Book Reviews

Nature via Nurture

Matt Ridley
4th Estate, London, UK; 2003;
ISBN 1-84115-745-7; 328 pp.;
UK £19

Harper Collins, New York, USA;
ISBN 0-0600-0678-1; 326 pp.;
US$26

Ridley's follow-up to the success of 'Genome' (4th Estate, 2000) develops some of the themes introduced there. 'Genome' gave readers a grand tour of recent discoveries in genetics and genomics, traversing the individual chromosomes in turn. 'Nature via Nurture' is loosely organised around the lives and thoughts of '12 hairy men'; late 19th and early 20th century researchers (possessing between them a large amount of facial hair) whose thoughts have influenced the long-running nature/nurture debate. Its main theme is outlined in the title: many traits of human behaviour, and consequently features of human culture and society, have a basis in enabling genes (nature), but the development and expression of these traits depends on complex regulatory mechanisms that are to some extent under environmental control (nurture), including control by the brain. The dragon that Ridley seeks to slay is the widespread popular fear of a genetic basis for human nature, whose cause and/or symptom is the idea that genes are destiny, the enemies of choice and meliorism: that 'a gene for' X is an unalterable sentence to suffer, or benefit, from X.

The starting point is the announcement in February 2001 that the human genome has about 30,000 genes, far fewer than had previously been thought. Ridley attacks Venter for spilling the news in advance of the press embargo deadline, and for packaging it in a myth subsequently promulgated by many major newspapers — that the small number of genes kills off the idea of biological determinism and leads to the conclusion that our environments must be responsible for much of human diversity. Ridley rightly ridicules this conclusion, and explains that human complexity has little to do with the number of genes, or even the fact that alternative splicing means that there are many more protein products than genes. The key factor is the subtle interplay of genes, and their promoters and enhancers, in regulatory networks: it is not only what genes you have, but how and when they are expressed. Gene expression is affected not just by other genes but also by the environment, broadly defined to include diet and exercise, as well the social environment and the mother's womb, whose effects can have lasting consequences. Moreover, not only is gene expression also influenced by the brain, the brain itself works in part (in laying down memory) via gene expression responding to external signals.

Thus, nature and nurture are not opposing forces, but their effects are subtly intertwined. This conclusion is hardly new, but Ridley is able to draw on the latest science — thanks to conversations with a large number of leading scientists — to spell out some of the emerging details to a generalist, educated reader. He also weaves in an intelligent discussion of their implications for our understanding of our bodies and minds, our families and human society.

So far, so good. Where Ridley is on weaker ground is in his claim to be occupying a non-partisan middle ground between the proponents of 'nature' and 'nurture' respectively. He detours, at some length, to attack the 'blank slate' social scientists whose views held sway over most of the academic establishment for several decades following the downfall of eugenics, predominantly in the 1960s and 1970s. These attacks are entertaining and largely justified, if somewhat repetitive to readers of 'Genome'. By contrast with Dawkins, however, whose overt partisanship is refreshingly frank, Ridley's attempt to deny partisanship (that his sympathies lie more with the 'nature' than the 'nurture' camp) is unconvincing.

While I found 'Genome' a delight, for me 'Nature via Nurture' was interesting and informative but less successful in its more ambitious aims. The central point that gene expression matters and is influenced by environment is correct, important and not well understood by the general public, and so it is right that Ridley has taken some care to spell it out in detail. But it does not succeed as a unifying theme for his wide-ranging tour around modern genetic discoveries and their impact on the prevailing intellectual environment. For me, much of the text was fascinating but only distantly relevant to the thesis, and conversely I felt that the thesis was not sufficiently spelt out, independent of any illustration. For example, the dust jacket speaks of genes that '... absorb formative experiences, react to social cues ...' This reflects the text accurately, given an appropriate interpretation of 'absorb' and 'react'. These terms may be misunderstood as suggesting that the environmental effects on gene expression are somehow capable of being passed on over generations, however, and Ridley does not take care to clarify this point. This potential misunderstanding is especially evident in a paragraph on the 'Flynn effect' of increasing IQ over successive generations. Inevitably, given our current limited knowledge of gene regulation, the details are hard-going in places. Similarly, the picture is still sufficiently fuzzy that it is unsurprising if Ridley's thesis fails to unify and compel. Nevertheless, his tour through neurogenetics and developmental genetics, as well as the genetic basis of language, culture and society, and the related, recent intellectual history, is a must for anyone interested in keeping abreast of the latest understanding of ourselves, our genetic inheritance and our social environments.

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DNA Microarrays and Gene Expression — From Experiments to Data Analysis and Modelling

Pierre Baldi and G. Wesley Hatfield
Cambridge University Press, Cambridge, UK; 2002; ISBN 0-521-80022-6; 230 pp.; £35.00;Hardback;

Microarray technology permits the gene expression profiles of tens of thousands of genes to be compared in a single experiment. This, and the advent of a number of other high-throughput technologies, extends the methods available for studying biological systems and facilitates the collection of unprecedented amounts of data. Extracting knowledge and insights from these data requires interdisciplinary collaboration among biologists, statisticians and computer scientists. 'DNA Microarrays and Gene Expression — From Experiments to Data Analysis and Modelling' is the product of such an interdisciplinary collaboration between Hatfield, a microbiologist, and Baldi, who has a background in computational genomics and bioinformatics. The book has been written to promote exactly this type of collaboration, to foster the 'two-way flow of information and ideas between biologists and computational scientists' by providing in-depth descriptions of DNA microarray technologies and the computational methods appropriate for analysis of the data.

The book is intended for a wide readership, from those who have a background in the life sciences to those with a computational or statistical background, from researchers who have only a rudimentary understanding of gene expression analysis to those actively engaged in collaborative research. Most of the text is accessible by anyone with a basic understanding of biology or maths, although, as the authors acknowledge in the preface, full appreciation of the computationally or biologically technical sections is likely to require input from colleagues from other disciplines. This strategy, which could have been problematic, works surprisingly well, not least because of the authors' success in providing concise explanations that can be read at a number of levels, and by providing frequent 'take home' messages. For example, text describing use of the scaled inverse gamma distribution as a conjugate prior (the book has a distinctly Bayesian emphasis) is interspersed with sentences such as: 'If you are not familiar with gamma distributions, think of this prior as a bell-shaped distribution, restricted to positive values'. Similarly, sections on molecular reactions begin with the Michaelis–Menten equation and an analogy between regulators of multiple genes as 'hubs' in maps that show the flight paths of aeroplanes from well-connected airports.

The book covers a wide range of subject areas, extending from a brief history of genomics in Chapter 1, through methods and instrumentation in Chapters 2 and 3, statistical data analysis in Chapters 4 to 7 and systems biology in Chapter 8. The first two chapters on statistical analysis of microarray data include standard topics such as inferring changes, dimensionality reduction, clustering, experimental design and interpretation, with the third chapter providing an example drawn from the authors' own research. This layout has the advantage that data analysis topics are presented in a logical sequence in Chapters 5 and 6 and are revisited within the context of the application and validation of the methods in Chapter 7. Appendices provide detailed experimental protocols, information on use of the authors' CyberT software and mathematical complements to the chapters on statistical analysis.

The strengths of the book are that it draws extensively on the expertise of its authors, includes a number of examples from their own research and has a cohesion suggesting that the authors collaborated closely on the text. This also means that there is a strong emphasis on both bacterial systems and Bayesian approaches to data analysis. Few books on microarray data analysis have discussed the merits of the Bayesian approach (for example, for the identification of differentially expressed genes) for a general audience, and their justification for this approach is very persuasive. Given that the merits of the Bayesian versus 'frequentist' approach are actively debated within the community of statisticians carrying out microarray data analysis, however, it would be interesting to have the counter argument presented. The authors' biases also represent a (minor) weakness. Discussion of basic problems that challenge researchers working on higher eukaryotes, such as cell-type heterogeneity and the problems of using micro-dissected tissue, might have been expected, as well as more detailed discussion of approaches to normalisation, for example Lowess or quantile-based methods.

Books such as these will increasingly be needed as the volume and complexity of biological data escalates. More researchers, from a widening variety of disciplines, will need to gain a conceptually sophisticated level of understanding of each other's subject areas, to facilitate critical interactions and stimulate yet more relevant and insightful means of data interpretation. Writing a book such as this was a challenging remit and one that the authors have achieved with great success.

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