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higher efficiency than Southern blotting, this has diagnostic implications, for example, the identification of intragenic deletions, such as within the Duchenne muscular dystrophy gene, and translocations, such as the t(11;14) that characterizes some lymphoid malignancies. Also, it is possible to enhance the FISH signals via tyramide amplification so that sequence-tagged site (STS) mapping can be performed and exons 1 kb apart can be identified within large genes.

Both Gert-Jan van Ommen in his Jubileum talk and speakers in the plenary session on the following day highlighted additional FISH inventions with bar-coding, using colour combinations obtained by hybridizing chromosome-specific monkey DNA against human, presented by Stefan Müller from Malcolm Ferguson-Smith's group (Dept of Pathology, Cambridge University, UK), and subtelomeric FISH probes by Sharon Horsley of the Lyndal Kearney laboratory (John Radcliffe Hospital, Oxford). The latter uses a clever device, developed in collaboration with a

company called Cytocell Ltd, whereby all the individual subtelomeric probes can be used on one chromosome slide. Interestingly, there are indications that even in normal people 'swapping' of telomeric sequences commonly takes place. Perhaps this is the result of the way chromosomes are spatially organized in the germ line, where, at first, meiosis telomeres are all bundled together at one end of the nuclear membrane, forming a so-called 'bouquet'.

In my own session on meiotic recombination and segregation there was a hotchpotch of DNA- and chromosome-based presentations, which I had arranged in the hope that there would be something for everyone. Fiona Benson (ICRF, London), and Dirk Lankenau (Dept of Developmental Genetics, Heidelberg), started the session with, respectively, a broad outline of proteins involved in meiotic recombination from *Escherichia coli* to humans, and a new DNA model on meiotic recombination mechanisms, based on work on *Drosophila*. The latter was found to be quite controversial,

creating many animated discussions into the late hours over many beers in the bar. Nobody, however, expressed any innovative ideas on the mechanism behind genetic interference, whereby one crossing-over/recombination event inhibits others around itself over huge physical distances, that is, on average 30 Mb in the human male. So this still remains an enigma. Anyway, I was very pleased that new antibody technology now allows clear-cut identification of the crossing-over/recombination points within chromosome pairs, the synaptonemal complexes. In humans and mice, at least, these points do correspond to the chiasmata in frequency and distribution; application of this new technology in other species should finally solve a lot of the past controversy (for example, see *Trends Genet.* 10, 112–115, 1994).

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BOOK REVIEWS



PCR all the way in molecular evolution

Molecular Systematics (2nd edn)

edited by David M. Hillis, Craig Moritz and Barbara K. Mable

Sinauer Associates, 1996. \$49.95 pbk (655 pages) ISBN 0 87893 282 8

The first edition of this book was hugely successful and quickly became a standard reference for all researchers in the fields of molecular systematics and molecular evolution. The ambitious goal of the book is to provide help in planning studies, laboratory design, data collection and data analysis. In the six years since the publication of the first edition, the field of molecular phylogenetics has continued to expand rapidly, mostly due to technical innovations involving the polymerase chain reaction (PCR). The continued explosion of the field is underscored, for example, by the fact that the bibliography almost doubled from 40 in the first edition to 75 pages in the second edition – and is, by necessity, still incomplete.

Although most of the chapters and contributors remained much the same, a new chapter (Chapter 7) on PCR by Steve Palumbi (one of the leading users of this technique who has continued to ask most interesting biological questions through the application of PCR techniques) was added, and the chapter on immunological techniques was

omitted. One of the driving forces behind the exponential growth of the field of molecular systematics was not only the technical ease of PCR, but also the development of 'universal' or versatile PCR primers. The technical challenge of having to make libraries, screen for clones, and determine DNA sequences of interest for every species became unnecessary because of these versatile primers. Most of the first sets of 'universal' PCR primers, designed to amplify homologous DNA sequences for a large set of species, and protocols for their usage, came from the laboratory of the late Allan Wilson. These primers have had a major impact on the speed, direction and common usage of a typical set of genes in the field. Chapter 7 contains a series of universal primer sequences and covers the basics of PCR for mitochondrial, chloroplast and nuclear DNA. Palumbi lists some objections to RAPD approaches because of technical and theoretical problems. In RAPD-PCR the often difficult step of primer design is circumvented by using short random PCR primers that amplify

random nuclear fragments for questions pertaining to population levels. However, this technique is fraught with potential difficulties and should only be used with the utmost care and for only a limited set of questions.

Also, the much expanded Chapter 8 by Dowling, Moritz, Palmer and Rieseberg on the analysis of fragments and restriction sites now includes newer PCR techniques and, importantly, work on microsatellites, which adds much to the value of this chapter. The latter set of population markers are widely applied already and their usage continues to grow rapidly. The recent realization that many PCR primers for particular microsatellite loci are of (often extensive) versatility in many, sometimes distantly related, species will lead to the even more widespread use of microsatellites in the near future.

What in this book will be of interest for readers of *Trends in Genetics*? One issue that continues to be of utmost importance in understanding developmental genetics and the issue of evolution of developmental mechanisms is homology. Still all too often one reads statements about, for example, '76% homology' when 76% similarity is meant; a statement that does not say anything about orthology or paralogy of two genes. Moreover, homology is often postulated by sameness of function (the most unfortunate term 'functional

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homology' is used) between two genes in two organisms. This reasoning could easily lead to incorrect conclusions (due to convergence and divergence) and the determination of orthology requires the generation of a gene tree, a phylogenetic tree that relates the evolutionary relationships of genes in its topology. Similarity of function or percent similarity are not valid criteria for determining orthology relationships. Only based on a phylogenetic analysis will one be able to distinguish between orthologous and paralogous copies of genes in different species and, hence, be able to determine the level of homology and whether the function of a gene changed during its evolutionary history. Lately, phylogenetic trees are found more commonly in the developmental biology literature and, although the recognition of the importance of evolution is a laudable development, it needs to be pointed out that these evolutionary trees are often constructed by the simplest phylogenetic algorithms and tend not make use of the

more sophisticated and more accurate methods.

In this regard, the chapter on Phylogenetic Inference by Swofford, Olson, Waddell and Hillis should be the main reason for readers of *TIG* to take a look at this book. If had I to single out one chapter that readers of *TIG* ought to read it would be this chapter, written by some of the leaders in developing and implementing phylogenetic algorithms. This chapter grew from 89 to over 100 pages in this second edition (and now contains an extensive list of available software), a reflection of the ever-growing complexity of phylogenetic inference. Knowledge of the processes of DNA and protein evolution can (e.g. in maximum likelihood models) be incorporated into phylogeny reconstruction, which yields more precise evolutionary trees. This chapter reflects best the trend that the boundaries between the fields of reconstruction of phylogenetic relationships between species based on molecular systematics

and the study of patterns and modes of molecular evolution are disappearing.

Chapters 1 and 12, by the editors, outline, with clarity and foresight, the multitude of approaches and questions that are covered under the vast, and somewhat artificial, heading: Molecular Systematics. Students of molecular evolution will find these chapters to be invaluable reading. Future editions will probably further increase the coverage of microsatellite work and analyses, and will possibly add chapters on conservation biology and on the construction of genetic linkage maps, a topic of great interest to workers in evolutionary biology who are trying to bridge the genotype-phenotype gap.

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Golden years

Discovering Molecular Genetics: A Case Study Course with Problems and Scenarios

by Jeffrey H. Miller

Cold Spring Harbor Laboratory Press, 1996. \$59.00 hbk (696 pages) ISBN 0 87969 475 0

The Eighth Day of Creation by Horace Freeland Judson is one of my favourite books. Not only is it a good read, but it influenced me to give up what I was doing at the time and become a molecular biologist, a decision that I have never regretted. I mention this because when I first looked at *Discovering Molecular Genetics* I thought to myself 'Aha! A companion to *Eighth Day*'. Here, reproduced in their original forms, are all the seminal papers from the 1950s and early 1960s: Watson and Crick (of course), Benzer's brilliant papers on rII, Gamow's curious half-page idea on the coding problem (complete with hand-drawn sketches and the teasing promise that a detailed account will appear in *Kong. Dan. Vid. Selsk.*), more believable coding papers by Crick, Brenner and Yanofsky, a couple by Hayes on conjugation, and the heroic 1961 review by Jacob and Monod, 38 pages of *Journal of Molecular Biology* that explained virtually everything. Altogether, 22 classic papers grouped into eight units, each with an excellent commentary by Jeffrey Miller putting the papers into historical context and helping us through the more tricky bits of what we now call 'data-handling'. This is not the

only book to reproduce important papers, but it is the first I have seen that covers specifically the period described by Stent as the 'dogmatic phase' of molecular biology, and the first to do the job so well.

I quickly decided that as a companion to *Eighth Day* this is a superb book. I particularly like the second section in which 18 later papers are reproduced to show how the foundations laid by the dogmatists have been built on since the 1960s. Here we see how Benzer's discovery of mutational hotspots was extended into a more complete description of mutagenesis in *Escherichia coli*, and how transposition was gradually understood. These 'updated' papers are also fascinating for the insights they bring into the evolution of research. Benzer, in 1959, needed less than one page of a 14 page paper to describe 'The Material and the Method'; 30 years later Cupples and Miller devote over half their text to the methods section. Oh to have lived in the Heroic Age!

I wish the book ended at p. 526 rather than p. 696. The problem lies with the subtitle: *A Case Study Course with Problems and Scenarios*, which reveals that the book is not simply a celebration

of molecular genetics, but another dreaded teaching text. So there are 'Sample Problems' and 'Scenarios', with answers in the *Solutions Manual and Workbook*. The laudable aim is to encourage students to understand concepts by working with data equivalent to those described in the classic papers. The *Sample Problems* do this in an orthodox way, but the *Scenarios* place the data in the context of historical or science fiction themes 'to make the exams more colourful'. I guess I have zero sense of humour because I found myself cringing at Munchkin Genetics (map of the *Escherichia yellow brick* chromosome) and 'Jurassic Engineering'. More to the point, I searched in vain for scenarios involving *Babylon 5*, *The X-Files* or some other theme that my current students are likely to find colourful.

I enjoyed this book. Parts of it puzzle me (I cannot work out why two stories by Edgar Allen Poe are reprinted at the back) but it is an excellent way in which to explore the development of molecular genetics. In the pressure cooker of UK university education I doubt if I will ever enjoy the luxury of being able to teach a module on 'Classic Papers', but for those more fortunate (and with a sense of humour) this is the perfect text.

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