# Book Reviews

*Genetic Instability in Cancer. Cancer Surveys, Vol. 28.*
Edited by Thomas Lindahl. Cold Spring Harbor
Laboratory Press, 1996. 353 pages. Price $90.00.
ISBN 0 87969 485 8.

When going on holidays I usually take an interesting
book with me. This year it was Volume 28 of the
'Cancer Surveys' series. Although a good novel would
probably have been more entertaining, I didn't regret
it.

Cancer research in the last decade or so has provided
abundant evidence that multiple genetic changes
initiate and drive the carcinogenic process. For
instance, at least eight alterations in specific genes are
necessary to convert a colon epithelial cell into a
malignant state. The bewildering spectrum of specific
mutations found in different tumours in the key
regulator P53 provides ample illustration of the
contribution of DNA alterations to oncogenesis. The
above mutation frequency is highly unlikely to occur
in a single somatic cell because normal cells have an
incredibly high replication fidelity resulting in one
mutation per cell, per generation per $10^9$ nucleotides.
This corresponds to a few sequence alterations when
copying the entire $5 \cdot 10^9$ basepair human genome. This
simple consideration implies that one or more of the
normal security systems that maintain genetic stability
must be compromised in the course of tumour
development.

Mechanisms of genetic instability are numerous
and surprisingly diverse. They range from DNA
damage repair pathways, replication error mismatch
correction and telomere shortening, to spindle func-
tion, cell cycle checkpoints and epigenetic changes
(such as DNA methylation). A prominent, and rather
alarming, role is played by DNA damage either of
endogenous origin or from exogenous sources
resulting in a time-dependent decay of our precious
carrier of genetic information. For instance, every day
as many as $10^4$ nucleotides in the human genome are
damaged by normal chemical reactions in each cell,
leading to inappropriate depurination, deamination,
oxidation and methylation of the nucleotides. Spon-
taneous deamination of 5-methylcytosine to thymine
causes a 12-fold increased mutation frequency relative
to unmodified cytosine. Damage accumulates in time
and may cause a substantial amount of mutation

even in differentiated, non-dividing cells, causing
cancer, and otherwise contributing to ageing.

The above observations clearly illustrate the im-
portance of the issue and the need to consider all
relevant aspects of this intricate story. These are
brought together in this volume. The book covers
almost all the areas mentioned above in relation to
genetic (in)stability, starting with basic information
about all known mechanisms involved in faithful
copying of DNA sequences, translesion DNA syn-
thesis, mechanisms of V(D)J recombination and
chromosomal aberrations. The knowledge presented
is collected from organisms as diverse as the bacterium
*Escherichia coli*, the yeast *Saccharomyces cerevisiae*
and man. The genetic stability processes implicated
are so fundamental to the development and continued
existence of life that they have hardly changed in the
evolution from unicellular pro- and eukaryotes to the
most sophisticated, multicellular mammalian systems.
The story of the discovery of the involvement of
mismatch replication error correction mechanism in
hereditary non-polyposis colorectal cancer (HNPCC)
has revealed how relevant the basic work done on *E.
coli* during the decade prior to this finding has been
for the understanding of the origin of HNPCC.

This volume brings together concise overviews from
a broad scientific area involving quite specialized
fields of research, such as mutagenesis and mutators,
replication fidelity, specific chromosomal aberrations
and genetic instability mutants, with each chapter
written by one of the leaders in the respective field. As
one might expect with multiple authorship, there is
some heterogeneity in style, format, presentation and
quality. There is also some redundancy, for example,
in the HNPCC–mismatch repair connection. How-
ever, this does not outweigh the important advantages
of multi-authorship: an up to date and expert
presentation of the situation in each specific area often
with emphasis on recent, sometimes still unpublished,
information (e.g. in the chapter on damage-induced
mutagenesis). Furthermore, it makes every chapter
readable on its own without the need to go through all
the previous chapters, before being able to understand
the part in which one is specifically interested.
Personally, I would have preferred to see more
illustrations and diagrams to explain structures and
mechanisms or depict crucial results, like the in-

formative figures used in the chapter on damage-inducible mutagenesis.

In short, *Genetic Instability in Cancer* is highly relevant for those with a clear interest in this broad field but with limited background knowledge, and also contains valuable information and useful references for those who are more familiar with some of the areas. Thus the book should be part of the library infrastructure of every cancer research laboratory and of experimental clinical departments of cancer institutes. It may be wise to borrow it for some time from your institute's library although it doesn't necessarily have to be during your holidays.

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*Sequence Data Analysis Guidebook. Methods in Molecular Biology*, *Volume 70*. Edited by SIMON R. SWINDELL. Humana Press, 1997. 324 pages. Price $69.50. ISBN 0 89603 358 9.

The backbone of this book is a large number of short chapters, each giving step-by-step instructions for individual items of sequence analysis, using particular program packages. This could only be of major use to those already having access to the software concerned, and presumably duplicates to a large extent the relevant manuals. There are some points of more general interest, but these are scattered through the text and consist mostly of unsupported assertions and precepts. The selection of packages covered appears to be arbitrary and inconsistent, and there is little or no reference to the vast array of sophisticated tools that are now available *via* the Internet.

These shortcomings can be illustrated by reference to chapters 22–25, which all deal with PCR primer design. Chapter 22 uses GENEJOCKEYII and repeats all the general information about the program to be found in the other seven chapters of the book which describe it. Chapter 23 uses a program called OLIGO, but does not say how the program can be obtained. Chapter 24 uses PRIME, a program from the 'gcg' package; this seems to be the only reference to this package, which I would guess is still the most widely used – certainly of multi-access sequence analysis packages. Chapter 25 uses part of the LASERGENE package, and repeats all the general information about the program to be found in the other six chapters which describe it; four of these chapters, including this one, are written by an employee of the company concerned. There is no comparison of the programs, nor any critical analysis of the algorithms or parameters used.

It has become a tediously repeated mantra that the pace of development in bio-informatics means that research molecular biologists are in desperate need of authoritative guidance in the selection and use of software tools. The back cover of this book explicitly promises to provide this help; but the book itself does not come close to fulfilling the promise.

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*C. elegans II*. Edited by DONALD L. RIDDLE, THOMAS BLUMENTHAL, BARBARA J. MEYER and JAMES R. PRIESS. Cold Spring Harbor Laboratory Press, 1997. Cold Spring Harbor Laboratory Hardback, 1222 pages. Price $175.000. ISBN 0 87969 488 2.

In 1988 Cold Spring Harbor Laboratory Press published *The Nematode Caenorhabditis elegans*, which presented the first 20 years of genetic study of 'The Worm', following Sydney Brenner's launch of this small (1·5 mm long) soil-inhabiting Nematode as a model organism for throwing light on more advanced eukaryote genetics and biochemistry. Most geneticists will know that the enthusiastic response from an ever-increasing number of laboratories has led to a startlingly rapid growth of knowledge on the worm.

The new book takes the story to 1996. It contains 30 substantial chapters and 4 appendices, the latter covering Genetics (Genetic nomenclature, List of laboratory strain and allele designations, Skeleton genetic map and List of characterized genes), Neurotransmitter assignments for specific neurons, Codon usage in *C. elegans*, and On-line *C. elegans* resources: and the book ends with a bibliography of about 2500 articles and 50 pages of index.

The 30 chapters start with a useful introduction to the worm for newcomers, and the following chapters mostly have a section called 'Prospects', which gives the reader a good idea of what is still unknown. Chapters 2–30 discuss an amazing variety of topics which study of the worm has illuminated. Chapter 2 describes work on the Genome, now estimated to have about 100 million base pairs, largely by reference to the *E. coli* genome whose size has been raised from 4 to closer to 5 million bp. The complete genome of *C. elegans* should be known by the end of 1998, and meanwhile the total number of genes is now estimated to be 14000–15000, much more than the expected number based on estimates of 2000 to 4000 essential genes garnered from genetic studies. About half the 6157 predicted genes in the region of the genome so far sequenced have significant homologies to genes previously characterized in other organisms, a smaller proportion than expected. These figures are doubtless changing rapidly as readers can find out by using Appendix 4.

Chapter 3 examines chromosome organization, mitosis and meiosis, and chapter 4 presents the enormous amount of information that has accrued on mutation. But here the biological information is lagging behind the sequence information, since only about 10% of the 15000 genes of *C. elegans* are

represented by mutations. Chapters 6–8 discuss RNA processing and gene structure, transcriptional factors and transcriptional regulation, and mRNA and translation, while chapters 9–12 cover sex determination, the germ line, spermatogenesis, and male development and mating behaviour. Chapter 14, on specification of cell fates in the early embryo, describes the origin of the five somatic founder cells from the first four cleavages of the embryo, which generate distinct sets of somatic tissues. These five blastomeres, called (rather confusingly) AB, MS, E, C, and D, yield complex series of unequal and later equal cleavages, whose genetic control is gradually being unravelled. Blastomere D, from the fourth initial cleavage stage, has a sister cell P4, which is the germ line precursor cell.

Chapter 15 discusses programmed cell death, or apoptosis, which plays an important part in *C. elegans* embryogenesis, since 131 of the 1090 cells generated during hermaphrodite somatic development undergo programmed cell death. These deaths are highly reproducible in terms of the identity of the dying cells and the time in development of their deaths, making it possible to study the phenomenon at single-cell resolution. Genetic screens have isolated over 100 mutations that identify more than a dozen genes affecting all programmed cell deaths as well as a few which alter the pattern of deaths. The pathway deduced contains four separable steps, including the decision of individual cells whether to live or die, and the execution of the death sentence in a cell which has decided to die; 11 genes which affect three of these stages (the *ced* series) have been studied in detail, and one of them (*ced-9*) is a negative regulator of programmed cell death with homology to the human and mouse *bcl-2* genes. This and homologies between other *ced* and mammalian genes strongly suggest that there is conservation of the cell-death pathway between nematodes and mammals, with the implication that the common genetic program for cell death predates the evolutionary separation of nematodes and vertebrates and possibly arose with the origin of metazoa or soon after. There is much more of great interest in this chapter, including the small number of cell deaths in *C. elegans* male development which occur by a different pathway that has led to them being called 'murders'.

Chapter 16 'Muscle: Structure, Function, and Development' leads the authors to quote Owl from A. A. Milne's *The House at Pooh Corner* (with a little updating), telling us we have to read this chapter twice to understand it. Owl's advice will doubtless help anyone struggling with 'The Twitchin Protein Superfamily', 'The Tropomin–Tropomyosin Complex', and certainly 'E. A Mystery: Acquisition of Muscle Cell Fates in the Mid-stage Embryo'.

The remaining 14 chapters are equally illuminating. Thus (17) 'Extracellular Matrix' concentrates on cuticle composition and genetics, especially the large family of 50–150 collagen genes; (19) 'Development of the Vulva' is described as a microcosm of events important in the development of all animals; (20) 'Patterning of the Nervous System' – the *C. elegans* nervous system consists of 302 neurons of 118 types that interconnect in a reproducible manner to form a variety of neural networks and pathways, and the recent progress reported here makes this the most important topic in worm genetics; (22) 'Synaptic Transmission' is on neurotransmitter metabolism and function and components regulating neurotransmitter release in all neurons; (23) 'Mechanotransduction' discusses the neural circuit and mechanosensory control of locomotion, touch receptor development and differentiation and the genes required for their function; (24) 'Feeding and Defecation' describes the complex processes by which the many-muscled pharynx takes in liquid plus bacteria, extrudes the liquid but not the bacteria (by an unknown process), grinds the bacteria and passes the paste to the intestine, the speed of consumption being controlled by muscles at the anus, and also discusses multifunctional neurons and redundancy (which is a pervasive theme in *C. elegans* nervous system function); (25) 'Chemotaxis and Thermotaxis' – very detailed analysis of complex behaviour including the regulation of chemotaxis and thermotaxis by experience; (26) 'Genetic and Environmental Regulation of Dauer Larva' – or how to escape from a tight situation and live longer; (27) 'Neural Plasticity' – synaptic plasticity during development and behavioural plasticity in the adult, including learning and memory; (28) 'Environmental Factors and Gene Activities that Influence Life Span' – the study of life span, theories of ageing, ageing in *C. elegans*, the search for genes that control the rate of ageing; (29) 'Evolution' – ingenious theories but much less certainty than elsewhere in the book, and doubts about the phylogenetic relationships of the Nematoda cast a slight shadow over the too enthusiastic use of *C. elegans* as a general model organism, but this is a very useful examination of the problems; (30) 'Parasitic Nematodes' 'Of every five animals on the planet four are nematodes' (Platt, 1994). Can this really be true? Most plants and animals have at least one parasitic nematode uniquely adapted to exploit them. This chapter discusses the nematode world, some important nematode parasites, antinematode compounds and their targets, the nematode surface, parasite genes and genomes, and, of course, future prospects.

'Who would have thought the little worm to have had so much genetics in it?' This must be one of the best ever Polygraphs to come from the Cold Spring Harbor Laboratory Press, and they, as well as the authors, editors and reviewers, are to be congratulated for creating such a splendid book.

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*Natural Hybridization and Evolution*. By Michael L. Arnold. Oxford University Press, 1997. 215 pages. Price £22.50. ISBN 0 19 509975 3 (pbk).

Hybridization between divergent populations challenges our ideas of 'species'. Should hybridizing taxa be regarded as part of one biological species, because they exchange genes, or be classed as separate, because they remain distinct despite gene flow? For most of this century, hybridization was seen as primarily a taxonomic problem. However, about twenty years back, a revival of the theory of clines (e.g. Slatkin, 1973; Endler, 1977) combined with the availability of electrophoretic markers to stimulate a new kind of research on hybrid populations – and, especially, on the narrow hybrid zones that subdivide so many taxa. This was seen as opening a window on the process of speciation, revealing the causes and consequences of reproductive isolation under natural conditions. The field has since burgeoned, with a steady increase in the rate of publication, up to the present total of about 30 papers per year.[1]

Arnold has now produced the first single-author book on natural hybridization since Anderson (1949). It is not a comprehensive review of the subject; rather, it is an argument for greater emphasis on the positive role of hybridization in evolution. Zoologists have in the main believed that the exchange of genes between distinct populations has been of little importance; gene flow has been seen as either impeding speciation (Mayr, 1963), or causing selection to reinforce reproductive isolation (Dobzhansky, 1940). In the botanical literature, there has been a greater emphasis on the origin of new species and new adaptations through hybridization (e.g. Anderson, 1949; Rieseberg, 1995). Arnold argues that this difference in emphasis is partly due to the more obvious hybrid origin of many plants, and partly because the proponents of the biological species concept (mainly zoologists) regarded hybrids as an evolutionary dead end.

In the broadest sense hybridization has played a key role in evolution. Maynard Smith & Szathmáry (1995) view the major transitions in evolution as involving the coming together of independent replicators into a single organism. For example, eukaryotes formed as a symbiosis between several free-living microbes (Irwin, 1994). Here, distinct sets of genes with complementary functions have combined to build up a more complex genome, whereas hybrids are usually taken to be recombinants between homologous sets of genes. However, the distinction is not so clear; hybridization most often leads to new species through allopolyploidy or hybrid parthenogenesis, in which both parental genomes are retained. Sexual reproduction may well have evolved as a means of generating evolutionary novelties through hybridization; the sporadic sex

[1] Numbers of papers in Science Citation Index with 'hybrid zone' in title or keywords.

found in bacteria is best seen in this way (Maynard Smith, 1990). Though Arnold focuses on hybridization between taxa of 'higher' plants and animals, the issues are relevant to this wider context.

After discussing species concepts, and the way these have shaped views on the role of hybrids, Arnold sets out in chapter 3 to assess the frequency of hybridization. There are really several questions here: how frequently do individuals find mates from other taxa; how often are genes exchanged; and what fraction of individuals trace their ancestry back through hybridization events? These questions are quantitative, yet evidence is too sparse to be more than suggestive. One problem which Arnold stresses is that rare events can have substantial consequences: for example, five species of cotton (*Gossypium*) trace back to a single allopolyploid ancestor (p. 38). He discusses evidence from comparative cytology; fossils (for example, inference of ploidy from the sizes of fossil guard cells – Masterson, 1994); taxonomic surveys of current hybridization; and phylogenies reconstructed from molecular evidence. This last should in principle be the most powerful. However, there are several difficulties. First, discordance between the ancestries of different loci may be due to errors in the phylogenies, or to 'lineage sorting', such that genes trace back to common ancestors much older than the present species (for example, primates share MHC polymorphisms which date back at least 30 Myr – Ayala & Escalante, 1996). Second, unless many loci are compared, one cannot tell whether hybridization involved introgression of individual genes, or mixing of whole genomes. The widespread reliance on just mitochondrial or chloroplast sequences is troubling, since these can be distorted by selection on any of the genes they carry. There is good evidence that human mtDNA derives from a recent 'selective sweep' (Hey, 1997), and cytoplasmic sequences show discordant distributions much more often than nuclear markers (Harrison, 1989). Finally, while many species may trace back to allopolyploid ancestors, it is not clear how many derive from regular diploid hybrids. Allopolyploids may be favoured by intrinsic physiological effects of increased ploidy (Thompson & Lumaret, 1992), and by heterosis: however, they are also easier to detect. Outcrossing diploids can generate hybrid species (as with the sunflower *Helianthus paradoxus* – Rieseberg *et al.*, 1990). However, extensive sets of reliable phylogenies will be needed to establish the importance of this mode of speciation, and to find what fraction of the genome is involved.

Arnold's thesis is that although the initial formation of recombinant hybrids may be rare, fit genotypes may be able to establish a stable hybrid population, or even spread to replace parental genotypes in at least some environments. In chapter 4, he discusses the various obstacles to hybridization, with particular emphasis on a barrier which has only recently received

attention: namely, incompatibilities which act after mating but before fertilization. In plants, the failure of foreign pollen may be the main cause of isolation; Arnold argues that the incompatibility here may be the same as that preventing self-pollination. Such self-incompatibility is of course absent in animals with separate sexes, but nevertheless, there are several examples of assortative fertilization. Although it is hard to know whether selection amongst gametes leads to reproductive isolation exceptionally often, it is tempting to suggest that fertilization systems diverge rapidly as a result of sexual selection (e.g. Aguade *et al.*, 1992; Metz & Palumbi, 1996).

The next chapter, on 'Concepts and Theory', is the most substantial, and to my mind, the most contentious. Arnold examines the various explanations for the maintenance of hybrid zones, and sets out his favourite: A model of 'evolutionary novelty'. This supposes that while hybridization may initially be rare, some hybrid genotypes are fitter than either parent in some novel environment, and are maintained there by selection. This scheme is close to Anderson's (1949) 'hybridised habitat', and Moore's (1977) 'bounded hybrid superiority' model. However, Arnold goes further, and argues that hybrids may often be fitter in parental as well as intermediate habitats. The difficulty then is in explaining why hybrids should be restricted to narrow regions. Arnold suggests two solutions: that contact is recent, and that the initial hybridization is rare, and most likely to occur in a disturbed region. Neither seems to me plausible; if spread is possible, it will be rapid, and yet many present-day hybrid zones are thought to be post-glacial ($\approx 10^4$ yr). Moreover, the extent of molecular divergence suggests that intermittent hybridization has occurred for $\approx 10^6$ yr (Barton & Hewitt, 1985).

The case for at least some hybrids having high fitness is a plausible one. Most hybrids are likely to be less fit, because they have never been tested by natural selection. However, some genotypes may be fitter than either parent. Indeed, that is to be expected if divergence involves several independent systems: a genotype combining one set of interacting genes from one parent, and one from the other, might well be superior. Particular hybrid genotypes are likely to be fit for another reason. Divergence is most likely to occur *via* a chain of relatively fit intermediates (Gavrilets, 1997; Orr, 1997); unless ancestral alleles have been lost, this can be reconstructed amongst hybrids. Environmental conditions may of course affect fitness, especially (but not exclusively) if divergence was driven by adaptation to divergent conditions. Rather than relying on such *a priori* arguments, Arnold concentrates on reviewing the evidence on hybrid fitness. This certainly does not show that hybrids are uniformly less fit, and in many cases suggest that they are the fittest class. However, there are problems. Measurement errors make it likely

that hybrids will often be classed as fittest; some statistical tests are needed. The 'hybrids' are sometimes F2 or backcrosses, and sometimes are collected from nature; the latter are expected to be fitter. The compilation in Table 1 is incomplete (for example, omitting *Podisma*, *Rana*, *Warramaba*, *Chorthippus*, and *Litoria* – Barton & Hewitt, 1985). Finally, many of these measurements are made in the laboratory. The inherent difficulties in measuring fitness make indirect arguments more compelling.

To understand what happens when divergent populations meet, one must think in terms of genes rather than genotypes: with sexual reproduction, there is no simple mapping of fitness onto abundance. Some individual alleles may be uniformly fitter, and will spread rapidly. Such introgression is inevitable, but may usually go undetected; the best examples come from bacteria, where genes for antibiotic resistance have spread between species that are highly divergent at other loci (Maynard Smith, 1990). Other genes may increase fitness only when in the right environment, or the right genetic background. They can then only be established if the whole gene combination is favoured in a large enough area, and becomes sufficiently frequent. Thus, even if a homozygous hybrid genotype is fitter, it may be very unlikely to be established in the face of gene flow and recombination. Arnold does not deal with this fundamental difficulty, largely because he thinks in terms of classes of 'hybrids', rather than genes and genotypes.

Arnold argues that for the most part, hybrid zones are not 'tension zones', maintained by 'endogenous' selection against hybrids, but rather, reflect 'exogenous' selection favouring hybrid genotypes in particular environments. It is important to appreciate that the question of how hybrid zones are maintained is separate from the question of whether some genotypes are fitter, and thus might be the source of novel species and adaptations. For example, crosses between two subspecies of the grasshopper *Chorthippus parallelus* give sterile F1 males, and yet no such sterility is seen in the field. This is because clines for the underlying loci are staggered, so that a fertile recombinant predominates in hybrid populations (Virdee & Hewitt, 1994). Provided this recombinant is not fitter than either parent (in which case it would spread over a wide area), epistasis can still maintain a narrow 'tension zone'.

The main weakness in Arnold's discussion of how hybrid zones are maintained is that he fails to separate two issues: first, whether there is a balance between selection and dispersal, and second, what kind of selection is acting. Thus, of his list of five features that are to be expected of a 'tension zone' (p. 123), four are also expected for a cline maintained by a balance between dispersal and 'exogenous' selection, which favours different genes in different places. Strong selection of any kind leads to steep clines ($\#$1);

dispersal will generate linkage disequilibrium (#4); clines will tend to be concordant as a result of linkage disequilibrium and (for neutral markers) shared history (#2); and fitness will be lower in hybrid populations because they include genes that are in the wrong place as well as the wrong genetic background (#5). One of the strengths (and also weaknesses) of the genetic analysis of hybrid zones is that it gives estimates of selection and gene flow that are independent of the mode of selection (Barton & Gale, 1993).

Arnold has written a clearly structured and stimulating review of current research on hybrid zones – especially valuable for its summary of his work on the Louisiana *Iris*, which gives us probably the best study of natural selection on field hybrids. My criticisms stem from the lack of a fully genetical perspective – a problem that afflicts most studies of hybrid zones. Despite Arnold's strictures against regarding diverse genotypes as simply 'hybrids', he himself thinks in terms of a limited number of classes defined by molecular markers. Such markers do give an exciting opportunity to study the genes responsible for reproductive isolation in nature. However, this will be a difficult enterprise, since field measures of fitness components suffer high environmental variance; existing methods for detecting quantitative trait loci must be extended to allow for epistasis and linkage disequilibrium; and any analysis must model interactions between individual genotypes that cannot be observed directly. *Natural Hybridization and Evolution* is a substantial step in the right direction; I hope it will encourage more studies that go beyond taxonomic description to a fuller understanding of the role of hybridization in evolution.

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*The Ecological Detective: Confronting Models with Data*. By RAY HILBORN and MARC MANGEL. Princeton University Press, 1997. 315 + xvii pages. Price £30.00 cloth, £16.95 paper. ISBN 0 691 03496 6; 0 691 03497 4 (pbk).

How should we judge the plausibility of our ideas about the world? This fundamental philosophical question took on quantitative form with the development of probability, and is the basic problem in statistical inference. It is remarkable that the idea of measuring chance by probabilities dates back only three centuries (Hacking, 1975), and that statistical inference was largely developed in this century. Indeed, even though hypothesis testing and estimation are the basis of so much of science, there still seems little agreement as to the merits of alternative approaches (Barnett, 1973). Perhaps because difficult and contentious arguments are involved, the whole issue is avoided in the statistics texts and courses which most scientists experience. As a result, most students have only a vague idea of one approach – the significance

test – and are unaware that they must choose from a range of fundamentally different philosophies.

This book is very welcome; it is the first I have seen that teaches the fundamentals of statistics and modelling in a thoughtful way. It grew from a work-shop in mathematical ecology, at which Hilborn and Mangel found that though most involved had experience in standard statistics, and in sophisticated modelling, they had little idea of how to connect the two: how to 'confront models with data'. The book alternates clear descriptions of the basic methods (sums-of-squares, likelihood and Bayesian techniques) with case studies ranging from management of hake fisheries in Namibia to predicting wildebeest numbers in the Serengeti. Rather than teaching recipes by rote, Hilborn and Mangel encourage the reader to work through simple computer examples, which illustrate how (and how not) to use these methods in practice. *The Ecological Detective* would thus best used as a class text: to really understand the issues, these simulated examples should be worked through. (To my mind, it is refreshing that the examples are given as simple algorithms, rather than as prepared code on a floppy disk which can be mindlessly spun.)

Though the examples are ecological, the book has much to offer any scientist – and, especially, geneticists. There is more of a tradition of using likelihood, simulation and Bayesian inference in genetics than in most fields – most notably, in gene mapping and human genetics. This tradition may be because genetical models are clearly defined, and often do not fit well with standard methods such as ANOVA. However, there is no book which shows how to deal with real data as clearly as *The Ecological Detective*, and the models of population dynamics are close enough to genetics to be easily accessible.

To be fully successful, this book really needs to be complemented by two others – which are to my knowledge not yet written. First, the reader needs to understand how to build mathematical models which are simple, yet capture the essence of the problem. This is a rare skill, which needs a good deal of mathematical insight even if the final model involves only simple algebra. Hilborn and Mangel give an excellent discussion of how to choose an appropriate range of models, but it is beyond the scope of their book to teach modelling as well as statistics. Second, the alternative statistical philosophies need to be understood. Hilborn and Mangel discuss these in some detail, but from a practical point of view; they also remain equivocal as to which approach they themselves prefer. Thus, the arguments are not laid out systematically, which could be confusing to any reader who thought too deeply about them. For example, Bayesian and likelihood approaches are discussed throughout, but the distinction between them is only made clear on p. 132. Edwards' (1992) *Likelihood* would be an excellent companion to Hilborn and Mangel but it would be good to see such clear statements of other philosophies. But do not wait until these hypothetical books are written: buy *The Ecological Detective*, read it and then confront your models with the data.

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