Fisher to O.W. Richards: 21 February 1927

I was glad to get your letter, but am sorry my pamphlet[85] was so obscure. I have evidently failed altogether to make clear the conditions for the initial kick-off. I do not know if you have ever had to select animals or men for a specific purpose. People who have to do so usually have their own little fads and preferences; a man who wants a good milking Shorthorn will feel if the shoulder blades are thin, and Capt. Fitzroy disliked the shape of Darwin's nose (was it not as an index of lack of determination!).

Imagine a genealogical census of all the members of a species in 1927, and ten generations before, say 1915. To every mature male of the 1915 enumeration there will correspond 0, 1, 2, ... descendants in 1927, with some millions in each of the principal classes. I imagine that these classes will be differentiated to a minute extent in every measurement you could make, and in growth curves, colour, seasonal responses, etc. In general, every characteristic will be either positively or negatively correlated with survival (zero is but a point of zero measure). If any one of the positively correlated characteristics is conspicuous, and if the conditions at the mating are such that some only of the males mate, or mate with different frequencies and at more or less favourable times, according to their success in exciting a physiological response in the females, then those females who by reason of coyness or differential excitability in fact succeed in mating with the better adapted males will themselves be more heavily represented in future generations, and their selective taste or differential excitability will be more and more strongly represented.

There is no necessity for a simultaneous competition, though this must often help. The differential excitability might show itself in the female, as she matures, being ready to mate with the more attractive males earlier than she would be with the less attractive.

In your second paragraph, why do you suppose that the difference in display should be *outweighed* by variations in maturity and environment? This implies a negative correlation, else such variations will on the average be equally distributed between the two scale pans; such differences would dilute, but not neutralize the effect of display. The evidence that the secondary sex characters are suddenly developed agrees well with the view that they are due to a runaway process[86] in which each increase in the secondary male equipment produces increased *selection* in the female temperament, and vice versa, so that both changes must go on at increasing speed until the conditions (ratio of sexes at mating, natural selection, etc.) are altered. For the same reason one would expect very seldom to catch the runaway process actually at work, just because it works so quickly when everything is favourable. In the majority of cases some check must already have supervened, and if this check is detected it may be used, quite illegitimately, as an argument that the structures observed are not due to sexual selection. ...

Fisher to J.A. Fraser Roberts: 18 January 1935

... There is one point in which Hogben and his associates are riding for a fall, and that is in making a great song about the possible, but unproved, importance of non-linear interactions between hereditary and environmental factors. J.B.S. Haldane seems tempted to join in this. What they do not see is that we ordinarily count as genetic only such part of the genetic effect as may be included in a linear formula and that we make a present to the environmentalists of such variation due to the combined action of genetic and environmental causes as is not expressible in such a formula. Consequently, the more important non-linear interactions were, the more thoroughly would we underestimate the importance of the genetic factors. This is, of course, another point in favour of speaking of the residue as non-genetic, rather than as environmental, though I have no doubt that in this residue the direct environmental effects are probably larger than the portion due to interaction.

Fisher to J.A. Fraser Roberts: 20 May 1935

... Yes, I do agree with you quite strongly that selection would be at its most efficient under uniform conditions, and, among these, probably at a higher than at a lower level of environmental well-being. That is, that any serious environmental disabilities scattered in the population would tend to frustrate any favourable selection for genetic potentialities. In expressing this argument, one has, of course, to admit that the existing selection is certainly very unfavourable, so that the less efficient it is, the better. But to anyone who seriously aims at improving the environmental conditions of the population and appreciates what has already been done in the last few generations, it is a most important point that this desirable action is making genetic differences more and more important, the more completely bad environments can be eliminated. ...

Fisher to R.N. Salaman: 10 February 1933

Moore has sent on your letter to me. Perhaps I can explain what was in the minds of the Editorial Committee when they discussed the point.[87] A large proportion of children are from families of 1 and 2, and if easy sex control were possible, I personally am quite confident that a very large proportion of the single children would be males, and that about half of the families of 2 would be of two boys. The larger families might be more equally distributed, and of this it is difficult to judge, but the question before most parents is not whether to have 9 boys and a girl or 6 boys and 4 girls, but whether their sole or few offspring will be, as things stand, something of an asset or something of a liability. Naturally this is only a judgement of the probable preponderant action, not a justification for it. I should personally

anticipate very high sex ratios in the age groups produced in the first 20 years after such a discovery.

I doubt myself if 'Society' would show any initiative in seizing control of any situation, before great and serious damage had resulted from action in private interests. In my view the present birth-rate is far below what any organized Society would aim at in the National interest; that, of course, is a matter of opinion, but the inertia of Society in the matter is an observable fact.

Fisher to E. Selous: 1 November 1932

I am venturing to write to you, through your publishers, to express my personal appreciation of your great book, *Realities of Bird Life,* ... I had heard a little of your work through Julian Huxley, though without appreciating its importance. I particularly regret that I knew nothing about it at the time of writing a chapter on sexual selection in my book, *The Genetical Theory of Natural Selection,* which came out in 1930.

From an arm chair, as you weather beaten adventurers still scornfully say, though, if you watched *our* activities, you would soon correct it to a laboratory desk, I had come to conclusions as to the value of Darwin's theory of sexual selection and of the criticisms of Wallace and others levelled against it, not so different from your own as you would expect from so suspicious a source, and had ventured to add an excrescence of my own on the psychic evolution, through the same selective process, of female taste. This aspect of the problem Darwin left alone, I cannot suppose he overlooked it, and I do not know how large a part in the reluctance of biologists to give due weight to this part of Darwin's theory has been due to an unwillingness to ascribe to the female bird, merely for the sake of its consequences, such extravagant and useless tastes as would seem to be necessary. However, the ecological situation which you have succeeded in observing and disentangling in the cases of the Ruff and the Blackcock fulfil so neatly the requirements of my runaway process, by which I believe particular preference patterns are evolved, as well as demonstrating the fact of preference itself, that I should particularly have liked to have had your facts (rather like a mannequin) to exhibit my theory on.

I do not know whether anything that I can say or do can avail to encourage you and your publisher to give us the second volume which you had, and I hope, still have, in mind. If so, let me say or do it.

Fisher to C.S. Sherrington: 22 January 1947

Talking to Mrs. Cameron[88] last night she gave me your kind message and made me recall that I had once attempted, though quite without success, to form ideas as to the bearing of the principle of indeterminacy on such questions as human character, moral responsibility, and so on.

I have been thinking a little further on the subject, and you may be amused, and I hope not bothered in any way, by the five disputable propositions that I have put down on the enclosed sheet. As, of course, everything depends on the development and workings of the nervous system, I hope you will peremptorily blue pencil anything which reads like absolute rot from this point of view.

Of course, my chief difficulty hitherto has been to allow the evolutionary process, which depends upon the permanent and therefore deterministic properties of genes, to take any part in the development of such a capricious quality as the possession of powers of individual choice. The enclosed is therefore essentially an attempt to set out a possible relationship between these two things.

Of the real existence of amplification on the scale required, there can be no doubt, since men, i.e. physicists, are in fact materially influenced by quantum events, amplified in succession by cloud chamber, camera, and the physicist's brain. It is, of course, quite another matter whether in the organization of the unity of the individual among higher organisms and the development of their capacity to be conditioned by experience, amplification on the same scale is an ordinary feature. I suppose for my own part that it must be.

[Enclosed sheet]

The development of a given genotype (even in given environmental conditions) is indeterminate in that undirected chance happenings intervene at all stages, each such event having perhaps permanent or increasing consequences, as development proceeds, on the integration of the nervous system and the formation of character.

Individual action, e.g. choice, is always in part predetermined by the genotype, in part by the subsequent effects of physically fortuitous developmental happenings in the past, and in part undetermined and ascribable to fortuitous contemporary happenings.

Both the course of development, and the instantaneous state of the nervous system, are such as to amplify the effects of initially minute (quantum) events, so as to have molar consequences.

This general principle of amplification has been of importance to survival, in some way at present obscure, perhaps connected with the organization of the whole bodily mass into individual unity, perhaps in orienting its reactions towards the future (as purpose or intention), and has evolved to its present high degree by reason of its survival value. It, though not the particular modifications which if favours, is determined by the genotype.

It is open to a man, religiously inclined, to assert that the primary elements of indeterminacy in development and choice are fortuitous only in the physical sense, being in reality divinely guided, much as the apparatus of games of chance were regarded as guided by the Goddess Fortuna.

C.S. Sherrington to Fisher: 3 February 1947

Thank you for writing, although your letter by its conundrums adds to the puzzlement of life. Your questions, beautifully clearly put, lie beyond the

boundaries of any special competence I can claim. In a wholly 'man-in-the-street' fashion I have been tempted to suppose that life's 'progress'—if that is the word—was an upshot of gene-heritage on one side and 'conditioning' on the other. E.g. the domestication of man's friend the dog, an upshot of generations where 'conditioning' disfavoured 'wildness' and encouraged 'tameness' by breeding from stock which evidenced this latter but not from such as evidenced the former. Of course that presupposes an *anlage* (e.g. genotype) which (material, though it be) disposes the individual rather to 'wildness' than to 'domesticity' or vice-versa. Is that permissible? Your questions gaily involve the matter-mind dilemma throughout. I interpret that as that you discount it? When I was first in Berlin the 'conditioning' there was toward evil, because Bismarck though a strong man was not a 'good soul', and the young Kaiser, who easily overthrew him, was worse. The Berliners were I take it conditioned to be what they are.

I always feel at a disadvantage about the gene because I find it always put forward as a purely *material* thing. I expect other physiologists feel the same. If the gene carries the psyche, might it not be clearer to start with it so *ab initio*. Inherited qualities are at least as clear in the 'psyche' as in the 'body'. Some of course adopt the term mystic, but that confuses worse and leads nowhere.

What you say about 'amplification' is very interesting to me—indeed exciting. Is not an outstanding example the life history of the gene itself as unfolded in the development of the individual organism? There it is met both in plant and animal, but in the latter it applies to transcendent reactions, through the nervous system, e.g. the toad immobilized by a tiny retinal image of a fly, or ourselves by the faint footfall of a supposed ghost—Hamlet when he caught the rustle of something behind the arras and lunged! It is creditably reported that a *single photon* can induce through our retina a *percept* and a percept can move the individual. Clearly, in the 'higher' animal, e.g. human, the system *par excellence* exhibiting amplification is the nervous system—in physiology we call the principle 'integration' rather than amplification, stressing that it is a principle which tends to make the whole individual react as a unity—that is the foundation of the 'ego', the 'self'. The old-time philosopher tended to suppose what he called the 'will' was the cause of solidarity of the 'individuum'. The truth is really the direct reverse as traced ontogenetically and physiologically. As you say —and no one I think can have put it forward better—'The general principle of amplification has been of importance to survival, in some way at present obscure, perhaps connected with the organization of the whole bodily mass into individual unity', i.e. integration and the system which does that most is the nervous, and it is *in* that system that mind has its seat.

Your remark about the goddess Fortuna and the piety of classic times is delightful! I wish glorious old Anatole France could have lived to read it. ...

Fisher to G.D. Snell: 9 November 1943

I have just received your letter of September 25th, a few days after the mice arrived, on the whole with very little loss. I should like to thank you immensely for co-operating so kindly with the Rockefeller Committee in obtaining these lines for me.

I have run a little mouse colony now for more than fifteen years, but it was only when I accepted the Arthur Balfour Chair of Genetics in Cambridge, formerly held by R.C. Punnett, that I decided to put into practice what I had long felt needed doing, namely the creation of permanent inbred lines covering all (or as near as makes no matter) of the genes recognizable in mice. I believe that the advantages offered by segregating inbred lines have never been fully appreciated. They give one the true single factor manifestations without disturbance due to other factors, such as ruins the value of so many specimens used for demonstration or museum exhibition. They can be used to illustrate all points of interest, such as factor interactions or linkages; they supply permanent standard material for quantitative studies and the means of obtaining improved standard genotypes in mice used as test material in human and veterinary medicine.

I daresay I shall run into plenty of difficulties, but it seems to me that only by doing the thing on a comprehensive scale will these be adequately explored.

Fisher to C.S. Stock: 24 October 1932

Thanks for your letter. ...

I think you have stated the functions of sex exactly. I imagine forms like the dandelion which are believed to be wholly non-sexual may thrive immensely for a time, but would eventually be so slow in modifying themselves to suit changed conditions that they will not contribute to the ancestry of the flora of the remote future. For this purpose, however, a very low percentage of crossing would, I believe, be effective. The penchant for obligatory cross-breeding seems to me explainable only by the predominantly unfavourable nature of mutations. ...

Fisher to C.S. Stock: 13 February 1936

... I am very glad you like the article on Determinism and Natural Selection [*CP* 121], as N.S. has so often been represented as a mechanistic, fatalistic or deterministic doctrine, whereas, in reality, it differs from nearly all causal laws in requiring no rigid determinism whatever. The only other important exception I know is provided by thermodynamics and statistical mechanics. ...

Fisher to C.S. Stock: 18 September 1943

Many thanks for your kind letter on my appointment at Cambridge. You

may be amused at one circumstance in connexion therewith. When in 1916, Dampier-Whetham, as he was then called, submitted a screed of mine, on the genetical intepretation of the biometrical work Galton had inspired, to the Royal Society, the referees appointed are rumoured to have been Karl Pearson and Reginald Punnett. The Society's action was impeccable; these were two leading lights in statistics and genetics respectively, with the additional advantage, when two referees are appointed, that they were not very likely to agree. In fact, I suspect that the rejection of my paper was the only point in two long lives on which they were ever heartily at one. Lest this sad story seem depressing, it has the point that the author of the paper was chosen to succeed each pundit in turn.

It is great news about your book. I suppose you must be right about it not selling, though really one can never tell, and the fact that a book is not understood doesn't prevent it being widely read. Anyway, I wish it the best of luck.

Fisher to C.S. Stock: 28 July 1945

... At the moment I suppose the principal safeguard[89] most obviously required is that the true father should be known and declared under personal attestation by the physician. This would, I suppose, regularize the business from a good many legal points of view, including that of the later possible incestuous marriage of the child produced, or, what is equally serious, suspicions or aspersions that such marriage was incestuous. I am not sure how far this would go to meeting the psychological requirements arising from the fact that our aesthetic and emotional nature must very largely have been hammered into its present shape, as in the case of other animals, through pressure of sexual selection.

Fisher to C.S. Stock: 31 July 1957

I am extremely glad you liked the Eddington Lecture [*CP* 241]. It was delivered in London and had a small and, I suppose, distinguished academic audience. I think they were interested at the time, but, on the whole, biological workers like those in physics are not much, or often, concerned with the larger issues, e.g. as to whether in the development of human character there are, in fact, developments of importance not to be ascribed either to nature or to nurture; as it were 'branch points', at which something happens, which, viewed from earlier in time, may be thought of in statistical terms as pure chance, which at least supplies a method of calculation appropriate to our state of uncertainty in such forecasts, but which, viewed in retrospect, may well seem providential to the individual most importantly concerned.

Fisher to P.V. Sukhatme: 6 May 1940

... Yes, I have followed with some interest Lotka's and Kuczynski's work in

the measurement of population growth, and your impression is correct that I developed the formal theory as expressed in 1930, in independence of both writers, some years earlier.[90] Actually, if I remember right, I set out the whole formulation, probably including the notion of reproductive value as a function of age, in correspondence with the late Dr Brownlee about the year 1925. You may remember that Brownlee was one of the first writers in England to stress the inadequacy of our birth-rate for maintaining a stationary population, expressing his ideas in terms of standardized birth- and death-rates. As I agree with him strongly on the importance of emphasizing the facts, I had a good deal of correspondence with him with a view to relating them more directly to the actual happenings, than is possible through standardized rates. I found later that Lotka is exceedingly touchy, and anxious to claim priority for his ideas, but as he (and apparently Kuczynski also) seems to have failed to grasp the notion of reproductive value, I should prefer it to be known that my own development is quite independent of theirs. I did not, however, publish anything on the subject prior to 1930,[91] though I could, when University College is again accessible, hunt up my correspondence with Brownlee.

Fisher to H.G. Thornton: 29 November 1950

Thanks for your note. Some time when you feel like it, you must tell me what is this tendency for 'increasing complexity in the inorganic world', which someone ought to start explaining.[92] I do not feel a comparable difficulty about new products of the human intellect, because after all, people are new, and each one capable perhaps, of doing some particular job usefully well, and meanwhile the jobs waiting to be done are changing. I mean both the aims and the tools available are different in each generation, so that a certain amount of novelty ought to result.

I quite agree that Smuts meant by Holism something much wider than evolutionary theory could explain, and it is really not very clear to me exactly what operational principles Smuts did mean to specify. Some such phrase as 'tendency to completeness of integration' is about as near as I can get.

Thanks also in other ways for your letter.

Fisher to R.E. Threlfall: 30 September 1953

Thanks for sending me the cutting from *The Glass Industry*.[93] To me it was an entire surprise that my work in *The Genetical Theory of Natural Selection*, 1930, which I presume was the source to which Dr. Preston refers, had been of any technological use. It just shows, to my mind, how well supplied with library and bibliographical facilities American workers in applied fields are, and how thoroughly, in fact, they must be used, for though my book is now fairly well known, very few copies of it were sold and it is quite

untrue to say that the technical details of its contents are at all well known. Yet someone must have read and noted the method and presumably from that point it has filtered through into some reference collections.

I find it all very astonishing. When are you going to be in Cambridge?

Fisher to J.F. Tocher: 20 June 1940

Thanks for your letter. I am not a little attracted by what you say, and by the suggestion you make,[94] and as there seems to be time for consideration, I will seriously try from time to time to get my ideas in order.

It is now full two generations since Galton began to point out that those rare men who make a success of administrative responsibilities in difficult times must owe their gifts principally to heredity, and must be growing rarer rather rapidly in countries with a distribution of birth-rate like that which has prevailed in our Island ever since. A crude prediction made at the time *Hereditary Genius* was published might well have been that in 1940 three posts out of four involving important decisions would be held by incompetents. Of course such predictions can never be verified, because, as in the later centuries of the Roman Empire, it always looks as though *circumstances* had changed so much. ...

Fisher to C. Todd: 23 April 1930

I am indebted to J.B.S. Haldane for calling my attention to the genetical importance of your most remarkable work[95] on the serology of oxen and poultry. If I am not mistaken, the methods you have developed may prove capable of elucidating some very obscure points in genetics and in evolutionary theory.

A genetic point of great interest to me, and I think of some general importance, is the biochemical relationship of alternative (allelomorphic) genes, and the meaning of 'dominance'. The rule you have discovered of the negative response of corpuscles of the offspring to serum exhausted for both its parents, suggests that the isolytic or agglutinative reaction is determined by the direct products of individual genes rather than of secondary reactions, which in many cases produce substances such as pigments which are absent from both parents. On this view your results can have two interpretations:—

(a) that the liability to respond by agglutination to any particular ingredient in the serum is always completely dominant, or
(b) the liability of recessives so to respond is always shared by the heterozygotes.

These two interpretations correspond to the two views (a) that dominance is a primary biochemical phenomenon, the recessive gene being defective, inactive or less active in some special respect than the corresponding dominant gene, and (b) that dominance is wholly a superficial or phenotypic

phenomenon, which has been brought about by the evolutionary modification of the heterozygote in a desirable direction, the two allelomorphic genes each initiating characteristic but different reactions.

Now is it possible that serological methods can discriminate between these two contrasted views? I am quite ignorant of the practical limitations of serological methods, so perhaps you will tell me without compunction if you think the following is impracticable:

> Make a serum using recessive donors.
> Exhaust with corpuscles from numerous dominant homozygotes (until reaction is negative with all dominant homozygotes in the group to be tested).
> Test with heterozygotes and recessives.

If (a) is true, the test should be negative in both cases; [if] (b) is true, it might be positive in both. The test fails if the exhaustion is inadequate, but this can be checked by a parallel test:

> Exhaust with corpuscles from numerous heterozygotes.
> Test with recessives; if the exhaustion is sufficient, the result should be negative on both theories.

The point is to obtain a serum sensitive to a particular gene. If this were possible, it would not only, as it seems to me, settle the dominance question, but throw a great deal of light on other points.

First, the magnitude of the reaction due to a single gene in comparison with those ordinarily observed would give an idea of the number of such genes in which the group of individuals tested ordinarily differ.

Next, if the technique can be pushed so far as to detect a single gene, the total mutation rate in genes having no visible effects would appear in a small proportion of perhaps feeble exceptions to your general rule as to parentage. Lethal mutations in *Drosophila* seem to be common enough to give an appropriate percentage of such exceptions.

I am sending a copy of this letter to Haldane. Please do not trouble to answer in any hurry. I know how troublesome it must be to have to deal with suggestions for laborious and perhaps useless side-lines, but I should much appreciate an exchange of ideas with a view ultimately to clearing up the genetic implications of your work.

Fisher to C. Todd: 6 October 1931

I was sorry to hear of the catastrophe at the farm and a little sorrier to hear that you have not yet been able to set up the complete experiment on the sex effect.[96] I am rather a fanatic on the subject of fully designed and complete experiments, but shall none the less be interested to hear if the other tests you mention give any guiding indications.

Your finding that two fowls immunized in parallel with the same corpuscles give qualitatively different antibodies is especially interesting to me as confirming the correspondence between immunological and genetical differences, for undoubtedly two sister fowls will generally differ qualitatively in their gene complexes and will therefore find different elements in the corpuscles, which are alien to them, and to which, on this view, they will react.

I believe you have made this point, though perhaps more tentatively, in your printed papers and I am glad to hear that you now regard it as fully confirmed.

I think I mentioned that in my experiment with wild *Gallus* I was developing lines differing in a single recognizable factor, such as Feathered feet, and at least not greatly different in the rest of their genetic outfit. If your accommodation is at the moment under-stocked, you might find it useful to take pairs of heterozygous birds which I could supply you with this winter and from each of which two homozygous strains and the heterozygote could be made available in two years' time, if, as I hope, after the sex effect, you will be attracted to the idea of developing sera reactive only to a specific gene.

Fisher to C. Todd: 5 February 1932

Seeing you yesterday afternoon, reminded me rather belatedly, that is, after getting home, that there was a point I wanted to put to you.

The point arises because I have been asked to serve on a newly formed committee of the Medical Research Council devoted to Human Genetics. As you know, I am inclined to think that your serological work is going to lead to a greater advance, both theoretical and practical, in the problems of human genetics than can be expected from any further work on biometrical or genealogical lines. This, at best, would be looking rather far ahead and I cannot hope to convince people until you have at least the sex effect pegged out; but I fancy expert committees are liable more usually to err, and therefore to waste public money, by taking too short rather than too long a view. What I want to know, is this: could you make any use of it if I were to persuade the committee that yours is the work best worth backing? You did not seem particularly keen on it when I suggested some time ago that an assistant might be useful, but I suppose a *good* assistant would always be useful in enabling you to explore by-paths, and in other cases might enable you to carry out tests on a scale which would be decisive, and which you could not undertake single-handed. ...

Fisher to C. Todd: 9 February 1932

... The present opinion that there are two mutually exclusive classes of genes, one capable of serological detection and having no other effects, and

the other familiar to geneticists, but having no serological effects, is firmly established, and will only be shaken by the direct demonstration that sera can be prepared sensitive to the genes that produce sexual differentiation and other effects.

This seems to me the primary point, beginning appropriately enough with the sex experiment, and this part of the work must be done with animals. It would seem all to the good in the meanwhile to have someone experimenting on the development of a parallel technique in man, i.e. one that will detect individual blood, and consequently sweep up a big aggregate of 'serological' factors. This would be useful for testing identity in twins and triplets, apart from what the animal work ought to lead to.

Fisher to C. Todd: 14 April 1932

I think that is very bad luck; also that it was very good of you to pursue the possibility so far.[97] You have shown that the reactions produced by the polyvalent cock were not conditioned by the sex of the corpuscles. He thus confirms the two other cocks, which, if I have the story right, failed to react at all to some hens' corpuscles. One might take these other two also as showing that the sex effect (if any) must be too slight to detect, within the range of the technique employed. (Your previous sex effect must on this view be due to sex-linked factors).

One possibility has occurred to me that might be of interest to you. I do not think there is any escape, unless your observational findings are revised, from the view that the whole of the reaction developed is a reaction to alien genes (or, of course, their immediate products). It is evidently possible to form antibodies to an enormous number of such alien genes, and perhaps to all, but your results do not prove that all possible reactions always take place; i.e. it may be that the reaction is conditioned by some other circumstance, as if the reacting mechanism needed to be stirred up somehow. Men, who do not react to alien human blood, might, on this view, do so if some bull or rabbit blood was injected at the same time, so that the serum would then react not only to the alien species, but to the alien human corpuscles. But, of course, the conditioning might have to be of an entirely different kind. The main point of my suggestion is that there may be conditions necessary to bring off the different kinds of reaction which are potentially available, and that your experience might well suggest some other sorts of conditions which might be effective.

Of course, on the sex question it may well be that the ♀ chromosome is entirely (genetically and serologically) inactive, and that the thing would work without difficulty in other factors.

Fisher to C. Todd: 22 November 1935

You might like to know that the serological research in human genetics that

I have long been planning is now a going concern here at the Galton Laboratory. Dr Taylor, who was formerly in Dean's School of Pathology at Cambridge, has been getting the laboratory into condition since the beginning of October, and we now have immune sera coming in from a number of rabbits.

I am planning to extend the animals utilized to sheep, pigs, and horses, and perhaps more widely.

In any case, I have long been looking forward to the possibility of your caring to keep in close touch with this work and giving us the benefit of your advice. Nothing, indeed, would give me greater pleasure than that you should, if convenient from time to time, make use of the bench room and facilities which we should always be glad to put at your disposal. I do not know, however, what your plans are, and whether you are likely to have time to maintain your interests in this line of research.

Perhaps you will be able, at all events, to give us a visit, to see the apparatus which Taylor has installed, and to discuss points of interest in connection with our programme.

Fisher to A. Vassal: [March 1930]

I am sending you a copy, which you may care to have, of a book of mine on Natural Selection. I wonder if you remember, in your lectures at Harrow, describing the numerical oddity of the neck vertebrae of the sloths, and if I remember right, of some odd manatee. The riddle interested me enormously at the time, and my interest was revived a few years ago when I heard that Tate Regan was using a rather similar group of facts in fishes as a basis for what seemed to be some rather fantastic Neo-Lamarckian conjectures. I had some correspondence with Tate Regan, making, I think, no impression upon *him*, but clarifying the matter so far to myself that when Ford and Bull published the herring data, which I quote in Chapter V, I was ready to spot its significance.

I hope at any rate that my shot at the riddle of the sloth will interest you, and that you will not turn down all the rest as unreadably mathematical.

Fisher to N. von Hofsten: 26 June 1950

... I suppose the difference between your 'actual curve' and your 'mixing curve' is that between two populations having the same gene ratio though different proportions of heterozygotes. This is a distinction which, if I were rewriting *The Genetical Theory,* I should certainly stress more heavily that I did there. For though the principal evolutionary agency is undoubtedly change of gene frequency, changes in the mating system with important secondary consequences can be brought about by changes in population frequencies without change of gene ratio.

I did not know about your paper, which is, I gather, of eugenic purport, though a trifle pessimistic. I do not see ground for pessimism in the genetic situation presented by Man, but I think it is quite inconceivable that any existing national state should have the courage to treat it as it requires.

Fisher to L.G. Wigan: 31 August 1942

... if the requirements of the environment fluctuate, and so are constantly inducing genotypic changes in the population of organisms, this will, at least slightly, hasten the extinction of genes, but I do not see that it does very much in this respect. I could well imagine the population of grasses in a region such as Syria adapting themselves progressively for 100 years at a time, or so, to moister or drier conditions without losing the capacity of reversing this change as quickly as ever. In fact, whereas in experimental populations extinctions of genes can occur with a gene frequency of only about 10^{-1}, it will need to be about 10^{-8} before it can conceivably occur in a really big population. ...

Fisher to E.B. Wilson: 2 August 1930

... As to the eugenic effect of class difference in fertility, I do not see that what you say about luck throws any doubt on it at all.

If desirable characters, intelligence, enterprise, understanding of our fellow men, capacity to arouse their admiration or confidence, exert any net average social advantage, then it follows that they will become correlated with social class. The more thoroughly we carry out the democratic programme of giving equal opportunities to talent wherever it is found, the more thoroughly we insure that genetic class differences of eugenic value shall be built up. Chance can only dilute this process, it does nothing to neutralize it. Of course, direct intelligence tests in this country show considerable differences between the children of parents of different occupations attending the same schools; but I do not stress this because a great many other qualities more important than intelligence must be sorted out by the same process. ...

Fisher to S. Wright: 6 June 1929

I was much interested in your note in the *American Naturalist* on the evolution of dominance, though of course sorry that you should consider the numerical values too small to be effective.[98]

I do not think there is any use in controversy except when the point at issue is perfectly clear to both parties, and I should therefore like to have your opinion of the enclosed,[99] which is the kind of thing I should now be inclined to write, before publishing anything on the matter.

Perhaps you would find it worth while to work out the case you cite making allowance for the effect of the more favourable factors on the frequency of the heterozygotes, and dropping the assumption that the modifier is dominant.

What I mainly want to know, however, is whether you agree with me that a very slight selective effect acting for a correspondingly long time will be equivalent to a much greater effect acting for a proportionately shorter time. Or, whether, on the other hand, you think I have underestimated the ratio of the selective intensities, or overestimated the ratio of the times. I cannot see how a conclusion can be reached without considering the latter.

Fisher to S. Wright: 10 July 1929

I was very glad to get your letter, and see what your point[100] really is. As others besides myself may have missed it, and fancied that you desired to establish insufficiency of selective intensity in relation to time available, I think it will be worth while to reply, little though either of us can know on the real point at issue.

I enclose what I am sending to the *American Naturalist* so that, if you think it desirable, you can have another go, in the same issue as mine. ...

Fisher to S. Wright: 13 August 1929

Many thanks for your interesting letter and the copy of your comment[101] on my reply. I am inclined to think your comment carries the discussion of your main point as far as it can be usefully carried in the present state of our knowledge, and I do not see that I can usefully add anything.

The point about using selective intensity[102] $i = \delta p/\{p(1-p)\}$ was of course aimed at comparisons with the selective value of 'multiple effects', in which also δp will contain the factor $p(1-p)$ depending on the gene ratio. From this point of view counter-mutation is infinitely powerful against the prevalent type of gene, as is illustrated by the power of mutation to keep a gene in existence against powerful selections.

You see, of course, that the principle of multiple effects, if carried far enough, greatly increases the number of factors available for modifying dominance, though possibly it does not increase the number whose fate will be settled by the effect in modifying dominance.

I am not sure that I agree with you as to the magnitude[103] of the population number n. To reduce it to the number in a district requires that there shall be *no* diffusions even over the number of generations considered. For the relevant purpose I believe n must usually be the total population on the planet, enumerated at sexual maturity, and at the minimum of the annual or other periodic fluctuation. For birds twice the number of nests would be good. I am glad, however, that you stress the importance of this number. ...

Fisher to S. Wright: 9 September 1929

Many thanks for your letter of August 28th, which is not only exceedingly

interesting in itself, but helps me to understand the larger paper,[104] which I have been puzzling over occasionally for some time.

I have so far published nothing on the diffusion problem,[105] but have in the Press a book on The Genetic Theory of Natural Selection, which has part of a chapter on the cohesion of species in relation to the problem of their fission. I think it must be generally true that the ancestry of all individuals of a species is practically the same except for the last 100 or perhaps 10 000 generations, and that a gene frequency gradient is maintained by selection between different parts of a species' range. So that well marked local variations may or may not be incipient species, according as real fission, cessation of diffusion, ultimately supervenes. My discussion of this point is necessarily superficial and qualitative, but may have some points to interest you. ...

Fisher to S. Wright: 15 October 1929

I have reason to be immensely grateful to you for sending me your paper, which, I fear, I have kept all too long, as I have now fully convinced myself that your solution is the right one.[106] It may be of some interest that my original error lay in the differential equation.

$$\frac{\partial y}{\partial t} = \frac{1}{4n}\frac{\partial^2 y}{\partial \theta^2}$$

which ought to have been

$$\frac{\partial y}{\partial t} = \frac{1}{4n}\frac{\partial}{\partial \theta}(y \cot \theta) + \frac{1}{4n}\frac{\partial^2 y}{\partial \theta^2}$$

the new term coming in from the fact that the mean value of δp in any generation from a group of factors with gene fraction p, is exactly zero, and consequently the mean value of $\delta\theta$ is not exactly zero but involves a minute term $-(1/4n)\cot\theta$. (You might care to give this correction from me when you publish.)

With this correction I find myself in entire agreement with your value $2n$ for the time of relaxation, and with your corrected distribution for factors in the absence of selection. Re-examining the whole work has been a great gain to me in clarifying my ideas, and I appreciate what I had not realized before, that selection, except when directed to an optimum value, is not important in keeping down the variance.

I have done a good deal of work on the terminal conditions, which, when it is fit to be seen, will, I hope, be of interest to you. A very striking result is that a mutation can only be regarded as effectively neutral if the selective intensity multiplied by the population number is small, so that the zone of effective neutrality is exceedingly narrow, and must be passed over, one way or the other, quite quickly in the course of evolutionary change.

Fisher to S. Wright: 19 March 1930

I am sending herewith a complimentary copy of my new book *The Genetical Theory of Natural Selection*. It was written too soon to include the later developments of dominance theory which threaten to be extensive. This is really an advantage for it would be a pity if the interest of this special development were to draw attention away from the more general questions.

In some ways the first chapter is the most important, and in some the second. The sixth chapter and the group on Man will attract very different sorts of readers. However, I am sure you will think it an attempt worth making, and should you happen to review it anywhere, remember that I shall be most interested to see your opinion.

S. Wright to Fisher: 10 June 1930

I wish to thank you very much for sending me a copy of your recent book. I have found it extremely interesting and stimulating. I presented my paper on the subject before the American Association for the Advancement of Science last December. It should appear soon in *Genetics*.[107] In reading your book I have naturally attempted comparison at every point with the views which I had reached. Our basic assumptions are, of course, very similar.

Certain differences in detail are of a rather superficial nature and can doubtless easily be ironed out. There appear to be some rather important differences in emphasis, however. You would probably not approve at all of the conclusions which I gave in the abstract of my paper which was published (*Anatomical Record*, 44:287, 1929). This somewhat exaggerates the difference, 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. The main differences all seem to trace to the greater role which I have attributed to random differences among local strains of a species brought about by local inbreeding.

I have not yet been able to follow the mathematics in Chapter IV to my satisfaction but hope to be able to do so. There appears to be substantially complete agreement with the results of my method in the case of no mutation and slight mutation. Your determination of the exact character of the terminal frequencies seems to agree well with the conclusions which I had drawn from consideration of very small populations. There may be a trifling discrepancy at the bottom of page 86 [*GTNS*, p. 94]. I obtained $1/(2N)$ as the exact rate of decay in the case of a population of monoecious organisms with completely random combinations of gametes, and a formula for the case of separate sexes which does not seem to be exactly the same as yours, but which applies exactly to the case of brother-sister mating. In the case of low mutation rates, my formula for the number of genes maintained by a

given mutation rate $2[0.577+\log(2N-1)]$ (in the case of one mutation per generation) differs only slightly from yours.

I was a good deal troubled by the difference between your formula for the selection effect (page 92) [*GTNS*, p. 99] and that which I had reached—$e^{2aNp}\{(C_1/p)+(C_2/q)\}$ in your symbols.

I had not considered the exact case which you give, flux equilibrium (because of the general difference in viewpoint) but on solving for it, I find a ratio of C_2 to C_1 in the above formula which gives results in close agreement up to a certain point ($a<1/(2N)$) but widely divergent beyond this. Your approximation is clearly a better one in this region, indeed, mine rapidly becomes wholly valueless in cases in which the terminal frequencies are large. Have you a general demonstration that the chance of fixation is $2a$? The example given on page 76 [*GTNS*, p. 83] for $a = 0.01$ seems to depend on repetition of a formula for the case in question. I have not, however, as yet gone carefully through the reasoning.

I liked very much your opening chapter with its comparison of the consequences of blending and particulate heredity, also the chapters on sexual selection, mimicry and human evolution.

I have been asked to review the book for the *Journal of Heredity*.

Fisher to S. Wright: 23 June 1930

Many thanks for your letter. I have not the summary from the *Anatomical Record,* so will await the appearance in *Genetics* before going into some of the small discrepancies you mention.

The method by which I should relate selective advantage when not necessarily small to chance of survival in a large population would be to say that the substitution of

$$f(x) = e^{c(1-x)} \text{ for } x$$

is without effect only if

$$x = e^{-c(1-x)};$$

writing the solution of this equation in the form $1-P$, P will be the limiting probability of survival, and

$$-\log(1-P) = P+\frac{1}{2}P^2+\frac{1}{3}P^3+\ \ldots$$

$$= cP$$

whence $$P = 2(c-1)$$ approximately,

or if a is the selective advantage

$$c = e^a$$

$$P = 2a-\frac{5}{3}a^2+\frac{7}{9}a^3-\frac{131}{540}a^4+\ \ldots$$

as far as I have worked it. ...

I do not think the equation has any biological interest except when a is small.

Did I tell you that the cases of polymorphism mentioned by Haldane in connection with dominance theory really fit in exceedingly well? I am publishing a note on them primarily to encourage workers on these species to pay attention to the further predictions of the theory.

I shall be very much interested in your review, and hope you will give yourself space enough to deal with the many different aspects of the book on which I want to know your opinion. I am particularly glad you like Chapter I, as I suspect many biologists will be tempted to leave it out (i) because they will naturally expect a first chapter to be trite as well as elementary, (ii) because they are tired of introductory expositions of Mendelism, and (iii) because they have believed almost since boyhood that they know all about what Darwin thought!

S. Wright to Fisher: 15 October 1930

I should have thanked you long ago for your letter of June 23rd, which entirely cleared up for me the derivation of your value $2a$ for the chance of survival of a mutation in a large population. I think that I have cleared up the apparent discrepancy between the result which I gave for the distribution of genes under selection ($s = -a$) and irreversible mutation (at a rate u such that $4nu$ is negligibly small), viz. $y=Ce^{2nsq}/1-q)$ and your value $(2dp/pq)\ (1-e^{-4nuq})/(1-e^{-4an})$ which seems clearly to be correct. The two formulae agree (with proper choice of coefficient) when ns is less than 1 but diverge rapidly above this. I had been aware of the limited range of applicability of my formula (which in fact I first reached in the form $y=C(1+2nsq)/(1-q)$), but had not seen how to deal with second order terms involving ns^2, n^2s^3, etc. in the derivation. I find now that these condense into a simple expression the inclusion of which gives identically your formula in this case. In the case of reversible mutation, however, the corrected formula appears to be $y=Ce^{4nsq}/q(1-q)$ for all values of ns (up to the point at which ns^2 approaches 1) in place of my previous formula $y=Ce^{2nsq}/q(-q)$, and for mutation rates (u, v) which are not negligible in comparison with $1/(4n)$, the formula seems to become $y=Ce^{4nsq}\ q^{4nv-1}\ (1-q)^{4nu-1}$ to at least a much better approximation than the result which I gave in one of my papers in the *American Naturalist* last fall, viz., $Ce^{2nsq}\ q^{4nv-1}\ (1-q)^{4nu-1}$.

Fortunately (assuming my present formula to be sufficiently accurate) I have merely had to make all my statements on interpretation in my forthcoming paper in *Genetics* apply to intensities of selection just half as great as before and my graphs merely needed relabelling.

I have included these corrections to my formula in the review of your book for the *Journal of Heredity* (which should appear next month) to show that there is now no mathematical difference between our results in the cases which can be compared. I have discussed at some length the rather different interpretations of the role of selection which we have reached and will be much interested in getting your criticism of my view.

I was much interested in your discussion of dominance in *Paratettix,* etc. The situation certainly seems to conform well to the expectation from your theory, and the objections which I made in the case of ordinary recessive mutations do not seem to hold here.

Fisher to S. Wright: 25 October 1930

Thanks for your letter. I am glad to hear the little discrepancies are clearing themselves up. With respect to the polymorphism work, the important thing from the mathematical standpoint is to ascertain in what manner the chance of success depends on selective advantage in the case of restricted recombination discussed in the last section [*CP* 87]. As far as I can see, this might be a matter of great difficulty, but this may be merely because I have not spotted some simple way of looking at it. It would evidently include the problem, the quantitative treatment of which I shirked at the beginning of Chapter VI, and would certainly throw light on the equally elusive problem of the effect of a stream of gene substitutions in loosening the linkage to which I refer in Chapter V.

Mathematicians always tend to assume that the hardest mathematics will be the most important, and this is perhaps true enough in the well worn topics. It is certainly not true of my book, where the apparently non-mathematical parts, where I have left the mathematics undone, are often of the greatest ultimate interest.

I shall be much interested to see your review for the *Journal of Heredity.*

Fisher to S. Wright: 19 January 1931

I was delighted to see your review of my book in *The Journal of Heredity* for August last, which for some reason has only just appeared in this country. Your opening paragraphs especially will be most valuable in getting the less genetical sorts of biologists to see that the evolutionary bearings of genetical discussion are not at all what they were supposed to be; but indeed I ought not to praise one part rather than another for I liked it all heartily. It is in fact the most understanding review of my book which has yet appeared anywhere, and apart from personal vanity, which will of course absorb any amount of mere praise, that is really what an author craves for.

I was extremely interested in your more critical discussion, but what a shame that they should have printed your formulae so illegibly. 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.

I hear that I have recently been attacked in the Zoological Society for daring to *intrude* in biological discussions; perhaps you have had occasionally a similar experience. I do not think it is this kind of thing which does any real harm; it makes a few old pundits feel more comfortable on their perches, but it carries mighty little weight with the younger men.

I had not intended to take up any special point in this letter, but I am tempted to mention this one, (p. 353) 'The formula itself seems to need revision in the case of another important class of genes, ones slightly deleterious in effect but maintained at a certain equilibrium in frequency by recurrent mutation' (I can leave migration aside here). The point here is that the average fitness *is* continually being increased by selection, at exactly the same rate as it is being decreased by mutation. This cause of deterioration of adaptedness, due to mutations of the organism, is, in my treatment, classed with the parallel deterioration due to changes in the environments. This supplies an amendment to the corresponding statement on p. 352, 'The only effective offset to undeviating increase in fitness, which he recognizes, is change of environment'. I think, if you happen to re-read p. 41 [*GTNS*, p. 44], you will see that I class deleterious mutations equally as an offset.

I wonder if you would agree that in attributing somewhat less weight than I to what selection always is doing, you are *ipso facto* attributing more to what it has already done. I mean that the situation sketched at the end of p. 353 would be undoubtedly right if selection had in the recent past been infinitely effective, or infinitely rapid, as a means of modification, and is only therefore ineffective now. This is what I was driving at in saying that the difficulties encountered by natural selection were chiefly of its own making, i.e. the high perfection of existing adaptation.

When the spirit moves you, I should be exceedingly interested to hear if you think this is rightly put.

Fisher to S. Wright: 17 February 1931

I very much hope I shall have a chance of seeing you again during the summer.

I do think that differential selective action in different stations or regions may be exceedingly important, even if there is a steady diffusion of germ plasm between them. ...

Fisher to S. Wright: 31 May 1931

I arrived in U.S. yesterday ... .

If I can catch you at Chicago I propose to come over on Saturday June 27 returning to Iowa the next day. ... I especially want to come on a day that will be convenient to you and when I can see something of the experimental work you are developing.

Let me know if the weekend I suggest will suit ... .

Your letter of Feb. 3rd contains a point about non-optimal points of genetic stability[108] which I should like to take up with you. In one dimension a curve gives a series of alternate maxima and minima, but in two dimensions two inequalities must be satisfied for a true maximum, and I suppose that only about ¼ of the stationary points will satisfy both. Roughly, I should guess that with n factors only 2^{-n} of the stationary points would be stable for all types of displacement, and any new mutation will have a half chance of destroying the stability. This suggests that true stability in the case of many interacting genes may be of rare occurrence, though its consequences when it does occur are especially interesting and important.

Fisher to S. Wright: [late June 1931]

This is just a note to thank you and Mrs. Wright for your kindness and hospitality to me in Chicago. I wish I could better understand your views on those points on which I differ from you, but on the points I have discussed with Lush,[109] I see little chance that I shall ever do so. However, there is a substantial body of theory on which I think we do agree and that after all is of infinitely more interest to the world at large than the very obscure points still in dispute.

Fisher to E. Wynter: 30 May 1945

... The subject of inbreeding especially with farm animals, interests me greatly, and I should be very glad to visit Dr. Corner's farm and discuss possibilities if ever this seems likely to prove useful. The preparation of inbred stocks is such a lengthy process that it should be started at once on [an] adequate scale and carried out by methods that will, as rapidly as possible, give closely inbred material. Of course, its importance will not be obvious to the farming community for another fifty years.

Notes

1. Dr J.R. Baker, Department of Zoology, Oxford University, had written asking Fisher whether he would agree that in the following statement, one part (the first and third sentences) was first pointed out in print by C.S. Elton though it was independently thought of by E.B. Ford, whereas the other part (the second sentence) was due to Fisher.

> When, after a period of great scarcity, a species is rapidly increasing in numbers, non-advantageous mutations tend to spread through the population. In the course of their spreading, they are likely to become incorporated with certain gene-complexes with which they give rise to characters having selection value. Thus periodical increases and decreases in numbers may result in more rapid evolution than stationary populations.

See also correspondence between Fisher and Ford (p. 196).

2. Lady Barlow, daughter of Charles Darwin's son, Horace.
3. Barlow, Nora (Ed.) (1945). *Charles Darwin and the voyage of the Beagle.* Pilot Press Ltd, London.
4. Barlow, Nora (Ed.) (1958). *The autobiography of Charles Darwin 1809-1822.* Collins, London.
5. For Fisher's review, see Appendix C (p. 292).
6. From Part iii of *The Rime of the Ancient Mariner* by S.T. Coleridge.
7. E.W. Barnes, Sc.D., F.R.S., who was Bishop of Birmingham, 1924-53, had been one of Fisher's mathematical teachers at Cambridge. Fisher had sent him a copy of *GTNS.*
8. Darwin, C.G. (1930). Review of *The genetical theory of natural selection. Eugenics Rev.* **22**, 127-30.
9. Bishop Barnes, in commenting on a lay sermon given by Fisher, had asked if he could offer an explanation of the relation between the divine and evil 'which seems to be the repellent part of the same mode of being.'
10. Julia Bell, M.A., F.R.C.P., (1879-1979), was a member of the Medical Research Council's external staff attached to the Galton Laboratory. She had stayed in London during the 1939-45 War and in February 1941 was seeing to the removal of various Laboratory records and other possessions for sake keeping.
11. The American biometrician, C.I. Bliss, writing to Fisher from the USSR, had enquired about the translation of Fisher's statistical books into Russian and had then added, 'Incidentally, if there has been a delay in translating your *Genetical Theory,* it is possibly caused by the anti-Marxian character of the last part of it, at least so several biologists have suggested. In the Soviet Union this is more than a slight technicality.' See also Fisher's letter of 10 February 1942 to K. Mather (p. 236).
12. Dr W.C. Boyd, Boston University School of Medicine, had written seeking Fisher's views on the role of selection and dominance in the human blood groups which he noted were not referred to in *GTNS.*
13. See Fisher's letters to C. Todd (p. 267).
14. See *GTNS,* p. 87.
15. Boyd had referred to studies with rodents which were said to show few blood-group differences and had then asked Fisher if he was justified in supposing that many genetic differences would be distinguished serologically.
16. Fisher was seeking advice from Dr L.P. Brower at Yale University on whether he should include a note on the butterfly *Limenitis* in the Dover edition of his book (see *GTNS,* p. 145). See also his letter of 25 November 1955 to E.B. Ford (p. 202).
17. Hope Professor of Zoology (Entomology), Oxford University, 1933-48.
18. See Fisher's contribution to the discussion of Protective Adaptations of Animals—especially insects, *Proc. R. ent. Soc. Lond.* **7**, 87-9 (1933), where he says, 'Approaching the problem of selective intensity from the genetical stand-

point, I have come to the conclusion that the effective selective intensity in Nature can seldom exceed 1 per cent per generation, else evolutionary modification would be a much more rapid process than it is known to be. Probably we should think of intensities of 0.1 per cent as more typical.'

19. Dr R.B. Cattell had just been awarded a Leonard Darwin Studentship by the Eugenics Society and Fisher was writing to him about his programme of work. See Cattell, R.B. (1936). Is national intelligence declining? *Eugenics Rev.* **28**, 181-203.
20. See Crosby, J.L. (1940). High proportions of homostyle plants in populations of *Primula vulgaris. Nature* **145**, 672-3.
21. Dr J.F. Crow had written asking Fisher to comment on a discussion paper on the roles of inter- and intra-population selection.
22. In 1947, Darlington and Fisher together founded the journal, *Heredity.*
23. Dr J. Davidson who had been a colleague at Rothamsted had recently become Head of the Entomology Department in the Waite Agricultural Research Institute in the University of Adelaide. He was an authority on the taxonomy of the *Aphidae.*
24. C. Tate Regan gave the Presidential Address on Organic Evolution to Section D (Zoology) at the Southampton meeting of the British Association for the Advancement of Science in 1925.
25. See Fisher's letter of 7 February 1927 to Regan (p. 252).
26. On the question of 'pouched mice', Davidson sought the advice of Professor F. Wood-Jones at the University of Melbourne; Wood-Jones said they were 'excessively difficult to deal with in any way' and that it was not practicable to obtain and ship such animals to England.
27. Muller, H.J. (1932). Further studies on the nature and causes of gene mutations. *Proc. 6th Int. Cong. Genet .*, Vol, 1, pp. 213-55.
28. Plunkett, C.R. (1932). Temperature as a tool for research in phenogenetics: methods and results. *Proc. 6th Int. Cong. Genet.* Vol. 2, pp. 158-60.
29. Fisher was awarded the Darwin Medal of the Royal Society in 1948 for 'distinguished contributions to the theory of natural selection, the concept of the gene-complex and the evolution of dominance'.
30. See *CP* 87, p. 402.
31. This letter and the following ones shed light on the development of ideas concerning the evolutionary effects of fluctuations in population size. See Fisher's letter of 24 April 1931 to J.R. Baker (p. 178).
32. See *GTNS*, p. 103.
33. Ford, H.D. and Ford, E.B. (1930). Fluctuations in numbers and its influence on variation in *Melitaea aurinia. Trans. R. ent. Soc. Lond.* **78**, 345-51.
34. Ford had said Fisher's suggestion that Mendel had reached his conclusions as a generalization of wide rather than local application raised a difficulty in regard to Mendel's strategy for it would then seem extraordinary that Mendel should have verified and demonstrated his conclusions with only a single species when, perhaps with no more work, he could have used two widely different organisms to strengthen greatly his position.
35. See Fisher's letter of 31 May 1931 to Wright and also *CP* 185.
36. Ford had asked Fisher if he would contribute to a volume on evolution in honour of Julian Huxley. See Huxley, J.S., Hardy, A.C., and Ford, E.B. (Eds.) (1954). *Evolution as a process.* Allen and Unwin, London.
37. Fisher was seeking advice on whether he should insert a note on the butterfly *Limenitis* in the Dover reprint edition of his book (see *GTNS*, p. 145). See also his letter of 29 November 1955 to L.P. Brower.

38. Hagedoorn, A.L., and Hagedoorn, A.C. (1921). *The relative value of the processes causing evolution.* Martinus Nijhoff, The Hague. See *CP* 17 and Darwin's letter of June 1921 to Fisher (p. 74).
39. Dr A.B.D. Fortuyn was Professor of Anatomy, Peiping Union Medical College, China.
40. See Section 32 of Fisher, R.A. (1925-70). *Statistical methods for research workers.* Oliver & Boyd, Edinburgh.
41. After reading *GTNS*, Professor R.R. Gates, Botany Department, King's College, London, had written seeking Fisher's views on the relative importance of migration and crossing in producing the observed differences in racial frequencies of the ABO blood groups. Gates wrote of two genetic factors being involved in the ABO blood groups which, he said, were apparently without selective effect.
42. See *CP* 87, p. 402.
43. See Fisher's letter of 23 April 1930 to C. Todd (p. 267), a copy of which Fisher had sent Haldane.
44. Haldane, J.B.S. (1930). A mathematical theory of natural and artificial selection. Part VII. Selection intensity as a function of mortality rate. *Proc. camb. Phil. Soc.* **27**, 131-6.
45. Haldane had lost track of the manuscript of the review of *GTNS* he had written for *Eugenics Review* after the editor (Mr Elton Moore) said he did not want it.
46. Edin, K.A. (1929). The birth rate changes. Stockholm 'upper' classes more fertile than the 'lower'. *Eugenics Rev.* **20**, 258-66. See Fisher's letter of 24 November 1938 to Sir James Marchant (p. 233).
47. Haldane, J.B.S. (1931). Mathematical Darwinism. A discussion of *The genetical theory of natural selection. Eugenics Rev.* **23**, 115-17.
48. At University College, London.
49. At the John Innes Horticultural Institution, Merton, where Haldane held a part-time appointment.
50. Haldane, J.B.S. (1939). The spread of harmful autosomal recessive genes in human populations. *Ann. Eugen.* **9**, 232-7.
51. See Fisher's letter of 10 February 1942 to K. Mather (p. 236).
52. Haldane, J.B.S. (1940). The conflict between selection and mutation of harmful recessive genes. *Ann. Eugen.* **10**, 417-21.
53. University College, London.
54. Rothamsted Experimental Station.
55. Heckstall-Smith, H. (1957). Review of *Nuclear explosions and their effects.* (Government of India) *Friend* **115**, 33-6.
56. Lancelot Hogben, Professor of Social Biology at the London School of Economics, had written asking if Fisher was working on the problem of the contribution of a sex-linked locus to the correlations between relatives.
57. See also Fisher's letter of 18 January 1935 to J.A. Fraser Roberts (p. 260).
58. Huxley, A. (1923). *On the margin.* Chatto and Windus, London.
59. See Fisher's letter of 1 November 1932 to E. Selous (p. 261).
60. Fisher was recovering from an operation and Huxley was to take his place at a discussion on Population in the Zoology Section of the British Association for the Advancement of Science.
61. See Darwin's letter of 30 April 1931 to Fisher (p. 138). Fisher's paper was not published until 1954 (*CP* 258). See Fisher's letter of 23 October 1951 to E.B. Ford (p. 202).

62. Huxley had asked Fisher about what he could say on selection for closer linkage in an article he was writing on polymorphism. See Huxley, J.S. (1955). Morphism and evolution. *Heredity* **9**, 1-52.
63. A draft of an article on Fisher's fundamental theorem of natural selection.
64. The term *genetic variance,* as used by Fisher, refers to the component of the genotypic variance which is now commonly called the *additive genetic variance.*
65. In the following two letters, Fisher discusses several points arising from a draft of Kimura, M. (1958). On the change in population fitness by natural selection. *Heredity* **12**, 145-67.
66. Fisher had once pulled Lowdnes up in conversation for stating that natural selection is concerned with the benefit of the species and had emphasized that in reality it is only concerned with the benefit of the individual. Later, when Lowdnes was unable to find a reference to this in *GTNS*, he wrote to Fisher for further information. Fisher's reply is notable for its reference to the evolution of altruism by kin selection and for the distinction drawn between individual and species benefit in natural selection. In 1958, Fisher inserted a passage dealing with this distinction in *GTNS* (p. 49).
67. After a broadcast on the BBC's Third Programme in which Fisher and three other British scientists—C.D. Darlington, J.B.S. Haldane, and S.C. Harland —gave their views on the Lysenko controversy (*Listener* **40**, 873), Mr A.H. Machino, Programme Organizer of the Russian Section, wrote saying that the BBC would like to include a shortened version of these talks in their Russian broadcasts for Soviet audiences. He suggested that the quotations from Lysenko could be omitted from Fisher's contribution 'as we think we can assume that the average Soviet listener is well acquainted with the various steps which led to the recent developments in biological research in the U.S.S.R. and with the role played by Lysenko in this matter'. The letter printed here is Fisher's reply. For Fisher's talk, entitled, 'What Sort of Man is Lysenko?', see *CP* 229.
68. Sir James Marchant, Secretary of the National Birth-Rate Commission, in writing to Fisher said doctors had experienced a greatly increased demand for information on birth control methods.
69. See Note 46.
70. See Note 27.
71. See Fisher, R.A. (1942). The polygene concept. *Nature* **150**, 154 (*CP* 191).
72. Early in 1935 Fisher had received an offer of 1000 roubles from the President of the State Publishing House of Biological and Medical Literature, USSR, for a translation of the first seven chapters of *GTNS*. See also Fisher's letter of 15 February 1937 to C.I. Bliss (p. 183).
73. Lewis, D. (1942). The evolution of sex in flowering plants. *Biol. Rev.* **17**, 46-67.
74. Mather, K. (1943). Polygenic balance in the canalization of development. *Nature* **151**, 68-71.
75. Jolly, A.T.H. and Rose F.G.G. (1943). The place of the Australian aboriginal in the evolution of society. *Ann. Eugen.* **12**, 44-87.
76. Morgan, T.H. (1932). *The scientific basis of evolution.* Faber, New York. See also Fisher's letter of 15 November 1932 to Darwin (p. 159).
77. After reading Fisher's Herbert Spencer Lecture, *The social selection of human fertility* (*CP* 99), Dr. C.S. Myers had written asking if Fisher regarded it as *proven* that 'those who rise in the social scale ... are involuntarily (i.e. congenitally) less fertile' and whether voluntary infertility could be excluded.

78. Fisher's letters to Dr R.K. Nabours, Department of Zoology, Kansas State College, have special interest becasue of their early and novel suggestions on practical and theoretical questions which arise in the study of polymorphic species involving dominance and close linkage. See *CP* 87 and *CP* 167.
79. Nabours, R.K., Larson, I., and Hartwig, N. (1933). Inheritance of colour patterns in the grouse locust *Acrydium arenosum. Genetics* **18**, 159-71.
80. See Fisher, R.A. (1939). Selective forces in wild populations of *Paratettix texanus. Ann. Eugen.* **9**, 109-22 (*CP* 167).
81. Dr J. Rasmusson, writing from Svalöf, Sweden, had asked about a comment attributed to Haldane that Fisher was in doubt concerning dominance theory.
82. This letter to Dr C. Tate Regan, Direct of the British Museum (Natural History), contains the earliest known outline of the argument which Fisher later presented in Chapter I of *GTNS*. See Fisher's letter to J. Davidson (p. 190) and also Darwin's letter of 27 April 1928 to Fisher (p. 84).
83. The correct value is $1.4\,n$ generations. See *GTNS*, p. 95.
84. See *GTNS*, p. 127. See also Fisher's letter to A. Vassall (p. 271).
85. Pamphlet on sexual selection, probably *CP* 6.
86. See *GTNS,* p. 152.
87. After editorial comment in *Eugenics Rev.* **24**, 174, (1932), Dr R.N. Salaman wrote questioning the assumption that the male ratio would be greatly increased if it were possible to control sex determination in Man. He suggested that 'Society' would seize control of the situation before that happened.
88. The wife of Dr J.F. Cameron, Master of Gonville and Caius College, Cambridge, 1928-48. Sir Charles Sherrington had resided in the Master's Lodge as a guest in 1943 when Fisher was also resident in Caius.
89. With Artificial Insemination Donor.
90. Dr P.V. Sukhatme had written asking if Fisher could confirm his impression that the theory of population growth included in Chapter II of *GTNS* had been developed by Fisher independently of the work of Lotka and Kuczynski and several years before publication of the book in 1930.
91. Fisher, in fact, published a short article on this subject in 1927 (see *CP* 60). Shortly afterwards, when a letter from Lotka appeared in *Eugenics Rev.* **19**, 257-8, claiming priority, it was accompanied by the following editorial note, 'Dr. Fisher writes: I am much interested to see how closely Dr. Lotka's work, which I had not previously seen, agrees in aim and method with the recommendations I have made. Evidently the only absolutely novel suggestion in my article lies in the estimation of a definite "reproductive value" for each age of life. Dr. Lotka's suggestions and mine are still unfortunately in the future as far as British official birth data are concerned.'
92. Dr H.G. (later Sir Gerald) Thornton, in commenting on Fisher's Eddington Memorial Lecture, *Creative aspects of natural law* (*CP* 241), had written that whilst Natural Selection must be the operative factor in the development of a higher structure in a living organism, it 'does not seem to explain the tendency for increasing complexity in the inorganic world or the appearance of new products of the human intellect such as works of art or original concepts.'
93. See Preston, F.W. (1953). Lecture version of Paper on annealing as genetics. *The Glass Industry* **34**, 485-6. Preston shows that Fisher's functional equation $f(x+1) = \exp(f(x)-1)$, considered in Chapter IV of *GTNS*, provides a good description of the process of annealing.
94. Dr J.F. Tocher, editor of *The book of Buchan,* had asked Fisher if he would contribute a chapter on 'National efficiency from the standpoint of heredity' in which he might 'give a lead in how to improve the physique, character, and

ability of the British Nation'. Fisher's contribution entitled, 'Heredity, environment, and national efficiency', was published as Chapter 4 of the Jubilee Volume of *The book of Buchan* (1943).

95. Todd, C. (1930). Cellular individuality in the higher animals, with special reference to the individuality of the red blood corpuscles. *Proc. R. Soc. B 106*, 20-44. See Haldane's letter of 29 April 1930 to Fisher (p. 209) for his comments on Fisher's letter to Todd. See also Fisher's letter of 25 November 1930 to Darwin (p. 134) and *FLS*, p. 338.
96. Fisher had suggested that Todd should test serologically for the female-determining chromosome. (See Fisher's letter of 10 June 1930 to Haldane, p. 212). On 2 October 1931, following Fisher's enquiry as to progress, Todd reported that he had not been able to tackle the complete experiment on the sex effect. In fact, there had been high mortality in his fowls which had been fed some alcohol-extracted protein residues in error. Todd went on to tell Fisher of his interesting finding that two fowls immunized in parallel with the same doses of the same red blood cells produced qualitatively different antibodies. This was an important discovery because it had been generally assumed until then that the nature of the immune antibodies produced depended solely on the character of the antigens used.
97. Todd had written that after spending much time trying to find a more delicate method of detecting small amounts of iso-agglutinin in the serum, he had not found any indication of a sex difference.
98. See Wright, S. (1929). Fisher's theory of dominance. *Am. Naturalist* **63**, 274-9. Wright suggested that the selective pressures on the modifying genes were too small to be effective.
99. An outline of Fisher, R.A. (1929). The evolution of dominance: a reply to Professor Sewall Wright. *Am. Naturalist* **63**, 553-6 (*CP* 81).
100. Wright had agreed that the main question at issue was whether a very slight selective pressure acting for a correspondingly long time would be equivalent to a much greater pressure acting for a proportionately short time. He said that his criticism of Fisher's theory rested on the assumption that modifying factors would nearly always be subject to other selective pressures more important than those involved in the modification of dominance.
101. Wright, S. (1929). The evolution of dominance. Comment on Dr. Fisher's reply. *Am. Naturalist* **63**, 556-61.
102. Wright maintained that it was proper to use δp, the change in frequency of a modifier gene, as the basis for comparison of the effects of selection and mutation. He had asked Fisher about the significance of his usage of the selective intensity i in *CP* 81.
103. Wright (see Note 101) had suggested that because of population subdivision and other factors, natural populations will often be of restricted size so that random drift will be important in affecting the frequency of genes subject to very small selective differences.
104. Wright's manuscript on gene frequency distribution which he had sent Fisher on 13 August 1929. See Chapter 1, p. 41.
105. Wright had asked Fisher if he had written anything on the effects of diffusion referred to in Fisher's previous letter.
106. See *GTNS*, p. 95 and *CP* 86.
107. See Appendix A (p. 287) for a review by Fisher of Wright's paper.
108. Wright's letter included an outline of his ideas on 'adaptive surfaces'.
109. J.L. Lush, Professor of Animal Breeding, Iowa State College, Ames.

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