

Fisher the evolutionary biologist

Alan Grafen

University of Oxford, UK

[At a meeting to commemorate the unveiling of a plaque to R. A. Fisher at Inverforth House, Hampstead, London, on May 17th, 2002]

Summary. Fisher's pioneering work in linking Darwinism and Mendelism is now built into biology, but the result that he viewed as holding the 'supreme position in biology', the fundamental theorem of natural selection, has a more chequered history. Recent work has shown the theorem to be true, despite many earlier refutations, but its interpretation has been in doubt. I defend Fisher's own evaluation of its significance and argue that it shows that non-random gene frequency changes are always adaptive, and that adaptation arises only through gene frequency changes: this *is* Fisher's 'genetical theory of natural selection'.

Keywords: Adaptation through gene frequency change alone; Fundamental nature of fundamental theorem; Genetical theory of natural selection; Licensed anthropomorphism; Truth of fundamental theorem

1. Introduction

I am proud and a little overwhelmed to have been asked to talk about Sir Ronald Fisher the evolutionary biologist, and I begin by expressing my gratitude to the Royal Statistical Society and to Professor Senn for inviting me.

I first read Fisher in the summer of 1975, in Sussex University Library. The *Genetical Theory of Natural Selection* was on my undergraduate reading list, set by my tutor Richard Dawkins. I felt an immediate attraction and interest in the book. Within a few months I was the proud possessor of my own copy of the 1958 edition, and it has formed a central part of my biological consciousness ever since. Later, about 1980, I met a young Australian biologist called Andy Bennett, and I said to him in jest 'no relation to the Bennett who published Fisher's collected papers, I suppose'. He replied 'Yeah, that's my da!' and went on to say that copies of the collected papers were still available. A few months later, and for the princely sum of AUS \$70, I became the proud possessor of the five volumes of Fisher's collected papers. I even make the proud boast that I have read them all.

The fascination of Fisher for me is that my research is mainly in evolutionary biology, which involves a certain amount of genetics from time to time, and I teach and have done some research in statistics. So I look to Fisher as a founding father in all three of the disciplines that we are celebrating. I must warn you that I am a Fisher fanatic and believe him to have been right about nearly everything in statistics, genetics and evolutionary biology.

It is evolutionary biology that I have been asked to speak about, and we should therefore begin with Darwin. Fisher Box (1978) tells us in her biography of her father that on his shelves when he went up to Cambridge as an undergraduate in 1909 were the complete works of Charles Darwin in 13 volumes, and it is clear that his knowledge of and appreciation of Darwin played

Address for correspondence: Alan Grafen, St John's College, Oxford, OX1 3JP, UK.
E-mail: alan.grafen@st-johns.oxford.ac.uk

a crucial role in Fisher's life work. The boundary between evolutionary biology and genetics is a grey one, and there is therefore a danger of overlap between Professor Edwards and me. But a good starting-point for a delineation of that boundary is to say that questions Darwin would have understood belong to evolutionary biology, whereas questions that rely on knowledge of chromosomes and deoxyribonucleic acid count as genetics.

We can apply this principle to the discussion of Fisher (1915) on the evolution of sexual preference, in which he introduces the famous runaway process. Sexual selection, of course, was the subject of Darwin's book of 1871 (Darwin, 1981). We see peacock's tails and hear black-bird song, and Darwin discussed both in the *Descent of Man*. Fisher's (1915) runaway process is a potential explanation of those biological phenomena and is therefore evolutionary biology.

A more conceptually fundamental paper emerged in 1918, the famous 'Correlation between relatives on the supposition of Mendelian inheritance' (Fisher, 1918). One question at issue in this paper is Fleeming Jenkin's objection to natural selection (Jenkin, 1867). Fisher triumphantly shows that Mendelian segregation results in the maintenance of variation and solves what Darwin himself viewed as the major outstanding difficulty with his theory. Darwin would certainly have understood the conclusion, and so this paper also counts as evolutionary biology. In both sexual selection and the correlation between relatives, Fisher used genetics to help to understand a biological question. Thus, genetics is never out of the frame—the question is whether genetics itself is the focus of attention, or whether it is playing a crucial but supporting role in the exploration of evolutionary biology.

The difference between evolutionary biology and genetics can be illustrated, literally, from the editions of *The Genetical Theory of Natural Selection*, Fisher's main opus in evolutionary biology. The frontispiece of Fisher (1930) shows some butterflies involved in mimicry systems (Fig. 1). Bates developed his theory of mimicry in 1861 (published in Bates (1862)), influenced by the *Origin of Species* published 2 years earlier. Darwin corresponded extensively with Bates and wrote after reading his publication

'I rejoice that I passed over the whole subject in the *Origin*, for I should have made a precious mess of it. You have most clearly stated and solved a wonderful problem'

(Burkhardt *et al.* (1997), page 540). Bates's ideas were included in the fourth edition of the *Origin of Species*. By our Darwinian test, then, mimicry is certainly evolutionary biology rather than genetics, and it is revealing that Fisher chose it as the frontispiece of his 1930 book. The second edition (Fisher, 1958) had a cover that we can put alongside (Fig. 2). This diagram shows phenotypes, lines of descent and the phenotypic effect of underlying genes. The publishers, Dover, clearly viewed the book as a book about genetics.

I am pleased and not surprised that Henry Bennett's *variorum* edition (Bennett, 1999) has butterflies on its cover (Fig. 3).

This determination to use genetics to support Darwinian biology was unusual among geneticists and was prosecuted by Fisher much further than by anyone else. His great contemporary Sewall Wright was a consummate geneticist. He was primarily concerned with genetics, with gene frequencies, linkage disequilibrium, epistasis, mutation and so on. Fisher was primarily concerned in his evolutionary work with sexual selection, mimicry, warning coloration, sex ratios, sexual reproduction and the heroic virtues, all Darwinian concerns.

My main theme so far has been the distinction between evolutionary biology and genetics. The same material can be viewed in another way, as showing the fundamental role that is played by statistics in Fisher's work. In Fisher (1918) he introduced into the statistical literature the term 'variance':

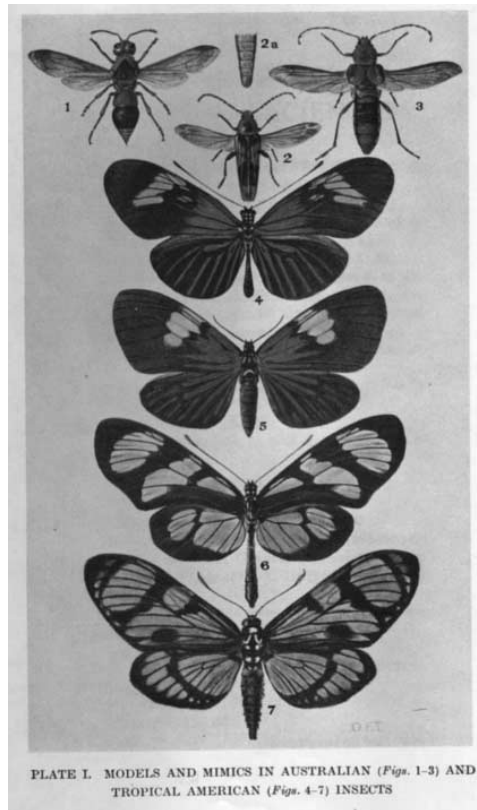


Fig. 1. Frontispiece of the first, 1930, edition of the *Genetical Theory*, which uses mimicry to emphasize the biological focus of the book

‘When there are two independent causes of variability capable of producing in an otherwise uniform population distributions with standard deviations σ_1 and σ_2 , it is found that the distribution, when both causes act together, has a standard deviation $\sqrt{\sigma_1^2 + \sigma_2^2}$. It is therefore desirable in analysing the causes of variability to deal with the square of the standard deviation as the measure of variability. We shall term this quantity the Variance of the normal population to which it refers, and we may now ascribe to the constituent causes fractions or percentages of the total variance which they together produce.’

This is a paper about the genetic underpinning of the maintenance of biological variability, resolving the outstanding issue in Darwinism, and the term variance first appears, along with the essential idea of partitioning that Fisher was to develop into the analysis of variance. How seamless indeed was Fisher’s work, which in this celebratory meeting we have divided into three!

2. The fundamental theorem of natural selection

But there is no doubt what Fisher considered to be his main contribution to evolutionary biology. As well as using genetics to support evolutionary biology, it employs statistics in an essential way. Combining, therefore, all three of the disciplines that we are celebrating, Fisher created his ‘Fundamental theorem of natural selection’, which must surely form the centre-piece of an encomium of this kind.

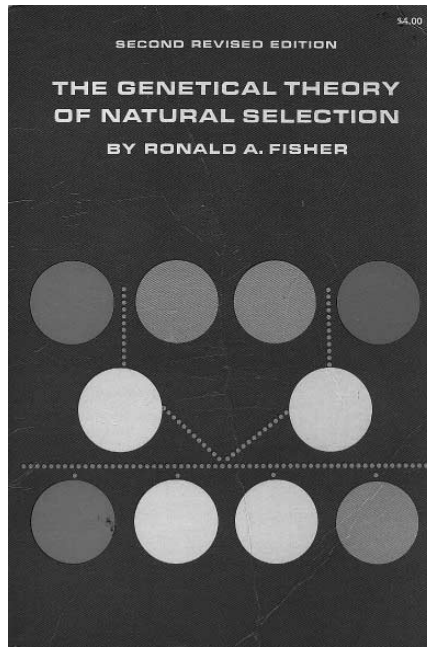


Fig. 2. Front cover of the Dover, 1958, edition of the *Genetical Theory*, which uses a simple Mendelian family tree to emphasize the genetical methodology of the book

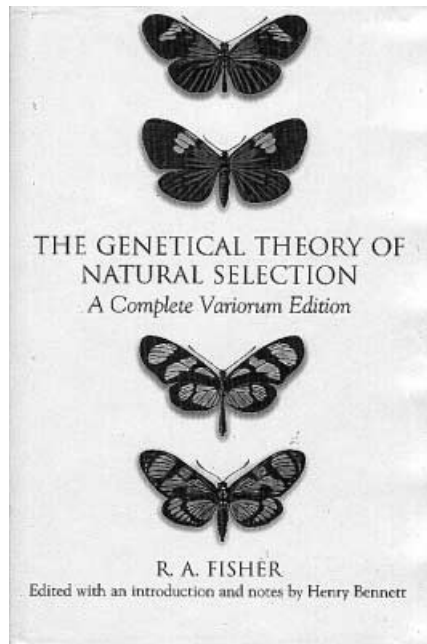


Fig. 3. Front cover of the *variorum*, 1999, edition of the *Genetical Theory*, which employs mimicry to restore the emphasis on the biological focus of the book

It may be an understatement to say that Fisher believed the fundamental theorem to be his main contribution to evolutionary biology. I suspect that he believed it to be the main contribution that anyone would ever make to evolutionary biology. However, I would characterize the modern evolutionary biologist's view of the fundamental theorem as a combination of 'what is that?' and 'is it not only an approximation?' and 'of historic interest only'. Putting these two views together, Fisher's and most of today's biologists', we have what might be called the fundamental enigma of Fisherian evolutionary biology.

It seems fitting, on an occasion to commemorate Fisher, to take seriously his own views about the significance of his work, and my aim is to persuade you at least that Fisher was much more nearly right than most modern biologists. I will make a further effort, which may carry fewer of you with me, to claim that Fisher was also absolutely right about the significance of his masterpiece.

The reception of the fundamental theorem was extraordinary. At this point I must acknowledge a debt to Professor Edwards, who has virtually written my talk for me. He has published an authoritative and fascinating account of the story up to then of the reception of the fundamental theorem (Edwards (1994); see also Frank (1997, 1998)) and also an important piece on the *Genetical Theory* more generally (Edwards, 2000). Let me give you a brief summary, suitable only for the narrow purposes of this argument, of Professor Edwards's marvellous paper. Fisher published the theorem in 1930, and it was virtually ignored at the time. When it was discussed later, it was seriously misrepresented. If your understanding of the theorem comes from reading Fisher himself, you should be aware that virtually no other biologists have understood what he meant. If you have encountered Karlin and Feldman's use of it, in remarks such as 'it appears that these attempts to save the fundamental theorem are quite pointless' (Karlin and Feldman, 1970) and 'we can say that the FTNS mostly fails' (Karlin, 1975) and in sections with headings such as 'Nonvalidity of the fundamental theorem of natural selection' (Karlin, 1975), be aware that they did not understand it. If there is a vague association in your mind between the fundamental theorem, \bar{w} increasing, Sewall Wright's adaptive landscapes, and hill climbing, be aware that Sewall Wright never understood the theorem, and that Fisher firmly denied the usefulness of adaptive landscapes and the inevitability of the climbing of hills. Most population genetics text-books either ignore the fundamental theorem or get it quite wrong.

So much for the sources of misunderstanding. Where is the path of enlightenment towards the fundamental theorem? It begins with Price (1972). Price was an American genius and eccentric who worked in biology for only a handful of years but made extraordinary contributions. One day, plaques will be unveiled to George Price. He explained what Fisher meant by the theorem and exhibited a tidied-up version of the derivation that proved the theorem to be indeed true as stated, and Fisher's derivation to be valid. But Price's paper itself was virtually ignored until Warren Ewens, having travelled to Damascus (see Ewens (1979)), wrote a further paper in 1989, which discussed Price's work, and derived extensions of the fundamental theorem, including to discrete time (Ewens, 1989). This succeeded in bringing the true version to more general notice, about 59 years after its first publication.

But I am trying your patience, by discussing the theorem without saying what it is. Fisher's original published version, in the eponymous *Genetical Theory of Natural Selection*, in 1930, was 'the rate of increase in fitness of any organism at any time is equal to its genetic variance in fitness at that time'. This appears to say that mean fitness can never decrease, as variances cannot be negative. This misinterpretation led Wright to invent his adaptive landscape, his flawed attempt to focus for once on evolution rather than on genetics. What, then, is the correct understanding of the fundamental theorem? The major point is that the rate of change in fitness on the left-hand side is not the total rate of change in fitness, but, as Fisher makes clear in the

original, only one component of the total rate of change. This partial rate of change is the part that can be ascribed to changes in gene frequencies.

What can this mean? The total rate of change in mean fitness can be viewed as due to a variety of forces, such as gene frequencies themselves, and ‘other forces’, namely segregation of those genes into genotypes, and environmental change, as well as the allocation of the genotypes to different parts of the environment. All the effects of epistasis and dominance and linkage are present in the ‘other forces’. Now Fisher seriously intended to isolate gene frequency changes from other changes in the genetic constitution and environment of the species. Henry Bennett quotes Fisher in his introduction to Bennett (1999) as follows:

‘if by extinction of certain insects a plant were rapidly to become generally self-fertilised and homozygous through lack of means to cross-pollination, I should, so long as the gene ratios remained unchanged, consider that the plant had not evolved but was responding passively to its changed environment’

(letter to O. Kempthorne in 1955, quoted on page xiii of Bennett (1999); letter published on page 228 of Bennett (1983)). So Fisher was serious about isolating the effect of gene frequency changes, and the left-hand side of the fundamental theorem, ‘the rate of increase in fitness’, is a certain kind of partial change in the mean fitness of a population, but we can ask how is this isolation to be done? Can this partitioning between the effect of gene frequency changes and the ‘other forces’ really be made precise? Fisher borrows from his own statistical work on multiple regression such as from Fisher (1922). We have for each individual a fitness, which will be considered as the dependent variable. We also have a list of the alleles that are present in that individual, which will be considered as independent variables. In technical terms, we have a dummy variable for each allele in the population. The entry for an individual contains the number of copies of that allele that she has.

We regress fitness on those dummy variables and obtain parameter estimates and fitted values in the usual way. The fitted values from this regression are the predicted fitnesses or, as they are nowadays known in genetics, the additive genetic values of fitness. We also have the coefficients for each allele (there is some aliasing, of at least one parameter per locus). We take the rate of changes of gene frequencies, then use the regression coefficients to predict what the rate of change in mean fitness is, on the assumption that those coefficients stay the same over time. And that is the partial rate of change of mean fitness.

This was the major revision that Price introduced. On the right-hand side, we need only to notice that the word ‘genetic’ would now be written ‘additive genetic’ or ‘genic’, just because words change their meaning over time. These terms both refer to the additive model that has just been described. Nowadays ‘genetic’ would refer to a model in which parameters were estimated for whole genotypes, and not for the alleles separately. For modern scientists lacking Fisher’s classical education, presumably, the ‘t’ in genetic makes it seem to be the adjective for genotype rather than for gene.

Here, then, is the theorem in modern terms suggested by Edwards (1994):

‘The rate of increase in the mean fitness of any organism at any time ascribable to natural selection acting through changes in gene frequencies is exactly equal to its genic variance in fitness at that time’.

Having proved it to be true, what did Price and Ewens make of it? They viewed the theorem as a valiant and valuable attempt to find an expression for the total rate of change in fitness. They saw the ‘partial’ aspect of the theorem in terms of its incompleteness. Ewens (1992) and more recently Lessard (1997) have tried to develop the fundamental theorem by completing it.

The verdict so far, then, is that the theorem is true but not so fundamental or, at the very least, in need of strengthening. Edwards (1994) quotes Nagylaki in 1991 as saying

‘the biological significance and analytical usefulness of the partial change in fitness remain to be demonstrated. . . . Fisher’s assertion is a theorem but does not seem to provide any fundamental insight into evolution under natural selection.’

3. The significance of the fundamental theorem

While preparing this paper, I have come to believe that Fisher was right in his beliefs about the importance of the theorem, and that the modern ‘completers’, to coin a term, are barking up the wrong tree or, at least, are barking up a non-Fisherian tree.

Fisher had a grand view of evolution, and we have already seen that his main interest in evolutionary biology, and I dare to say his main interest in genetics also, was providing an underpinning in genetical terms for Darwin’s ideas about natural selection. Indeed, the title of his book was *The Genetical Theory of Natural Selection*. Darwin’s natural selection *informally* was that fitter organisms left more offspring; their offspring resembled those parents, and so the population came to resemble the fittest forebears. Fisher was perfectly aware that population genetics was more complicated than that, and that mean fitness could, like the value of modern investments, go up or down. Come to think of it, as Fisher was writing in 1929, the value of investments was plummeting throughout the western world. Where, in the complexities of population genetics models, could he find an expression of Darwin’s principle of natural selection? In my view, Fisher thought that his fundamental theorem isolated what we might call the adaptive engine of Darwinian natural selection.

Thus the partial nature of change is not an inability to find a stronger result. Fisher believed that this partial change was the only aspect of the changes in a population’s genetic constitution that was progressive, that could create design. Environmental change, of course, generally messes things up, presenting new challenges, and demanding new responses. Fisher explicitly lumps the segregation of genes into genotypes with environmental change as non-adaptive, as non-design-creating.

We can write an interpretation of the fundamental theorem as stating that

‘Non-random changes in gene frequency always change mean fitness positively. No other aspect of the genotypic changes of a population has a systematic optimizing tendency.’

Can we make this interpretation in a more formal mathematical way? I believe that we can (Grafen, 2002). The essential technical point is this. Population genetics uses the mathematics of motion, with difference or differential equations tracking gene and genotype frequencies. Nowadays, we study design and optimization with optimization programs, as used in economics, game theory and operations research. The interpretation of the theorem can be made precise by proving links between the mathematics of motion and the mathematics of optimization, expressing in a formal way Fisher’s connection between population genetics and Darwinian design.

I have a suggestion about the fundamental enigma of the misapprehension of the fundamental theorem, at least from 1970 onwards. The idea of optimization was an acceptable part of the operation of population genetics in the 1950s and 1960s, but it became increasingly frowned on because the arguments based on optimization were dynamically insufficient. This was one of the arguments of Lewontin (1974). Thus ideas of optimization, which I have argued are key to understanding the meaning and importance of the fundamental theorem, became methodologically disapproved of.

Returning to the theorem, under my suggested interpretation it is of great interest. If we consider the differences between humans and chimpanzees, the non-random differences in gene frequencies must all be due to natural selection. If we thought species differences might be due to segregational differences, or to environmental differences, this result might be disappointing.

But I am sure that the majority view is that we differ from chimpanzees because gene frequencies have changed, and that our differences in height, hairiness, gait and encephalization are down to changes in gene frequency, not to changes in segregation.

Now Fisher used his fundamental theorem in various ways in his book and subsequently. The major effect was that he used it as a licence for regulated anthropomorphism. He discussed organisms as acting to maximize their fitness as though, in line with our discussion of optimization programs, they were rational creatures maximizing a utility function.

Let us ponder this licence a little. Why is a licence needed? Anthropomorphism has been a besetting sin of biologists and others for centuries in understanding organic design. It is essential for a materialist explanation of design to avoid requiring a ghost in the machine. Yet it is also virtually impossible to discuss design without using terms of purpose, so-called intentional terms. To say the eye is *for* seeing is to invoke intention, just as to say that the kidney *processes* waste products, the liver *regulates* blood sugar, or the eye blink is a reflex *to protect* the eye. But a good materialist needs an excuse for using intentional terms, unavoidable though they are, and a good excuse, a written and logically argued excuse, may be called a licence.

In what sense does the licence regulate the anthropomorphism? For one thing, it tells us exactly what is being maximized. The fundamental theorem tells us what it is that the design-creating capacity of evolution regards as good design. It must increase the partial fitness of the individual: not the individual's longevity, or happiness, or intelligence or complexity. There is no scope for Teilhard de Chardin's increase in consciousness here, or for Lamarck's striving of a species, or indeed for group selection in which the group benefit is favoured. Thus the precise form of the theorem matters for the nature of the licence. We see from a section added in Fisher (1958), entitled 'The benefit of the species', that Fisher was explicitly making the point about group selection, essentially answering the question: what is the organism's maximand under natural selection?

Fisher published a game theory analysis of the card game *Le Her* in 1934, finding a Nash equilibrium before Nash (though not before William Waldegrave, who found the same solution in 1713; see Hald (1990)), and showing that it was a mixed, or randomized, strategy (Fisher, 1934). Fisher was therefore familiar with game theory calculations of rational creatures, and when he discussed organisms maximizing their fitness he was clearly thinking in those terms.

Regarded as a licence for regulated anthropomorphism, Fisher's theorem flourished. Taking their cue perhaps from the general sense of the theorem, but mainly perhaps from Fisher's consequent willingness to discuss the design of organisms in terms of optimization, evolutionary biologists took up Fisher's licence with enthusiasm. Hamilton (1964) developed inclusive fitness and also his idea of 'unbeatable strategies'. Maynard Smith and Price (1973) invented the theory of evolutionarily stable strategies. Game theory in particular was not technically linked to the fundamental theorem, but I regard inclusive fitness and the theory of evolutionarily stable strategies as parts of a Fisherian tradition of treating individual organisms as optimizing agents.

I mentioned earlier a research project of my own. Until preparing this paper, I did not realize quite how much I was building on the fundamental theorem. What building is necessary? Why is it not already complete? Fisher's derivation makes various assumptions that rule out some later developments, and I shall give three examples. First, it assumes that an individual's fitness depends on its own genotype and not on the genotypes of others. This assumption rules out for one thing the study of social behaviour, including parental care. Hamilton (1964) invented inclusive fitness as a generalization of the fundamental theorem, in which one individual's fitness is allowed to depend in a very general way on the genotypes of others. Second, Fisher's derivation is at least not explicit about frequency dependence, i.e. the fitnesses depending on gene or genotype frequencies. Game theory in biology creates frequency dependence of the fitnesses

of genotypes. Thus we can extend Fisher's derivation and theorem by permitting frequency dependence of the fitnesses. As a final example, Fisher's fitnesses were fixed. But the study of stochastic environments raises questions about whether the arithmetic or geometric mean of fitness is maximized. By allowing random fitnesses, the fundamental theorem can be brought into play (see Grafen (1999, 2000)).

In all three of these possible extensions, biologists have sought an optimization principle, and it is by following the logic of the fundamental theorem, but relaxing its assumptions appropriately, that we can most effectively provide one.

In conclusion on the theorem, the theorem was fundamental in 1930 because it isolated the adaptive engine in evolution and made an extraordinary link between gene frequencies and adaptive change. It really did show how Darwinian natural selection worked simply and consistently and persistently amid the maelstrom of complexities of population genetics. The theorem is just as important today for that reason. This is not popularly realized by biologists because most take for granted an informal sense that natural selection leads to organisms maximizing their fitness, but they do not ask how that sense can be justified. Furthermore, I claim that the right way forward in developing and justifying optimization approaches in biology is extending and developing the fundamental theorem.

4. Eugenics

One topic is left that should be mentioned, and that is Fisher's espousal of eugenics. The final five chapters of Fisher (1930) deal with selection in humans, and Fisher considered these an essential part of the whole. Today's biologists do not much read those chapters, I guess partly because of fear, essentially of social Darwinism and through an association with genocide, and partly because we are narrower technicians now and tend to suspect grand altruistic applications of our subjects. There is so much still to emerge from chapters 1–8 of Fisher (1930) that it would be surprising if a close study of the remaining, largely neglected, chapters did not yield important ideas.

Fisher's discussions of eugenics always strike me as idealistic and hopeful and intelligent, and I cannot fully explain why I am unpersuaded by them. But it may be of interest that Fisher's great successor in evolutionary biology, W. D. Hamilton, also held strong eugenic beliefs. You can read them in the recently and posthumously published second volume of Hamilton (2001). I find them similarly difficult to assimilate. Perhaps a historian of science will explain to us why the views of these great evolutionists are not shared by their many admirers and followers; and perhaps it will be a historian of science at a sufficiently distant date that they can view us as well as Fisher and Hamilton with historical distance.

5. Conclusion

How, then, to conclude, would Fisher have liked to be remembered as an evolutionary biologist?: as Darwin's mathematician, as the reconciler of Darwinism and Mendelism, and as the discoverer of the first consistent 'Genetical theory of natural selection', namely his fundamental theorem.

I end with tributes from Hamilton and Darwin. Hamilton's tribute is direct and is found on the back cover of Bennett (1999). It is much quoted, and rightly so, as a tribute of one great evolutionist to his immediate predecessor. For those of you who do not know, I should warn you that it is especially poignant, as Bill died tragically early, within a year of the publication of this tribute:

‘This is a book which, as a student, I weighed as of equal importance to the entire rest of my undergraduate Cambridge BA course and, through the time I spent on it, I think it notched down my degree. Most chapters took me weeks, some months. . . . And little modified even by molecular genetics, Fisher’s logic and ideas still underpin most of the ever broadening paths by which Darwinism continues its invasion of human thought.’

‘Unlike in 1958, natural selection has become part of the syllabus of our intellectual life and the topic is certainly included in every decent course in biology. By the time of my ultimate graduation, will I have understood all that is true in this book and will I get a First? I doubt it. In some ways some of us have overtaken Fisher; in many, however, this brilliant, daring man is still far in front.’

Darwin’s tribute must, obviously, be indirect, as Fisher was born in 1890 and Darwin died 9 years earlier. The passage is taken from Darwin’s autobiography, and is about his struggle with mathematics.

‘I attempted mathematics, and even went during the summer of 1828 with a private tutor (a very dull man) to Barmouth, but I got on very slowly. The work was repugnant to me, chiefly from my not being able to see any meaning in the early steps in algebra. This impatience was very foolish, and in after years I have deeply regretted that I did not proceed far enough at least to understand something of the great leading principles of mathematics; for men thus endowed seem to have an extra sense’

(quoted in Burkhardt and Smith (1985), page 63).

In reading Fisher, ‘an extra sense’ is a phrase that often springs to my mind, and it is that mathematician’s sense which Darwin coveted. In Fisher it was present to an extraordinary degree. Fisher’s chief aim in his evolutionary work was to employ that extra sense in the development of Darwin’s idea of natural selection. We are only today beginning to appreciate the extent to which Sir Ronald Fisher fulfilled that noble aim.

References

- Bates, H. W. (1862) Contributions to an insect fauna of the Amazon valley: Lepidoptera: Heliconidae. *Trans. Linn. Soc.*, **23**, 495–515.
- Bennett, J. H. (ed.) (1983) *Natural Selection, Heredity and Eugenics (including Selected Correspondence of R. A. Fisher with Leonard Darwin and Others)*. Oxford: Oxford University Press.
- Bennett, J. H. (ed.) (1999) *The Genetical Theory of Natural Selection, variorum* edn. Oxford: Oxford University Press.
- Burkhardt, F., Porter, D. M., Harvery, J. and Topham, J. R. (1997) *The Correspondence of Charles Darwin*, vol. 10, 1862. Cambridge: Cambridge University Press.
- Burkhardt, F. and Smith, S. (1985) *The Correspondence of Charles Darwin*, vol. 1, 1821–1836. Cambridge: Cambridge University Press.
- Darwin, C. R. (1981) *The Descent of Man and Selection in Relation to Sex*, facsimile edn. Princeton: Princeton University Press.
- Edwards, A. W. F. (1994) The fundamental theorem of natural selection. *Biol. Rev.*, **69**, 443–474.
- Edwards, A. W. F. (2000) The genetical theory of natural selection. *Genetics*, **154**, 1419–1426.
- Ewens, W. J. (1979) *Mathematical Population Genetics*. Berlin: Springer.
- Ewens, W. J. (1989) An interpretation and proof of the Fundamental Theorem of Natural Selection. *Theoret. Popln Biol.*, **36**, 167–180.
- Ewens, W. J. (1992) An optimizing principle of natural-selection in evolutionary population-genetics. *Theoret. Popln Biol.*, **42**, 333–346.
- Fisher, R. A. (1915) The evolution of sexual preference. *Eugen. Rev.*, **7**, 184–192.
- Fisher, R. A. (1918) The correlation between relatives on the supposition of Mendelian inheritance. *Trans. R. Soc. Edinb.*, **52**, 399–433.
- Fisher, R. A. (1922) The goodness of fit of regression formulae, and the distribution of regression coefficients. *J. R. Statist. Soc.*, **85**, 597–612.
- Fisher, R. A. (1930) *The Genetical Theory of Natural Selection*. Oxford: Oxford University Press.
- Fisher, R. A. (1934) Randomisation, and an old enigma of card play. *Math. Gaz.*, **18**, 294–297.
- Fisher, R. A. (1958) *The Genetical Theory of Natural Selection*, 2nd edn. New York: Dover Publications.
- Fisher Box, J. (1978) *R. A. Fisher: the Life of a Scientist*. New York: Wiley.
- Frank, S. A. (1997) The Price equation, Fisher’s fundamental theorem, kin selection, and causal analysis. *Evolution*, **51**, 1712–1729.

- Frank, S. A. (1998) *Foundation of Social Evolution*. Princeton: Princeton University Press.
- Grafen, A. (1999) Formal Darwinism, the individual-as-maximising-agent analogy, and bet-hedging. *Proc. R. Soc. Lond. B*, **266**, 799–803.
- Grafen, A. (2000) Developments of the Price equation and natural selection under uncertainty. *Proc. R. Soc. Lond. B*, **267**, 1223–1227.
- Grafen, A. (2002) A first formal link between the Price equation and an optimisation program. *J. Theoret. Biol.*, **217**, 75–91.
- Hald, A. (1990) *A History of Probability and Statistics and Their Applications before 1750*. New York: Wiley Interscience.
- Hamilton, W. D. (1964) The genetical evolution of social behaviour. *J. Theoret. Biol.*, **7**, 1–52.
- Hamilton, W. D. (2001) *Narrow Roads of Gene Land*, vol. 2, *Evolution of Sex*. Oxford: Oxford University Press.
- Jenkin, F. (1867) Review of Darwin's *The Origin of Species*. *N. Br. Rev.*, **46**, 277–318.
- Karlin, S. (1975) General two-locus selection models: some objectives, results and interpretations. *Theoret. Popln Biol.*, **7**, 364–398.
- Karlin, S. and Feldman, M. W. (1970) Linkage and selection. *Theoret. Popln Biol.*, **1**, 39–71.
- Lessard, S. (1997) Fisher's fundamental theorem of natural selection revisited. *Theoret. Popln Biol.*, **52**, 119–136.
- Lewontin, R. C. (1974) *The Genetic Basis of Evolutionary Change*. New York: Columbia University Press.
- Maynard Smith, J. and Price, G. R. (1973) The logic of animal conflict. *Nature*, **246**, 15–18.
- Price, G. R. (1972) Fisher's "fundamental theorem" made clear. *Ann. Hum. Genet.*, **36**, 129–140.