the article by Burley *et al.* on X-ray crystallographic studies of eukaryotic transcription factors.

The classical problem of the functions of DNA methylation in vertebrates is discussed by Adrian Bird. In the vertebrates almost all regions of the genome are subject to methylation, while in non-vertebrates, which include nearly all animal species, most of the genome appears free of methylation at all times, and the methylation that does occur in these genomes is confined to a small fraction of the nuclear DNA. To explain this striking difference Bird suggests that DNA methylation acquired a new function at the start of the vertebrate lineage, which made possible the increase in the number of usable genes necessary for the dramatic progress in vertebrate evolution.

Telomeres and telomerase are a subject of great interest at present, since telomeres, the structures at the ends of eukaryotic chromosomes, serve the two vital functions of maintaining the length of the chromosomes in the face of the inability of DNA polymerase to replicate linear DNA ends completely, and of distinguishing natural chromosome ends from double-stranded breaks in the DNA, which must be rapidly repaired. Most eukaryotes have a short, tandemly repeated, evolutionarily conserved sequence on their chromosome ends, and these arrays, shortened at replication as indicated above, are extended by a specific reverse transcriptase, which carries its own internal RNA template. *Drosophila*, however, maintains chromosome length by tip-specific transposition of a small set of retrotransposons (James M. Mason & Harald Biessmann (1995) The unusual telomeres of *Drosophila*. TIG Vol. 11, No. 2, 58–62). Several papers in the book under review present experimental evidence on eukaryote telomeres and telomerase (pp. 707–746), but *Drosophila* was not included. Another article which probably everyone will want to read is 'The replicon: thirty years later' by Francois Jacob, whose beautifully composed English and impeccable logic was a great pleasure to read when I first studied bacterial genetics.

This might just be the book to be marooned with on the desert island reserved for Desert Island Disks, and if you are allowed a second book and your knowledge of molecular biology needs upgrading, there is the Encyclopedia of Molecular Biology edited by John Kendrew assisted by 11 stars (Blackwell 1994).

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Lords of the Fly by R. E. KOHLER. University of Chicago Press. 1984. 321 pages. Price £14.25. ISBN 0 226 45063 5

This book is by a science historian who adopts an unconventional approach: he attempts to write 'a material, cultural and social history of scientists at work'; specifically, the story of the research community using *Drosophila*. However, the author has a thesis that 'scientists work neither out of pure curiosity nor to win rewards... but rather to gain the continuing privilege of working under ideal conditions'. Why do science historians have to have theses to live by even when their own studies refute such simple-minded categorizations? I remember Kitty Brehme telling me that she went into Bridges' darkened hut at Cold Spring Harbor when he was drawing the details of salivary gland band patterns and heard him repeat the mantra, 'Christ, what a life for a man!' Ideal conditions/no curiosity, I ask you? But despite this bias the book is a success, and all new (and recent) entrants to the *Drosophila* fellowship should read it.

This is not a history of *Drosophila* as an experimental organism for it says little about the physiological studies of Loeb, Northrop, Guyenot and others whose successors still pursue some of the issues raised around the turn of the century. It is about how *Drosophila* was developed as a tool for genetical research: in the first place, it is the story of the Columbia Fly Room established by the embryologist T. H. Morgan with his eye on the exploitation of mutations for the understanding of evolution and development. But this is not how things worked out during 1909–10, after Sturtevant and Bridges decided to classify the mutations they found not according to affected organs but by chromosomal groups. This started the great flurry of activity around chromosome mapping and by 1914, thanks to Muller and Bridges, to the construction of multiple marker stocks and balancer chromosomes, which became the ever improving tools of the trade. At this point, domesticated *Drosophila* had a capital value; namely, the intellectual and practical investment in these specialized stocks and technology. *Drosophila* effectively took over the laboratory (Kohler calls its the 'breeder reactor') and determined its ethos; or in E. P. Thomson's phrase which he uses, its 'moral economy'.

That 'moral economy' owed something, no doubt, to the fact that *Drosophila* was of no commercial value, but very much more to the gross overcrowding of the Fly Room. This was the working space for Morgan and the Carnegie Trust supported Sturtevant, Bridges and Muller (and that Trust merits a vote of thanks from all Drosophilists) and a succession of graduate students and visitors. It was a small (16 × 25 ft), exciting world of great activity and shared experiences. As Jack Schultz said to me, 'there were no patents on ideas, they were bandied about freely'; publication was the mark of recognition. There is a tendency to think that these first years of *Drosophila* genetics reflected the true, impersonal pattern of science, with a capital S; but it would be fairer to say that this highly competitive group of workers recognized rules that were to their mutual advantage; and, essentially, this was to share everything – information, technology, fly stocks and ideas, without reservation. So *Drosophila* rapidly became the dominant organism in genetic research, carrying this ethos with it. And that was a great tradition for us, accepted without