Genet. Res., Camb. (1999), **73**, *pp.* 85–89. Printed in the United Kingdom

Book Reviews

Interpreting DNA evidence: statistical genetics for forensic scientists. By I. W. Evett and B. S. Weir. Sinauer Associates Inc. 1998. ISBN 0 87893 155 4. 278 pages. Price £25.95.

The interpretation of DNA profile evidence was a topic of considerable controversy during the early 1990s. Indeed, this reviewer has had differences of opinion with both authors on statistical and population genetics aspects. The publication of their book marks a maturation of the debate, in which a consensus seems to be emerging on many previously debated topics.

The basis of some of the dispute was the clash of philosophies which underlies the Bayesian/frequentist divide in statistics. Most statistical geneticists, including one of the authors, have generally adhered to the frequentist paradigm. Many forensic scholars, among them the other author, have found that approach to be unsatisfactory in the legal setting, not least because courts are concerned with individual events and not long-run performance of methods. One common objection to Bayesian methods, concerning the subjectivity of the prior, provides no difficulty in jury trials as it is the jury's role to subjectively assess, for example, eyewitness' statements. But the authors also recognise that the forensic scientist's work is inevitably based on professional judgment accumulated from training and experience. Although "objectivity" in the sense of non-partisanship is crucial, the pursuit of, for example, "objective" DNA profile match probabilities is doomed to failure. Match probabilities reflect the current state of knowledge: if everyone's DNA profile were known, match probabilities would be irrelevant.

The authors draw on methods from both frequentist and Bayesian traditions, but the overall framework for assessing evidence is firmly rooted in the Bayesian approach. They thus achieve a coherence which evaded the most prominent reference work in the field, the 1996 report of the US National Research Council (NRC). The NRC report was based on the work of a committee, and contains much that is worthwhile, but also errors and misunderstandings. These arise most clearly in its flawed treatment of the database search scenario, and in its failure to appreciate the central role of four-gene joint probabilities at each locus (two genes from the defendant, and two from the alternative possible culprit).

Forensic scientists working with DNA evidence will need to refer to the NRC report, but they should learn from Evett and Weir's book first, and follow the latter when the two authorities disagree. The book is divided roughly 50/50 between general background on statistics and population genetics, and the specific application of these ideas to the interpretation of DNA profile evidence. A final chapter deals with issues of presentation in court, including a discussion of some recent judgments. It is aimed at forensic scientists having perhaps an undergraduate degree in the biological sciences but not a strong background in statistics or population genetics. I am not a member of this target audience, but it seems to me that the authors have succeeded in their goal of providing an accessible introduction to the field, striking a good balance between practical details and general principles. Mixed profiles and relatedness testing, are discussed in separate chapters, but the full range of possibilities cannot be covered, consequently principles are presented along with illustrative examples. Exercises are provided, together with solutions in an appendix.

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Molecular Embryology of Flowering Plants. By Valayamghat Raghavan. Cambridge University Press. 1997. ISBN 0-521-55246-X. 690 pages. Price £95.00.

This ambitious work deals with most aspects of angiosperm reproductive biology, from flower development, through formation of gametes, self-incompatibility, pollination and fertilisation to embryogenesis *in vivo* and *in vitro*, and concludes with a

https://doi.org/10.1017/S0016672398249858 Published online by Cambridge University Press

chapter on genetic transformation of embryos. It aims to present the results of recent molecular genetical analysis in the context of a large body of classical evidence from studies of morphology, physiology, tissue culture and genetics. Sadly, it falls far short of its objective. In presenting the results of molecular genetics it is often factually incorrect (errors range from gene nomenclature to confusion of homeotic and homeobox genes). Experimental results are presented inaccurately or interpreted wrongly. A particularly confusing example is a discussion of viviparous mutants in maize which assumes that mutations at five different *viviparous* (*vp*) loci are allelic. The error is then compounded by a lengthy attempt to explain the different phenotypes of *vp* mutants in terms of pleiotropy. On occasion, experimental results are hardly interpreted at all. For example, a homeobox gene expressed in soybean embryos induced to form from tissue culture cells is suggested to play an important part as a transcription factor during embryoid development. It is left to the reader to make the connection with the expression of the closely-related *Knotted1* gene of maize (used to isolate the soybean sequence) which is described as the earliest marker of meristem formation during maize embryogenesis 128 pages earlier. Although the subject matter should be visually appealing, many of the illustrations, for example the nucleotide sequences of genes with unknown developmental functions, are uninspiring and uninformative.

Although this book provides a useful guide to the 40 years of classical research contained in the 4,500 cited references, it is not to be recommended as an introduction to the new molecular genetics of plant development. It could confuse or, at worst, mislead.

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Molecular Biology Lab Fax (*2nd Edition*) *Vol. II Gene Analysis*. Edited by T. A. BROWN. Academic Press. 1998. ISBN 0-12-136110-1. 255 pages. Price $59.95.

The 2nd edition of the Molecular Biology Lab Fax manual has undergone a radical transformation to accommodate the huge expansion in molecular methodology that has occurred over recent years. It is presented in two volumes, the first dealing with Recombinant DNA and this second volume on Gene Analysis. The Lab Fax series is designed to be a quick reference source for the experimenter. Primarily it is a collection of useful data but also provides basic details and advice on commonly used experimental procedures. It is a compact hardback volume, sufficiently robust to survive life in labs. Considerable effort has been put into making it more user friendly than some of the other large detailed molecular lab manuals and despite its small size it is surprisingly comprehensive. It is rare for a lab manual to be read in its entirety but I found it generally well balanced, nicely presented and easy to read. In doing so I came across a surprising number of useful facts that I hadn't been aware of, or had forgotten.

Volume II contains comprehensive chapters on commonly used procedures in gene characterisation. Each chapter begins with a concise introduction covering history and application followed by choice of methods and some basic recipes that are conveniently placed alongside the relevant section of the text. A section at the end covers some of the more commonly encountered problems and suggests some approaches to tackling them. Throughout the book, information is presented in a short, snappy style. For the person who needs more information the whole manual contains adequate references to more detailed manuals or original references. In general the data displayed in table format are very useful and collectively they should save much searching through manufacturers' instruction manuals or catalogues.

The introductory chapter concerns approaches to nucleic acid blotting and hybridisation and deals with a range of factors affecting transfer/hybridisation though, surprisingly, there is no mention of the widely used SDS-phosphate method of Church and Gilbert. Throughout there are tables showing, for example, how to convert oligonucleotide moles to μg, calculate T_m values, and choose the right transfer membrane and fixation method. Suppliers are also listed. Current methods of DNA sequencing with a brief guide to sequence analysis, software packages and databases are covered in another chapter. Though many labs now have automated sequencing, the emphasis here is on manual sequencing, which is a perfectly feasible undertaking for the beginner given the excellent kits which are available and listed here. It would have been worth pointing out that there are now several concerns which offer complete sequencing services, and it may be more cost effective and time saving for labs without sequencing facilities to pop their DNA samples in the post. Other chapters deal with nucleic acid probe labelling and methods of detection, agarose gel electrophoresis and centrifugation, all with tabulated technical data. A clear and concise beginners' guide to PCR amplification is also included. The penultimate chapter is a reference index, with brief definitions of virtually all the compounds that the average molecular biologist is likely to come across. The last chapter deals with the essential aspects of safety in the laboratory. It is presented in Table format and contains helpful information, for example, on EC guidelines on risk assessment of reagents, chemical and heat resistance of plastics and gloves.

There is some inconsistency between chapters in the level of experimental detail. The longest chapter, on

agarose gel electrophoresis, is to my mind too detailed. A simple table recommending agarose types and appropriate buffers for different purposes would have satisfied most users. And the 26 pages devoted to DNA size markers, some of them generated by rare restriction enzymes that most laboratories will not have, would have been better used to expand other sections where some important detail is missing. For example, one finds no recommendation on the concentration of ethidium bromide to use for staining DNA in agarose gels, no guidance on depurination (mentioned in the troubleshooting section), and no table listing the composition and appropriate use of different scintillation cocktails

However, these are minor criticisms of a manual that, overall, presents a brisk overview of relevant facts for the molecular biologist. It is not intended to compete with the heavier and more detailed Methods books, but to provide a compact no-nonsense source of information for novices and more experienced researchers alike. By and large it fulfils these criteria very well, and should be a useful purchase for most labs.

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Molecular Genetic Analysis of Populations. 2nd Edition. Edited by A. R. Hoelzel. Oxford University Press. ISBN 0 19 963634 8 (hard); 0 19 863635 5 (paper). 445 pages. Price £29.95.

It is perhaps an indication of the willingness of scientists studying natural populations to apply (and develop) molecular techniques, that the first edition of this book was fairly dated as soon as it appeared. This second edition is timely, and covers reasonably well the new laboratory techniques that have become widespread since the earlier edition. There are three new chapters: on microsatellites, on gel methods for detection of variation in DNA conformation and denaturability, and on the use of automated fluorescence-based technologies. The appendices have been extended and include a section on computer software useful to molecular ecologists. The original chapters have seen little change, with the exception of those on DNA isolation. The first edition suffered slightly from an overemphasis on mitochondrial and plant DNA. Brook Milligan's revised chapter, now titled 'Total DNA isolation', covers a wider variety of source tissues and extraction techniques, with useful guidelines on when to apply which protocol.

To my mind the major failing of the first edition was the lack of a chapter on microsatellites. Microsatellite DNA variation is arguably the most widely used tool in the molecular analysis of natural populations, and was just becoming popular when the earlier edition was published. Christian Schlötterer's chapter on microsatellites is an essential addition to the book, and is clearly written. Sections include cloning protocols, the nature of microsatellite mutation, the interpretation of gels, and the use of primers for amplifying loci conserved across species. Additionally there is a section on amplifying microsatellites from 'difficult' sources such as faeces or bone; although I would have liked to see more on this theme included in Milligan's chapter on DNA isolation. Schlötterer also points out a number of the potential pitfalls associated with microsatellites, such as homoplasmy biasing estimates of genetic distance, and 'null alleles' causing confusion in paternity inference.

The other new chapters are also useful. The use of single strand conformational polymorphisms (SSCPs) has become more widespread and is now covered. The last chapter is on the use of automated technology and fluorescent labelling methods in detecting DNA variation. Six years ago only the huge genome mapping 'factories' used such sophisticated methodology. Nowadays literally thousands of researchers studying natural populations have access to this technology. The chapter covers both DNA sequencing and microsatellite genotyping using these systems. As in earlier chapters useful guidelines are given detailing the relative merits of the various subtle variations in the methods that may be employed. Of the new appendices the most welcome is that listing computational resources available to workers in the field. I feel this topic deserved a chapter in it's own right. As a consequence of the brevity of this section there are some glaring omissions; for example there is no mention of Queller and Goodnight's Relatedness and Kinship programs.

Generally this book succeeds in its aim. It is comprehensive, the protocols are clear and easy to follow, and every chapter is well referenced. The biggest problem is that the techniques available are advancing so rapidly. Already, one can anticipate what new chapters might be in any third edition. More on Amplified Fragment Length Polymorphisms (AFLPs) for instance, a technique becoming very popular in analysis of plant populations and genomics. However, this criticism could probably be levelled whenever a book such as this appears. New techniques will always emerge. On the whole then, a useful, if not quite essential manual to a great many laboratories studying genetic variation in natural (and captive, why not?) populations.

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Darwinism's Struggle for Survival: Heredity and the Hypothesis of Natural Selection. By Jean Gayon. Cambridge University Press 1998. 516 pages. Price £65/$95. ISBN 0 521 56250 3 hardback.

Darwin's idea that evolution had happened was never seriously controversial – at least not among biologists. But his proposed mechanism, natural selection of small differences, was the subject of more or less acrimonious dispute, which still persists in some quarters. Jean Gayon's scholarly work takes us through the controversies up to their resolution (at least to the satisfaction of the majority) by the Modern Synthesis.

The story begins with Darwin's politely conducted argument with Wallace about the unit of selection. Wallace thought that selection was a matter of competition between species or varieties, whereas Darwin insisted that it was the individual that was selected. To maintain that view, Darwin needed a theory of individual heredity, and here he ran into difficulties. He did not rule out selection of discontinuous variants, but he replaced the emphasis on the slow accumulation of individually imperceptible differences. As early as 1867 Henry Jenkin, not a biologist but a Professor of Engineering, pointed out the difficulty. Selection could hardly make progress on the basis of small heritable differences that would soon, according to the prevailing idea of blending inheritance, be blended out of existence. Darwin was troubled by this objection and clearly needed some particulate model of inheritance, but had nothing to suggest except the theory of pangenesis, which never attracted much support. Eventually, as we now know, Mendelism came to the rescue, but too late for Darwin.

An important influence at the end of the nineteenth century was Galton's Law of Ancestral Inheritance, according to which each individual was a blend with contributions from all forbears: half from parents, one quarter from grandparents, and so on back, totalling to one. Gayon does well to explain the rather messy and dubious approximations that led Galton to this neat conclusion. Galton came to agree with Jenkin that selection could not work on this basis, and fell back on what amounted to a mutational, antigradualist hypothesis of shifts of species type to new positions of stability. Pearson, the leader of the Biometrical school, revised Galton's Law to a more flexible form that he thought would allow selection of quantitative differences. His ally, W. Weldon, worked hard in an attempt to demonstrate stabilizing selection on shell width in crabs – an experiment that excited William Bateson's derision. Bateson believed that continuous variation was not heritable, and held to this view with an obduracy that today seems more to do with his personal feud with Weldon than with logic.

Following the rediscovery of Mendel's work in 1900 Bateson and his fellow Mendelian enthusiasts were confirmed in their anti-quantitative position. They thought that heredity was demonstrably and exclusively about clear-cut segregating differences – the origin of which de Vries was thought to have demonstrated with his ever-sporting evening primroses, later shown to be a misleading special case.

With hindsight, it is hard to see why the demonstration of large hereditary effects should have been thought to preclude a role for small ones. Indeed, as early as 1902, the statistician Udny Yule pointed out the clear possibility of reconciling quantitative inheritance and Mendelian theory. But neither the Mendelians nor the Biometricians were in the mood for reconciliation at that time. The dispute over large versus small heritable differences is not obviously relevant to the principle of natural selection – after all, even the most hopeful of monsters must be subject to the viability test. But somehow natural selection, the essence of Darwinism, became firmly associated with slow quantitative change. There was (and to some extent still is) a gulf between two views of natural selection: on the one hand as a creative force, like a sculptor slowly chipping away, and on the other as an arbitrator giving yes-or-no verdicts on new organisms arising ready-made.

Gayon reviews, comparatively briefly, the advances that eventually led to the rehabilitation of Darwinism – the demonstration of the selectability of quantitative characters, the examples from the growing Drosophila school of the subtle effects of allelic differences, and so on. He could have made more of the dawn of the chromosome theory (though he does quote W. S. Sutton's extraordinarily prescient publication of 1902), which Bateson resisted almost to his dying day. At the very least, the demonstration of a physical base for the genes must have made them easier to take seriously.

Later in the book Gayon deals with the contrasting approaches to population genetics of Fisher and Wright. A fair summary of his reasonable verdict, I think, is that Fisher's models had precision and clarity (though readers may have some difficulty in understanding them from Gayon's account), but were clearly a great simplification of real evolving populations; Wright's adaptive landscapes, on the other hand, tended to impressionism but provided insights into real population complexity. Perhaps surprisingly, there is no mention of punctuated equilibrium, seen in some quarters as the new and major challenge to gradualist Darwinism. Perhaps it is less of a hot topic for the French than it has been for us.

This is, on the whole, an admirable book, well translated from the original French, and with extensive

notes and illuminating quotations from original sources. However, it has some rather glaring faults. Though the author has read widely, he has not understood everything. For example, in discussing the maintenance of polymorphisms he dismisses heterozygous advantage or heterosis as "verbal sleight of hand", but surely it is a testable hypothesis. Then, lower down the page, he equates heterozygous advantage with frequency-dependent selection. Another place where he is confused, or at least much less than clear, is in his account of mimicry, which he stresses because of its importance as an example of selection in action. He writes that Bates, of Batesian mimicry, was unwilling to accept Mullerian mimicry, probably, he says, because the latter "implied a hardening of the concept of natural selection". But the following paragraphs totally fail to explain, at least to me, in what way Batesian mimicry was less hard-line in this respect.

A more serious obstacle for the reader is the book's verbosity. One among many examples is in Gayon's account of the development of population genetics, where he writes that two parameters, mutation rate and population size, "have a rigorous and measurable empirical significance". As the author helpfully explains in the next sentence, that just means that in principle they can be measured – in other words, the previous verbiage was redundant! In fact, perhaps half the words in the book could with benefit have been omitted; though perhaps (my prejudice) that would have diminished it in the eyes of the philosophers and sociologists of science who (to judge from the author's occasional apologies for neglecting sociology) form part of the intended readership.

In spite of, and to some extent because of, the problems that it sets for the reader, this book is well worth reading. Most geneticists will emerge from the experience knowing much more about the chequered history of their subject than they did before.

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https://doi.org/10.1017/S0016672398249858 Published online by Cambridge University Press