NATURAL SELECTION, HEREDITY, AND EUGENICS

Including selected correspondence of R.A. Fisher with Leonard Darwin and others

Edited with an introduction
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PREFACE

This volume consists of a selection from R.A. Fisher's letters on natural selection, heredity, and eugenics, along with such comments and other material as are required for the elucidation of the correspondence and for giving continuity to the whole.

The structure of the book has been greatly influenced by Fisher's extensive correspondence with Leonard Darwin over more than 20 years. Many of their letters in the period 1915-29 were concerned with questions later considered in Fisher's book *The genetical theory of natural selection* (1930). This fact and the considerable influence of that book on much of the other correspondence have necessitated a somewhat lengthy introduction. Chapter 1 is concerned with the circumstances in which *Genetical theory* was written, its main features, the reception it was given, and its impact on evolutionary thought. Chapter 2 contains two unpublished papers by Fisher from 1911-12 dealing with Mendelism, biometry, and selection. The Darwin-Fisher letters, separated into pre- and post-*Genetical theory* periods, are presented in Chapters 3 and 4, respectively, and Fisher's letters to other correspondents in Chapter 5. Fortunately, it has been possible to add to the interest of this material by including in Chapters 3 and 4, extracts from Darwin's letters to Fisher and, in Chapter 5, some relevant correspondence from a few of the eminent individuals to whom Fisher was writing. Before 1930 Fisher had very little correspondence on natural selection and heredity with anyone other than Darwin, whereas after *Genetical theory* was published, various readers wrote with questions and comments stemming from the book. A number of Fisher's letters in Chapters 4 and 5 may be seen as providing an extension or elaboration of arguments contained in *Genetical theory*. Of the four appendices in the present volume, A and C comprise reprints of two reviews by Fisher referred to in the text, whilst B and D contain material hitherto unpublished—a review by Fisher of J.B.S. Haldane's book *The causes of evolution* and Fisher's last paper on natural selection which he read at a meeting in Adelaide in 1959. In this article he contrasts the scope and magnitude of Charles Darwin's achievements with the work of those who are still sometimes put forward as the progenitors of his ideas.

A graphic description of how *Genetical theory* was written has been given by Joan Fisher Box (1978) in her outstanding biography of her father, *R. A. Fisher. The life of a scientist* (John Wiley, New York).

Like his other genetical work, it was done at home with his wife. He would stride about the room, or mull over a pipe, as he dictated and she took down his words in

> longhand ... Fisher seemed to know exactly what he wished to say, holding the whole ordered argument in his head, and even his deliberation over the detailed expression of his thoughts did not often give pause to the pen of his amanuensis. Yet, once he had set a passage down on paper, he rarely changed a word or needed to rearrange the order or insert omissions. His capacity to hold in mind the numerous details of a complex argument was remarkable, as was his precision in expressing what he meant.

This passage could equally well describe Fisher dictating letters to his secretary. The letters provide a fascinating record of one of the most brilliant intellects in modern evolutionary biology discoursing in characteristic manner on numerous subjects, many of them complex, with great care, precision, and some subtlety, and showing at the same time much good humour and charm.

The Darwin-Fisher letters are presented in chronological order but the letters in Chapter 5 are arranged, for ease of reference, in alphabetical order according to the names of the correspondents. My object when selecting correspondence has been to include material of scientific or historical interest, avoiding unnecessary repetition and personal references of no scientific relevance. Editorial insertions in the correspondence have been kept to a minimum; such material is shown in square brackets. When a word or passage has been omitted, this is indicated by the symbol ... . Occasional changes in punctuation or spelling have been made without comment.

I am indebted to Lady Barlow and Professors E.B. Ford and S. Wright for their gracious permission to reproduce material from their letters to Fisher as shown in Chapter 5; to Lady Barlow and Professor H.B. Barlow for their kind assistance with Leonard Darwin's letters; to Naomi Mitchison, Laura Huxley, Anthony Huxley, and Unity Sherrington for permission to reproduce material from the letters of Professor J.B.S. Haldane, Aldous Huxley, Sir Julian Huxley, and Sir Charles Sherrington, respectively; to Dr W.B. Provine for kindly sending copies of Fisher-Wright correspondence; to the Oxford University Press for information on the sales of *Genetical theory* and for permission to reproduce extracts from Mr K. Sisam's letters to Fisher concerning publication of that book; to the Secretary of the Royal Society of Edinburgh for information on the refereeing of Fisher's 1918 paper on the correlation between relatives; to the Eugenics Society and *Nature* for permission to reprint the material in Appendixes A and C respectively; and to the University of Adelaide for permission to quote various passages from *R. A. Fisher correspondence* held at the University.

Mrs Joan Fisher Box kindly read the whole work and made many valuable suggestions. I am indebted to Professors W.F. Bodmer and D.J. Finney for their comments on the typescript and to Professor R.J. Berry

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J.H.B.

Adelaide, South Australia
September 1982

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EDITOR'S ABBREVIATIONS

CP	*Collected papers of R.A. Fisher* (ed. J.H. Bennett). University of Adelaide (1971-4). (Numbered references to papers can be identified from the reference list on p. 298.)
FLS	*R.A. Fisher. The life of a scientist* by Joan Fisher Box. John Wiley, New York (1978).
GTNS	*The genetical theory of natural selection* by R.A. Fisher. Clarendon Press, Oxford (1930); 2nd edn, Dover Publications, New York (1958). (Page numbers refer to the 1958 edition.)

1 INTRODUCTION

Since Charles Darwin developed the theory of natural selection in ignorance of the true nature of heredity, it was inevitable that it should be redeveloped later on a genetical basis. However, the relevance of genetics for an understanding of evolutionary theory was not widely appreciated by biologists until well into the twentieth century. Fisher's (1930) book *The genetical theory of natural selection* was the first major work to provide a general synthesis of Mendelism and Darwinism. Written at a time when Darwinism was neglected or ignored, it marked an important turning point in the development of evolutionary thought, leading to the emergence of neo-Darwinism.

To appreciate fully what it was that Fisher accomplished with this book we must recall the general attitude of biologists to natural selection and evolution in the period 1920-30. D.M.S. Watson in his Presidential Address to the Zoology Section of the British Association for the Advancement of Science in 1929 expressed it as follows.

> Whilst the fact of evolution is accepted by every biologist the mode in which it has occurred and the mechanism by which it has been brought about are still disputable.
>
> The only two 'theories of evolution' which have gained any general currency, those of Lamarck and of Darwin, rest on a most insecure basis; the validity of the assumptions on which they rest has seldom been examined and they do not interest most of the younger zoologists.

Such views were widely held by botanists as well as zoologists. D.H. Scott in his Presidential Address to the Botany Section of the British Association in 1921 said,

> There is a strong tendency in these days to admit natural selection only as a 'merely negative force' and as such it has even been dismissed as a truism.
>
> It may be that the theory of natural selection as Darwin and Wallace understood it may some day come into its own again: but in our present total ignorance of variation and doubt as to other means of change we can form no clear idea of the material on which selection has had to work and we must let the question rest. For the moment, at all events, the Darwinian period is passed. We can no longer enjoy the comfortable assurance which once satisfied so many of us that the main problem had been solved. All is again in the melting pot. By now a new generation has grown up that knows not Darwin.

E. W. MacBride,[1] writing in 1927, explained his view of natural selection as 'a purely negative agent': 'it weeds out but does not create; it accounts for the elimination of the unfit, but not for the appearance of the fit.'

The above quotations have come from British biologists but the views involved were widespread and general. Similar comments can be found in the writings of contemporary scientists from North America and elsewhere. For example, in 1926 the American paleontologist, H.F. Osborn, in an article in *Science* entitled, 'The problem of the origin of species as it appeared to Darwin in 1859 and as it appears to us today', concluded, 'The causes of "variation", to use the term (Darwin) employed for the evolutionary process, lie in the way before us. They may be resolved or they may prove beyond human solution.' R.K. Nabours[2] gave frank expression to the general view in 1930: 'We are still in a morass, it may as well be admitted, with regard to the ultimate problems of evolution.'

Amongst the few biologists who accepted natural selection as an agency of adaptive modification—a positive force for evolutionary change—there was often confusion and lack of understanding of the means by which it could work. C. Tate Regan in his Presidential Address on Organic Evolution to the Zoology Section of the British Association in 1925 said, 'I am inclined to accept Darwin's theory as a whole, including both natural selection and the inherited effects of use and disuse, at any rate until some better explanation of the facts is forthcoming.'

Biological variation and inheritance

Confusion as to the role of natural selection in evolution had become widespread among biologists in the generation after Darwin. The basic difficulty was an inadequate understanding of the nature of biological variation. There were really three closely connected problems involved here for what was missing in Darwin's theory of natural selection was (i) a satisfactory distinction between the different *types* of biological variation, especially heritable versus non-heritable and continuous versus discontinuous (or discrete) variation, (ii) a convincing explanation for the *origin* or causes of heritable variation, and (iii) an adequate theory of the *inheritance* of such variation. Darwin had seen that it was essential for there to be heritable variation if evolution by natural selection were to occur. He distinguished between 'individual differences' which were small and occurred frequently and 'sports' which were large and occurred rarely. He suggested that natural selection acts on the individual differences which he thought were mostly heritable. As to the origin of new variation, Darwin imagined that 'changed habits' produced individual differences which were heritable. On heredity, he wrote in the first edition of the *Origin of species* in 1859, 'The laws of inheritance are quite unknown'; in the fifth edition (1869), he replaced 'quite unknown' in this sentence by 'for the most part unknown'.

In 1868, in *The variation of animals and plants under domestication*, Darwin had put forward his 'provisional hypothesis of pangenesis'. This was a vague and speculative proposal to explain the hereditary transmission of individual differences including those caused, as Darwin believed, by

environmental effects. Each part of an organism was imagined to throw off small invisible particles called gemmules. These supposedly came together in the germ cells from where they were transmitted to the next generation. Some gemmules, he thought, controlled the development of various parts of the new organism although many remained in a dormant state to be transmitted to the next generation. Although this scheme of inheritance was in a sense particulate, Darwin did not conceive of his gemmules as particles segregating unchanged throughout successive generations. Hybridization, he thought, led to a blending of the parental differences. Pangenesis did not lead to any change of approach in the *Origin* where Darwin in effect accepted the traditional view of heredity as involving a blending of the parental contributions.

Darwin's theory of natural selection had a profound influence on his half-cousin Francis Galton who was intensely interested in variation of all kinds. Seeing the central place which biological variation had in Darwin's theory, Galton carried out a number of investigations into heredity. He soon perceived that Darwin's theory of pangenesis was unsatisfactory. A very important contribution was his demonstration of the role of heredity in continuous variation. In attempting to measure the intensity of heredity in Man, Galton was led to introduce the concept of regression and to develop the analysis of correlations. In this way he helped lay the foundations of biometry. His law of ancestral heredity[3] was formulated in an attempt to predict the average value of a character in an individual from a knowledge of the given character in the ancestors. He suggested that the average contribution of each parent to its offspring is one-quarter or, in other words, that half of the qualities of the child can be accounted for when we know the father and mother; likewise, the four grandparents together contribute one-quarter and so on.

In his celebrated paper of 1865 on experiments in plant hybridization, Gregor Mendel[4] wrote,

> It requires indeed some courage to undertake a labour of such far-reaching extent; this appears, however, to be the only right way by which we can finally reach the solution of a question the importance of which cannot be overestimated in connection with the history of the evolution of organic forms.

Did Mendel appreciate the importance of his particulate theory of heredity in understanding the evolutionary process? Whilst he does not mention Darwin in his 1865 paper, four years later in the paper on *Hieracium*, he refers to 'the spirit of the Darwinian teaching'; he clearly knew of Darwin's work. But can we be sure that he was referring to Darwin's work in the above passage? Fisher evidently thought so. He wrote to D.J. Finney on 19 November 1948,

> Evolutionary problems were, of course, not the subject of Mendel's paper, but as a side issue he points out that the view of inheritance at which he had arrived does

remove one of the principal difficulties which Darwin and others had felt about the theory of selection. Indeed, Mendel was so clear about the theoretical implications of the particulate view of inheritance, that one rather wishes he had written a paper on the theory of evolution.

Mendelism, Darwinism, and biometry

Following the rediscovery of Mendel's paper in 1900, the question as to whether ancestral heredity was consistent with Mendelism soon aroused much interest and controversy. It was not till more than 30 years later that biologists generally came to realize that Mendel's work provided a firm foundation for Darwin's theory of natural selection.

How did it come about that this general understanding of the importance of Mendelism for natural selection took so long to follow the Mendelian rediscovery of 1900? A major reason must be that some of the most influential early advocates of Mendelism were found amongst those who were already opposed to Darwin's theory of natural selection by small variations. In an unfortunate chapter in the history of biology, Mendelism became involved in a bitter controversy as though its principles were basically opposed to natural selection. As Fisher (*CP* 165, 1939) put it,

> The Mendelian discovery, since it embodied some facts unknown to Darwin, was eagerly seized on, and an antagonism between these facts and Darwin's theory was assumed and asserted, though never conscientiously examined. The early advocates of Mendelism, such as Bateson, had already before its discovery embroiled themselves in anti-Darwinian controversy.

In his book, *Materials for the study of variation treated with special regard to discontinuity in the origin of species*, William Bateson had written in 1894 (p. 567), 'the Discontinuity of which Species is an expression has its origin not in the environment, nor in any phenomenon of Adaptation, but in the intrinsic nature of organisms themselves, manifested in the original Discontinuity of variation.' Whereas Darwin had suggested that natural selection acts generally and gradually on small individual differences which he assumed were for the most part inherited, Bateson maintained that the evolutionary process was a discontinuous one which depended essentially on the occurrence of large, definite or discontinuous differences between individuals. It is not altogether surprising then that, when Mendel's work was rediscovered in 1900, Bateson mistakenly seized on the discontinuity in heredity as supporting evidence for his own ideas of the discontinuity of the evolutionary process.

In 1901, Hugo de Vries,[5] on the basis of what he thought were mutations in the evening primrose, put forward a general explanation for the origin of heritable variation which could itself account for evolutionary change. He claimed that species arose by saltations or single large mutations and that the small individual differences observed in natural populations had nothing to do with the origin of species. Although the variants in the evening primrose were later shown to involve chromosomal rearrangements and not mutation at all, de Vries' mutation theory of evolution had a considerable influence on many biologists and it led to a widening of the gap not only between Mendelism and Darwinism but also between Mendelism and biometry. Bateson[6] wrote of de Vries that 'for the first time he pointed out the clear distinction between the impermanent and non-transmissible variations which he speaks of as *fluctuations*, and the permanent and transmissible variations which he calls *mutations*' which are 'those alone by which permanent evolutionary change of type can be effected'. Thus the early Mendelians came not only to regard mutation as involving discontinuous or large differences which determined directly the course of evolutionary change, but also to think of fluctuations or continuous variation as non-heritable.

At the same time a bitter controversy developed in England between the biometricians and the Mendelians over the question as to whether the correlations between relatives could be accounted for in terms of Mendelian inheritance. Karl Pearson[7] and his associates, the biometricians, maintained that the observed correlations for continuous characters could not be accounted for in terms of Mendelism where they assumed complete dominance to be essential. Pearson accepted Darwin's view that evolution proceeded gradually by selection acting on small or continuous differences whereas, as we have seen, Bateson rejected Darwinism and believed in discontinuity in evolution. It thus came about that Mendelism was represented as opposed to both biometry and Darwinism. The feud which developed between the Mendelians and the biometricians had serious repercussions on ideas of the relevance of genetics for an understanding of evolutionary theory well into the twentieth century.[8]

Though G.U. Yule[9] had suggested in 1902 that, with a multiple-factor hypothesis for continuous characters, ancestral heredity was reconcilable with Mendelism, it was not until 1918 with the publication of Fisher's comprehensive paper, 'The correlation between relatives on the supposition of Mendelian inheritance' (*CP* 9), that Mendelism and biometry were brought properly together. In this paper Fisher developed the basic quantitative theory for the analysis of the variation in a population for a continuous character affected by a large number of genes. He took account of the most general assumptions as to the individual peculiarities of the genes (for example, in respect of dominance, gene frequency, and magnitude of the gene effects) and showed that the genetical behaviour to be observed does not become more complex as the number of genes is increased. Fisher established that with such a general system there was very good agreement between the correlations of relatives actually found and those calculated.

He showed how the variance (a term which Fisher introduced with this paper) could be partitioned into heritable and non-heritable fractions and that the heritable variance could itself by analysed into various genetically meaningful components attributable to additive gene effects, dominance, and other genic interactions. This analysis was of particular importance, for selection can act directly only on the additive genetic component.

Whilst the 1918 paper rightly marks the grand synthesis of Mendelism and biometry, and the birth of biometrical genetics, Fisher had already in 1911, at a meeting of the Cambridge University Eugenics Society, pointed out the essential basis for the synthesis of biometric results and Mendelian theory (see *FLS*, p. 1). Fisher's 1911 paper on Mendelism and biometry was not published but at least two typewritten copies have survived; an uncorrected copy is in the Minute Book of the Cambridge University Eugenics Society kept at the office of the Eugenics Society in London, whilst the other is Fisher's corrected copy complete with illustrations and footnotes. We are indebted to Mrs Joan Fisher Box not only for first drawing attention to the existence of this paper but also for giving the corrected copy for safe keeping with the Fisher Papers in Adelaide. This copy has been used for the reproduction included in Chapter 2.

By 1911 Fisher not only appreciated that the results of the biometricians could be accounted for in terms of the simultaneous action of many genes with additive effects, but he also saw the valuable contributions to be made to the study of quantitative characters by both biometrical and genetical methods of analysis. His 1911 paper contains a number of original ideas quite apart from those taken up in the 1918 paper on the correlation between relatives. For example, it is interesting to see the way in which Fisher suggests that the concepts of population genetics can be used in the study of inbreeding. After referring to the large number of dominant defects known in Man, he says that there must be a still larger number of recessive defects 'by one or more of which almost everyone is affected'. He indicates how a knowledge of the frequencies of defective children born to consanguineous unions may be used to estimate the number of recessive genes for serious defects which are carried in the heterozygous state by a healthy member of the population. He also shows that with cousin marriage and uncle-niece unions the probability of any progeny having two genes identical by descent from a gene in a common ancestor is 1/16.

Fisher's 1911 paper is not concerned directly with evolution but it contains a clear reference to the basic relationship of Mendelism and biometry to evolution and to the need to involve population and statistical studies: 'The value of biometrical work is largely due to the fact that the actual evolution of new species in the past is a question of populations, and must have taken place in the way indicated by statistical methods.' In view of this, we may certainly share Fisher's regret, expressed in his introductory remarks, that he has made no mention of de Vries' mutation theory of evolution—even though we might well wonder why he should refer to de Vries' theory at all in a paper on Mendelism and biometry. Perhaps it is significant in this connection that Fisher ends his introductory remarks by saying that his object has been to give a fair view of the merits of the two methods (i.e. Mendelism and biometry) 'whose advocates have shown so little appreciation of the other school'.

Fisher had received no formal education in either of these new disciplines. His undergraduate education at Cambridge was in mathematics and physics but at the same time he maintained and extended biological pursuits begun in his schooldays. After his election to the Royal Society in 1929, Fisher wrote to Arthur Vassal, who had been his biology master at Harrow,

> It would have worked out much the same, I fancy, if I had taken your suggestion and taken biology for Scholarship purposes at school. I still think the scholarship would have been more chancy and I suppose, without being sure, that a mathematical technique with biological interests is a rather firmer ground than a biological technique with mathematical interests, like D'Arcy Thompson.

Joan Fisher Box (*FLS*, p. 19) records how Fisher had excelled at school in biological and physical science as well as mathematics. The choice of some of the numerous books awarded as school prizes reflects his early and developing interest in biology. At the age of 11 he was given E. Stanley's *A familiar history of birds*, and a year later Gilbert White's *Natural history and antiquities of Selborne*, both as prizes for mathematics. His prizes at Harrow include O. Schmell's *Introduction to zoology* and G. J. Romanes' *Jelly-fish, starfish and sea urchins*. In 1909, during his last year at Harrow, Fisher chose for one of his prizes the complete works of Charles Darwin. His choice of these 13 volumes was of special significance. As he later recorded (*CP* 217), 'it was the year in which the centenary of Darwin's birth and the jubilee of the publication of the *Origin of species* were being celebrated'. Later in 1909 when he went up to Cambridge, Fisher eagerly seized on three remarkable books, all published at just that time by the Cambridge University Press: (i) *The foundations of the origin of species: two essays written in 1842 and 1844 by C. Darwin* (ed. F. Darwin); (ii) *Darwin and modern science* (a collection of essays assembled by A.C. Seward); and (iii) *Mendel's principles of heredity* by W. Bateson. Fisher's copy of the *Foundations*, a gift from C.S. Stock, his friend and contemporary at Cambridge, bears the inscription, 'In memory of many delightful conversations on the subject matter of this book, June 1913'. *Darwin and modern science* was given to Fisher as a College prize. Bateson's book he bought as a freshman (see his Bateson Lecture, *CP* 248, 1951). Another book published in 1909, which seems also to have come under Fisher's early scrutiny, was W.C.D. and C.D. Whetham's *The family and the nation*, which emphasizes the selective effect of differential birth-rates, a subject to which Fisher himself later attached much importance.

To judge from his 1911 paper on Mendelism and biometry, Fisher's knowledge of heredity at that time was determined to a very large extent by his reading of Bateson's book. Bateson, who had been appointed as Professor of Biology at Cambridge in 1908, was in the forefront of workers in 'genetics', to use the name he had himself chosen for the new discipline in 1905. There can be little doubt that Fisher would have noted with ready approval Bateson's statement on p. 288. of his book that, 'With the discovery of the (Mendelian) factors precise analytical treatment can at length be applied to the problem of Evolution.' On the very next page, however, Bateson says, 'The conception of Evolution as proceeding through the gradual transformation of masses of individuals by the accumulation of impalpable changes is one that the study of genetics shows immediately to be false.' The reference to evolution in Fisher's 1911 paper suggests that he had by then seen not only that Bateson's position on this last point was wrong, but also how Mendelism and Darwinism would have to be brought together in a quantitative theory of natural selection. Fisher's introductory remarks suggest that he also saw that it would be difficult to obtain a fair view of the matter in the controversial atmosphere for which Bateson and Pearson were largely responsible.

In 1910 Bateson left Cambridge to become the first Director of the John Innes Horticultural Institution and his colleague R.C. Punnett was appointed as Professor of Biology in his place (the title was changed to Genetics in 1912). Punnett had been a Fellow of Caius College since 1901 and in 1911 he must have known Fisher, not only as a Caius Scholar, but also as one of the small group responsible for the formation of the Cambridge University Eugenics Society, a fellow Council member of the Society, Chairman of its undergraduate committee, and the author of original ideas on Mendelism, biometry, and evolution. (Like Fisher after him, Punnett was a Scholar and then Fellow of Caius College, and also Professor of Genetics at Cambridge.) In 1911 Punnett was only 36 years old and it may well be that Fisher was thinking of the possibility of new and exciting developments for genetics and evolution in Cambridge following Bateson's departure. If these were Fisher's dreams it must have soon become clear that they were not to be realized. In 1915, when Punnett's book *Mimicry in butterflies* was published by Cambridge University Press, it included a mutationist's explanation for the evolution of complex mimetic resemblances between members of unrelated species. The evolution of mimicry was later described by Fisher as the greatest post-Darwinian application of natural selection.

Punnett's references to selection in his book on mimicry are of particular interest. Central to his discussion is an appendix with a table (prepared by H.T.J. Norton) showing the numbers of generations required for various selective intensities (0.50, 0.25, 0.10, and 0.01) to bring about given alterations in the frequencies of the three genotypes in a dimorphic population mating at random. Punnett commented (p. 96), 'it is remarkable in how brief a space of time a form which is discriminated against, even lightly, is bound to disappear. Evolution, in so far as it consists of the supplanting of one form by another, may be a very much more rapid process than has hitherto been suspected, for natural selection, if appreciable, must be held to operate with extraordinary swiftness where it is given established variations with which to work.' Punnett referred to evidence from the study of melanism in the peppered moth *Biston betularia* in some parts of England as confirmation that such rapid changes in the constitution of a dimorphic population exhibiting Mendelian heredity do take place and he concluded that the melanics must have some selective advantage over the pale form. He also mentioned the experience of breeders who found that melanics were 'somewhat hardier, at any rate in captivity'. After suggesting that 'it is not at all improbable that the establishing of a new variety at the expense of an older one in a relatively short space of time is continually going on', Punnett wrote, 'a census of a polymorphic species, if done thoroughly, and done over a series of years at regular intervals, might be expected to give us the necessary data for deciding whether the relative proportion of the different forms was changing—whether there were definite grounds for supposing natural selection to be at work, and if so what was the rate at which it brought the change about.' Punnett's book is thus noteworthy for calling attention not only to the remarkable efficacy of selection as a factor for change in a population involving what E.B. Ford later called *transient* polymorphism, but also to the value of regular field surveys in such a situation. That these interesting early suggestions on selection by Punnett have not received greater recognition may, perhaps, be due to the curious circumstance that he included them in his book in support of his mutationist explanation of mimicry. As no rapid change had been recorded in the frequencies of the different mimetic forms in the various populations under observation, Punnett suggested that natural selection must be non-existent in this case. In fact, as Fisher showed in 1922 (*CP* 24), a quite different situation exists with a stable selectively balanced polymorphism, as when selection favours the heterozygote, the genetic composition of the population being maintained unaltered from generation to generation. Then the stability of the gene ratios of factors controlling the polymorphism could be seen as implying not the absence of selection, as Punnett had imagined, but the existence of selective differences (possibly large differences) between the different forms. In 1927, Fisher (*CP* 59) suggested not only that polymorphic mimicry in butterflies was an example of such a selectively balanced equilibrium but also that the polymorphism could itself undergo evolutionary development by the selection of modifying factors. The twin concept of allelic genes acting to switch on one or another of the possible alternatives in a polymorphism and of the alternatives themselves being subject to modification by selection in the course of evolution were entirely novel in 1927. These suggestions were later confirmed by field and laboratory studies.

Fisher's view of the role of selection in the maintenance of balanced polymorphisms represented a marked change not only from Punnett's approach but also from Darwin's attitude to common differences. In Chapter II of the *Origin,* Darwin refers to an 'extremely perplexing' point concerning species presenting 'an inordinate amount of variation' and he suggests these are variations 'which are of no service or disservice to the species and which consequently have not been seized on and rendered definite by natural selection'. Again, in Chapter VII of *The descent of man,* he says, 'The great variability of all the external differences between the races of man ... indicates that they cannot be of much importance; for if important, they would long ago have been either fixed and preserved or eliminated.' He then refers to polymorphic forms 'which have remained extremely variable, owing, as it seems, to such variations being of an indifferent nature, and to their having thus escaped the action of natural selection'. With blending inheritance, common differences maintained in a population could only be seen as selectively neutral. Fisher's demonstration in 1922 that a polymorphism can result from a balance of selected forces was important in showing that selection can maintain genetic variation in a population with a constant homogeneous environment.

Norton's table in Punnett's book provided an early demonstration of the value of a mathematical treatment of the effect of selection in population genetics. Both J.B.S. Haldane and the Russian geneticist S.S. Chetverikov acknowledged the stimulus it supplied when they began their work in population genetics. Norton was a mathematician who during the period 1910-15 was a Fellow of Trinity College, Cambridge. He worked on various problems in population genetics but it seems his only publication was his 1928 paper,[10] 'Natural selection and Mendelian variation', describing work he had completed many years earlier. It is interesting to speculate on what the early development of genetics at Cambridge might have been like if Punnett had sought the mathematical assistance he needed from Fisher rather than Norton. Perhaps it was Punnett's friendship with the mathematician G.H. Hardy of Trinity which led to Norton being asked to consider genetical problems. We know that in 1908 Punnett had taken the problem of the genotypic frequencies to be expected in a random mating population to Hardy who as a result published his note,[11] 'Mendelian proportions in a mixed population'. Fisher apparently did not know about Norton or the work on which he was engaged in Trinity, right alongside Caius; he wrote to R.F. Harrod in 1951 that he had not heard of Norton till he read about him in Harrod's book[12], *Life of John Maynard Keynes.*

Fisher's early interest in and original approach to the evolutionary process are clearly evident in a number of his writings apart from the 1911 paper on Mendelism and biometry. For example, in his 1912 paper on Evolution and Society (see p. 58), he considers the possibility of selection acting generally on *any* entities having the properties of variation and heredity; after discussing the co-ordination of individuals into groups or societies, he touches on the evolutionary problem presented by altruism. In 1916, commenting upon an article by W.E. Castle entitled, 'Is selection or mutation the more important agency in evolution?', he wrote, 'Mendelian characters take their place within the Darwinian scheme; they can be modified by selection and no doubt have come into existence by that agency.'[13] Apparently Fisher was already thinking of Mendelian characters as the product of previous selection in the gene-complex. This was a remarkable departure from the generally accepted view. Had not Bateson[14] written in 1909 that the order in heredity 'cannot by the nature of the case be dependent on Natural Selection for its existence, but must be a consequence of the fundamental chemical and physical nature of living things'? In 1920, at the end of a review of H.J. Muller's 1918 paper on balanced lethals, Fisher raised the possibility of the evolution of a co-adapted gene complex; 'The process of evolution would seem to require that selection should act separately upon many minute variations, but as soon as mutual adjustment and adaptation is obtained, it might thereafter be advantageous if the whole group were cemented into a single factor.'[15] Reviewing *The relative value of the processes causing evolution* by A.L. and A.C. Hagedoorn, Fisher (*CP* 17, 1921), wrote, 'The whole process is worthy of a thorough discussion, but the authors evidently lack the statistical knowledge necessary for its adequate treatment.' Fisher's two papers, 'On the dominance ratio' (*CP* 24) and 'Darwinian evolution by mutations' (*CP* 26), both published in 1922, mark the start of his thorough quantitative discussion of the evolutionary process, a work which went on growing and led ultimately to the production of *GTNS.*

Major Leonard Darwin and the Eugenics Society

By 1911 Fisher had clearly seized on the essentials of both biometry and Mendelism and saw the important role which both of these disciplines were destined to play in developing a proper understanding of natural selection. It was natural that he should follow these ideas through to questions of ultimate human concern. Mankind was becoming responsible for the future course of human evolution. The recognition of excellence and its promotion for future generations were clearly most important. What could an understanding of Mendelism, biometry, and natural selection contribute to a discussion of the future path of human evolution?

The improvement of the biological inheritance of man, or eugenics as Galton called it, was a subject that attracted increasing attention in the years following the Mendelian rediscovery in 1900. Galton not only had arranged for the establishment of a Eugenics Laboratory at University College London and financed the appointment of a Research Fellow but also, on his death in 1911, he left an endowment for a Chair in Eugenics with Karl Pearson designated as the first incumbent. A separate organization, the Eugenics Education Society (later called the Eugenics Society), was formed in London late in 1907 with the object of spreading a knowledge of eugenics and the laws of heredity among the public; shortly afterwards Galton became its President. The Cambridge University Eugenics Society was set up in 1911 with the aim of increasing the awareness of eugenics and heredity in members of the University; its Council included A.C. Seward[16] (President), Horace Darwin, R.C. Punnett, W.C. Dampier Whetham, J. Maynard Keynes (treasurer), C.S. Stock (secretary), and Fisher. The First International Eugenics Congress was held in London in 1912 with Leonard Darwin as president; Fisher attended as a steward. The two men had met before this in Cambridge but it was perhaps at the London Congress that Fisher had his first opportunity to appreciate fully the unusual qualities of Leonard Darwin. A man of exceptional character, intellect, and background, Darwin soon came to exert a profound influence on Fisher's life and work.

Leonard Darwin (1850-1943) was the second youngest and the longest surviving of Charles Darwin's five sons. For 20 years in the Royal Engineers he was engaged mostly with teaching and administration but also occasionally as a member of scientific expeditions. He resigned from the army at the age of 40 with the rank of Major, and then entered public life, serving for three years as a member of the House of Commons. Shortly after Galton retired as President of the Eugenics Education Society in 1909, Leonard Darwin succeeded to this office. In this position he found when he was over 60 that he was at last doing work which he felt to be of importance. For 18 years as president he devoted all his energies to the welfare of the Eugenics Society.

Leonard Darwin was, by all accounts, a remarkable man. Sir Arthur Keith[17] has written of him, '... in physical appearance, ... in his attitude to life and in the disposition of his mind he bore a closer resemblance to his father than did any of his brothers. He had his father's honesty of expression, openness of mind, charitable disposition, subjection of self, an excess of candour, and also his father's happy sense of humour. He was completely devoid of personal ambition.' Gwen Raverat, in her enchanting book, *Period piece*, about life in the Darwin family, includes the following verse on 'Uncle Lenny':

> Serenely kind and humbly wise,
> Whom each may tell the thing that's hidden,
> And always ready to advise,
> And ne'er to give advice unbidden.

When, shortly after Leonard Darwin's death, another niece, Margaret Keynes, sent Fisher a copy of a memoir she had written about her uncle, Fisher in writing to her said, 'My very dear friend Leonard Darwin ... was surely the kindest and wisest man I ever knew.'

Fisher acknowledges his indebtedness to Darwin in several of his early papers (*CP*9, 10, 70). His study of the correlation between relatives (*CP*9) was first undertaken, he says, at Darwin's suggestion and it was to Darwin's 'kindness and advice' that it owed its completion. *GTNS* itself was dedicated to Darwin 'in gratitude for the encouragement given to the author during the last fifteen years by discussing many of the problems dealt with in this book'. The advice and encouragement of Charles Darwin's son Leonard must have provided a powerful stimulus for Fisher to press on with the big job of work involved in laying the foundations for the neo-Darwinian synthesis.

From 1915 for about 20 years, Fisher and Darwin met and wrote to each other frequently, exchanging their views on natural selection, heredity, eugenics, and many other questions. During much of this time they corresponded with one another every few days. Fisher kept most of the letters which Darwin sent him. He also kept carbon copies of the typewritten letters which he sent Darwin from about 1928 onwards. Unfortunately, Fisher's earlier handwritten letters to Darwin, which would be of the greatest interest, seem not to have survived. Sometimes, however, it is possible to catch a reflection in Darwin's letters of ideas and suggestions which Fisher must have introduced previously.

Darwin's earliest letters in 1915 set out various problems which he hoped Fisher would solve; these are concerned mostly with biological variation and inheritance, Galton's law of ancestral heredity, parental correlation and regression, as well as natural selection and mutation. Darwin said he was 'building up ideal conditions and seeing how far they work like nature does work'. He was especially anxious to know if Galton's work on ancestral heredity could be given a Mendelian interpretation. In 1902, Bateson[18] and Weldon[19] had each suggested that Mendelism and ancestral heredity were inconsistent. Yule[9] had criticized this view and suggested instead that Mendelism and ancestral heredity were 'perfectly consistent the one with the other and may quite well form parts of one homogeneous theory of heredity'. This problem must have come forcefully to Leonard Darwin's attention in 1914 when his brother Francis[20] gave the first Galton Lecture before the Eugenics Education Society. Francis said that Mendelism requires that we 'look at variation in a very different way to that of Galton' and that whilst 'a progressive study of heredity must necessarily be on Mendelian lines', it 'does not follow that the laborious and skilful work of Galton and his school is wasted'. Biometrics, he said, 'may illuminate a problem which cannot as yet be solved in Mendelian fashion'. Leonard apparently judged that Fisher could provide the light that was needed. From 1915 onwards, he unfailingly gave stimulus, support, and encouragement to Fisher for his mathematical studies of biometry, heredity, and selection, constantly plying him with questions and suggestions, and sending various notes and papers of his own on evolution with requests for Fisher 'to pull them to pieces'. Fisher was always glad to hear Darwin's ideas, for as he once wrote, 'I have been learning bit by bit that there is generally the germ of something uncommonly well worth thinking about in what you say.' After receiving Fisher's detailed counter-notes to his suggestions, Darwin sometimes referred to his difficulty in 'sucking the whole juice' out of Fisher's letters, and to his concern that Fisher took so much trouble and treated his suggestions so seriously.

Some of Darwin's early letters show the kind of clarification which he thought was needed in the ideas surrounding biological variation. Others show how he was ready with wise counsel when Fisher encountered difficulties in getting his papers published. This had some important consequences. For example, we can see that it was only because of Darwin's interest, initiative, and support that Fisher's big paper on the correlation between relatives, after having effectively been rejected by the Royal Society of London in 1916, was published by the Royal Society of Edinburgh in 1918. In August 1920, when Fisher's paper, 'On the probable error of a coefficient of correlation deduced from a small sample' (*CP* 14), was refused publication in *Biometrika* and then in the *Journal of the Royal Statistical Society,* Darwin wrote at once with helpful advice. Early in 1923, when Darwin agreed that the Royal Statistical Society had treated Fisher badly in refusing to publish a paper on χ^2, he wrote to Fisher, 'You may well feel that I preach to you unwarrantedly but please remember it is friendship to you which makes me risk annoying you'; he urged Fisher to 'push on quietly avoiding as far as possible all controversy'. Darwin said that at home he was brought up to believe controversy with individuals was a great waste of time and should be avoided. Here and elsewhere in Darwin's letters, we find ourselves reminded of his father, if not explicitly, then perhaps by the ideas or sentiments expressed or by the use of a particular turn of phrase. Sometimes we find Fisher urging Darwin to try and recall his father's spoken words, 'especially when explaining his dissent from some view which he felt, rather than saw, to be unsound'. The Darwin-

Fisher letters thus shed light not only on the development of Fisher's thinking in natural selection and related areas, but also to some extent on Charles Darwin's writings and ideas. They also reveal the growth of the fascinating friendship which developed between these two exceptional men—Leonard Darwin, President of the Eugenics Society, himself with two happy but childless marriages, and Ronald Fisher, 40 years younger, initially an unknown and rather isolated schoolmaster, producing brilliantly original papers which could not be published in England because of opposition from the leading authorities in biometry and genetics. For Fisher the friendship with Darwin, with his close links with Charles Darwin and Francis Galton, had special significance. It seems that Darwin soon became as a revered father whose counsel on many questions was eagerly sought and always greatly respected. Darwin's nobility of character, his modesty, and charm shine through his letters. He repeatedly excuses himself for being 'muddle-headed' and 'stupid about mathematical things'. His letters to Fisher were, he said, an opportunity to 'let off steam'—'I like blowing off steam to you and expect you to take *no* notice of it.' The Darwin-Fisher letters were certainly not written with an eye to posterity or publication. They were exchanges between trusted friends who knew well how to receive them. They are, however, full of good things and are of interest not only for the scientific content but for the stimulating discussion of a great many general questions as well as for the personal touches and expressions of humour. There are fascinating exchanges on chance, indeterminism, and free will, the economic and social order, family allowances, tropical agriculture, food production, the level of population, and many other questions of lasting interest. Darwin wrote that he always liked getting Fisher's letters because they made him *think*. He once summed up his feelings on receiving a letter from Fisher as 'somewhat like that of a pig genuinely admiring a necklace of pearls, but not knowing quite how to put it on and feeling sure that he had not deserved such a present'. There are indeed many gems in this correspondence and much to make the reader *think*.

From 1914 onwards, Darwin encouraged Fisher to write reviews, mostly of biological books and articles, for the *Eugenics Review*, a quarterly journal published by the Eugenics Society. Fisher no doubt appreciated the ready access to genetical and other literature thus provided. Over the next 20 years he published about 200 reviews in this journal. During much of this time Darwin was president of the Society and Fisher was an honorary secretary. It seems that one of Fisher's major objectives in his work with the Society was to get it re-organized as a predominantly scientific body. He wished to see it encouraging and promoting scientific research in human heredity. There is an interesting exchange of letters with Darwin on this theme in October 1930 when Fisher was exploring the possibility of diverting funds from publicity into research. Fisher wrote that he was concerned to answer the question, 'Are there any ways in which I can do good through my connection with the Society?' Fisher's concern on this score seems to have grown as Darwin's influence on the Society diminished. Darwin retired as president in 1928, and before long, Fisher became increasingly disillusioned with those who took control. Writing to Darwin on 16 November 1933, he referred to 'the small group of non-scientifics who control the Society' and said he was 'more than ever convinced that Eugenics will make no progress ... unless it has widespread sympathy and some active support from professional men of Science.' Fisher was then a vice-president of the Society and his recent appointment to the Galton Professorship as Pearson's successor had given Darwin much pleasure. When Pearson was in charge of the Laboratory, relations with the Society were badly strained. Fisher tried to encourage co-operation between the two groups. Shortly after he took over from Pearson, the Society agreed to share the cost of publishing the Laboratory's *Annals of Eugenics*; from 1934 till 1941, the *Annals* was issued jointly by the Laboratory and the Society. Pearson's subtitle for the *Annals*, a journal 'for the scientific study of racial problems', was replaced by Fisher's new description of it as one 'devoted to the genetic study of human populations'. Fisher had helped prepare the Society for the opportunity to support a journal of human heredity. In December 1932, the Society's council had agreed to take the initiative in forming 'a non-propagandist organization to study human heredity' and its Human Heredity Committee had been authorized to enquire into the financial aspects of initiating and running a journal devoted to this subject. When Fisher became Galton Professor and editor of the *Annals*, the Society dropped these plans and supported the *Annals* instead. In 1934, Fisher persuaded the Society to support post-graduate research by funding studentships in honour of Leonard Darwin. Several of these were later awarded to individuals who worked in the Galton Laboratory.

The Eugenics Society was able to greatly extend its financial commitments at that time because of a large bequest from Henry Twitchin. For about six years before his death in 1929, Twitchin, a grazier in Western Australia, had been giving £1000 annually to the Society to help it extend the knowledge of eugenics among the general public. During those years, Darwin helped maintain Twitchin's interest in the Society by writing to him about its work and occasionally meeting him or his solicitor in London. Twitchin[21] died on 19 March 1929, leaving an estate valued at about £80 000 to the Society. This bequest not only made possible a much larger annual expenditure but also led to increased discussion about the Society's programme. It is against this background that we should see Fisher's letters to Darwin in October 1930 pressing the case for the Society to fund research in human heredity. Though Fisher failed in 1930 to win Darwin to the view that Twitchin money should be used to support research, in particular on human blood groups, yet by 1934, as we have seen, he had gained Society support for funding research scholarships and sharing the costs of publishing the *Annals*. However, by a strange irony, Fisher came to feel at about that time that those who had gained control of the Society were 'almost without eugenic knowledge or ideas'. C.P. Blacker had become general secretary of the Society in 1931 and, with his active encouragement, Society funds went more and more to support work on chemical contraception, whilst the grant in support of the *Annals* was gradually reduced and finally removed altogether. Writing to P.F. Fyson in September 1938, Fisher said the directors of policy in the Society were strongly entrenched and 'almost impervious to scientific advice'; he had therefore not attended the Council for some years though he had allowed his name to remain as vice-president. After 1937 Fisher was no longer vice-president; he remained a member of the Society's council till 1942 but apparently attended no meeting in this period. He resigned from the council in 1942, shortly before Leonard Darwin's death. Fisher's involvement with the Eugenics Society over many years seems to have derived much of its strength from the close bond he had formed with Darwin and it did not last long after Darwin's strong influence on the Society came to an end.

All the evidence from Fisher's published work, his biography, and his correspondence, shows, I believe, that his biological interests were primarily in natural selection (which had aroused his interest at school), secondly in heredity (which had stirred his imagination as a freshman at Cambridge in 1909), and that, from these, stemmed his interests in human heredity and eugenics. After he was awarded the Darwin Medal of the Royal Society in 1948, Fisher wrote to D.J. Finney that this was 'an immense satisfaction ... as I have worked for a good many years, and indeed saw the need nearly forty years ago, to reverse the trend then prevalent of misrepresenting and minimizing the importance of Darwin's achievement'. Recently, however, several writers have proffered a different view of Fisher's priorities and aims in his biological work, based upon a sociological or ideological approach. B. Norton[22] has written about the neo-Darwinian synthesis, 'Fisher's decision to become involved in this sort of work has remained somewhat mysterious'; he then suggests that the 'mystery' would be removed if one were to accept his belief that 'Fisher's problems were ideological rather than biological'. The classic 1918 paper on the correlations between relatives (*CP* 9) should now be seen, Norton says, 'predominantly as a contribution to the hereditarian social ideology of eugenics'. According to Olby,[23] 'Fisher was both a eugenicist and a Mendelian biometrician but not an evolutionary biologist', while MacKenzie[24] believes Fisher 'sought not to *reconcile* Mendelism and biometry but to *use* Mendelism to vindicate biometric eugenics'. I hope that the contents of this volume will help readers in judging what weight should be given to these different views.

The writing of *GTNS*

The first indication that Fisher was writing a book on selection occurs as early as 1919 when he prepared several chapters dealing with the selective situation in Man. Although never completed it was probably a useful preparation for the writing of *GTNS* ten years later. In August 1919, Darwin wrote, 'it wants more orderliness. It is worth taking great pains with your first book, even though a book is an awful grind. ... You must not take your facts only when they fit your theories and neglect theoretical conclusions when facts are not available.' In some respects, Darwin seems to have filled a role not unlike that of a research supervisor. Over several years, he tried to stir Fisher 'to write a great work on the mathematics of evolution'. In August 1921, he told Fisher that papers are of comparatively little use in permanently affecting opinion and that he hoped 'when you are fully ready—not before—you will put your ideas into a book'. He kept returning to this point urging Fisher on at a time when the leading biologists saw no need or place for mathematical arguments. A few years later Darwin wrote, 'You will have a small audience, but it will gradually be realized that many of these problems [of selection] can be attacked in no other way.' In 1928, when Fisher began to put together material for *GTNS,* he lost no time in seeking Darwin's comments, especially on his reconstruction of Charles Darwin's arguments which was to have an important place in his first chapter.

Except for the mathematical chapters (IV and V), the whole manuscript of *GTNS* was written out by Mrs Fisher at Fisher's dictation between October 1928 and June 1929. Fisher's letters to Darwin at this time tell us about the author's attitude to the work in progress. On 13 November 1928, after thanking Darwin for the care he had given to reading Chapter I, he wrote, 'I wish I could believe it was worth the trouble. I have decided to write on, sometimes ahead of my convictions, with a view to subsequent careful revision, which I hope may be less difficult than making a fresh start.' On 18 February 1929, when sending Chapters IV and V, he wrote, 'I have made an abominable mess of the whole thing and failed to get out an adequate solution of nearly all the problems, but I hope that it may at least show what further work is needed.' Darwin replied, 'if you have not covered the whole surface, it is because the ground is very very stiff. In pioneer work of this kind, no one can be expected to solve all the problems.' Within a few months, Fisher had done much of the further work needed and in October 1929 he was able to incorporate it in Chapter IV. As Fisher recorded both in *GTNS* (p. 95) and *CP* 86 (p. 458), during 1929 he had received from Sewall Wright in manuscript a study in which 'while confirming many other conclusions of my [1922] paper [*CP* 24], he arrives at a time of relaxation of only $2n$ generations' instead of $4n$ and this 'has led to a more exact examination of the whole problem.'

On 19 March 1929, when sending Darwin the first of the chapters on Man (Chapter VIII) Fisher wrote, 'I do not expect you to agree that I am necessarily right about Man, but only that I am approaching the subject in a rational spirit.' It was to be another three months before the further chapters on Man were finished, and by then, on the basis of what they had seen of the early part of the book, the Clarendon Press, Oxford, had agreed to publication.

Although Fisher viewed his deductions regarding Man as 'strictly inseparable' from the more general chapters, he was concerned that the publishers, who had agreed to publication after seeing only Chapters I-VIII, might view Chapters IX-XII rather differently. When sending the final chapters on Man, he therefore told them that they must feel perfectly free to change their mind about publication. Their reply, however, was quick and encouraging. They recognized Fisher's quantitative genetical theory of natural selection as an outstanding and lasting achievement. But they also saw that the book would require a considerable effort from the reader. They no doubt paused at some of the long, complicated sentences—sentences which had led Darwin to recommend to Fisher 'one idea—one sentence' as a good rule to follow. The letters which passed between Fisher and Kenneth Sisam of the Clarendon Press show not only the encouraging responses and the helpful suggestions of the publishers, but also the author's characteristic reactions to the particular questions raised.

K. Sisam to Fisher: 13 May 1929

Our representative, Mr. Crowther, has safely delivered to us part of your MS. in which you examine statistically the theory of natural selection, etc. Our advisers are very much interested, and it would help me, for short reference, if you could give me an idea of the title you propose (which ought to be explicit). From reading a little of the MS., I assume that you would preface it by an introductory chapter on aims and methods, and I understand that the chapters on Man are still to be completed. I have not yet had time for a detailed report from our advisers, but I am sure the Delegates will be interested in this new method of approach.

Fisher to K. Sisam: 14 May 1929

I should call the book something like

THE GENETICAL THEORY OF NATURAL SELECTION

I cannot easily get the words statistical or mathematical into the title, but genetical is essential. My impudence in treating the subject as a branch of mathematics, I must justify in a preface; very short and historical, was my intention, not dealing there with methods, and only hinting at aims.

There will be four or five chapters on Man as the subject is generally shirked by geneticists, and I know of no historian who knows what Natural Selection means.

K. Sisam to Fisher: 28 May 1929

Our advisers have now had an opportunity of reading the chapters of *Natural selection*, which they find full of good things. They urge two points very strongly in the interest of the book:

(1) That the Introduction on its scope and results should not be too brief or too stiff.
(2) That, as the text at present is decidedly hard reading, it would be improved if you could get a comparative layman in the subject to go over it, and if you could then meet his difficulties. They do not suggest that the book could be make intelligible to a person who knew no mathematics, but they think that the exposition could sometimes be easier without loss of accuracy. The matter itself they consider well chosen.

In its present form the book would be very useful to specialists; but—though it could never be 'popular'—the circle of readers would be increased considerably (especially in America) if the treatment were simplified in hard places, so as to bring more of it within reach of those not highly equipped already.

These are suggestions for making the book more successful, which would be in your interest and ours. But if you say the present treatment is the only one possible to you, we should still be ready to publish for the narrower group of specialists only. ...

I hope this will enable you to go on and finish the work, which will, we are sure, be of great value to biologists, not many of whom have the full command of statistical method.

Fisher to K. Sisam: 31 May 1929

Many thanks for your letter of May 28. I shall do my best to improve the presentation in the way you suggest, though of course most of what you say is so probably true that I have worried about it a good deal already. ...

I want to get a largish class of biological teachers who often do not know what to say about the present position of Selection Theory, and in consequence say nothing to the point.

Fairly large print is a real antidote to stiff reading, though of course I must do my best too.

K. Sisam to Fisher: 4 June 1929

Thank you for your Preface; I shall take advice upon it. I am afraid we did not keep notes of particular passages, but our advisers did feel that in the interests of brevity, you plunged into the middle of the subject, and that an introductory guide to the purposes of your research would help a reader to follow. ...

K. Sisam to Fisher: 24 June 1929

We find, and our advisers find, your Preface interesting and original, though we still think that a little more explanation of the scope of the work is desirable, even if it is only a single paragraph. At least we suggest that each chapter should have a short summary heading, indicating the thread of its content. You see, our whole concern is to help the reader to follow your argument easily, instead of having to double back on his tracks in order to pick up points he has missed at the outset.

I am returning the Preface, and we shall be very glad to set to work upon your completed MS. ...

Fisher to K. Sisam: 25 June 1929

I have now completed the part on Man and it comes to 5 chapters (VIII to XII). I will send them when I have the MS in order (quite soon).

I am conscious that the Chapters on Man will, from your point of view, tend to alter the character of the whole book, and I want you to feel perfectly free to change your mind about publication. In particular I had great hesitation in writing Chapter XII at all, and would willingly stop at the end of Chapter XI, if it seemed at all possible.

I think the provision of contents at the beginning of each Chapter is an excellent suggestion. I have also selected quotations for most of them.

I think two colour plates should be enough, but will put the point to Poulton.

K. Sisam to Fisher: 1 July 1929 [sic]

Thank you for your letter of 27th June with the good news that your chapters on Man are complete. We shall look at them with interest when they come, but on the whole our nerves are strong and I hope no reasonable and well-based position will lead us into difficulties. If we have any suggestions, I shall let you know as soon as possible after the MS comes in. But I hope that we shall be able to proceed with the composition almost at once.

K. Sisam to Fisher: 25 July 1929

Thank you for your letter of 22nd July, in accordance with which we have returned Chapter VII for revision.

So far we are brave enough for the later chapters, but in order to save time we are having them set straight up into slip proofs, without previous reference to our official advisers, and it is just possible that they may have some suggestions to make. To me personally your latter chapters were of very great interest, and I know no reason why biologists should not consider the ultimate ends of their science.

Fisher to K. Sisam: 27 July 1929

Thanks for your letter. I am glad you are not prostrated. We have had no contract yet, but I suppose you will send one, when you have been more fully advised.

Fisher to K. Sisam: 15 October 1929

I send herewith corrected galley proofs completed, and have indicated the positions of Figs. 6-11. The first five are in the part you already have, and I think their positions are clear. The end of Chapter IV has been rewritten, and the new versions of Figs. 6 and 8 will follow soon. I have not yet heard, however, of further progress with colour plates.

I am exceedingly sorry to have to make a big alteration at this stage, which is in every sense due to my own fault. I became convinced that my mathematical treatment was all wrong, and I am lucky to have the chance to put it right. Of course I must pay for it.

Fisher's choice of title for his book was doubly significant. It served not only to direct the attention of biologists back to the theory of natural selection as the mechanism of evolution but also to emphasize the genetical basis for this theory. Fisher had rethought the whole of Darwin's theory in terms of genetics. In *GTNS* the theory of natural selection was considered for the first time on its own merits. The work of biologists during the 70 years after publication of the *Origin* had thrown very little light on the evolutionary process. Natural selection was neglected or ignored. Leonard Darwin himself had written at the start of his *Organic evolution*[25] that 'evolution is the great thing, not natural selection' and he even suggested 'if a recollection of about 50 years standing may be trusted', that his father had once expressed this view. Fisher gently revealed his response to this when writing to Darwin on 28 March 1929: 'I am particularly anxious to avoid misrepresenting your father's views; though I do not agree in emphasis with the earlier pages of *Organic Evolution*. *If* Lamarckism had seemed acceptable I think it would have done all that your father said about Natural Selection and would therefore have been as important as Natural Selection really is. To me it all hangs on the if.'

When *GTNS* appeared in April 1930, Fisher promptly sent copies to a number of friends. Included amongst these was James Davidson, an entomologist and a former colleague at Rothamsted who had taken up a post at the University of Adelaide. From the covering letter which Fisher sent him, we can catch a glimpse of what the Rothamsted fellowship, at once stimulating and congenial, had meant to the author when considering the problems dealt with in *GTNS*. During the previous ten years as statistician at Rothamsted, Fisher was daily in close touch with some very able research biologists. The role of natural selection in evolution must have come into a number of their discussions. It was, no doubt, after one such discussion that Davidson tried to get Fisher to talk at the 1925 meeting of the British Association for the Advancement of Science when Tate Regan gave his presidential address to the Zoology Section on Organic Evolution, but Fisher says he 'funked it quite shamelessly'. However, Regan's Lamarckian conjectures to account for some observations on vertebra numbers in fishes aroused Fisher's interest. In 1927, the year in which Regan became Director of the British Museum of Natural History, Fisher sent him an alternative interpretation involving selection. This correspondence, which apparently made no impression on Regan, is of special interest because it contains the first known outline of the argument which later became the subject of Chapter I of *GTNS*.

Some features of *GTNS*

The first two chapters of *GTNS* were considered by Fisher to be the most important. Chapter I involves a comparison of the consequences of blending and particulate inheritance for the theory of natural selection. With the traditional blending theory accepted by Charles Darwin, heritable variation is shown to be rapidly dissipated, whereas with Mendelian or particulate inheritance it is conserved. With particulate inheritance the mutation rates needed to maintain a given amount of variation are therefore considerably smaller than those required with blending inheritance, where new variation would have to be snapped up by selection within a few generations before it disappeared. Fisher suggests that it was because Darwin accepted the logical consequences of blending inheritance that he was led into considerable speculation as to how new variability could be generated. Although Darwin thus came to believe that increased food and changed conditions were causes of variation, he was clear that, as regards evolutionary change, such factors were unimportant compared with selection. Fisher supports his contention by a masterly reconstruction and analysis of Darwin's reasoning, based largely on the rough essays of 1842 and 1844.

Darwin's essays were published in *The foundations of the origin* in 1909 and we know that Fisher studied them carefully when he was a student at Cambridge. A suggestion from Leonard Darwin may have provided the stimulus for Fisher to undertake his reconstruction of Charles Darwin's reasoning. He wrote to Fisher in the autumn of 1926 that his father's extremely modest nature led him to pay too much attention to criticism and therefore his earlier opinions should perhaps be given not less but more weight than the later ones. The analysis which Fisher carried out shed light not only on Charles Darwin's concern with new variation and especially with environmentally induced modification but also on the early Mendelians' view of the role of mutation in evolution. He alluded to these two aspects through the quotations he inserted below the heading to Chapter I.

But at present, after drawing up a rough copy on this subject, my conclusion is that external conditions do *extremely* little, except in causing mere variability. This mere variability (causing the child *not* closely to resemble its parent) I look at as very different from the formation of a marked variety or new species (C. Darwin, 1856).

As Samuel Butler so truly said: 'To me it seems that the "Origin of Variation", what ever it is, is the only true "Origin of Species".' (W. Bateson, 1909).

The first quotation indicates that although Darwin believed that almost every individual must involve new variation (or mutation as we would now say), he nevertheless drew a sharp distinction between the origin of variation and the origin of species. The second quotation shows that over half a century later Bateson was proclaiming that the origin of species was the same as the origin of variation. As Fisher (*CP* 279) later commented, Darwin 'showed a deep understanding in resisting the easy notion that evolutionary progress was, so to speak, worked by mutation'.

These carefully chosen quotations placed in thought-provoking juxtaposition at the start of the book seem particularly apt when one considers that the introductory chapter contains a comprehensive discussion showing that the bearing of Mendelian inheritance on evolutionary theory is indeed the opposite of that which the pioneers of Mendelism such as Bateson took it to be. The author's presentation of this argument is a model of clarity. Nevertheless it has not always received the attention it deserves. In two books on evolution published in 1963 and 1976, Mayr[26] describes the quotation from Bateson as the 'motto' for Chapter I of *GTNS* and claims that it shows Fisher believed that mutation is the only true origin of species! In reality, as any reader of *GTNS* can see, the very opposite is the case. One of Fisher's aims in Chapter I was to dispose of the point of view represented by Bateson's statement and so prepare the way for a discussion of the pioneering advances in selection theory made possible by developments in population genetics. The early Mendelians had ignored the distinction between mutation and ~~evolution~~ selection latent in Charles Darwin's work and 'thought of Mendelism as having dealt a deathblow to selection theory whereas in reality it had swept the field of all its competitors' (Fisher, *CP* 279).

Fisher had shown that the logical argument on which Darwin relied, and which governed the opinions expressed in the *Origin*, finds expression only in the essays of 1842 and 1844. Writing to M.J. Feldstein in 1929, Fisher related his finding to a more general question in the history of science: 'The history ... of the development of fundamental ideas has been much obscured by the hesitation of great men to publish incomplete work ... The bearing of Mendelism upon evolutionary theory could scarcely have been so misunderstood as it has been, if these essays had first put Darwin's views incompletely before the world.'

Chapter II, which Fisher described as 'heavy', is noteworthy for three reasons: (i) the development of the quantitative ideas necessary for a precise examination of the nature of selective advantage; (ii) the derivation of the Fundamental Theorem of Natural Selection; and (iii) the discussion of the nature of adaptation. Fisher first shows how to take account of the age structure of a population to define what he called the 'Malthusian parameter of population increase' to represent the fitness of the population. A Malthusian parameter may be defined similarly for any genotypic class in the population so giving a measure of that genotype's fitness. In this formulation, which involves an integral equation and age-specific birth- and death-rates, each age group is weighted by what Fisher called its *reproductive value*. This is a measure of the extent to which persons of given age contribute to the ancestry of future generations. This concept was entirely new with *GTNS*. As Medawar and Medawar[27] ascribe the Malthusian parameter to A.J. Lotka and say it was 'borrowed without acknowledgement by R.A. Fisher in his treatise on the Genetical Theory of Natural Selection', it should perhaps be noted that Fisher has recorded that he developed these concepts independently of Lotka. In fact, the intrinsic rate of population increase, which Lotka introduced into demography in 1925, has the same value as Fisher's Malthusian parameter if, ignoring all differences in reproductive value, it is assumed that the population has attained its steady-state age distribution.

Fisher wrote to Darwin on 27 June 1929 with an interesting application of his new concept: 'The reproductive value at different ages must determine the extent to which parental care pays.' He considers the case of an old oak in a forest having a greater expectation of posterity than a young one and concludes that 'it would be a bad bargain for the father oak to benefit his offspring unless he could do so by losing considerably less than the offspring gains.' For crocodiles, assuming they could recognize their mature progeny, 'I suppose they would co-operate with them not only on terms of mutual advantage, but on terms of joint advantages so long as the loss of either did not exceed half the gain of the other. Hence society starts with the family.'

In a short section headed, 'the genetic element in variance', Fisher (*GTNS*, p. 30) shows how, taking account of the genotypic composition of the population, a part of the population variance for a quantitative character may be identified as the genetic variance (now widely called the additive genetic variance), being the variance of the relative genetic values (also called the additive genetic or breeding values) which are built up of the average effects of the genes. He sets this out for the general case of a non-random mating population, introducing the concepts of average excess as well as average effect of a gene or gene substitution. Fisher then applies this method of analysis to the case where fitness is the quantitative character and arrives at what he calls the Fundamental Theorem of Natural Selection: 'the rate of increase in fitness of any organism at any time is equal to its [additive] genetic variance in fitness at that time.' The fundamental theorem specifies the relationship between the instantaneous rate of evolutionary advance in fitness and the additive genetic variance in fitness when *all* genes are taken into account. In an interesting article entitled, 'Fisher's "fundamental theorem" made clear', G.R. Price[28] came close, I believe, to Fisher's meaning in a number of respects but he went on to describe Fisher's 'device of treating non-additive gene effects as "environment"' as a 'defect'. Writing to O. Kempthorne in 1955, Fisher elaborates on his reasons for regarding the components of fitness attributable to dominance, epistasis, and environment as 'all in the same boat' in respect of their effect on the evolution of the species. He says these components cannot by themselves have any evolutionary effect on the species but they may induce selection in favour of genes which enable the organism to exploit these components of variance in fitness. He considers the situation in which, by the extinction of certain insects, a plant species rapidly becomes self-fertilized and homozygous; the genotypic frequencies are changed but, so long as the gene frequencies are unaltered, Fisher suggests that the plant cannot be said to have evolved but is just reacting passively to its changed environment. Fisher's letters to M. Kimura throw further light on these questions.

In considering Fisher's achievement with the quantitative analysis of selection in Chapter II, it should be remembered that the concept of individual characteristics being advantageous or adaptive, even when strikingly cryptic or warning coloration was involved, was not generally accepted in 1930. For many biologists adaptation remained as a puzzle. In 1909, Bateson had written 'Mendelism ... provides no fresh clue to the problem of Adaptation' and 'we look on the manner and causation of adapted differentiation as still wholly mysterious',[29] and again in 1924, 'modern discoveries have given little aid with the problem of the origin of adaptation'.[30] The early Mendelians regarded large mutations as the stuff of progressive evolution. Believing there was no evidence for large differences resulting from many small changes, they saw it simply as a matter of chance that a mutant should arise conforming closely to its environment in a great many particulars. Some biologists regarded the high degree of improbability of such an event as an argument against Darwinism. Writing to A.J. Nicholson in 1955, Fisher said '... I feel sure that Darwin would never have made his discovery had he not been remarkably strongly impressed with the reality and intensity of adaptations. It was, I think, only the fading of this impression towards the end of the nineteenth century which opened the door to theories of de Vries' "mutation theory" type.' In Chapter II, Fisher considers adaptive improvement as an interaction between the organism and its environment and concludes that it must generally involve many separate differences and also a large number of small evolutionary steps. With a well-adapted organism, large mutations must be harmful. Small mutations were thus seen to have far greater biological importance than those of large extent. This was contrary to the belief of the early Mendelians; according to Bateson, 'the smaller the steps, the less could Natural Selection act upon them'.[31] Having earlier shown that Lamarckism, orthogenesis, and other theories of evolution worked by mutation are inconsistent with the observation that the great majority of mutations are deleterious, Fisher concludes that natural selection is the only known mechanism which can gradually accumulate and combine the various contributory changes. Since natural selection leads to combinations of genes which otherwise would be extremely unlikely, it could be described as a mechanism for generating an exceedingly high degree of improbability. Such an outlook involved a fundamental change from the earlier description of evolution as a chapter of accidents. The objection that the principle of natural selection depends on a succession of favourable chances is, Fisher says (*GTNS*, p. 40), 'more in the nature of an innuendo than of a criticism, for it depends for its force upon the ambiguity of the word chance, in its popular uses'. His opinion of the supreme importance of Darwin's conception of natural selection is perhaps best summarized in the following sentence (*CP* 258), '... it was Darwin's chief contribution, not only to Biology but to the whole of natural science, to have brought to light a process by which contingencies *a priori* improbable, are given, in the process of time, an increasing probability, until it is their non-occurrence rather than their occurrence which becomes highly improbable.'

Chapter III on the 'Evolution of dominance' was written in November 1928 only a few months after Fisher had first developed the relevant theory (*CP* 68). Dominance, he suggests, should be regarded as a modifiable property of the phenotype, which, in suitable circumstances, could have evolved over a long period through selection acting on modifying genes in the genetic background of the organism. It will be advantageous for the organism if rare deleterious mutants, repeatedly produced over a great many generations and generally carried in a single dose, are rendered recessive. Most mutants are deleterious and are thus expected to be recessive but with selectively neutral or advantageous mutants the theory gave no reason for expecting dominance or recessiveness to have evolved.

Fisher's theory of the evolution of dominance provoked much discussion. It was first criticized by Wright[32] who questioned whether there were modifier genes sufficiently numerous and so nearly neutral in relation to all other evolutionary forces for Fisher's proposed scheme to give a plausible explanation for the common phenomenon of dominance. This comment reflected a basic difference between Fisher and Wright regarding the efficacy of minute selective intensities. We shall return to this point later.

Fisher's theory of the evolution of dominance was based on the same principle which he had applied in 1927 to account for the evolution of mimicry, the essential idea being that the genes of an organism comprise an interacting system, the effect of any gene being capable of gradual modification by selection acting on the rest of the genetic system. This work led the way to a wider recognition of the importance of interactions of numerous genes in the evolutionary process. Elsewhere in *GTNS* Fisher draws on the same principle in considering the selective modification of linkage values. These discussions of the role of selection in the evolutionary modification of mimicry, dominance, and linkage values contributed in an important way to the growth of the concept of the gene-complex. Fisher's work in this area is also noteworthy for drawing attention to the valuable contribution which evolutionary theory can make to an understanding of genetic phenomena—as distinct from the contribution which genetic theory makes to an understanding of evolutionary phenomena.

Fisher had found that when two factors in the same chromosome are both in equilibrium in a population in such a way that each greatly affects the selective advantage of the other, selection will tend to produce progressively closer linkage. If the genotype is not to congeal, this tendency to closer linkage must be counterbalanced in some way. Fisher suggested in *GTNS* that such an agency 'may be found in the advantage of combining different advantageous mutations which, unless they occur consecutively, can only be done by recombination', although he observed that this would probably mean that 'the stream of favourable mutations would need to be a considerable one'. Writing to Wright on 25 October 1930, he said 'the apparently non-mathematical parts [of *GTNS*] where I have left the mathematics undone, are often of the greatest ultimate interest' and he referred to the 'elusive problem of the effect of a stream of gene substitutions in loosening the linkage' mentioned in Chapter V. Writing to R.K. Nabours on 22 March 1933, Fisher said he had never been able to see how his suggested linkage-loosening agency could be great enough quantitatively but it 'might, I suppose, be much enhanced in a species which had recently experienced great changes in environment either by spreading into new habitats or by its ecological situation, including its predators, being much affected by human occupation. ... Perhaps the ideal form of selection for loosening linkage in general would be one in which one set of pattern combinations was highly selected for a few generations and a totally different complementary set were just as highly selected a few generations later. Seasonal selection, e.g. fertility in summer versus viability in winter, might perhaps really work in some such way ...' He was urging Nabours to collect suitable field data with his grouse locusts which might shed light on this problem. Writing to J.S. Huxley on 5 July 1954, Fisher said he was rather puzzled in 1930 as to 'how, in spite of such widespread tendency to closer linkage, free recombination had in fact been retained, as is needed if different improvements are to be combined, though I find it difficult to understand how this *effect* is itself effective in promoting recombination.'

The stage was now set for Fisher to present (in Chapters IV and V) a quantitative assessment of the consequences of Mendelian heredity for the maintenance of population variability taking into account selection, mutation, and finite population size. This was essential for the rehabilitation of natural selection, for as Fisher later put it (*CP* 258), 'Darwin had no deductive basis from which to infer the quantitative efficacy of a selective process in producing evolutionary change ... [and] he was undoubtedly led consistently to underrate the rapidity with which, in favourable circumstances, evolutionary changes can be brought about by natural selection.'

The problem of the survival of an individual mutant gene in a large population is examined using the branching-process model and functional iteration. So long as there are few copies of the mutant present, chance effects predominate in determining survival. For a mutant with a selective advantage s, the probability is approximately $2s$ that it will ultimately sweep through the entire population. It follows that an advantageous mutant can occur only a small number of times before its substitution in the population becomes practically certain. Fisher attached much importance to this result.

In *CP* 24 (1922), Fisher had initiated the study of change in population gene frequency as a random process evolving in time. Treating gene frequency as a continuous variate, he introduced the chain binomial model and diffusion methods involving partial differential equations into the study of gene frequency distributions in a population. In particular, he considered the effect of random sampling of gametes in a small population on both gene frequency and the decrease of variability—the case of steady decay—as well as the statistical equilibrium established between a supply of neutral mutants and the causes of extinction of such genes. In *GTNS*, this work is greatly extended. Noting that the solution of the diffusion equation for steady decay and neutral mutation give gene frequency distributions whose integrals fail to converge, Fisher derives the exact forms for the terminal class frequencies using the method of functional equations. Considering the statistical equilibrium maintained in a finite population by a supply of mutations each having a small selective advantage, he develops some far-reaching conclusions concerning the selective process. Perhaps the most important is that in a species with n individuals living to reproduce in each generation, selective intensities greater than $1/n$ exert entirely regular and calculable effects. He wrote (*GTNS*, p. 102),

The very small range of selective intensity in which a factor may be regarded as effectively neutral suggests that such a condition must in general be extremely transient. The slow changes which must always be in progress, altering the genetic constitution and environmental conditions of each species, must also alter the selective advantage of each gene contrast. Slow as such changes in selective advantage must undoubtedly be, the zone separating genes possessing a definite selective advantage from those suffering a definite selective disadvantage is so narrow, of the order of the reciprocal of the breeding population, that it must be crossed somewhat rapidly. Each successful gene which spreads through the species must in some measure alter the selective advantage or disadvantage of many other genes. It will thus affect the rates at which these other genes are increasing or decreasing, and so the rate of change of its own selective advantage. The general statistical consequence is that any gene which increases in numbers, whether this increase is due to a selective advantage, an increased mutation rate, or to any other cause, such as a succession of favourable seasons, will so react upon the genetic constitution of the species, as to accelerate its increase of selective advantage if this is increasing, or to retard its decrease if it is decreasing. To put the matter in another way, each gene is constantly tending to create genetic situations favourable to its own survival, so that an increase in numbers due to any cause will in its turn react favourably upon the selective advantage which it enjoys.

Writing to E.B. Ford on 24 March 1930, Fisher described this as 'rather a subtle principle'.

Fisher's theoretical deduction that the more numerous species tend to be the more variable genetically gave support to Darwin's suggestion that abundant species make the most rapid evolutionary progress. He wrote (*GTNS*, p. 132), 'An evolutionary consequence of some importance is that in general a smaller number of large species must be increasing in numbers at the expense of a larger number of small species, the continuous extinction of the latter setting a natural check to the excessive subdivision of species which would ensue upon a too fine and detailed specialization.'

In 1922, in the first discussion of selectively balanced polymorphism, Fisher (*CP* 24) suggested that factors involving heterozygote advantage would accumulate in the stock and should therefore be commonly found. In *GTNS* (p. 113), he considers the more general situation of a polymorphism where 'one gene has a selective advantage only until a certain gene ratio is established, while for higher ratios it is at a selective disadvantage'. He emphasizes that selective differences and therefore the conditions of stability must change during evolution. Such polymorphisms cannot therefore be absolutely permanent but as there is a tendency for them to accumulate, they must exist 'with a frequency quite disproportionate to the probability of occurrence of the conditions on which the stability is based' (*GTNS*, p. 114). Fisher suggests in several letters that he would have included more about polymorphism if *GTNS* had been written a little later. In 1929 he began corresponding with Nabours on genetical and ecological aspects of his work with polymorphic grouse locusts. His letters to Nabours contain many suggestions which were then quite novel. On 8 August 1932, he told Nabours that it would be 'of the very highest interest if you found that the proportion of dominants, and therefore the selective advantage of the colour

pattern, varied from place to place, for this would open up a whole new field in the quantitative study of ecological conditions.'

In Chapter VI, 'Sexual reproduction and sexual selection', Fisher at first discusses a question he had touched on in 1922 (*CP* 26), namely the evolutionary advantage of sexual reproduction. He suggests that evolution will occur more rapidly with sexual than with asexual reproduction because beneficial mutants involving different gene loci can more readily be brought together in a single individual. Writing to Wright in October 1930, Fisher says he had shirked the quantitative treatment of this problem. However, he does offer the following conclusion which is surely remarkable for 1930: 'the only groups in which we should expect sexual reproduction never to have been developed, would be those, if such exist, of so simple a character that their genetic constitution consisted of a single gene.' (*GTNS*, p. 137).

After considering the concept of a species as a natural group whose members are bound together by a constant interchange of their germ plasm via sexual reproduction, Fisher turns to the question of how it is possible for selection acting on small individual differences to lead to speciation. Noting that it is 'characteristic of unstable states that minimal causes can at such times produce disproportionate effects', he remarks that this problem 'involves complexities akin to those that arise in the discussion of the fission of the heavenly bodies'. He suggests that selection acting differently on different parts of a species will generate genetic heterogeneity and that an element of instability may then be introduced by genetic modification affecting gene flow between the parts. Under sufficiently intense selection, this would lead to speciation 'even in the absence of geographical or other barriers'. Fisher examines these ideas using a model of speciation with a geographical gradient in gene frequency, the gradient gradually becoming steeper until fission occurs.

An important means of fission in higher animals may be provided, Fisher suggests, by sexual preference where females in different parts of a species display a preference for differently characterized suitors. He is then led into a discussion of Darwin's theory of sexual selection. As Fisher wrote to E. Selous in 1932, he 'had ventured to add an excrescence of my own on the psychic evolution, through the same selective process, of female taste'. Fisher had discussed the evolution of sexual preference in 1915 (*CP* 6) but in *GTNS* he takes the argument much further and shows that in certain circumstances sexual selection will act by increasing the intensity of preference to which it is due and so lead to a 'runaway process which, however small the beginnings from which it arose, must, unless checked, produce great effects, and in the later stages with great rapidity'(*GTNS*, p. 152). In such a situation, sexual selection might ultimately be checked by natural selection.

Also in Chapter VI, Fisher uses his concept of reproductive value to show

how natural selection will lead to a sex ratio which equalizes the parental expenditure devoted to the production of the two sexes. He thus solves the problem of the influence of natural selection on the sex ratio, of which Darwin wrote in *The descent of man*, it is 'so intricate that it is safer to leave its solution for the future'.

Mimicry, the subject of Chapter VII was seen by Fisher as having special interest because of 'the great disparity between the views formed by the pioneers of Mendelism and those of selectionists' (*GTNS*, p. 187). The question of how the polymorphic mimetic resemblances for colour pattern in butterflies could have evolved presented a considerable challenge to the early Mendelians because the different forms not only mimicked models belonging to different genera or families but also were controlled by a single gene switch mechanism. Punnett's suggestion that the mimicry could be explained by parallel mutations in model and mimic required, as Fisher had noted (*CP* 59, 1927), 'the gratuitous assumption that no evolutionary change has taken place in the two alternative forms since the dimorphism was first established'. Fisher's explanation, which has been fully substantiated by later work, involved the gradual evolution of a gene-complex by selection operating on an interacting genetic system.

The rest of *GTNS* (Chapters VIII-XII), comprising one-third of the book, is devoted to the selective situation in civilized man. Fisher had first intended social selection in human fertility to follow sexual selection and mimicry as a third application of natural selection. He found, however, that the argument in this case needed more extensive development and as this section grew in size he was concerned that the reader might not easily see it as a whole.

Fisher begins with the assertion that human characteristics, whether of a physical, mental, or moral kind, have evolved under natural selection and may be studied just as are the characteristics of any other organism. In particular, individual differences in human behaviour, especially those associated with fertility, must be seen as capable of leading to important evolutionary changes. In examining the main agencies at work in the evolutionary modification of man and his social organization, genetical variation must be considered equally with sociology and the historical record. The rise and fall of numerous civilizations calls for some very special explanation. The advantages of civilization would surely be enhanced and prolonged 'if, as it was formerly thought could be safely assumed, life in the civilized condition, as in the barbaric state, favoured the survival and reproduction of those human types who could most effectively promote the prosperity of their society and who on the other hand were most apt temperamentally to appreciate and exploit its advantages' (*GTNS*, p. 199). Why, then, has it been otherwise?

Fisher first considers the role of selection in the evolution of co-operative behaviour and specialization of labour in civilized man and in the social insects. In his 1912 paper on social selection, he had said that in the social insects, 'there is no conflict between the interests of family and the nation, which in human society constitutes the central problem in Eugenics: where those individuals who are of most use to the state, and who will sacrifice themselves most readily for the common good, are often prevented by that very sacrifice from procreating their valuable kind.' In insect communities, reproductive specialization has eliminated intracommunal selection as an evolutionary agent. In *GTNS*, Fisher suggests that when human societies adopted an economic system of individualizing property, this might have been expected to control intracommunal selection in a socially advantageous way, with social success and accumulated wealth reflected in high fertility. However, this expectation has not been realized. Fisher says that differences in behaviour associated with fertility have been of major importance in the evolution of human societies. He suggests that the human species is unique in having differential fertility instead of mortality as the main factor affecting selection and, on the evidence available, he concludes that there is an important genetical component in fertility differences. In Chapter X Fisher considers the relation between fertility and social class; for all civilized societies for which data are available he says the birth-rate has a larger value in the lower than in the higher social classes. He suggests that it is important that we recognize 'the absolute failure of the economic system to reconcile the practice of individual reproduction with the permanent existence of a population fit, by their mutual services, for existence in society', for in his view it is the inversion of the birth-rate with respect to social class which has led to the decline of apparently successful civilizations.

In Chapter XI Fisher develops his theory of the selective process by which the inversion of the birth-rate becomes established in civilized societies. The two essential elements are (i) the social promotion of the less fertile and (ii) a genetical component in characteristics affecting reproduction. He points out that in primitive societies having a tribal organization the more eminent individuals are generally the more fertile and the effects of natural selection are greatly enhanced by social and sexual selection. Altruistic qualities such as those associated with heroism, recognized as socially valuable in such groups, may then be developed considerably further than could be ascribed to individual advantage alone. Fisher suggests that the higher mental qualities of man, and especially his appreciation of them, may also be ascribed to social selection acting in a similar way.

Having found that in civilized man the main selective influences act through the birth-rate and that such selection is very intense and against all the factors of social success, Fisher in the final chapter offers his suggestions for countering the social promotion of infertility so as to provide conditions thought necessary for a permanent civilization. The financial burden of raising children should not rest with the parents but should be distributed equally throughout the members of the same social class by means of family allowances *proportional to income.* If this were done, there should be an equal standard of living for equal work irrespective of the size of the family. When the introduction of family allowances was being widely discussed in Britain after the First World War Fisher argued against flat allowances and for a system of proportional allowances to be regarded as an integral part of wages and salaries. Such allowances, he suggested would be comparable in principle with the proportional deductions made widely for superannuation benefits. Fisher attached great importance to proportional family allowances as part of a long-range population policy. It is a subject which comes into a number of his letters to Darwin and other correspondents.

In developing his argument that there is a biological basis for expecting the decline of civilized societies in which there is a reduced fertility amongst those who are socially successful (where socially valuable qualities making for leadership, enterprise, high endeavour, etc., are generally most frequent) Fisher referred to the economic system of individualizing property, 'which, diverse as are the opinions which different writers have formed about it, appears to the writer to be one of the unconscious triumphs of early human organization' (*GTNS*, p. 201). Writing to C.V. Drysdale on 4 October 1929, he said, 'free competition is invaluable in stimulating the production of wealth, but should be excluded on economic and eugenic grounds from the question of the reproduction of children. Unless it is so excluded, you cannot fail to recruit the next generation preferentially from the least prudent, or the most bigotted.' After reading *GTNS*, J.B.S. Haldane told Fisher that he regarded this part as 'highly controversial' and that if he were convinced by it, he would have to become an extreme form of socialist. J.S. Huxley reacted to the final section of *GTNS* by suggesting that to work against individualism was eugenic.[33] Aldous Huxley wrote on 26 September 1931 that 'after reading in your book about the effects on the human stock of a social organization based on economic reward I think we have a right to a good deal of gloom and alarm'. Fisher's response to his finding that class differences were an essential feature of the dysgenic process in civilized life was quite different. As he wrote to Darwin on 16 March 1931, he had tried to conceive of biologically progressive societies which were classless, but he found this always led to an impasse: 'Man's only light seems to be his power to recognize human excellence, in some of its various forms... Promotion must be a reality.' Fisher's attitude is consistent with his general view of the human condition and the nature of evil which he expressed when writing to Bishop Barnes on 12 January 1952: 'Man is in process of creation, and that process involves something we can call improvement, in which Man's own co-operation is necessary. Hence the need to become acutely conscious of evil or quasi-evil in ourselves and in the world, just as the increase of natural knowledge requires a corresponding consciousness of ignorance. Complacency in either respect would seem quite deadly to progress.'

Reception of *GTNS*

With its novel approach to the theory of natural selection, *GTNS* presented a challenge to readers and reviewers. Fisher wrote to L.C. Dunn in 1930,

> The book will be really difficult to review owing to new arguments being developed (though from a central viewpoint) on questions which hitherto have been discussed in isolation, and which consequently appear at first sight to be very distinct. If I had to review it I should waver much between giving the reader an idea of Chapter I, and alternatively, of the arguments in Chapter VI. The human chapters are more manageable being really the development of a new evolutionary argument as to social selection, comparable with such developments as Sexual Selection and Mimicry; and it is done more fully as is necessary in breaking new ground.

The review in *Nature* by Punnett[34] was a great disappointment to Fisher. Punnett's approach was revealed in his opening paragraph: 'Probably most geneticists today are somewhat skeptical as to the value of the mathematical treatment of their problems' believing that 'in their own particular line it is, after all, plodding that does it'. Most readers, he said, would find the final section of *GTNS* dealing with Man, 'the brightest part of the book for apart from the absence of mathematical formulae, it is full of shrewd comments and odd bits of learning'. The significance of *GTNS* evidently went unrecognized: 'Throughout the book one gets the impression that Dr. Fisher views the evolutionary process as a very gradual, almost impalpable one, in spite of the discontinuous basis upon which it works.' When Darwin read this, he wrote at once to Fisher saying how sorry he was that *Nature* had picked 'an old discontinuous stick-in-the-mud like Punnett'. Then, characteristically, he added 'to get 5 columns is an excellent advertisement. My father would have been much pleased by such a review of the *Origin,* and merely carefully noted the points to answer in his next edition'. However, Fisher thought he should tidy up such 'troublesome trifles' at once; he published a rejoinder to Punnett in the same volume of *Nature.*

Some biologists realized quickly the worth of Fisher's book. Writing in the *Eugenics Review* under the heading 'Mathematical Darwinism', Haldane[35] said *GTNS* laid the foundations of a new branch of science and that 'no serious future discussion, either of evolution or eugenics can possibly ignore it ...; during the next generation any discussions of the problem of gradual evolution which are likely to be of permanent value will take the form of a development, discussion, and perhaps in some cases, a refutation of the arguments stated in the book before us.' In a review in the *Mathematical Gazette,* Haldane[36] wrote that *GTNS* 'should serve not only to raise the discussion of the evolution problem to a higher level but to introduce mathematicians to a new growing point of their subject'. Interestingly enough, Haldane added that Fisher's runaway process (*GTNS*, p. 152) had special value in explaining orthogenesis and he believed this process was more important than Fisher's 'fundamental theorem'.

Long and favourable reviews of *GTNS* were published in a number of English periodicals. An anonymous reviewer in *The Times Literary Supplement* of 28 August 1930 described it as 'the most important contribution to biological theory which has appeared in any country in the last quarter of a century', and added, 'it may well be the beginning of a new phase in the endeavour to understand the living world'. A reviewer in *The Spectator* of 24 May 1930 said the task of considering the theory of natural selection on its own merits 'certainly has never been performed with anything like the skill and subtlety now brought to bear upon it' in *GTNS*. C.G. Darwin wrote in the *Eugenics Review* that the 'masterly quality of the book can be seen even by reading the four short pages of the Preface'. A. Bradford Hill in a long review in the *Journal of the Royal Statistical Society* quoted from Fisher's preface, 'no efforts of mine could avail to make the book easy reading' and then commented, 'From Dr. Fisher this is no mean threat; anyone at all conversant with his scientific works knows that they are invariably difficult to read—though, equally invariably, exceedingly well worth the effort demanded.'

Upon publication of *GTNS*, Fisher had arranged for complimentary copies to be sent to a number of American scientists, including L.C. Dunn, H.H. Laughlin, T.H. Morgan, H.J. Muller, R. Pearl, E.B. Wilson, and S. Wright. Whilst the book was not unknown in America in 1930, it appears to have taken longer there than in England for it to be widely appreciated. According to Dobzhansky, Ayala, Stebbins, and Valentine,[37] 'The reception of Fisher's book is a clear indication of the climate of its time. One searches in vain through the issues of *Science* for 1930 and 1931 for a review of it. Apparently the editors did not consider it important enough to be worth reviewing.' At least two American journals carried reviews of *GTNS*. In the *Quarterly Review of Biology,* of which R. Pearl was editor in 1931, it was dismissed in a brief note, which described as 'paradoxical' Fisher's conclusion that the direction of evolution is determined not by the direction of mutation but by that of selection. The *Journal of Heredity* published a long review by Wright[38] who described *GTNS* as 'a book which is certain to take rank as one of the major contributions to the theory of evolution'. He went on to give a critical discussion of Fisher's concept of evolution which he described as 'pure Darwinian selection' and indicated that in his view less weight must be given to what individual selection is doing.

Shortly after publication of *GTNS*, Fisher's interest in the role of selection turned to the exciting possibilities opened up by the study of polymorphisms and the human blood groups. Several early readers, noticing that blood groups were not referred to in *GTNS*, wrote seeking Fisher's views on the role of selection, mutation, and migration in determining the different racial frequencies of the ABO blood types. When R.R. Gates suggested that these serological differences were apparently without selective effect, Fisher replied (1 July 1930), 'There are a good many climatically limited blood diseases, such as malaria and yellow fever, so I would not be too sure of the absence of selection.' On 18 October 1934, Fisher wrote to W.C. Boyd, 'I cannot see any escape from the view that the frequencies have been determined by more or less favourable selection in different regions, governed not improbably by the varying incidence of different endemic diseases in which the reaction of the blood may well be of slight but appreciable importance.' These must be some of the earliest suggestions put forward for natural selection acting via climatically limited endemic blood diseases in the maintenance of human polymorphism.

When Charles Todd's work on the individuality of red blood cell antigens in chickens was brought to Fisher's attention, he wrote at once (23 April 1930) suggesting that Todd was detecting primary gene products and proposing further experiments. A. H. Sturtevant[39] in his book *A history of genetics* says that Todd's remarkable results were 'soon interpreted to mean that the antigens were close to immediate gene products, and might furnish useful materials for the study of the action of genes, relatively free of the complications of developmental interactions. It is not clear who first formulated this idea; I first heard it in conversation with Haldane in the winter of 1932-1933. However, the results of this assumption have been of far-reaching importance in the study of the developmental effects of genes.' Several of Fisher's letters to Todd and Haldane in 1930 shed interesting light on this question.

Fisher was soon predicting on the basis of Todd's work that serological methods would uncover many genic differences in Man and that this would lead to a revolution in human genetics. He was anxious to see a start made in 1930 and tried in vain to persuade Darwin that the Eugenics Society should support a research worker in this area. In 1933, Fisher moved to the Galton Laboratory and shortly afterwards he set up the Serum Unit which soon made important contributions to knowledge of the human blood groups, especially with the Rhesus system.

Fisher's early interest in blood groups stemmed largely from his ideas on the evolution of dominance. His letters to Todd and Boyd show that he was at first contemplating the possibility of many, if not most, genes being detectable via serological effects. An excellent account of the development of his ideas in this area is provided by Joan Fisher Box in Chapter 13 of *FLS*.

Second edition of *GTNS*

Shortly before publication of *GTNS*, Darwin had written telling Fisher not to be disappointed at a small sale. It was, he said, 'the kind of book to work through others'. In fact, there was a gratifying early demand for *GTNS* and more than one-third of the 1500 copies printed were sold in the first 12 months. However, sales soon declined markedly and the last copies of *GTNS* were not sold until 1947.

In 1930 Darwin repeatedly urged Fisher to prepare extra material in readiness for a second edition. Early in 1931 Fisher wrote a review of the criticisms raised against the theory of natural selection 'with a view to repairing something like an omission from my book'. He thought of including this as an extra chapter in a proposed German translation of *GTNS*. However, as sales of *GTNS* fell away, the prospects of a German translation and a second English edition receded. In November 1931 Fisher sent a copy of the article to Julian Huxley and asked if he knew an editor who would care for it. The paper remained unpublished and Fisher filed it away. Twenty years later he brought it out and sent if off as his contribution to *Evolution as a process*, a volume of essays on evolution published in honour of Huxley. Unfortunately, Fisher did not add a note explaining when and why he had written this paper, 'Retrospect of the criticisms of the theory of natural selection' (*CP* 258, 1954). In 1980 it was cited by Mayr[40] as an example of 'post-synthesis literature' with 'an extraordinary amount of space ... devoted to the refutation of anti-Darwinian arguments'.

When Fisher sent this article to Ford in 1951, he dismissed the possibility of a second edition of *GTNS*: 'the most I should be inclined to attempt would be a book of essays taking up particular topics such as this one'. In 1955 Dover Publications expressed interest in reprinting the original text. When their paperback edition of *GTNS* appeared in 1958, it contained various changes and additions supplied by the author. Though widely referred to as the second edition, Fisher did not like to call it that. Whilst he acknowledged that he could not give the amount of work necessary to bring the original text up to date in its various aspects—genetical, evolutionary, sociological, etc.—it was probably also his historical sense which led him to prefer that *GTNS* should stand as 'the first attempt in strictly genetical terms to appraise the weight of evolutionary theories going back for nearly a century'.

The additions and alterations introduced with the Dover edition were collected up from the author's interleaved copy of *GTNS* where he had noted them down as they occurred to him over the years. Some of this material had been prepared a quarter of a century earlier. As slightly smaller print was used for the new material in the Dover edition, it is not difficult to see where changes or additions have been made. There was no major alteration but several of Fisher's additions deserve comment. In Chapter II, when considering the analysis of genetic variance, he introduces a more general formulation taking account of multiple alleles which he had developed about 1930. Unfortunately, the presence of a number of typographical errors detracts from the presentation of this new material.[41] An insertion which should not be overlooked occurs on page 40 where Fisher explains how, in his Fundamental Theorem of Natural Selection, the evolutionary effects ascribable to the dominance component of the genotypic variance are credited to gene substitutions at other loci.

An addition of particular interest is the reference to individual and group selection on page 49. As Fisher wrote to A.G. Lowndes on 23 June 1945, '... natural selection will only explain adaptations insofar as they are effective in preserving the germ plasm of the individuals concerned.' In the Dover edition, he says it is doubtful if any character, with the possible exception of sexuality itself, could be interpreted as having evolved for specific rather than for individual advantage. In his letter to Lowndes, Fisher emphasized that individual selection 'does not preclude adaptations which are effectual through the survival of relatives, for these share to a great or less extent the germ plasm of the individual'.

The most extensive changes in the book are in Chapter III on the evolution of dominance where Fisher said the tentative and apologetic approach adopted in 1930 was inappropriate in 1958, given the progress made during that period in understanding the important role of systems of interacting genes in evolution.

A significant addition to Chapter VI (p. 153) is Fisher's non-genetic early nesting model which he developed in order to account for Charles Darwin's suggestions on sexual selection in monogamous birds. This was the subject of several letters between Fisher and Leonard Darwin who wrote (20 August 1930) that he thought his father would have been 'a bit surprised that such a complicated explanation was needed'. There are several slips in the passage as printed which make it hard to follow but Fisher's letters to Darwin (27 June and 7 August 1930) show what he intended and also how some of the slips came about. Also in Chapter VI Fisher added a section referring to butterflies of the genus *Limenitis* in the eastern USA as 'an example of a species in process of fission, in which sexual preference is evidently playing an important part' (*GTNS*, pp. 145-6). Fisher was doubtful about the validity of this example, the information on which had come to him from E.B. Poulton about 1935. Late in 1955 when preparing material for the Dover edition, he sought advice on this from E.B. Ford and L.P. Brower. The passage which was ultimately inserted in *GTNS* in its original form was later criticized by Platt and Brower (1968).[42] Referring to examples of phenotypic intergradation in areas of geographic overlap between populations which are elsewhere distinct and relatively homogeneous, as a key to understanding the process of the origin of species, they say,

> one of the most historically significant concerns two North American nymphaline butterflies of the genus *Limenitis*, *L. arthemis* Drury and *L. astyanax* Fabricius. Fisher (1930) regarded the available data on these butterflies as evidence for their being incipient species on the verge of attaining complete genetic isolation. This example proved important to understanding not only the role of sexual selection in interspecies evolution (Huxley, 1938a, b) but also laid the foundation for Dobzhansky's (1937) theory that, following allopatric separation and divergence, speciation can be completed by selection in the zone of secondary overlap. Notwithstanding the absence of subsequent substantiating data, this interpretation of the *arthemis-astyanax* complex was accepted by Hovanitz (1949), reasserted by Fisher (1958), and again put forward by Mayr (1963).

Platt and Brower found that mating occurs at random in the zone of overlap of *L. arthemis* and *L. astyanax*, and they offer a plausible explanation for the maintenance of this narrow zone based on mimicry. Evidently Fisher was right to have had misgivings about the passage on *Limenitis*, but despite what Platt and Brower suggest in the above quotation, his insertion of this passage in the Dover edition of *GTNS* in 1958 can scarcely have misled other writers on this subject in publications which appeared 10 or 20 years earlier.

Fisher, Haldane, and Wright

The publication of *GTNS* was followed shortly afterwards by S. Wright's (1931) paper, 'Evolution in Mendelian populations', and J.B.S. Haldane's (1932) book, *The causes of evolution*. Wright's view of the role of selection in evolution differed markedly from Fisher's. This difference, described by Fisher and Ford (*CP* 239, 1950) as 'the widest disparity which ... has so far developed in the field of Population Genetics', became the subject of much argument. Can Fisher's correspondence add to our understanding of the issues involved?

It seems that Fisher first wrote to Haldane and Wright when they published criticisms of his theory of the evolution of dominance in 1929-30. The correspondence with Haldane continued for many years but that with Wright stopped in June 1931. The Fisher-Wright letters, however, are of great value for the light they shed on the development of their differing views of the roles of selection and random drift in evolution.

As far as we know, Fisher first wrote to Haldane on 15 March 1930 enclosing a draft of his paper on the evolution of dominance in certain polymorphic species (*CP* 87). Fisher clearly valued the stimulus provided by Haldane's suggestions in this area. Over the next ten years they seem to have enjoyed exchanging letters, discussing questions of natural selection, and

sometimes sending drafts of their papers to one another for comment. Their letters are perhaps of greatest interest for what they reveal of their relationship in that decade, especially in 1933 when Fisher was about to join Haldane at University College London and again in 1940 when Haldane was about to join Fisher at Rothamsted.

Fisher first wrote to Wright on 6 June 1929 with a draft reply to Wright's paper criticizing dominance theory.[32] Wright had claimed that the selective pressures on the modifying genes were too small to be effective. When Wright replied that this criticism rested on the assumption that modifiers would nearly always be subject to other selective pressures more important than those concerned with dominance modification, Fisher wrote back encouraging him to publish a second paper since, he said, others also might have missed this point in the earlier paper. When Wright published a second paper,[43] he introduced the suggestion that the most important selective action on a gene is not necessarily the controlling factor. I think this exchange may be seen as the first of a series of misunderstandings between Fisher and Wright. Wright was proposing that natural populations are often of such restricted sizes that random drift is important in determining the frequencies of genes subject to very small selective differences. Fisher wrote (13 August 1929) questioning the importance of this factor; he suggested that in considering the interference of population number n with selection, n must be based on the entire species unless isolation in districts were substantially complete.

Now Fisher had met Wright in 1924 during a visit with a party of mathematicians to the US Department of Agriculture centre at Beltsville. Almost 30 years later, when writing to a friend about organization of the biological sciences, Fisher recalled that occasion.

> In the Dark Ages of 1924, I had the pleasure of visiting a research centre at Beltsville ... and was impressed even then to find that there was a department for research on horses and one for cows, and I think there was also one each for sheep, pigs and poultry, but none for Physiology or for Pathology or for Parasitology, Nutrition, etc. There was, however, newly injected and shining like a star, Sewall Wright with a Department of Genetics, an enormous corrugated iron building crammed from floor to roof with guinea pigs. I am afraid I held up the progress of the party sitting in the hot sun outside this building surrounded by tiers and tiers of guinea pig skins.

Later in 1924 Fisher sent Wright a copy of his 1922 paper (*CP* 24) dealing with gene frequency distribution in populations. In 1929 Wright wrote to Fisher that, stimulated by that paper, he had himself made a comparable study and had arrived at the value $1/(2n)$—instead of $1/(4n)$ as given by Fisher (*CP* 24)—for the rate of decay of gene frequency in a random mating population of n individuals with no mutation or selection. On 13 August 1929, the same day as that on which Fisher wrote to Wright suggesting that the relevant population number must be that for the whole species, Wright wrote to Fisher enclosing a copy of his manuscript on gene frequency distribution. He sought Fisher's comments saying that he was not clear as to the cause of the discrepancy between $1/(2n)$ and $1/(4n)$. Two weeks later, replying to Fisher's letter of 13 August 1929, he agreed that the population number n must be based on the entire species, unless isolation in districts is substantially complete, and he acknowledged that isolation would need to be much more nearly complete than he had at first realized if it were to lead to random fixation of strains. Was not Wright suggesting that he now saw isolation as a less important factor affecting gene frequency than he did when he wrote the big manuscript? Perhaps this was what Fisher had in mind when he wrote (9 September 1929) that Wright's letter of 28 August 1929 'is not only exceedingly interesting in itself, but helps me to understand the larger paper, which I have been puzzling over occasionally for some time'. I think this exchange contained the germ of a second misunderstanding since Wright's later writings showed that he continued to regard the relevant population number n as that for the local population and not the species.

The discrepancy between $1/(2n)$ and $1/(4n)$, which Wright found, required Fisher to re-examine the diffusion approach used in his 1922 paper (*CP* 24). He soon found that he had neglected a small term in the diffusion equation; when this was included there was complete agreement with Wright's result for the case of no mutation and selection. This experience led Fisher to undertake a more detailed study of the terminal class frequencies using the method of functional equations which he had outlined in *CP* 24. He took the opportunity to include an account of this work and the corrected diffusion equation in *GTNS* at the proof stage in October 1929.

On 1 January 1930, Wright read a short paper, 'Evolution in a Mendelian population', to a meeting of American geneticists. The published abstract ends with the following passage.[44]

> In too large a freely interbreeding population, there is great variability but such a close approach of all gene frequencies to equilibrium that there is no evolution under static conditions. ... With intermediate size of population, there is continual random shifting of gene frequencies and consequent alteration of all selection coefficients, leading to relatively rapid, indefinitely continuing, irreversible, and largely fortuitous, but not degenerative changes, even under static conditions. The absolute rate, however, is slow, being limited by mutation pressure. Finally, with a large but subdivided population, there is continually shifting differentiation among the local races, even under uniform, static conditions, which, through intergroup selection, brings about indefinitely continuing, irreversible, adaptive, and much more rapid evolution of the species as a whole.

Wright's concern with the lack of evolution in a large freely interbreeding population under 'uniform, static conditions' is plainly evident, as is the way this led him to propose an important role for population subdivision and intergroup selection in his 'shifting balance theory of evolution', as he later called it. On 10 June 1930, writing to thank Fisher for a copy of

GTNS which he had just received, Wright suggested that the above abstract —written before he saw *GTNS*—exaggerated the differences between them since 'I was forced by limitation of space to express my views in a balder and more unqualified form than I would care to maintain fully.' Shortly afterwards, when reviewing Fisher's book, Wright spelt out clearly a basic difference in their points of view. He wrote,[38] 'throughout the book (Fisher) overlooks the role of inbreeding as a factor leading to the non-adaptive differentiation of local strains, through selection of which, adaptive evolution of the species as a whole may be brought about more effectively than through mass selection of individuals.' Wright emphasized that, in his view, inbreeding has an essential role in the theory of evolution. His confident statement on this point seems to have come as a surprise to Fisher. Upon seeing the review, he wrote at once to Wright (19 January 1931):

> You must really take some later opportunity to set out your views more fully, for I am willing to be convinced, not of the importance of subdivision into relatively isolated local colonies, which I should agree to at once, but that I have overlooked here a major factor in adaptive modification which is what at present I am not convinced of. The point is very well worth going into in detail. I fear though that an adequate discussion will be above the heads of many biologists.

Evidently, Fisher expected Wright to have developed a mathematical theory justifying his view of isolation as a primary factor in adaptive modification. Writing on the same day to E.B. Ford for his opinion on this question, Fisher said that whilst he could see that random survival in small isolated colonies may be of special importance in some cases, he did not appreciate how it could *generally* favour a more rapid progress in *adaptive* modification, and he added, 'at present I doubt if the adaptive modification of the species as a whole would in general be at all retarded by a complete mixture of every generation.' In fact, Fisher seems to have come to the conclusion well before this that isolation would have to be very extreme to be worth anything genetically. He had written as much to Darwin on 15 January 1929 and to Wright himself on 13 August 1929. Now, however, that Wright had published such a definite statement about partial isolation as a primary factor in adaptive modification, Fisher was inclined to emphasize that the different views of Wright and himself on this point were ones held 'at present'. On 20 April 1931, for example, he wrote to A.B.D. Fortuyn,

> As far as I can see at present, isolation, whether geographical or physiological, whilst of immense importance to the problem of fission, is not a primary factor in adaptive modification, save in the subordinate sense that fission is a necessary condition for divergent adaptation. Sewall Wright, however, at present thinks otherwise, and there are very few men who have a better right to form their own opinions.

At the end of May 1931, when Fisher arrived at Ames, Iowa, for a six-week period as visiting professor, he wrote at once to Wright in Chicago asking when he could visit him there. No doubt Fisher was anxious to hear about Wright's theory, to judge for himself what significance should be given to it, and to see if they could then agree on the role of random survival in adaptive evolutionary modification. Fisher's next letter, written after he had visited Chicago, was evidently the last one he sent Wright. After thanking the Wrights for their kindness and hospitality, Fisher gives a hint of exasperation that his visit to Chicago, made especially to talk with Wright, and which no doubt involved long and searching discussions, had not led him to a better understanding of Wright's views on those points on which they differed. There is a rare touch of finality about Fisher's remark that he saw no chance of ever understanding Wright's views on those points which he had discussed with J.L. Lush in Ames. Perhaps it is significant that, shortly afterwards, when reviewing Wright's paper, 'Evolution in Mendelian populations', Fisher drew a distinction between Wright's 'scientific conclusions' and his 'philosophical observations on the nature of the evolutionary process, which are of great interest, although necessarily more personal and subjective' (See Appendix A, p. 287). Commenting on Wright's concern with the lack of evolution in large outbreeding populations under uniform static conditions, Fisher said that not only had Wright overlooked the advantages of a large population with respect to mutation, but also that, since the environment must be continually changing, static conditions in the evolutionary sense do not occur.

In 1932, both Fisher and Wright were in Ithaca, New York for the Sixth International Congress of Genetics. Fisher's paper, 'The evolutionary modification of genetic phenomena' (*CP* 97), included the following reference to Wright: 'Sewall Wright, if I understand him, has suggested ... that very small selective intensities do not, as one would naturally assume, exert effects proportional to their magnitude; but I have so far found it impossible to set up any reasonable scheme of genic interaction which would justify this conjecture.' Wright, in his paper, 'The roles of mutation, inbreeding, crossbreeding and selection in evolution', concluded, 'The course of evolution through the general field [of possible gene combinations] is not controlled by direction of mutation and not directly by selection, except as conditions change, but by a trial and error mechanism consisting of a largely non-adaptive differentiation of local races (due to inbreeding balanced by occasional cross breeding) and a determination of a long time trend by intergroup selection ... the average adaptiveness of the species thus advances under intergroup selection, an enormously more effective process than intragroup selection.'

In June 1933, when Wright took up again his criticism of Fisher's theory of the evolution of dominance, he appeared to place the argument in a wider setting.[45]

> Fisher used the observed frequency of dominance as evidence for his conception of evolution as a process under complete control of selection pressure, however small the magnitude of the latter. My interest in his theory of dominance was based in part on the fact that I had reached a very different conception of evolution (1931) and one to which his theory of dominance seemed fatal if correct. As I saw it, selection could exercise only a loose control over the momentary evolutionary trend of populations. A large part of the differentiation of local races and even of species was held to be due to the cumulative effects of accidents of sampling in populations of limited size. Adaptive advance was attributed more to intergroup than intragroup selection.

Replying, Fisher (*CP* 119, 1934) quoted Wright's statement that 'there should always be other evolutionary pressures of greater magnitude acting in one direction or the other' on the modifiers, and he added, 'Wright appears to think that this implies that a selective intensity of lesser magnitude has therefore no effect', but such an argument, Fisher claimed, was fallacious. Wright[46] replied that he could not follow Fisher's reasoning but probably more significant for their future relationship were the complaints he included in this paper about Fisher's handling of his 1929 manuscript. Though this question had not been mentioned in any of a dozen letters which had passed between them since 13 August 1929, Wright evidently came to believe that Fisher had made use of his manuscript without adequate acknowledgement. After this exchange, there was, it seems, little chance of reconciliation.

Fisher certainly had reason to be immensely grateful to Wright for sending his manuscript in August 1929. Fisher wrote as much to Wright on 15 October 1929 and he included acknowledgements to Wright in *GTNS* (p. 95) and *CP* 86 (1930). These acknowledgements might, perhaps, have been more happily constructed but there is nothing in the Fisher-Wright letters, or elsewhere that I know of, indicating that Fisher had done anything more or less with Wright's manuscript than he stated.

Fisher's next major reference to Wright's work was in 1941 (*CP* 185) when he questioned Wright's concept of an adaptive surface and his formulation of selective tendencies in terms of a potential function $\bar{W}$—with the implication that selection is governed by the average condition of the species or interbreeding group rather than by its action on individuals. Fisher had touched on the first of these points in a letter to Wright on 31 May 1931. His letters to E.B. Ford (2 May 1938) and M. Kimura (3 May 1956) also refer to these questions. In one of his last references to this subject, Fisher wrote (*CP* 277, 1958), 'the existence of such a "potential function" as that which Wright designates by $\bar{W}$ is not a general property of natural populations ... selective tendencies are not, in general, analogous to what mechanicians describe as a conservative system of forces. To assume this property is one of the gravest faults of Wright's formulation.

The only other major references to Wright's work in Fisher's later publications concern the question of selection and random drift. They occurred in two papers with E.B. Ford—*CP* 219 (1947) and *CP* 239 (1950)—and in a prefatory note written for the reprinting in 1950 of Fisher's paper, 'The distribution of gene ratios for rare mutations' (*CP* 86, 1930). In this note Fisher recorded that he did not share Wright's 'conviction that evolutionary progress is favoured by the subdivision of a species into small, imperfectly isolated populations, save in the case stressed by Darwin in which the environmental conditions of these are sufficiently diverse to induce divergent evolutionary tendencies. Wright, on the other hand, has maintained that random survival in such populations leads to the testing of a greater variety of genotypes, and to the more rapid discovery of successful combinations, while my own studies have not led me to believe in any such effect, as a factor contributing to organic evolution.' This view Fisher had expressed repeatedly since he first wrote to Wright about this question on 19 January 1931. This point and the issues involved have not always received the attention they deserve—to judge from Provine's[47] recent summary statement that Fisher 'began to realize that Wright was correct in arguing that evolution would proceed more rapidly in a population subdivided into partially isolated subpopulations'. Fisher and Ford (*CP* 219) gave a useful summary of their reasons for not agreeing with Wright on this question.

> Those evolutionists who find it difficult to attach any great evolutionary significance to such chance effects have urged that the normal segregation of all factors in each generation continually supplies new genotypes selected at random from a number usually much greater than the number in a single generation of even a numerous population, and that the selective increase or decrease of any gene is determined by the totality of the life experience of all these ... combinations: that the number of genotypes tried will generally be larger in more numerous than in less numerous populations; and that the existence of very small and completely isolated populations, such as Wright seems to postulate, will generally be terminated by extinction in a period which must be thought of as short on an evolutionary scale of time.

Fisher never accepted Wright's view that inbreeding is an essential factor in adaptive evolutionary modification and that intergroup selection acting on random non-adaptive changes in local groups is a more effective process than intragroup selection in the adaptive modification of species.

Wright[48] has suggested that he saw intergroup selection as the only process by which the selection of interaction systems could occur. He evidently saw Fisher's Fundamental Theorem as 'a refutation of the possibility of any selection among interaction systems'; his suggestion that interaction systems had been neglected by Fisher apparently stemmed from that view. Fisher expressed his view of intergroup selection when he wrote to J.F. Crow in 1955 that the conditions needed for isolation to be worth anything genetically must be taken to preclude real competition between the imagined groups.

It is interesting, and perhaps needs emphasizing, that both Fisher and Wright considered systems of interacting genes to be of critical importance in evolution. A fundamental difference in their views of the evolutionary process concerned the *means* by which interaction systems could be exploited.

As we have already seen, Fisher, from quite early on, attached importance to the role of individual selection in the evolution of systems of interacting genes. He wrote to Darwin on 7 August 1928,

> I am inclining to the idea that the main work of evolution lies in the discovery by trial of perhaps rare combinations of its existing variants, which work better than the commoner combinations. A slight increase in the number of individuals bearing such a favourable combination will then set up selection in favour of all the genes in the combination, with marked evolutionary results. Many of these genes would have been previously rare mutant types (not necessarily rare mutations) unfavourable to survival. I think of the species not as dragged along laboriously by selection like a barge in treacle, but as responding extremely sensitively whenever a perceptible selective difference is established.

In *CP* 147 and elsewhere, Fisher recorded his belief that the selective intensities effective in evolutionary change were generally very small—of the order of 0.1 to 1 per cent per generation.

Considering what is now known about genetic variation in natural populations, it is interesting to see Fisher's early recognition of the large amount of latent variability and that he believed much of it was due to effectively neutral mutations whose ultimate fate would be governed largely by changes in the environment, including the genic environment. In *CP* 87 (1930) he wrote,

> It is indeed certain that many species contain a large amount of latent variability by the selection of which their instantaneous rates of evolutionary improvement are maintained. There is no need, however, to suppose that the whole of this is due to a stream of mutations beneficial from their first appearance in process of spreading over the species rather than that much of it may be due to effectively neutral mutations which have occurred in the past and the ultimate fate of which is at present in process of decision.

Writing to Regan in February 1927, Fisher had considered the case of a 'tolerably good' mutant which 'in certain circumstances, or in certain gene combinations, may be advantageous but on the whole is neutral'. In *CP* 81 (1929), he wrote that 'factors suffering the feeblest selective action will at any one time be the most numerous ... It is the idlers that make the crowd and very slight attractions may determine their drift.'

Near the end of the Preface to *GTNS*, and after a warning that the book was not easy reading, Fisher wrote, 'I believe no one will be surprised that a large number of the points considered demand a far fuller, more rigorous, and more comprehensive treatment.' Nowadays there is, of course, a fine tradition of quantitative research in theoretical and applied population genetics. The indispensable contribution of such studies to evolutionary biology is now widely recognized. This certainly represents a marked change of view since 1930. Whilst *GTNS* did much to help bring about this change, the book was, as Fisher said, not easy reading. For some readers this added to its fascination but for others it undoubtedly limited their understanding of Fisher's contributions.[49] As A.L. Bowley[50] remarked about some of Fisher's statistical work, not all of the goods are in the window. It was perhaps with some such thoughts in mind that Darwin wrote to Fisher in June 1930, as he began to reread *GTNS*.

> my impression is confirmed that it will be slowly recognized as a very important contribution ... but I am afraid it will be slow, because so few will really grasp all that it means. You must ... trust to ultimate results.

Notes

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4. See Bennett, J.H. (Ed.) (1965). *Gregor Mendel. Experiments in plant hybridisation. With introduction by R.A. Fisher*. Oliver and Boyd, Edinburgh.
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> Fisher [...] for the sake of manageable mathematics made all sorts of simplifying assumptions, such as: population size large, epistatic effects and linkage negligible, accidents of sampling unimportant, effects of individual genes usually slight. As necessary as all of these assumptions were during the infancy of population genetics, they contained the germ of much of the trouble that plagued the field during the ensuing forty years.

50. See *FLS*, p. 85.

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