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Perspectives

Anecdotal, Historical and Critical Commentaries on Genetics

Edited by James F. Crow and William F. Dove

D. S. Falconer and *Introduction to Quantitative Genetics*

William G. Hill*,[1] and Trudy F. C. Mackay†

School of Biological Sciences, University of Edinburgh, Edinburgh EH9 3JT, United Kingdom and †Department of Genetics, North Carolina State University, Raleigh, North Carolina 27695

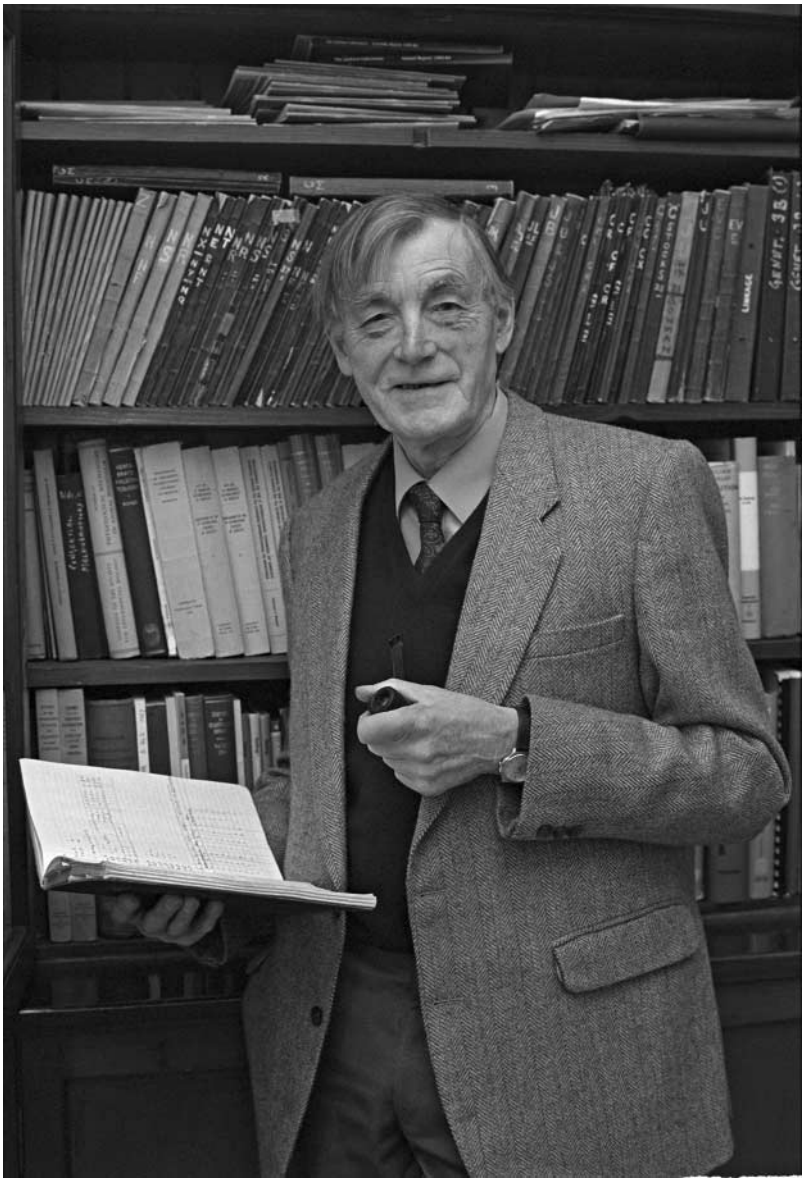
DOUGLAS Falconer died on February 23, 2004, in Edinburgh. In his career he made many important contributions to quantitative genetics and to the genetics of the mouse. Undoubtedly, however, his greatest impact was through his textbook, *Introduction to Quantitative Genetics* (Falconer 1960a), which for many throughout the world has been both their lead into and their lifelong reference on the subject. The first edition was published in 1960 when one of us (W.G.H.) was an undergraduate student in agriculture and becoming interested in animal breeding; the book (albeit advanced for that naïve student) gave a lead into the science behind the practice. The fourth edition in 1996 was co-authored by T.F.C. Mackay (Falconer and Mackay 1996). We both have read it many times, consulted it, and taught from it. The book has been part of our lives. In this *Perspectives* we shall give some brief biographical information about Douglas, who was our teacher, colleague, and friend, and a summary of some of his most significant research. We shall concentrate, however, on the development and impact of *Introduction to Quantitative Genetics*.

Douglas Falconer's family, which came from Edinburgh, had no significant tradition of science. His father was a minister in the church when Douglas was born on March 10, 1913, in Old Meldrum, Aberdeenshire, but the family soon moved back to Edinburgh, where Douglas went to school. There he developed an interest in science, although no biology was taught. He was accepted for university but his studies were delayed by 5 years when he contracted tuberculosis. During those long years of recuperation he read widely, including Morgan's *Theory of the Gene*. Finally, in 1936 he resumed his education at St. Andrews University, where he shone in science, being both more able and older than his contemporaries and, judging by his later years, a clearer thinker and more organized. He took an honors degree in zoology under D'Arcy Thompson (of *Growth and Form* fame), but did not study any genetics. Falconer (unpublished notes) wrote that Thompson presided over the final year course, "but did almost nothing. I asked him at the beginning for recommendations as to what to read and he said 'Just browse, my boy, just browse.' So I worked away on my own . . . and at the end of the year he came along to me and said 'Well, Douglas, my boy, you're a very good lad and I don't think we need give you an examination this year.'" But the Dean prevailed and Douglas had to take an exam, in which he received First Class Honors. He was unfit for military service and took his Ph.D. in 1943 under James Gray at Cambridge on "The behavior of wireworms in relation to temperature and light," which is less esoteric than it appears as the wireworm is a major crop pest and there was a wartime need to increase agricultural production; but Douglas did not find it inspiring.

While still a student he met and married Margaret Duke, a classicist, and they had two sons; all three survive him. Among their shared interests was a love of music, which they played together. Douglas played the flute and continued to do so until he was well into his eighties. In midlife Douglas developed diabetes, which he managed well, but he became increasingly blind in his last years. To those who met him from at least the 1960s onward, he already appeared a frail individual, but his frailness belied his determination and toughness. He was still coming into work and writing long after his retirement in 1980, not the least on further editions of his book, and he still kept an interest and enjoyed scientific discussion until his death.

Subsequent to completing his Ph.D., Douglas had a temporary lectureship at Queen Mary College London, then based in Cambridge, where his teaching included a course in genetics. At the end of the war, the Agricul-

[1]*Corresponding author:* Institute of Cell, Animal and Population Biology, School of Biological Sciences, University of Edinburgh, West Mains Rd., Edinburgh EH9 3JT, United Kingdom.
E-mail: w.g.hill@ed.ac.uk



Douglas Falconer in his office in 1987. (Photograph by Antonia Reeve.)

tural Research Council (ARC) was planning an institute for the study of genetics in relation to animal breeding and was bringing a group together, initially near London, but later to move to Edinburgh. Seeing this prospect, in 1945 Douglas took the opportunity to work with R. A. (Sir Ronald) Fisher at Cambridge (whose mouse labs were in his own house). Douglas set to work on mapping mutant genes and also to work on the inheritance of milk yield in mice (recording the trait as the increase in litter weight after feeding, not with a mechanical milking machine) but his time with Fisher was not entirely satisfactory. He recalls in an anecdote:

> Fisher was engaged in a complicated experiment involving a large number of mouse genes, and also involving inbreeding, that is, brother by sister mating. Inbreeding is well known to reduce fertility, and I thought it would be interesting to see how much the fertility would be reduced in the next two or three generations, and see whether he would have sufficient animals to choose suitable pairs to mate, and I found out that he would not, that he would find that many of his lines would become extinct because there was not a suitable pair to continue them. I thought I ought to tell him of this finding and see what he thought about it, so I did one day at tea. He listened to what I said and then without uttering a word, he turned round and walked out of the room. The next day he came to me and said, "I think you should arrange to go to Edinburgh as soon as you can."

Douglas Falconer was appointed to the Genetics section of the ARC Animal Breeding and Genetics Research Organization in Edinburgh in 1947, under the direction of Professor C. H. Waddington, newly appointed to the Buchanan Chair of Animal Genetics at the University of Edinburgh. A very illustrious group were brought together. In addition to Falconer, those in quantitative genetics included Alan Robertson, Jim Rendel (who left in 1951 for Australia), Eric Reeve, Forbes Robertson, and Ian Mason and, later, Crad Roberts and George

Clayton. In related areas in the ARC or university during the late 1940s and 1950s were Alan Beatty, Charlotte Auerbach, Geoffrey Beale, Mick Callan, Toby Carter, Ruth Clayton, Henrik Kacser, Mary Lyon, James Sang, and Barnet Woolf. In an earlier *Perspectives*, Falconer (1993) gives a much fuller account of the personnel and activities of their groups. (We joined the group much later: W.G.H. was a student of Alan Robertson from 1963 and then on the university staff from 1965; T.F.C.M was a student of Alan Robertson from 1976 to 1979 and then a staff member from 1980 to 1987.) Waddington essentially allowed people to work with little direction; in fact, the set up was much more like a modern university department with independently funded, self-directed groups, rather than the traditional hierarchical European university department.

INTRODUCTION TO QUANTITATIVE GENETICS, FIRST EDITION

Quantitative genetics was then a little-known subject and training was necessary. Douglas had spent time with Fisher but had worked mostly on linkage. Alan Robertson, however, spent a period in the United States with Sewall Wright and Jay L. Lush prior to coming to Edinburgh; and there were important sabbatical visitors to Edinburgh in the early days. Notable were Michael Lerner in 1948, who wrote much of his *Population Genetics and Animal Improvement* (Lerner 1950) while in Edinburgh, and Wright in 1949, who gave a course of lectures, parts of which appeared in a long methodological paper (Wright 1952), which were the basis of the first volume of his treatise (Wright 1968). Notwithstanding the contact Douglas and the Edinburgh group had with Wright and Lush, it was the analysis of variance structure and the methodology of Fisher (1918) rather than the path coefficient approach of Wright that Douglas used in his book.

In the late 1940s there was a dearth of teaching of any branch of genetics in Britain, and from 1949, in addition to honors undergraduate courses, a postgraduate Diploma in Genetics was started at the University of Edinburgh, taught by the university, ARC, and other staff. This included courses in quantitative genetics and its applications to livestock improvement, taught by Douglas and colleagues.

At that time no textbooks that covered all or indeed much of the relevant material were available. C. C. Li's (1955) *Population Genetics* dealt mainly with the subject at the level of individual genes, and the books or long papers by Fisher, Haldane, and Wright provided neither a comprehensive nor a simple coverage. Among the most relevant books were Lerner's (1950) *Population Genetics and Animal Improvement* and *The Genetic Basis of Selection* (Lerner 1958), but their aims were more limited; Lush's (1945) *Animal Breeding Plans*, which contained even less background theory; Mather's (1949) *Biometrical Genetics*, which dealt little with the kinds of randomly mating outbred populations and selection issues encountered by animal and human geneticists; and Kempthorne's (1957) *An Introduction to Genetic Statistics*. Perhaps the most comprehensive source was Lush's (1948) notes, *The Genetics of Populations*, but these were then available only as a mimeograph (posthumously published; Lush 1994).

Aimed at filling this void, and specifically to help students in the Edinburgh courses, Douglas Falconer wrote *Introduction to Quantitative Genetics*, the first edition of which was published in 1960 (Falconer 1960a). In the preface he states his objectives:

> My aim in writing this book has been to provide an introductory textbook of quantitative genetics, with the emphasis on general principles rather than on practical application, and one moreover that can be understood by biologists of no more than ordinary mathematical ability. In pursuit of this latter aim I have set out the mathematics in the form that I, being little of a mathematician, find most comprehensible, hoping that the consequent lack of rigour and elegance will be compensated for by a wider accessibility. The reader is not, however, asked to accept conclusions without proof. . . . I have no particular class of reader in mind, but have tried to make the book useful to as wide a range of readers as possible (p. v).

In the preface, he also gave some significant specific thanks:

> It is no exaggeration to say that without Dr. Alan Robertson's help this book could not have been written. Not only has his reading of the manuscript led to the elimination of many errors, but I have been greatly assisted in my understanding of the subject, particularly its more mathematical aspects, by frequent discussions with him (p. vi).

He also thanks Waddington for provision of facilities, Crad Roberts for reading the entire manuscript, and the honors and diploma students for raising questions that led to the improvement of many topics.

The first five chapters dealt with the genetics of single genes, perhaps more appropriately termed population genetics, namely Hardy-Weinberg, selection, inbreeding, and genetic drift. This is, however, important background for the quantitative genetics that follow from chapter 6 on, and indeed was and remains a succinct and clear introduction to the subject. It is again instructive to show Falconer's insight and clarity of writing by quoting from the beginning of chapter 6, "Continuous Variation":

> It will be obvious, to biologist and layman alike, that the sort of variation discussed in the foregoing chapters embraces but a small part of the naturally occurring variation. One has only to consider one's fellow men and women to realize that they all differ in countless ways, but that these differences are nearly all matters of degree and seldom present clear-cut distinctions attributable to the segregation of single genes. If, for example, we were to classify individuals according to their height, we could not put them into groups labeled "tall" and "short," because there are all degrees of height, and a division into

> classes would be purely arbitrary. Variation of this sort, without natural discontinuities, is called *continuous variation*, and characters that exhibit it are called *quantitative characters* or *metric characters*, because their study depends on measurement instead of on counting. The genetic principles underlying the inheritance of metric characters are basically those outlined in the previous chapters, but since the segregation of the genes concerned cannot be followed individually, new methods of study have had to be developed and new concepts introduced. A branch of genetics has consequently grown up, concerned with metric characters, which is called variously *population genetics*, *biometrical genetics* or *quantitative genetics*. The importance of this branch of genetics need hardly be stressed; most of the characters of economic value to plant and animal breeders are metric characters, and most of the changes concerned in micro-evolution are changes of metric characters. It is therefore in this branch that genetics has its most important application to practical problems and also its most direct bearing on evolutionary theory (p. 104).

After this introductory paragraph, in which only stylistic changes have been made through the fourth edition, Falconer goes on to explain how "the intrinsically discontinuous variation caused by genetic segregation is translated into the continuous variation of metric characters."

LATER EDITIONS

The first edition of his book was a major success. It was reprinted five times by Oliver & Boyd and twice by Longman. Douglas realized the increasing need for a new edition, but other commitments prevented his giving time to it.

He had been appointed Deputy Director of the ARC Unit of Animal Genetics under Waddington, but "Wad" became less interested in genetics and also went on a long sabbatical. In 1968 Falconer was appointed to a Personal Chair in Genetics at the University of Edinburgh and also Director of the ARC Unit. The following year he was appointed Head of the Department of Genetics with responsibilities for all the diverse groups, including other major ones in mutation research, epigenetics, and protozoan genetics, housed in several buildings (later known as the Genetics Village) on the King's Buildings campus. This was a heavy task, which Douglas undertook in an even-handed manner, notwithstanding the competing claims of many prima donnas, giving it all the commitment he gave to other work including his research, which he continued throughout this time. In 1977 he was able to give up the Headship of the Department following John Fincham's appointment to the Buchanan Chair. He could then devote time to revising his book, both prior to his formal retirement and consequent closure of the ARC Unit of Animal Genetics in 1980 and subsequently when he continued research and writing but ceased active experimental work with the mouse.

The second edition was published in 1981, with the following comments in the preface (Falconer 1981, p. ix):

> In preparing this revised edition, my aims have been (1) to keep the character of the book, and its length, unchanged; (2) to include some account of all the main developments in the last twenty years; and (3) to be less neglectful of plants.

The headings of the 20 chapters were unchanged, except chapter 16, "Inbreeding and Crossbreeding: III. The utilisation of heterosis," became more broadly "… III. Applications." Apart from adding new experimental data, including some from his own selection lines, the main changes were inclusions of new or expanded sections on the influence of assortative mating on correlations among relatives, on the effects of selection on variance in the infinitesimal model (the "Bulmer effect"), on variability among replicate selection lines, on selection limits theory, and on interpretation of long-term response. Chapter 18 on threshold characters was substantially changed, not least to reflect his own important work. In response to a query from Cyril Clarke, Falconer (1965, 1967) had proposed and used a method for analysis of human data on diseases with all-or-none expression but complex inheritance, including, for example, diabetes from which Douglas himself suffered. In this he showed that the heritability of "liability" (a term he did not introduce until the second edition) could be computed simply from two numbers, the incidence of the disease in the population and in relatives of affected individuals. The method uses the population incidence to compute the base mean and selection intensity and the incidence in relatives to compute the "response," thereby providing the realized heritability of liability.

The third edition (Falconer 1989) contained less revision. The main changes in the text were to incorporate more on mutation in quantitative genetics and a little on mixed model analysis, including REML and BLUP, and to incorporate his set of problems, previously published separately (see below).

Recognizing that some sections were becoming outdated and that he was less up to date with the subject (he was in his eighties), Douglas asked T.F.C.M. to join as a co-author of the fourth edition, published in 1996 (Falconer and Mackay 1996). The basic structure of the book was unaltered, but the main changes are outlined in the preface:

> Quantitative genetics is now merging with molecular genetics and this very active area of the subject needs more consideration than it was given in the previous edition. Accordingly, a new chapter has been added, on quantitative trait loci (QTL)—the location and characterization of the genes causing quantitative variation. Chapter 20, on natural selection, has been largely rewritten, with fuller treatment of mutation and the maintenance of genetic variation; we hope these additions will make the book more useful to students of evolutionary quantitative genetics. In the earlier chapters, the treatment of polymor-

> phism has been expanded, and some sections in the chapters on inbreeding have been shortened (p. ix).

The total length of the book was increased by little more than that of the additional chapter on QTL, which, together with chapter 20, was written mainly by T.F.C.M.

PROBLEMS ON QUANTITATIVE GENETICS

The first and second editions did not include sets of problems, but Falconer knew that these would improve the utility of the book for students. He had already prepared a large number as part of his teaching, but set out to provide a more complete set using, as far as possible, real rather than synthetic data. These were first published separately as *Problems on Quantitative Genetics* (Falconer 1983), but then incorporated into the third and fourth editions of *Introduction to Quantitative Genetics*. The problems vary in difficulty and do not necessarily, as is the case for most real data, have simple right or wrong answers, as the aim was to get students to think. Here is one in that category from chapter 10, "Heritability," raising the sort of problem frequently encountered in analysis of metric data (the interested reader can consult the book for Falconer's answer; p. 183):

> A study of morphological variation in a population of *Geospiza fortis*, one of Darwin's finches in the Galapagos, provides the following data on the depth of the bill. How would you interpret these data?
>
> Regressions, ± s.e.
> Offspring-midparent 0.82 ± 0.15
> Offspring-father 0.47 ± 0.17
> Offspring-mother 0.48 ± 0.13
> Correlations, ± s.e.
> Full sibs 0.71 ± 0.12
> Father-mother 0.33
>
> Data are from Boag, P. T. & Grant, P. R. (1978) *Nature*, **274**, 793–4.

While we were delighted to have the problems available, some of us teaching the course in Edinburgh would rather that he had not published his answers, as we had to create another batch of problems to test the students.

RESEARCH ACHIEVEMENTS

Falconer's major contributions in quantitative genetics were on the response to artificial selection in mice, the concept of the cross-environment genetic correlation, and, as noted above, development of the theory for understanding the genetics of complex human diseases in terms of an underlying continuous liability. This research also provided much illustrative material for the book. Particularly in his early years of mouse genetic research, Falconer also worked on identification and mapping of individual genes and notably identified the first sex-linked gene in the mouse, *Tabby* (Falconer 1952a).

The impact of Douglas's work can best be appreciated by considering what was understood about the genetics of quantitative traits in the late 1940s and early 1950s. There were many unanswered theoretical and empirical questions to be addressed. How effective is artificial selection in changing the mean of a trait? How long does response to selection continue? How closely do observed responses to selection match theoretical predictions? What deductions about the nature of genetic variation can be made from results of selection experiments? How important is recombination and linkage in patterning natural variation for quantitative traits and governing response to selection? The latter questions arise from the puzzle of abundant genetic variation for quantitative traits, yet relatively stable mean values in most populations. Could this be explained by the action of the population genetic processes of mutation, natural selection, migration, and genetic drift on genes affecting quantitative traits? Or are genes affecting such traits qualitatively different from those affecting Mendelian variation? The latter hypothesis was espoused by Mather (1941, 1949), who proposed that natural variation for quantitative traits was caused by multiple polygenes with individually undetectable but similar and supplementary, largely additive, effects, which are organized in balanced polygenic systems of alleles increasing and decreasing the trait value (*i.e.*, genes in linkage disequilibrium).

Strong predictions regarding the response of quantitative traits to artificial selection arise from extrapolating population genetic models of response of single genes to selection. Assuming that many genes affect the trait and that allele frequencies are not correlated with the magnitude of their effects, a symmetrical response to divergent selection for increasing and decreasing values of the trait is expected, the rate of which should gradually decline as the frequencies of genes affecting the trait in each direction approach fixation. Ultimately, limits to selection will be reached at which all favorable alleles are fixed and no genetic variation remains. Douglas's results of artificial selection on mice and those of his colleagues with Drosophila (*e.g.*, Robertson and Reeve 1952; Clayton *et al.* 1957; Clayton and Robertson 1957) rather surprisingly revealed that these predictions generally did not hold well in practice!

For example, after 30 generations of selection for increased and 24 generations of selection for decreased 6-week body weight in mice, Douglas observed that the absolute magnitude of response appeared equal in both directions (Falconer 1955). (This work was reported at the 1955 Cold Spring Harbor Symposium, a major event in the history of quantitative genetics. Figure 2.) However, Douglas proposed that one should describe the selection response in a manner that takes account of the amount of selection applied. He invented the

Douglas Falconer (left) with Mel Green at the Cold Spring Harbor Symposium in 1955 (photograph courtesy of Cold Spring Harbor Laboratory).

concept of "realized heritability" (h^2), obtained by regressing the cumulated selection response on the cumulated selection differential, the latter weighted by the number of progeny measured. (Douglas credited the origin of this concept to his colleague Barnet "Woggy" Wolfe.) When described in this manner, it was apparent that the resulting realized heritabilities were markedly different in the high ($h^2 = 0.18$) and the low ($h^2 = 0.52$) lines. This important result indicates that predictions of response to selection from heritabilities estimated from correlations among relatives in the base population could be misleading. Further, asymmetrical responses to selection *de facto* imply that one or more of the assumptions underlying the simple prediction must be false. For example, alleles increasing size may have been more frequent than those decreasing size in the base population; there might be directional dominance, and inbreeding depression could accelerate response in one direction and hinder it in the other. Douglas had the biological insight to realize that in this case the asymmetry was most likely attributable to a maternal effect. He speculated that 6-week body weight could be partitioned into weaning weight at 3 weeks, largely determined by the mother, and growth between 3 and 6 weeks, largely a property of the individual. Remarkably, the asymmetrical response was due to weaning weight alone. For some reason, selection for reduced body size was accompanied by a correlated response in decreased mothering ability, but there was not a concomitant increase in mothering ability in the lines selected for increased weight. In addition to the unexpected asymmetrical responses, neither realized heritability nor phenotypic variance tended to decline as predicted over the course of the experiment; indeed, the phenotypic variance of the small line actually increased. Douglas also proposed that the relationship of body size to fitness could at least be partially assessed by comparing the expected and realized selection differentials. These were nearly equal in the large line, but the realized selection differentials were much lower than the expected differentials in the small line as selection proceeded, indicating that natural selection was countering artificial selection for reduced body size.

To assess whether patterns of response to artificial selection differ between traits, Douglas initiated long-term divergent selection for litter size (also an important character in farm animals). An immediate and unexpected result was that the response was opposite to the direction of selection for the first two generations, although continued selection yielded an average realized h^2 of 0.17 (Falconer 1955). This anomalous result was attributed to a negative nongenetic maternal effect whereby females reared in large litters were smaller and consequently had smaller litters. Again, the selection response was asymmetrical, with realized h^2 of 0.08 in the high line and 0.23 in the low line (Falconer 1963). In this case, Douglas demonstrated quite elegantly that the asymmetry was because the "trait" selected—"litter size"—is actually a composite of ovulation rate and embryonic survival rate. Increased litter size was due to an increase in the ovulation rate. Ovulation rate was not changed in the line selected for decreased litter size; a decrease in embryo survival accounted for this response. An explanation that fits these observations is that genes affecting embryonic survival would be deleterious recessives and rare in the initial population, and hence selection for reduced litter size would increase their frequency and thereby yield a greater response than would reducing the frequency further in the high line. Segregation of rare recessive alleles affecting embryo survival could lead to a limit to selection for high litter size at which some genetic variance remains. If so, inbreeding with continued selection, followed by crossing the newly derived inbred lines, could break the selection limit by purging some of the deleterious alleles. This was exactly what was observed when this experiment was conducted (Falconer 1971).

Douglas also made a major contribution to the practical problem of deciding in what environment artificial selection should be applied, if the selected individuals are to be reared in a wide range of environments. Should selection be conducted in a good environment, giving maximal expression to the desired character, as Hammond (1947) had argued, or should it be carried out under the conditions in which the organisms will eventually live?

Douglas showed that the answer depends on the extent to which the trait exhibits genotype by environment interaction ($G \times E$). If the rank order and relative magnitudes of phenotypic expression for genotypes affect-

ing the trait are the same across a range of environments, then there is no $G \times E$ and it does not matter in which environment the selection is conducted. However, if the expression of the trait changes rank or magnitude among the different genotypes, there is $G \times E$ and it might be best to select in the environment in which the organisms will ultimately be reared. To analyze this, Douglas made a major contribution to quantitative genetic theory by showing that the magnitude of $G \times E$ could be quantified by the cross-environment genetic correlation, r_{GE}, in which the same character measured in two environments is considered to be two different characters. The magnitude of $G \times E$ declines as r_{GE} approaches unity and increases as r_{GE} approaches zero. Thus the answer to the question regarding the appropriate environment in which to select comes from evaluating the relative magnitude of the correlated to the direct response to selection (Falconer 1952b). Here the correlated response (CR_Y) is the response of the trait in the environment (Y) in which it is expected to perform, given selection in a different environment (X), while the direct response (R_Y) is for selection in the environment in which the organisms will ultimately be reared. Assuming equal selection intensities in the two environments, $CR_Y > R_Y$ if $r_{GE}h_X > h_Y$, where h_X and h_Y are, respectively, the square roots of the heritabilities of the trait in the environment in which selection is made and in the environment in which the individuals are expected to ultimately perform. If the genetic correlation is low, selection should be conducted in the environment in which the strain is expected to perform, as was demonstrated by Douglas's classic experiment describing direct and correlated responses of growth weight of mice reared on high and low "planes" of nutrition (Falconer 1960b).

We outline only some highlights of Douglas's subsequent research, which continued to 1990 when he came back to theoretical issues of selection in different environments (Falconer 1990) and which included the demonstration of genetic variability in susceptibility to tumors obtained by selection of mice for the number induced by urethane exposure (Falconer and Bloom 1964). In his later selection experiments Douglas sought to find out more about the genetic basis of the responses to selection obtained. First he appreciated the need to replicate experiments because one selection line is just a single sample, subject to sampling by genetic drift, and so he initiated selection for high and low 6-week body weight with six each of high-selected, low-selected, or unselected controls (Falconer 1973). He then sought to find what had contributed to the genetic changes. Perhaps his most elegant experiment was to make aggregation chimeras of embryos from high, control, and low lines (Falconer *et al.* 1981). Such chimeras vary in the contribution that they get from each "parent," both overall and between organs and tissues. The lines were genetically marked so that the origin of tissues in the adult animals could be detected. Falconer and colleagues found that body weight was linearly related to the mean cell proportions, which accounted for most or all of the chimeric variance of body weight, and that no single organ was found to have a predominant effect on growth. Hence they concluded that control of growth must be systemic and not under the control of any single organ or tissue. It will be interesting to see how these results come to be explained in the modern era of functional genomics.

LOOKING BACK

One or more editions of *Introduction to Quantitative Genetics* have been translated into at least nine languages, sometimes eccentrically. For example, Carlos Lopéz-Fanjul explained to us that in the first Spanish translation by F. M. Sanchez (*Introducción a la Genética Cuantitativa*, CECSA, Mexico, 1970), Drosophila "bristle number" was translated as "número de setas." While in archaic Spanish "seta" means "hair," in current Spanish lexicon "número de setas" translates to "number of mushrooms."

What is remarkable is that *Introduction to Quantitative Genetics* has lasted over 40 years, with only evolution and not revolution of content, and is still used for courses. There have been many predictions of the death of quantitative genetics as a subject, as new techniques have been introduced. This has not happened. When the book first appeared, the most obvious market was for students and researchers in animal and, to a lesser extent, plant breeding. Subsequently, as the numbers involved in such industries have declined, there has been a heightened interest in quantitative genetics in those studying natural populations and in conservation genetics. The complex nature of the inheritance of much human disease has been realized, such that quantitative genetics of humans is now a fashionable and heavily researched subject.

The expansion of the subject is illustrated by *Genetics and Analysis of Quantitative Traits* by Lynch and Walsh (1998), which is over twice the length of Falconer's *Introduction to Quantitative Genetics* and is purportedly only the first of two volumes. (We look forward to the second, but have stopped holding our breath.) Other books deal with particular parts and their titles illustrate the breadth of the subject, for each relies heavily on quantitative genetic methods, including Roff's (1997) *Evolutionary Quantitative Genetics*, Frankham *et al.*'s (2002) *Introduction to Conservation Genetics*, and several books covering aspects of animal and plant breeding. That of Kearsey and Pooni (1996) focuses more on the approach of the Birmingham school, but brings the notation and coverage of Mather and Jinks' (1971) *Biometrical Genetics* closer to that of texts such as Falconer's. Aspects of the theory of quantitative genetics have been covered by Crow and Kimura (1970) in *An Intro-*

duction to Population Genetics Theory, by Bulmer (1980) in *The Mathematical Theory of Quantitative Genetics*, and recently by Bürger (2000) in *The Mathematical Theory of Selection, Recombination, and Mutation*. Modern methods of statistical analysis of quantitative genetic data are presented by Sorensen and Gianola (2002).

Undoubtedly Douglas Falconer has had an enormous and lasting impact on quantitative genetics; indeed, he essentially defined the subject. He will be greatly missed.

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