encyclopedia.com

Ronald Aylmer Fisher | Encyclopedia.com

Complete Dictionary of Scientific Biography COPYRIGHT 2008 Charles Scribner's Sons
20-25 minutes

(*b*. London, England, 28 February 1890; *d*. Adelaide, Australia, 29 July 1962),

statistics, *evolutionary genetics*. For the original article on Fisher see *DSB*, vol. 5.

Fisher's monumental influence on mathematical statistics is no greater or lesser than his influence on evolutionary genetics. Indeed, while he was at Rothamsted Experimental Station at Harpenden in Hertfordshire, England, between 1919 and 1933, Fisher not only revolutionized statistics, he helped usher in modern evolutionary theory and the historical period of evolutionary biology denoted the "evolutionary synthesis." This update deals with Fisher's contribution to evolutionary genetics, as it has only been since the mid-1980s that precisely what that contribution is has been fully understood.

The Evolutionary Synthesis . With J. B. S. Haldane and Sewall Wright, Fisher originated the field of theoretical population genetics, which synthesized the recently (1900) rediscovered principles of Mendelian heredity with Darwinian natural selection. Among the three, however, Fisher made the greatest contribution to the origins of population genetics. Fisher, of course, published much on that topic, but the three works that establish him as the dominant theorist among his contemporaries are his "The Correlation of Relatives on the Supposition of Mendelian Inheritance" in 1918; his "On the Dominance Ratio" in 1922; and the locus classicus of evolutionary genetics, *The Genetical Theory of Natural Selection*, in 1930. These three works form one long argument that defends the reconciliation of Mendelian heredity and Darwinian natural selection from the then-pervasive critics by eliminating speculative evolutionary causes or, to use William Provine's term, *constricting*, the causes correctly attributable to evolution.

In "On the Dominance Ratio," Fisher discusses, as he says, "the distribution of the frequency ratio of the allelomorphs of dimorphic factors, and the conditions under which the variance of the population may be maintained" (1922, p. 322). He saw this paper as linked to the earlier "Correlation of Relatives on the Supposition of Mendelian Inheritance." In broad brush strokes, this means that where the 1918 paper defended the principles of Mendelian heredity against the criticisms of the biometricians (and in fact showed the two schemes to be compatible),

the 1922 paper continues by carrying through its mathematical methods and concepts as well as defending Darwinism's using the principles of Mendelian heredity. Specific to "On the Dominance Ratio," Fisher's aim was to respond to a set of criticisms to the effect that Darwinian natural selection cannot be the correct explanation of the modulation of genetic variation in populations because the genetics of populations are such that there is not enough variation available for selection to act upon. In his response, Fisher considered the interaction of natural selection, random survival (genetic drift), assortative mating, and dominance. During the course of the paper, Fisher eliminated from consideration what he took to be insignificant evolutionary factors, such as epistatic gene interaction and genetic drift, and argued that natural selection acted very slowly on mutations of small effect and in the context of large populations maintaining a large amount of genetic variation.

Analysis of Random Drift . Consider drift, or what Fisher referred to variously as random survival, steady decay, or the Hagedoorn effect. The phrase *random drift* comes from Wright's landmark paper of 1931, "Evolution in Mendelian Populations." Notwithstanding Wright's obvious contributions to the development of the concept and mathematical modeling of drift, it was Fisher who, in his 1922 paper, was the first among the architects of population genetics to explore mathematically the evolutionary consequences of drift in a Mendelian population.

In finite populations, the variation in the number of offspring between individuals may result in random fluctuations in allele frequencies. These random fluctuations affect the chances of survival of a mutant allele in a population. Fisher argued that the survival of a rare mutant depended upon chance and not selection. Indeed, he argued that such a mutation would be more likely to remain at low frequencies in a large rather than in a small population, since in a large population the mutant would have a greater probability of survival. Random fluctuations in allele frequencies also reduce a population's genetic variation. In *The Relative Value of the Processes Causing Evolution* (1921), Arund L. and Anna C. Hagedoorn argued that random survival is an important cause of the reduction of genetic variation in natural populations. Fisher argued that the Hagedoorns were mistaken. Fisher determined two key quantities for the situation in which a population is under the influence only of the steady decay of genetic variation, that is, the Hagedoorn effect: the first quantity describes the time course in generations of the Hagedoorn effect; the second describes the "half-life" in generations of the effect. Fisher determined the time course to be $4N$ (where N is population size) and the half-life to be $2.8N$. This means that the Hagedoorn effect requires $4N$ generations to reduce the genetic variation in the population to the point that all alleles are identical by descent. The "half-way" point is reached in $2.8 N$ generations. (Wright demonstrated in a 1929 letter to Fisher that his, Fisher's, calculations were twice too high: the time-course in generations is $2N$ and the half-life of the Hagedoorn effect is $1.4N$. In his paper, “The Distribution of Gene Ratios for Rare Mutations” [1930], Fisher showed that the correction had only a minor effect on his argument.)

Fisher used these quantities to weight the significance of the effect of steady decay; the longer the time course, the weaker the effect. Given that the time course of the Hagedoorn effect depends on the population size, the larger the population, the weaker, or less significant, the effect. It is evident that as population size increases over 10^4, that the time course becomes considerable. Indeed, Fisher says, “As few groups contain less than 10,000 individuals between whom interbreeding takes place, the period required for the action of the Hagedoorn effect, in the entire absence of mutation, is immense” (1922, p. 330). According to Fisher, then, the Hagedoorn effect is evolutionarily insignificant and populations are large.

Fisher’s insights regarding the evolutionary effects of genetic drift reflect his strong Darwinian assumptions, as he (Fisher) says: “a numerous species, with the same frequency of mutation, will maintain a higher variability than will a less numerous species: in connection with this fact we cannot fail to remember the dictum of Charles Darwin, that ‘wide-ranging, much diffused and common species vary most’” (1922, p. 324).

Gene Interaction . In his 1918 paper, Fisher considered the statistical consequences of dominance, epistatic gene interaction, assortative mating, multiple alleles, and linkage on the correlations between relatives. Fisher argued that the effects of dominance and gene interaction would confuse the actual genetic similarity between relatives. He also knew that the environment could confuse such similarity. Fisher here introduced the concept of variance and the analysis of variance to the scientific literature:

> When there are two independent causes of variability capable of producing in an otherwise uniform population distributions with standard deviations σ_1 and σ_2, it is found that the distribution, when both causes act together, has a standard deviation . It is therefore desirable in analyzing the causes of variability to deal with the square of the standard deviation as the measure of variability. We shall term this quantity the Variance of the normal population to which it refers, and we may now ascribe to the constituent causes fractions or percentages of the total variance which they together produce. (1918, p. 399)

Fisher then used this tool to partition the total variance into its component parts.

Fisher labeled that portion of the total variance that accurately described the correlation between relatives the “additive” genetic component of variance. The “nonadditive” genetic component included dominance, gene interaction, and linkage. Environmental effects, such as random changes in environment, comprised a third component of the total variance. In 1922, on the basis of his 1918 work, Fisher argued that the additive component of variance was important for evolution by natural selection. Indeed, he argued that, particularly in large populations ($>10^4$), nonadditive and environmental components of the total variance are negligible. He further claimed that selection would remove any factor for which the additive contribution to the total genetic variance is very high and leave those for which the contribution is low. Indeed, Fisher says, “It is therefore to be expected that the large and easily recognized factors in natural organisms will be of little adaptive importance, and that the factors affecting important adaptations will be individually of very slight effect” (1922, p. 334). Ultimately, for Fisher, evolution proceeds very slowly, with low levels of selection acting on mutations of small effect and in large populations holding considerable genetic variation.

The Genetical Theory of Natural Selection . Fisher’s work discussed above and other work on, for example, the evolution of dominance and mimicry, would culminate in his book, *The Genetical Theory of Natural Selection* (1930), one of the principal texts—along with Haldane’s *The Causes of Evolution*(1932) and Wright’s “Evolution in Mendelian Populations” (1931) and “The Roles of Mutation” (1932)—completing the reconciliation of Darwinism and Mendelism and establishing the field of theoretical population genetics (and, for Fisher, its application to eugenics). *The Genetical Theory* is celebrated as the locus classicus for the reconciliation of Darwinian natural selection and Mendelian heredity. Remarkably, the book manuscript was produced by Fisher’s dictating to his wife, Ruth, during the evenings. It was revised and reis-sued in 1958 and most recently in a variorum edition issued in 1999 (edited by J. H. Bennett).

The first seven (of twelve) chapters of *The Genetical Theory* set out Fisher’s synthesis of Darwin’s mechanism of natural selection and Mendelian genetics. Fisher considered the first two chapters, on the nature of inheritance and the “fundamental theorem of natural selection,” the most important of the book. Indeed, these two chapters accomplish the key piece of the reconciliation. Moreover, the general argument strategy Fisher used in 1918 and 1922, of defending the principles of Mendelian heredity and defending Darwinism under the rubric of Mendelian heredity, is carried through. Fisher’s aim in *The Genetical Theory* was to establish particulate inheritance against the blending theory and then demonstrate how plausibly Darwinian natural selection may be the principal cause of evolution in Mendelian populations.

Fisher’s first chapter considers implications of a synthesis of natural selection with, alternatively, blending and Mendelian inheritance. He demonstrates that on the Mendelian theory, natural selection may be the main mechanism of a population’s variability. The demonstration importantly resolved a persistent problem for Darwin’s theory of descent with modification, one that had led biologists to abandon natural selection as an evolutionary mechanism: Darwin’s acceptance of blending inheritance required him to imagine special mechanisms controlling mutation because of enormous mutation rates demanded by the blending theory. Because Mendelian heredity did not demand such enormous mutation rates, Fisher was able to eliminate these controlling mechanisms and, so, revive natural selection as an important evolutionary mechanism.

Fisher's second chapter develops, mathematically, his genetical theory of natural selection. The arguments are drawn largely from his "On the Dominance Ratio" of 1922 and "The Distribution of Gene Ratios for Rare Mutations" of 1930, the response to Wright's aforementioned correction of Fisher's 1922 paper. Three key elements may be distilled from Fisher's "heavy" mathematics in the second chapter of *The Genetical Theory*. The first is a measure of average population fitness, Fisher's Malthusian parameter—that is, the reproductive value of all genotypes at all stages of their life histories. The second is a measure of variation in fitness, which Fisher partitions into genetic and environmental components (based on his distinctions from his 1918 and 1922 papers). The third is a measure of the rate of increase in fitness, that is, the change in fitness due to natural selection. For Fisher, "*the rate of increase of fitness of any organism at any time is equal to its genetic variance in fitness at that time*" (*The Genetical Theory of Natural Selection*, 1930, p. 37; emphasis in original). This last element is Fisher's fundamental theorem of natural selection and is the centerpiece of his natural selection theory.

Understanding the Fundamental Theorem . Interestingly, inasmuch as Fisher considered his fundamental theorem the centerpiece of his evolutionary theory, it happens that the theorem is also the most obscure element of it. The theorem was thoroughly misunderstood until 1989, when Warren Ewens—in "An Interpretation and Proof of the Fundamental Theorem of Natural Selection"—rediscovered George Price's 1972 clarification and proof of it in "Fisher's 'Fundamental Theorem' Made Clear." Fisher's original statement of the theorem in 1930 suggests that mean fitness can never decrease because variances cannot be negative. Price showed that in fact the theorem does not describe the total rate of change in fitness but rather only one component of it. That part is the portion of the rate of increase that can be ascribed to natural selection. And, actually, in Fisher's ensuing discussion of the theorem, he makes this clear. The total rate of change in mean fitness is due to a variety of forces, including natural selection, environmental changes, epistatic gene interaction, dominance, and so forth. The theorem isolates the changes due to natural selection from the rest, a move suggested in Fisher's 1922 paper. The key change that Price and Ewens make in the statement of the theorem, the change that clarifies it, is to write "*additive* genetic variance" for "genetic variance" (since "genetic variance" includes both an additive and nonadditive part). With the theorem clarified and proven, Price and later Ewens argue that it is not so fundamental. Given that it is a statement about only a portion of the rate of increase in fitness, it is incomplete. The Price-Ewens interpretation of the theorem is the standard one. However, Anthony Edwards –in his 1994 paper, "The Fundamental Theorem of Natural Selection"—argues that Fisher's isolation of change in the genetic variance due to selection is biologically deep, that is, fundamental, and so the charge of incompleteness is impotent.

Fisher compared both his 1922 and 1930 explorations of the balance of evolutionary factors and the "laws" that describe them to the theory of gases and the second law of thermodynamics, respectively. The received view of these comparisons is that Fisher's interests in physics and mathematics led him to look for biological analogues. No doubt this is part of the story. However, a more plausible interpretation of the comparison comes from treating Fisher's major works of 1918, 1922, and 1930 as one long argument. If this is done, one finds that Fisher's strategy in synthesizing Darwinian natural selection with the principles of Mendelian heredity was to defend, against its critics, selection as an evolutionary mechanism under Mendelian principles. Following this argument strategy, Fisher built his genetical theory of natural selection piecemeal, or from the bottom up. That is, Fisher worked to justify the claim of his fundamental theorem by constructing plausible arguments about the precise balance of evolutionary factors. Thus, his piecemeal consideration of the interaction between dominance, gene interaction, genetic drift, mutation, selection, and so on led to his theorem. It is not, at least not primarily, the search for biological analogues to physical models and laws that underwrites the theorem.

Eugenics . The last five chapters of *The Genetical Theory* explore natural selection in human populations, particularly social selection in human fertility. According to Fisher, the decline of human civilizations is due in part to the point in economic development where an inversion in fertility of the upper classes to that of the lower classes is reached. Fisher's central observation, based upon England's 1911 census data, was that the development of economies in human societies structures the birth-rate so that it is inverted with respect to social class—low birth-rates for the upper class and high birth-rates for the lower class. Families who, for whatever reason, were not capable of producing many children rose in class because of the financial advantage of having few children. In the final chapter of *The Genetical Theory*, Fisher offers strategies for countering this effect. He proposed the abolishment of the economic advantage of small families by instituting what he called "allowances" to families with larger numbers of children, with the allowances proportional to the earnings of the father. In spite of Fisher's espousal of eugenics in this part of the book, he means the discussion to be taken as an inseparable extension of the preceding part.

No one has thought that Fisher's contribution to evolutionary genetics was less than groundbreaking. Rather, precisely what Fisher established, its nature and scope, and exactly how he did so has been less than clear. With Fisher's work on variance in 1918, his work on the balance of factors in evolution in 1922, and his fundamental theorem of natural selection in 1930, we have a unified argument setting aside pervasive anti-Darwinism, originating a new mathematical approach to the evolution of populations and establishing the very essence of natural selection. All of which are good reasons for the universal approbation of Fisher's work in evolutionary genetics.

SUPPLEMENTARY BIBLIOGRAPHY

There is a wealth of material on Fisher's contributions both to statistics and to evolutionary genetics, including unpublished correspondence. See J. H. Bennett's Natural Selection, Heredity, and Eugenics: Including Selected Correspondence of R. A. Fisher with Leonard Darwin and Others *(Oxford: Clarendon Press, 1983) and* Statistical Inference and Analysis: Selected Correspondence of R. A. Fisher *(Oxford: Clarendon Press, 1990). These works contain a bibliography of all of Fisher's*

publications. *See also* The University of Adelaide Digital Library: R. A. Fisher Digital Archive; *available from http://digital.library.adelaide.edu.au/coll/special/fisher/*.

WORKS BY FISHER

"The Correlation of Relatives on the Supposition of Mendelian Inheritance." *Royal Society of Edinburgh* 52 (1918): 399–433.

On the Dominance Ratio." *Proceedings of the Royal Society of Edinburgh* 42 (1922): 321–341.

"The Distribution of Gene Ratios for Rare Mutations." *Proceedings of the Royal Society of Edinburgh* 50 (1930): 205–220.

The Genetical Theory of Natural Selection. Oxford: Clarendon Press, 1930. Released in a revised, second edition in 1958 from Dover Publications. Released in a variorum edition by Oxford University Press in 1999, edited by J. H. Bennett.

OTHER SOURCES

Edwards, Anthony W. F. "The Fundamental Theorem of Natural Selection." *Biological Reviews of the Cambridge Philosophical Society* 69 (1994): 443–474.

Ewens, Warren J. "An Interpretation and Proof of the Fundamental Theorem of Natural Selection." *Theoretical Population Biology* 36 (1989): 167–180.

Gayon, Jean. *Darwinism's Struggle for Survival: Heredity and the Hypothesis of Natural Selection*, translated by Matthew Cobb. Cambridge, U.K., and New York: Cambridge University Press, 1989.

Hagedoorn, Arund L., and Anna C. Hagedoorn. *The Relative Value of the Processes Causing Evolution*. The Hague, Netherlands: M. Nijhoff, 1921.

Haldane, John B. S. *The Causes of Evolution*. London:Longmans, 1932.

Hodge, M. Jonathon S. "Biology and Philosophy (Including Ideology): A Study of Fisher and Wright." In *The Founders of Evolutionary Genetics: A Centenary Reappraisal*, edited by Sahotra Sarkar. Dordrecht, Netherlands, and Boston: Kluwer Academic Publishers, 1992.

Price, George R. "Fisher's 'Fundamental Theorem' Made Clear." *Annals of Human Genetics* 36 (1972): 129–140.

Provine, William. "Founder Effects and Genetic Revolutions in Microevolution and Speciation: A Historical Perspective." In *Genetics, Speciation, and the Founder Principle*, edited by Luther Val Giddings, Kenneth Y. Kaneshiro, and Wyatt W. Anderson. New York: Oxford University Press, 1989.

———. *The Origins of Theoretical Population Genetics*. 2nd ed. Chicago: University of Chicago Press, 2001.

Wright, Sewall. "Evolution in Mendelian Populations." *Genetics* 16 (1931): 97–159.

———. "The Roles of Mutation, Inbreeding, Crossbreeding, and Selection in Evolution." *Proceedings of the Sixth Annual Congress of Genetics* 1 (1932): 356–366.

Robert Skipper