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Book Reviews

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Is It in Your Genes? The Influence of Genes on Common Disorders and Diseases that Affect You and Your Family. P. R. REILLY. Cold Spring Harbor Laboratory Press. 2004. 304 pages. ISBN 0 87969 721 0. Price $19.95 (paperback). ISBN 0 87969 719 9. Price $29.95 (hardback).

This book is about the influence of genes on common disease and disorders. It is written for a general audience so that little prior knowledge of genetics or biology is required to understand its contents. It is organised into four parts, Pregnancy (~20 pages), Infancy (~10 pages), Childhood (~30 pages) and Adulthood (~160 pages). Each part comprises a number of sections (usually 1 to 2 pages) that deal with a particular disorder. The sections start with a type of question that the author encountered during or after giving public talks about genetics and disease, for example "*My uncle has cerebral palsy. Does this mean my children are at increased risk*?" and "*My mom has glaucoma. How much of the risk for glaucoma is genetic*?". Most sections end with a paragraph trying to answer the question posed at the beginning. The number of disorders and traits that are discussed are too numerous (>100) to reproduce but here is a sample: Endometriosis, Twinning, Spina Bifida, Deafness, Stuttering, Handedness, Asthma, Longevity, Inflammatory Bowel Disease, Diabetes, Cancers, Mental illness and human behaviour.

The book is accompanied by a website, www.is-it-in-your-genes.org, which, according to the book, 'is planned to become available by May 2003' (the book was published in 2004 …). I checked the website in the first week of August 2004. It exists but there is no information (apart from how to buy the book) other than 'the site will go live in June 2004'. Ah, the wonders of modern day web technology.

I very much enjoyed reading this book. It gives an up to date summary of the knowledge regarding genetic risk for common disease and disorders, is written very clearly and contains a large amount of information that is easy to find. To my knowledge, the information provided is factually correct and an excellent condensation of the primary literature (33 pages of primary literature and further information are provided at the back of the book). It tries to avoid jargon and by-and-large achieves this. The main source of information regarding risk for disorders in relatives of affected individuals comes from twin, family and genetic epidemiological studies. Essentially, for the majority of disorders, a positive family history and an individual's relationship to affected relatives, rather than specific known gene variants in the individual, are the main predictors of risk. This is a sobering thought in the age of gene mapping and genomics because very few polymorphisms or mutations have been found that reliably predict risk and have a large enough effect to be of clinical or counselling importance.

It will be interesting to speculate how much this book will change if it is (re-)written in 10 years' time. The author is very optimistic about 'personalised medicine' and gene/mutation discovery. However, in my view he makes gene discovery for common disorders sound a bit too easy – there has been relatively little success for common diseases such as psychiatric disorders and diabetes. In addition, there is a growing consensus that the relative risk of common variants that predispose to disease are small, say around 1·5, which suggests that the actual risk for carriers will not differ substantially from the average (background) population risk.

I only had a few minor issues with the book. It appears to be written for an American audience, with funny units (feet, inches, pounds) and examples of population prevalence preferably quoted from studies of the US population. When reporting results from gene mapping studies usually no difference is made between within-family (linkage) and population-wide (candidate gene) studies. Arguably the difference between these two is not important for the intended audience, but the route from the initial study to identifying putative causal polymorphisms is usually (much) longer for the former.

In conclusion, this is a very readable book that I will recommend to friends and colleagues who are interested in the area of genetics, medicine and public health.

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Microbial Functional Genomics. J. Zhou, D. K. Thompson, Y. Xu and J. M. Tiedje. John Wiley & Sons. 2004. 590 pages. ISBN 0 471 07190 0. Price £58.95 (hardback).

This book is a worthy attempt to put together several disparate strands emerging from the genomics/post-genomics 'revolution'. (Incidentally, one could fault the Kuhnian paradigm in 'The Structure of Scientific Revolutions' for failing to note that a revolution need not be in how we interpret nature, but may rather be in the methods regarded as appropriate for studying it). The first four chapters deal with genomics. Among the virtues of chapter 3, 'Computational genome annotation', is an explanation of Markov chain models comprehensible to the non-specialist. Chapters 1, 2 and 4 treat various aspects of microbial diversity and evolution. Chapter 4, 'Microbial evolution from a genomics perspective', presents objective accounts of the molecular clock and horizontal gene transfer, and a clear account of the various ways of creating phylogenetic trees.

The remainder of the 15 chapters deal with gene function. Chapter 5 is again computational, on prediction of gene function. It deals as expected with sequence and structure-based methods, but also says what can be said at this time about systems-based approaches. Chapters 6–10 are methodological. Chapters 6 and 7 are on DNA microarrays and the analysis of gene expression data from them. The descriptions here of the printing of arrays, hybridisation and detection, and image processing are extremely clear. The following chapter gives a useful account of the problems in normalisation and also a helpfully non-technical view of data clustering; again as with the same author's chapter 5, there is sufficient maths to provide solidity but the explanations are clear enough for the non-expert to follow. Chapter 8 is allegedly on mutagenesis, but is in fact aimed at how to knock out gene function, whether genetically or via antisense RNA. The genetic tools are those that can be applied on a genome-wide scale – *in vitro* transposon insertion, signature-tagged mutagenesis (STM) in the context of pathogenicity, and gene disruption via homologous recombination. Chapter 9 provides an excellent outline of mass spectrometry methodologies. Chapter 10's title, 'Identification of protein-ligand interactions', is slightly misleading since it deals with protein-protein interactions, again focussing on ways of obtaining genome-wide information. It starts with high-throughput gene cloning, then provides a detailed account of yeast two-hybrid methodology followed by a less detailed one of phage display, ending with protein and peptide arrays and a somewhat perfunctory description of surface plasmon resonance.

The next 4 chapters show how these methods can provide whole-genome approaches to important microbial systems: the *E. coli*/*B. subtilis*/*S. cerevisiae* models, pathogens, antimicrobial drug discovery, and microbial detection. The pathogenicity chapter, for example, details the extra genes present in pathogens (often in pathogenicity islands), as well as those deleted, in comparison with non-pathogenic relatives; the use of microarray-based comparative genomics to find pathogenicity-related genes; STM, an especially useful tool in this context; and transcriptome and proteome analysis to suggest candidate pathogenicity-related functions. The chapter on antimicrobial drug discovery provides a detailed and sober description of how new potential drug targets may be identified and validated. The final chapter looks at future prospects, including for the novel forms of systems biology that are predicted to be evolving, and for the genomics of microbial communities ('metagenomics') – 'genomics beyond single cells'.

The book is authored by a small group from Oak Ridge, Tennessee, and Michigan State University, and consequently has clarity and unity of tone. The approach throughout is thoughtful and blessedly hype-free. Descriptions of methods are for the most part excellent, as are the diagrams that illustrate them. In sum, I found this an interesting and highly recommendable attempt to provide a new kind of microbial genetics text focussed on the largely technical developments of the past decade. The authors will probably share the misfortune of most pioneers, in that (a) others will copy them and inevitably will sometimes do even better, and (b) because of the continued rapid advance of the field (or rather, collection of not always related fields), for the book to continue to be useful it will have to be frequently revised. Who will find it useful? The more advanced and academic undergraduates; new postgraduates and postdocs lacking familiarity with the ideas and techniques; and many senior research supervisors, both in academic and commercial contexts, who have had to assimilate the new information in a hurry and consequently are aware of gaps in their knowledge.

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Recipes for ecological genetics

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Ecological Genetics: Design, Analysis and Application. A. Lowe, S. Harris and P. Ashton. Blackwell Publishing. 2004. 326 pages. ISBN 1 4051 0033 8. Price £29.99 (paperback).

The phrase 'ecological genetics' evokes images of EB Ford searching English fields and hedgerows for meadow brown butterflies (Ford, 1945). However,

although the authors of this book credit Ford with coining the phrase, the subject of their book bears little relation to Ford's studies of butterfly eyespot variation. Instead this book is resolutely about a topic that is perhaps more commonly referred to as molecular ecology – the application of molecular and protein based genetic markers to the study of wild populations.

Starting as it does with a comparison of types of markers (Chapter 2) and methods of analysis (Chapter 3), it feels very much like a recipe book for beginning graduate students. There is a great deal of welcome and useful information of the kind that is hard to obtain from the primary literature, such as tables comparing the merits and otherwise of AFLPs, microsatellites, RAPDs, allozymes and RFLPs. Authors rarely address the reasons why a particular marker was chosen, although that is perhaps because it is often because Joe had some primers for a related species, rather than the result of a careful analysis of the merits of different options.

There is plenty more useful information here. A detailed consideration of the sample sizes required for different goals, such as sampling rare alleles or estimating allele frequencies, a concise description of different types of data analysis such as Fst statistics, genetic distance and genetic diversity measures, and a consideration of the relative merits of estimating gene flow by indirect methods such as Fst versus direct methods such as assignment tests, are all sections that one might recommend to a beginning PhD student. Indeed, a second year PhD student of mine, Silvia Perez-Espona, who is carrying out a study of population structure in red deer, enjoyed these early chapters and says she is likely to use the book in the future.

Nonetheless, the value of any reference volume is called into question by factual errors, and there were a few here. A box entitled 'Understanding linkage disequilibrium' states that 'If two alleles from different genes on the same chromosome tend to be associated … linkage disequilibrium is said to exist', alongside a drawing of two physically linked markers. In fact, linkage disequilibrium refers to associations between alleles within individuals in a population, but the markers need not be linked in a physical sense. In other cases, the coverage of the literature is patchy, for example Coyne and Orr's analysis of reproductive isolation in *Drosophila* is specifically criticised on the grounds that 'premating isolation was not included.', even though several papers by the same authors that were not cited have considered pre-mating isolation in detail (Coyne *et al*., 1989; Coyne *et al*., 1989; Coyne *et al*., 1997).

The authors also missed an opportunity to challenge the established dogma of their field. Despite mentioning in the introduction that studies of adaptive markers might be informative, virtually all of the subsequent analysis assumes that markers under study are neutral. Thus, for example, differences in population structure between mtDNA and nuclear markers are attributed to sex differences in gene flow. However, there is considerable evidence that mitochondrial genes are under selection and are likely to be subject to both occasional selective sweeps and background selection (Gemmell *et al*., 2004). This provides an alternative to sex differences in dispersal as an explanation for the common observation that mtDNA is more highly structured and has an effective population size even less than that expected relative under neutrality, when compared to nuclear markers such as microsatellites. Another piece of dogma is that neutral markers should be used to estimate dispersal. In fact, linkage disequilibrium between selected loci is likely to provide a much better estimate of dispersal, because a selection-migration balance is more stable and returns to equilibrium more rapidly than a neutral drift-selection balance (Mallet *et al*., 1990; Lenormand *et al*., 1998). However, estimates based on selected markers are far more difficult to obtain, as there are few cases in which the genetic basis of traits involved in local adaptation are known. A comparison of the two approaches would have been useful.

However my major disappointment was that this book simply failed to live up to its title. In my mind, ecological genetics is about understanding adaptation and the interaction between genetic variation and ecology. To illustrate this, I will briefly mention two recent studies that epitomise the kind of approach that I think should characterise the field. In remembrance of Ford, modern studies of butterfly eyespots are a good place to start. Work on the African species *Bicyclus anynana* has shown that what appear to be hard-wired correlations between different traits can in fact be readily separated by artificial selection (Beldade *et al*., 2002). This suggests that allometry and correlated evolution, often used as evidence for developmental constraint, may in fact be a result of ecological selection pressures channelling traits in particular directions. And staying with butterflies, a recent study of *Melitaea cinxia* has shown that local adaptation in host preferences affected the probability that butterflies would colonise nearby habitat patches (Hanski *et al*., 2001), an elegant demonstration of the interaction between genetic adaptation and population ecology. So in summary, I recommend this book as a primer for studies of population structure using neutral markers, but there is a whole other book on ecological genetics that remains to be written.

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