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R. A. Fisher, Lancelot Hogben, and the Origin(*s*) of Genotype–Environment Interaction

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Abstract. This essay examines the origin(*s*) of genotype–environment interaction, or $G \times E$. "Origin(*s*)" and not "the origin" because the thesis is that there were actually two distinct concepts of $G \times E$ at this beginning: a *biometric* concept, or $G \times E_B$, and a *developmental* concept, or $G \times E_D$. R. A. Fisher, one of the founders of population genetics and the creator of the statistical analysis of variance, introduced the biometric concept as he attempted to resolve one of the main problems in the biometric tradition of biology – partitioning the relative contributions of nature and nurture responsible for variation in a population. Lancelot Hogben, an experimental embryologist and also a statistician, introduced the developmental concept as he attempted to resolve one of the main problems in the developmental tradition of biology – determining the role that developmental relationships between genotype and environment played in the generation of variation. To argue for this thesis, I outline Fisher and Hogben's separate routes to their respective concepts of $G \times E$; then these separate interpretations of $G \times E$ are drawn on to explicate a debate between Fisher and Hogben over the importance of $G \times E$, the first installment of a persistent controversy. Finally, Fisher's $G \times E_B$ and Hogben's $G \times E_D$ are traced beyond their own work into mid-20th century population and developmental genetics, and then into the infamous IQ Controversy of the 1970s.

Keywords: analysis of variance (ANOVA), biometry, developmental biology, eugenics, genetics, genotype–environment interaction ($G \times E$), IQ controversy, Lancelot Hogben, nature–nurture debate, population genetics, R. A. Fisher

Introduction

Genotype–environment interaction, or $G \times E$, refers to cases in which different genotypic groups respond differently to the same array of environments. Such phenotypic responses are often visually displayed by means of reaction norm graphs.[1] For instance, Figure 1 reveals

[1] For histories of the reaction norm concept, see Griffiths and Tabery (Forthcoming) and Sarkar (1999).

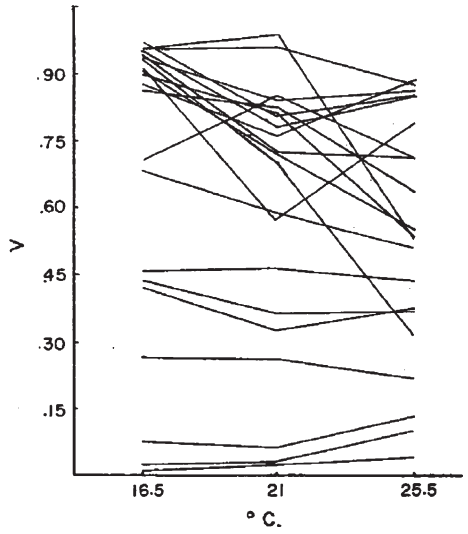

Figure 1. Lewontin's reaction norms for viability (V, *y*-axis) of fourth chromosome homozygotes of *Drosophila pseudoobscura* raised in different temperatures (°C, *x*-axis). From Lewontin (1974, Figure 2). Reproduced with the permission of the University of Chicago Press.

phenotypic curves for various strains of *Drosophila* raised at different temperatures (*x*-axis) and graphed for viability (*y*-axis). Cases of G × E have important implications for the study of variation. First, if G × E exists for a particular trait in a population, then a scientist cannot assume that phenotypic variation for that trait in a population is simply the sum of genotypic differences and environmental differences (the "main effects"). The presence of G × E adds another source of variation which must be taken into consideration. If no G × E exists, then an "additivity relation" may be assumed, and the statistical analysis of variance (ANOVA) may be employed to partition the total phenotypic variance (V_P) into genotypic variance (V_G) and environmental variance (V_E):

$$V_P = V_G + V_E. \quad (1)$$

When additivity applies, scientists can also talk about the *proportion* of total phenotypic variation attributable to either genotypic variation or environmental variation. For example, the concept of heritability[2] (h^2) is measured as:

[2] It is important to note here that this is the definition of heritability in the *broad* sense. Following Jay Lush's distinction, this concept can be contrasted with heritability in the *narrow* sense, which only accounts for the proportion of total phenotypic variance arising from the additive genetic component of genotypic variation (Lush, 1943).

$$h^2 = V_G/V_P. \quad (2)$$

But when the effect of genetic differences is modified by the environmental distribution and the effect of environmental differences is modified by genetic distribution, Eq. 1 must be modified so as to include variation due to $G \times E$ ($V_{G\times E}$):

$$V_P = V_G + V_E + V_{G\times E}. \quad (3)$$

A heritability measure is now no longer possible unless the variation due to $G \times E$ can be eliminated from the equation. This statistical maneuver is called a *transformation of scale*. It is employed to alter the scale on which the variables are measured, thereby transforming the scale, eliminating the variation due to $G \times E$, and returning to an additivity relation. Such a maneuver, however, is obviously controversial, since it essentially manipulates the measured variables simply to statistically eliminate the variation detected.[3] As we will see below, the legitimacy of this move has figured prominently in debates over $G \times E$.

There is also a second implication which is related to the first point. Since instances of $G \times E$ can be to such a degree that norms of reaction actually change rank across different environments (as is the case in Figure 1), then it becomes clear that even if one genotypic group performs better than another genotypic group in one environment, this does not necessarily mean that this will be the case in other environments. As a result, scientists must be wary of inferences made about the performance of different genotypic groups in untested environments simply from the knowledge of how those groups performed in limited, tested environments.[4]

Because of these implications for the study of variation, $G \times E$ has often sat at the heart of debates over how to best study variation and over what conclusions may be inferred from such studies. Perhaps the most (in)famous instantiation of such a debate was the IQ Controversy of the 1970s. Arthur Jensen sparked the dispute with his appeal to heritability measures to explain the gap in IQ scores between black and white populations in the US; the gap, Jensen claimed, was a result of *genetic* differences and so would remain undiminished by efforts to eliminate it via environmental interventions, such as compensatory education.[5] But critics, such as Richard Lewontin and David Layzer,

[3] Falconer and Mackay (1996); Lynch and Walsh (1997).

[4] Falconer and Mackay (1996); Lynch and Walsh (1997).

[5] Jensen (1969).

pointed to G × E to criticize Jensen's heritability measures.[6] For developmentally complex traits such as IQ, Lewontin and Layzer argued, scientists should expect G × E to be the norm; they encouraged seeking out cases of G × E in nature because of the information it revealed about variation. Indeed, Lewontin introduced Figure 1 in the context of the IQ Controversy so as to provide an empirical example of G × E. Jensen, however, was unimpressed. He doubted that such cases of G × E were common in nature; and, even when they were, he simply encouraged a transformation of scale to make the complication go away.[7]

The dispute over G × E did not end with the IQ Controversy; it persists into the present. (For a more recent example, see the target article by Gilbert Gottlieb, along with the commentary by Turkheimer, Goldsmith, and Gottesman, and Gottlieb's reply.[8]) For some scientists, G × E is fundamentally important for understanding variation in a population. For others, G × E is simply a nuisance (albeit an eliminable one) that complicates statistical efforts to partition sources of variation in a population.

This essay examines the origin(*s*) of the concept of G × E. "Origin(*s*)," and not "the origin," because the thesis is that British biologists and statisticians R. A. Fisher and Lancelot Hogben actually came to consider the concept by quite different routes. Fisher, working in the biometric tradition of biology, began by searching for accurate ways to assess the relative importance of nature and nurture; in developing methodologies for the task, he recognized that genotype–environment interactions (or, as Fisher called them, "non-linear interactions") created a potential complication for such assessments. Hogben, working in the developmental tradition of biology,[9] began by evaluating different sources of variability in a population; while he recognized the widely emphasized genetic and environmental sources of variability, he also drew attention to a *third class of variability*: that which arises from the combination of a particular genetic constitution with a particular kind of environment. For Hogben, this third class of variability was inherently developmental in nature. These different routes in these separate research traditions ultimately led Fisher and Hogben to distinct

[6] Layzer (1972, 1974); Lewontin (1974).

[7] Jensen (1972, 1973).

[8] Gottlieb (1995a, b); Turkheimer et al. (1995).

[9] The notion of a *tradition*, along with the separate biometric and developmental traditions, will be explicated below.

concepts of genotype–environment interaction. Fisher introduced what will be called the *biometric* concept of $G \times E$, or $G \times E_B$, while Hogben introduced what will be called the *developmental* concept of $G \times E$, or $G \times E_D$. Finally, these distinct concepts led Fisher and Hogben to disparate conclusions when considering the consequences of genotype–environment interactions for assessments of variation in populations. Fisher took the non-linear interactions to be of potential, but unproved, importance; Hogben claimed that they were standard and fundamentally important for understanding variability. Thus, the debates over $G \times E$ that still play out today are divided up along lines similar to those found in the Fisher–Hogben exchange. The Fisher–Hogben exchange, then, offers the historian a case that marks both the origin of a persistent dispute and the origin, I will argue, of the distinct concepts of $G \times E$ that have fueled that dispute.

In the next section, Fisher's route to $G \times E_B$ within the biometric tradition is traced. It will be seen that his consideration of genotype–environment interaction was a by-product of his developing appreciation for the potential importance of environmental sources of variation along with his development of biometric techniques for assessing such variation. Hogben's route to $G \times E_D$ within the developmental tradition is then taken up in Section 3. After a brief biographical introduction, Hogben's consideration of genotype–environment interaction is examined, where it will be seen that his interest in the concept emerged out of an earlier appreciation for experimental embryology. Next, Fisher and Hogben's opposing positions on the importance of genotype–environment interaction are compared in Section 4. Here the focus will be on revealing how their different routes to $G \times E$ and the resulting distinct concepts of $G \times E$ contributed to their disparate positions when it came to the question of importance. Finally in Section 5, the legacies of Fisher's $G \times E_B$ and Hogben's $G \times E_D$ will be traced beyond their own work and into the IQ Controversy.

R. A. Fisher and the "Non-linear Interaction of Heredity and Environment"

Ronald Aylmer Fisher (1890–1962) looms large in the history of 20th century biology and statistics (Figure 2). His contributions to population genetics, experimental design, significance tests, and general statistical methodologies combined with his ardent and infamous endorsement of eugenics to create a scientist who both revolutionized the biological and statistical sciences, and also vigorously pursued

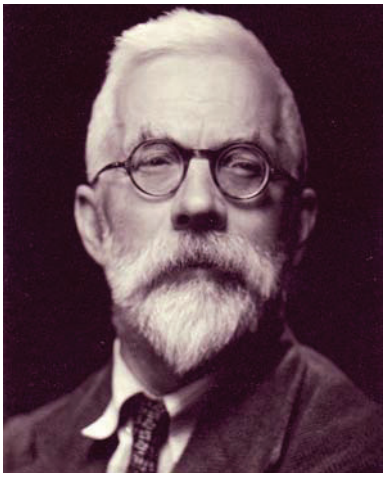

Figure 2. R. A. Fisher. Fisher papers, Barr Smith Library, University of Adelaide Library, MSS 0013/Series 25. Reproduced with the permission of the University of Adelaide Library.

the social and political implications of that revolution.[10] Because Fisher's biography and his contributions to biology and statistics have already been closely examined by historians, philosophers, and sociologists of science, the goal of this section will not be to rewrite this history. Rather, the focus here will be on tracing Fisher's path to genotype–environment interaction, a previously unexamined story. The aforementioned histories, however, will be drawn on quite heavily to reveal how Fisher's attention to genotype–environment interaction was situated within his larger biometric and eugenic research, since the concept was related to each of these domains.

[10] The most complete biography of Fisher comes from his daughter, Box (1978); however, shorter treatments can be found in Mahalanobis (1964) and Yates and Mather (1963). Fisher's contribution to population genetics can be found in Mather (1964), Plutynski (2006), Provine (2001), Skipper (2002), and Thompson (1990). His work on the design of experiments is discussed in Preece (1990) and Yates (1964), and his "logic" of significance tests is examined in Johnstone (1987). Fisher's development of now-classical statistical methodologies is discussed in Anderson (1996), Bennett (1990), Cochran (1980), Finney (1964), MacKenzie (1981), and Rao (1964). The relationship between these biological/statistical contributions and Fisher's interest in eugenics is examined in, for example, Bennett (1983), Kevles (1995), Ludmerer (1972), Mackenzie (1981), Mazumdar (1992), and Soloway (1990). Much of Fisher's scientific correspondence along with Bennett's (1983, 1990) volumes are now available online at the University of Adelaide Library's website as a part of the R. A. Fisher Digital Archive: http://www.library.adelaide.edu.au/digitised/fisher/.

The Environment Expunged

In October 1918, at only 28 years of age, Fisher published "The Correlation between Relatives on the Supposition of Mendelian Inheritance."[11] Fisher's project was the resolution of the supposed incompatibility between the biometrical theory of continuous variation and the Mendelian theory of discontinuous variation.[12] Biometrician George Udny Yule, 16 years earlier, had considered the same problem and argued that the Mendelian principles of inheritance could be seen as a special case of the biometric law of ancestral heredity[13]; Fisher, in contrast to Yule, took the reductive relationship between the Mendelian principles and the biometric law of ancestral heredity in the opposite direction.[14] Fisher instead concluded that he came upon "the Law of Ancestral Heredity as a necessary consequence of the factorial mode of inheritance."[15]

But assessing the relationship between biometry and Mendelism was not the only feat accomplished in Fisher's (1918). In the process of deriving the mathematical relationship between the Mendelian principles and the law of ancestral heredity, Fisher also introduced a new statistical concept – *variance*.[16] Fisher was interested in accounting for the sources of variation in a population. Traditionally, populations were statistically evaluated solely with an eye towards averages, but averages shed no light on variation. Fisher noted, though, that if a trait under investigation, such as stature in humans, manifested itself in a population with a normal distribution, then the mean could be calculated along with the standard deviation. Fisher's novel contribution to the statistical analysis of variation in a population was to go beyond the standard deviation and analyze the *square* of the standard deviation:

> When there are two independent causes of variability capable of producing in an otherwise uniform population distributions with standard deviations σ_1 and σ_2, it is found that the distribution, when both causes act together, has a standard deviation $\sqrt{(\sigma_1^2 + \sigma_2^2)}$. It is therefore desirable in 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

[11] Fisher (1918). For a commentary on Fisher (1918), see Moran and Smith (1966).

[12] Norton (1978); Provine (2001).

[13] Yule (1902).

[14] Tabery (2004).

[15] Fisher (1918, p. 421); Sarkar (1998, p. 106).

[16] Box (1978, p. 53).

> 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.[17]

The earlier generation of biometricians, such as Karl Pearson and Yule, had already introduced the concept of the *correlation coefficient* as a numerical measure of association.[18] Thus, correlation tables were, by 1918, common; and parental correlations along with fraternal correlations were frequently calculated from these correlation tables by the biometricians. Fisher employed this correlation technique for partitioning sources of variance in 1918 as a means towards assessing the relative importance of heritable and non-heritable sources of variation, explaining, ''For stature the coefficient of correlation between brothers is about .54, which we may interpret by saying that 54% of their variance is accounted for by ancestry alone, and that 46% must have some other explanation.''[19]

To what cause should this remainder of the total variance be attributed? Perhaps environmental variation? No! Fisher, in 1918, was quick to eliminate this possibility from the minds of his readers: ''It is not sufficient to ascribe this last residue to the effects of environment. Numerous investigations by Galton and Pearson have shown that all measurable environment has much less effect on such measurements as stature.''[20] So with environmental variation expunged from the list of possible causes of variation, Fisher had to find another explanation for the 46% of the total variance left unaccounted for by ancestry. Fisher responded, ''The simplest hypothesis, and the one which we shall examine, is that such features as stature are determined by a large number of Mendelian factors, and that the large variance among children of the same parents is due to the segregation of those factors in respect to which the parents are heterozygous.''[21] Drawing on data collected by Pearson and Alice Lee,[22] Fisher then calculated the variance between siblings attributable to Mendelian segregation and the effects of dominance. With variances due to ancestry, segregation ($\frac{1}{2}\,\tau^2$), and dominance ($\frac{3}{4}\,\varepsilon^2$) all accounted for, Fisher could finally sum up the sources of the total variance[23]:

[17] Fisher (1918, p. 399).

[18] Mackenzie (1981); Norton (1975); Porter (2004).

[19] Fisher (1918, p. 400).

[20] Fisher (1918, p. 400).

[21] Fisher (1918, p. 400).

[22] Pearson and Lee (1903).

[23] Fisher (1918, p. 424).

Ancestry		54%
Variance of sibship		
½ τ^2	31%	
¾ ε^2	15%	
Other causes	–	
		46%
		100%

Fisher famously concluded, "it is very unlikely that so much as 5% of the total variance is due to causes not heritable, especially as every irregularity of inheritance would, in the above analysis, appear as such a cause."[24]

Rothamsted and the Environment Reconsidered – the Origin of $G \times E_B$

Ending an assessment of Fisher's evaluation of the relationship between heredity and environment in the causes of variation, though, would be incomplete if it terminated with his conclusion made in 1918. Historians of genetics and eugenics have often characterized Fisher as a "reformed" or a "new" eugenicist, emphasizing his ultimate recognition of the potential importance of environmental causes of variation.[25] Pauline Mazumdar, in particular, detailed the evolution in Fisher's understanding of the environment's role in variation in her history of the British Eugenics Society.[26] According to Mazumdar, Fisher's (1918) was, from the very beginning, designed to accommodate the ideals of the Eugenics Society: (a) the compatibility of biometry and Mendelism, and (b) the negligible importance of environmental causes of variation.[27] But in 1919, Fisher left Cambridge and the "loving pressure of the eugenists" to join the Rothamsted Agricultural Research Station in Harpenden as a statistician employed to investigate the effects of environmental variables on crop yield.[28] At Rothamsted, Fisher was forced to examine environmental variation rather than assume it to be a randomly distributed variable, as he had in his 1918.[29]

In 1918, Fisher explained that sources of variation could be summed as long as the causes of variability were *independent*. Prior to undertaking

[24] Fisher (1918, p. 424).

[25] Allen (1986); Barkan (1991); Kevles (1995); Mazumdar (1992); Soloway (1990).

[26] Mazumdar (1992).

[27] Mazumdar (1992, p. 110).

[28] Mazumdar (1992, p. 114). Fisher's time at Rothamsted is also discussed in Box (1978, Chapter 4) and Mackenzie (1981, Chapter 8).

[29] Mazumdar (1992, p. 121).

the work at Rothamsted, the environment could be treated as independent for the simple reason that Fisher took it to be negligible. In making *no* contribution to variability, there was no need for Fisher to concern himself with how environmental variation might be causally related to the other sources of variation. But the research at Rothamsted forced Fisher to reconsider the environment as a possible source of variation. With the environment now on the list of possible sources of variation, Fisher had to also consider the relationship between environmental variation and heritable variation. He judged this possible complication in the second installment of his "Studies in Crop Variation" series, published with W. A. Mackenzie in 1923. He began by warning, "…if important differences exist in the manurial response of varieties a great complication is introduced into both variety and manurial tests; and the practical application of the results of past tests becomes attended with considerable hazard."[30] The possible difference in manurial response was the possible presence of genotype–environment interaction. "Only if such differences are non-existent, or quite unimportant," Fisher continued, "can variety tests conducted with a single manurial treatment give conclusive evidence as to the relative value of different varieties, or manurial tests conducted with a single variety give conclusive evidence as to the relative value of different manures."[31] Fisher, here, was making explicit the implications that genotype–environment interaction had on the evaluation of group differences: if genotype–environment interaction existed for a trait under investigation, then examining several varieties' values in just one environment ("a single manurial treatment") would not give conclusive evidence for the relative values of those different varieties in untested environments.

To test for this interaction, Fisher examined the manurial responses of 12 different potato varieties. A relatively small field (0.162 acres) had been first divided into two equal parts, one part receiving a farmyard manurial treatment while the other receiving no treatment. Each half was then itself divided into 36 plots, and each of the 12 potato varieties then planted in triplicate in a chessboard arrangement within each field. Finally, each individual plot was divided again, so that three rows of seven plants were set in each plot; one row received only the basal manuring of the series to which it belonged, while the other two rows received in addition either a dressing of sulfate of potash or a dressing of muriate of potash.

[30] Fisher and Mackenzie (1923, p. 311).

[31] Fisher and Mackenzie (1923, p. 311).

Table 1. Fisher's analysis of variation due to manuring, variety, deviations from summation formula, and variation between parallel plots

Variation due to	Degree of freedom	Sum of squares	Mean square	Standard deviation
Manuring	5	6,158	1231.6	35.09
Variety	11	2,843	258.5	16.07
Deviations from summation formula	55	981	17.84	4.22
Variation between parallel plots	141	1,758	12.47	3.53
Total	212	11,740	–	–

From Fisher and Mackenzie (1923, Table 3). Reproduced with the permission of Cambridge University Press.

With this experimental design, Fisher was able to use the data to undertake one of his very first applications of an analysis of variance, now a standard resource in any statistician's toolbox. He measured the weight of produce lifted from each of the rows, determining both the mean yield of each of the 12 varieties irrespective of the manuring applied, and the mean yield of each of the manurial treatments irrespective of the variety grown. What followed was, as Box has pointed out,[32] the first presentation of the familiar ANOVA table (Table 1).

The "Deviations from summation formula" category was the measure of the differences between the potato varieties in their manurial response – that is, the measure of interaction. In yet another innovative leap in this same article, Fisher noted that the deviations from the summation formula were not significantly greater than would occur by chance, leading him to conclude, "In the present material evidently the varieties show no difference in their reaction to different manurial conditions."[33] This comparison of a source of variation against chance was an early statistical test of significance, or what is now called an "*F*-test" in honor of Fisher's development of the method. Fisher evidently took the results of "Studies in Crop Variation, II" to be quite conclusive. Two years later, in his extremely influential *Statistical Methods for Research Workers*, Fisher again warned of the "interaction of causes" when he introduced the analysis of variance. However, he again used the potato variety-manurial response results from "Studies in Crop Variation, II" to introduce the possible complication and again came to the same conclusion: "There is no sign of differential response among the varieties…"[34]

[32] Box (1978, pp. 109–112).

[33] Fisher and Mackenzie (1923, p. 317).

[34] Fisher (1925, p. 209).

We are now in a position to reflect on Fisher's route to genotype–environment interaction. For Fisher, the concept of interaction was situated in his larger biometric program devoted to measuring the relative contributions of nature and nurture to variation in populations, a program initiated by Fisher's mentor and eventual rival, Pearson, the founder of biometry.[35] Fisher, operating in this biometric tradition, was focused on the causes of variation (i.e., the genotypic and environmental differences) responsible for variation in populations. He asked questions about how much of the variation in populations could be attributed to differences in genotype or differences in environment, and he then developed many of the now-standard statistical methodologies designed to answer these questions, such as ANOVA and the statistical test of significance. Non-additive interactions potentially posed a complication for Fisher's summing of variances. But this interaction was understood to be (and, in fact, was defined as) simply a statistical measure – a deviation from the summation formula – which would be detected by Fisher's methodologies if it existed. This notion will be called the *biometric* concept of genotype–environment interaction, or $G \times E_B$. It may be defined as *a statistical measure of the breakdown in additivity between genotypic and environmental sources of variation, which is generated by a statistical methodology such as the analysis of variance*.

We are also now in a position to take stock of the various components of the biometric tradition, in which Fisher was operating. The concept of a research tradition has been developed by Larry Laudan.[36] For Laudan, a particular research tradition is situated around a particular *problem*. Science, Laudan pointed out, was fundamentally a problem-solving activity, and so understanding a particular research tradition began with identifying the problem on which that tradition was focused. This problem then specified the metaphysical and methodological commitments of members of the research tradition; it established the appropriate entities and processes to investigate, the appropriate questions to ask about those entities and processes, and the appropriate methodologies to employ in seeking to answer those questions. A research tradition, Laudan explained, "is a set of general assumptions about the entities and processes in a domain of study, and about the appropriate methods to be used for investigating the problems and constructing the theories in that domain."[37] On Laudan's model, then, the concepts employed by members of a particular research

[35] Porter (2004).

[36] Laudan (1977).

[37] Laudan (1977, p. 81).

Table 2. The components of the biometric research tradition

Components	Biometric research tradition
Problem	Variation in populations
Approach to causation	Causes of variation
Causal question	How much?
Methodology	Statistical
Concept of interaction	Biometric – $G \times E_B$

tradition, the questions asked about those concepts by those members, and the methodologies employed by those members to answer those questions are all intimately related to each other and focused on the particular problem to which the research tradition is devoted.

Laudan's framework may be applied to the case of the biometric tradition. The main problem on which Fisher was focused was the partitioning of the *relative contributions of nature and nurture responsible for variation in populations*. His approach to causation involved an investigation into the *causes of variation*, or the genotypic and environmental differences, responsible for such variation. He asked, *how much* of the variation in a particular population was due to individual differences in heredity or environment? And he sought to answer those questions with his population-level, *statistical methodologies*. Fisher's route to genotype–environment interaction was in this biometric tradition, and his biometric concept of interaction – $G \times E_B$ – bore the marks of that history. The various components of the biometric tradition, now teased apart, are organized in Table 2.

Lancelot Hogben and the "Interdependence of Nature and Nurture"

In contrast to Fisher, whose name is known to any historian, philosopher, or sociologist of biology, Hogben has received much less attention from those in science studies (Figure 3). As a result, it will be useful to pause before examining Hogben's discussion of genotype–environment interaction and examine the man himself. His sarcasm, quick temper, and tendency to enter public disputes all combined to generate a scientist whose personality, like Fisher's, was just as large as his scientific pursuits. Moreover, those scientific pursuits were considered throughout much of the early 20th century to be on par with the contributions of contemporary biologists who are now considered more notable, such as Fisher, J. B. S. Haldane, and Julian Huxley. Influential geneticist C. D. Darlington, as just one instance, wrote of Hogben after his death,

Figure 3. Lancelot Thomas Hogben, Hogben papers, special collections, University of Birmingham Library. Reproduced with the permission of the University of Birmingham Library.

"When I was very young, Galdane, Guxley, and Gogben (as the Russians called them), seemed to be the three Magi."[38]

Lancelot Thomas Hogben (1895–1975) described his "larval existence" like that of many prominent biologists: obsessively collecting newts, beetles, and butterflies; identifying birds and recognizing them by their eggs; and exploring local geography. "I wanted to be a biologist long before I was 12," he recalled 60 years later.[39] Biology, however, was not what God had intended for Hogben…at least that was how his

[38] Darlington to Wells, 6 June 1976, Lancelot Hogben Papers (A.44), University of Birmingham Library.

[39] Hogben (1998, p. 2). Hogben wrote his autobiography, *Look Back with Laughter* (*LBL*), in the early 1970s. G. P. Wells (H. G. Wells' son) drew on much of this to write his biographical memoir of Hogben, as a Fellow of the Royal Society (Wells, 1978). Wells also edited Hogben's *LBL* with an eye towards publishing it in the late 1970s but could not succeed in the endeavor (Tabery, 2006). More recently, Hogben's son and his daughter-in-law have published a heavily edited version of *LBL*, under the title, *Lancelot Hogben*, *Scientific Humanist*: *An Unauthorized Autobiography* (Hogben, 1998). More limited biographies of Hogben can be found in Gurdon and Hopwood (2000), Kevles (1995), Mazumdar (1992), Sarkar (1996), Tabery (2006), and Werskey (1978). For the purposes of this essay, biographical references will be made to Hogben (1998); when material is to be cited that was edited out of Hogben (1998), references will be to Wells' edited version of *LBL* held at the University of Birmingham Library (listed as A.9 and A.10 of the Hogben Papers).

mother saw it. He was born 2 months prematurely, and to ensure that he would survive the ordeal, his mother dedicated him from birth to the mission field.[40] This religious devotion was no less powerful on the paternal side of his parenting. Thomas Hogben,[41] a self-employed Methodist preacher, spent his days ministering to seamen at the local port under a banner extolling the benefits and burdens of the Christian God: ''In the foreground was the lake of brimstone and fire. Across the middle was the edge of a cliff where stood the theatre, the brothel, the casino, the racecourse, the tavern, the *Palais de Danse* and other haunts of Satan. From the edge of the cliff the lost departed were falling in different stages of incandescence. Above the cliff was a solitary pilgrim pursuing a winding road to the rising sun; and, ironically, below it across the flames the legend: *God is Love*.''[42] Fortunately, the young Hogben and his parents were able to reach a compromise during these formative years; the field of medicine allotted the boy the time to study biology while also preparing himself for service as a medical missionary.[43]

Largely self-educated at the Stoke Newington Public Library, Hogben excelled academically and won a Major Entrance Scholarship to attend Trinity College Cambridge in 1913.[44] At Cambridge, Hogben cultivated his biological interests and replaced his parents' religious teaching with a devotion to socialism. He studied botany, physiology, and zoology (winning the Frank Smart Prize for the last in 1915), and also embryonic development at the Marine Biological Laboratory in Plymouth.[45] Hogben entered social life with an equal vigor. Assessing the social societies available to him at the time, Hogben recalled, ''I still regard the Union Debating Society of Cambridge (even more that of Oxford) as a potting shed for the cultivation of mentally retarded politicians. The most lively discussions at an intellectually high level were those which took place at the *Moral Sciences*, colloquially *Moral Stinks*, *Club*, where Bertrand Russell and [G. E.] Moore minced words with their philosophical competitors, in the Fabian Society and its study

[40] Hogben (1998, p. 1).

[41] Wells wrote a follow-up essay to his biographical memoir entitled, ''Father and Son'' (A.38), which detailed the Hogben family along with Thomas Hogben's influences on his son; however, Wells could not convince The Royal Society to publish the sequel (Wells, n.d.).

[42] Hogben (1998, p. 4).

[43] Hogben (1998, p. 13).

[44] Hogben (1998, pp. 24–25).

[45] Hogben (1998, pp. 40–41).

circles, and in the *Heretics* founded by C. K. Ogden of Basic English fame."[46] The Fabian Society at Cambridge was a particularly accommodating match for Hogben; he met his first wife, Enid Charles, there and eventually became its secretary, changing the Society's name to the University Socialist Society.[47]

At the outset of World War I, Hogben joined noncombatant Quaker relief organizations – first the War Victims contingent, which helped house French civilians rendered homeless by the combat, and then the Friends' Ambulance Unit.[48] When the British government introduced compulsory military service, though, in 1916, Hogben, a pacifist, protested this action as a conscientious objector and spent several months imprisoned in Wormwood Scrubs for the decision.[49] After the War, Hogben entered the academic life, teaching and leading research in London at Birkbeck and the Royal College of Science (1917–1922), in Edinburgh at the Animal Breeding Research Laboratory (1922–1925), in Montreal at McGill University (1925–1927), at the University of Cape Town (1927–1930), at the London School of Economics (1930–1937), at the University of Aberdeen (1937–1941), at the University of Birmingham (1942–1943), in London at the War Office (1944–1946), and finally at the University of Birmingham again where he retired (1947–1961).

In his early career at Birkbeck, Edinburgh, McGill, and Cape Town, Hogben was primarily devoted to experimental embryology and physiology. He worked on the mechanisms of amphibian metamorphosis with Julian Huxley and on the amphibian pigmentory effector system with Frank Winton.[50] The investigations were largely interventionist by nature; for example, he isolated the role of the pituitary in the pigmentory effector system by surgically going through the roofs of frogs' mouths and removing various portions of the gland, then noting the subsequent lack of pigmentation (see Figure 4). Hogben, while at Edinburgh and with the help of Haldane, Huxley, and Frank A. E. Crews, also founded the Society for Experimental Biology and its accompanying *British Journal of Experimental Biology*.[51]

It was Hogben's 7 years at the LSE, however, that produced his most lasting contributions to science and society. During these years he wrote

[46] Hogben (1998, p. 33).

[47] Hogben (1998, p. 51).

[48] Hogben (1998, pp. 48–49).

[49] Hogben (1998, Chapter 7).

[50] Hogben and Winton (1922a, b, 1923); Huxley and Hogben (1922).

[51] Crews et al. (1923); Erlingsson (2005); Hogben (1998, p. 79).

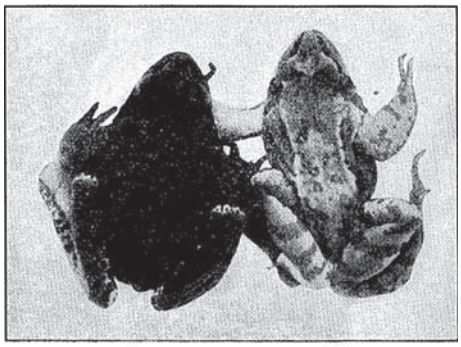

Figure 4. Two frogs, 19 days after pituitary operation by Hogben. (A) Partial removal of only anterior lobe. (B) Complete removal. From Hogben and Winton (1923, Figure 2). Reproduced with the permission of The Royal Society.

his first two, hugely successful, Primers for the Age of Plenty: *Mathematics for the Million* and *Science for the Citizen*.[52] He also attacked Britain's eugenics movement with a tenacity unmatched even by the standards of other anti-eugenicists of his day.[53] Sir (later Lord) William Beveridge, then the director of the LSE, sought to bridge the divide between the natural and the social sciences and so announced the search for a Chair of Social Biology in 1929, which would be funded by the Rockefeller Foundation.[54] Fisher applied for the position,[55] but it was Hogben who was ultimately invited to take the post. In his autobiography years later, Hogben recalled this vocational victory with glee, noting, "…the brass hats of the Eugenics Society were already congratulating themselves on the prospect of one of their co-religionists getting the job."[56] Hogben, however, only agreed to take the appointment after some reluctance, later explaining, "At that time human genetics was a morass of surmise and superstition. … Should I prosper in the Herculean task of cleaning the Augean stables of human heredity, I should be contributing to the overdue disposal of a manure heap of

[52] Hogben (1937, 1938).

[53] Hogben's role in the anti-eugenics response to the eugenics movement is discussed in Barkan (1991); Blacker (1952); Kevles (1995); Ludmerer (1972); Mazumdar (1992); Paul (1995, 1998); Soloway (1990); and Werskey (1978). Those historians that consider the origins of Hogben's attention to the role of environmental sources of variation (such as Werskey 1978; Mazumdar 1992) will be discussed below when that topic is addressed.

[54] Kevles (1995); Mazumdar (1992); Werskey (1978).

[55] Box (1978, p. 202).

[56] Hogben (1998, p. 121).

insanitary superstitions."[57] Ultimately, Hogben recalled, it would be one of his fellow-"Magi" that convinced him to take on the responsibility: "Conversation with J. B. S. Haldane jerked me out of indecision concerning my fitness for the task."[58] Hogben accepted the position and left Cape Town, joining the LSE in 1930.[59]

Cleaning the Augean Stables

Hogben's first full-fledged assault on the eugenics movement came with the publication of his *Genetic Principles in Medicine and Social Science*.[60] "This book does not undertake to set down all that is known and has been surmised about human inheritance," Hogben admitted. Instead, it was the first step in his Herculean task: "It is an attempt to separate the wheat from the tares, to indicate where a sound foundation of accredited data is available, to discuss what methods can be applied to the extremely elusive nature of the material with which the human geneticist deals, and to re-examine some of the biological concepts which have invaded other fields of inquiry in the light of modern advances in experimental genetics."[61] The underlying thread that guided the discussion was his persistent emphasis on the role that the environment played in the development of pathological, behavioral, and social traits. For instance, with respect to pathological traits, Hogben emphasized the importance of environmental agencies contributing to "deficiency diseases" such as rickets.[62] And when arrested social behavior in the case of Mongolism was discussed, Hogben drew attention to the effect of birth order and the uterine environment on the incidences of such a trait.[63]

The role of the environment was of such prominence in the pages of *Genetic Principles* because Hogben felt that biologists had generally learned to neglect it in response to theoretical developments of the previous century. More specifically, the death of Lamarckism, the discovery of cellular fertilization, and finally the rise of Weismann's theory

[57] Hogben (1998, p. 122).

[58] Hogben (1998, p. 122).

[59] A thorough discussion of Hogben's appointment at the LSE can be found in Mazumdar (1992, Chapter 4).

[60] Hogben (1932a). "Full-fledged" because Hogben had addressed critically the science of eugenics to a limited extent prior to *Genetic Principles* in earlier book chapters and lectures (see, for example, Hogben, 1927, 1931a, b).

[61] Hogben (1932a, p. 9).

[62] Hogben (1932a, p. 64).

[63] Hogben (1932a, pp. 99–103).

of the germ plasm ushered in a generation of biologists with no theoretical interest in the environment. Hogben, however, also noted that this tendency to ignore the environment was gradually eroding in the face of experimental biology, and especially experimental embryology:

> Weismann's teaching had a profound influence on the form which the hypothesis of natural selection assumed in the closing years of the nineteenth century. It has left a profound impress upon biological discussion of social evolution. During the present century the rise of experimental methods in the study of heredity and development has shown the immense importance of environment in determining individual variability among animals and plants. Strictly speaking, it is meaningless to speak of hereditary characters. Characters as such are the end-product of a prolonged and immensely complex series of reactions between the structural materials contributed by the sperm and the egg on the one hand, and all the characteristics of the physical medium which the cells descended from a given fertilised egg develop.[64]

In addition to describing the state of early-20th century biology, this quote also revealed Hogben's prescription for formulating the relationship between heredity and the environment. "Genetical science," Hogben claimed, "has outgrown the false antithesis between heredity and environment productive of so much futile controversy in the past."[65] Since every character is the end-product of an immensely complicated series of reactions between external agencies and the hereditary material, "Differences can be described as determined predominantly by hereditary or predominantly by environmental agencies if, and only if, the conditions of development are specified."[66] To drive this point home, Hogben pointed out that variation in a population could arise from hereditary variation (emphasized by eugenicists), environmental variation (emphasized by anti-eugenicists), and an often-ignored *third class of variability*: that which "arises from the combination of a particular hereditary constitution with a particular kind of environment."[67] It will be especially important to keep this conception of the relationship between heredity, environment, and development in mind when Hogben employed this relationship to criticize Fisher the following year.

[64] Hogben (1932a, p. 40).
[65] Hogben (1932a, p. 201).
[66] Hogben (1932a, p. 98).
[67] Hogben (1932a, p. 98).

But in 1932, Hogben had not yet criticized Fisher, and in his review of *Genetic Principles* Fisher welcomed Hogben's position at the LSE, despite the fact that his application was turned down in favor of Hogben's.[68] Fisher began, "[Hogben's] recent appointment as Professor of Social Biology at the London School of Economics gave the welcome assurance that his keenly analytic brain, and training in a severe experimental discipline, would be put to important service in the study of the biology of man. The rapid appearance of his new book, 'Genetic Principles in Medicine and Social Science,' will therefore be received with more than ordinary interest by all those who recognize the need, in this field, of whole-time workers with an adequate biological training."[69] Fisher was especially impressed by Hogben's assimilation of the most recent work in the field and in his "strong taste for analytic precision of statement."[70] However, Fisher also worried that this attention to "purely academic considerations" led to an exclusion of "aspects of more practical importance."[71] "Throughout the book," Fisher complained, "those who consider that the practical importance of the problem renders it urgent, will receive a disturbing impression that they are being asked to wait, in solemn hush, outside the laboratory door, until the Professor sees fit to announce that the ultimate truth has at last been revealed."[72]

Fisher also took issue with Hogben's discussion of the environment. With regard to Hogben's account of the source of some biologists' neglect for the role of the environment, Fisher called it a "historical misapprehension" to suggest that Galton and Weismann's rejection of the Lamarckian inheritance of acquired characters "led to a neglect of the somatic importance of such modifications."[73] In contrast to Hogben's claim that Galton and Weismann's influence led to conceiving of all differences between parents and offspring as genetic, "It would be truer to say that this was so while the influence of the Lamarckian doctrine persisted, for it was the distinctive dogma of this doctrine that such differences, even if environmentally induced, were inherited. Only when Lamarckism had been overthrown could the problem of the relative importance of the congenital and the induced differences be

[68] Fisher (1932). For other prominent reviews of Hogben (1932a) by his contemporaries, see Huxley (1932) and Haldane (1932).

[69] Fisher (1932, p. 147).

[70] Fisher (1932, p. 147).

[71] Fisher (1932, p. 147).

[72] Fisher (1932, pp. 147–148).

[73] Fisher (1932, p. 149).

clearly formulated."[74] And when Hogben summarized the connection between mental defect, scholastic success, and birth order by writing, "This connection leaves little doubt that environmental influences play a very significant rôle in determining the manifestation of mental defect,"[75] Fisher concluded, "We can only hope that when Professor Hogben has had sufficient leisure to produce the authoritative work, which we may later hope for, that he will think it better to omit, or radically to rewrite, his discussion of this type of material."[76]

The William Withering Memorial Lectures

That same year (1932), the Medical Faculty of the University of Birmingham invited Hogben to deliver their William Withering[77] Memorial Lectures, and Hogben chose medical genetics as the theme of his Lectures.[78] Hogben, in preparation for the Lectures, contacted Fisher in February of 1933 on a point of clarification:

> Dear Fisher, I am at present engaged in preparing a course of lectures in which I shall be dealing with your own contributions to the genetic theory of correlation. There is one point in your 1918 paper which worries me very much. When you speak of the contribution of hereditable and nonhereditable causes of variance in a population, what exactly do you mean? I often use the same form of words myself and lately I have been searching for a more explicit formulation of the problem. Suppose you say that 90 per cent of the observed variance is due to heredity, do you mean that the variance would only be reduced 10 per cent, if the environment were uniform? Do you mean that the variance would be reduced by 90 per cent, if all genetic differences were eliminated? Perhaps you will think the question silly; but if you could suggest an alternative form of words, it might help.[79]

[74] Fisher (1932, p. 149).

[75] Hogben (1932a, p. 106).

[76] Fisher (1932, p. 150).

[77] William Withering (1741–1799) was a botanist and physician (discovering the medical implications of foxglove's active ingredient – digitalis), a member of the Lunar Society, and a chief physician at the Birmingham General Hospital (Aronson, 1985).

[78] Hogben (1998, p. 123).

[79] Hogben to Fisher, 17 February 1933, R. A. Fisher Papers (available on-line at http://www.library.adelaide.edu.au/digitised/fisher/). Quoted with the permission of Leslie Hogben.

Fisher responded the following day:

> Dear Hogben, Your question is a very sound one. The point is this:-If the differential effects of environment and heredity are not correlated, i.e. if each genotype has an equal chance of experiencing with their proper probabilities, each of the available kinds of environment, then the variance is additive, and the statements you have are equivalent. If they are not independent, then the *practical* choice of a form of statement will depend upon what the correlation is due to.[80]

Fisher took Hogben's question to be one concerning genotype–environment *correlation*, and so answered Hogben's question with a discussion of a genotype's "chance of experiencing" a particular environment. The concept of genotype–environment correlation refers to cases where an individual's genotype correlates with exposure to particular environments. Genotype–environment correlation, however, was not Hogben's target, and he took several days to construct a lengthy rebuttal. "Dear Fisher, I don't think you quite got the difficulty which I am trying to raise. It concerns an inherent relativity in the concepts of nature and nurture…"[81] Hogben then introduced an example to clarify his concern.

> Let me take an example which is particularly pregnant because the character can be defined either as an all or none reaction or in metrical terms. I refer to the bar eye series in Drosophila. From Krafka's data you will see the following values for facet number are given at 15° and 25°C.[82]

	Low bar	Ultra bar
15°C	189	52
25°C	74	25

> Consider the elementary population with the following structure. The genotypes are Low bar and ultra bar in equal numbers, equally distributed between two environments, namely an incubator at

[80] Fisher to Hogben, 18 February 1933, R. A. Fisher Papers (available on-line at http://www.library.adelaide.edu.au/digitised/fisher/). Quoted with the permission of the University of Adelaide Library.

[81] Hogben to Fisher, 23 February 1933, R. A. Fisher Papers (Series I, Hogben, L.), University of Adelaide. Quoted with the permission of Leslie Hogben.

[82] Krafka (1920).

> 15°C and one at 25°C. There is zero correlation between the distribution of environmental and genetic variables. Yet I cannot agree that the two statements "*y* per cent of the variance is due to environment," and "the variance would be reduced by *y* per cent if all differences of environment were eliminated," are equivalent nor that there is equivalence between the two statements "*x* per cent of the variance is due to heredity" and "the variance would be reduced by *x* per cent if there were no genetic differences."

Hogben then pointed out that the result was a "lack of singularity."

> The fact is that there is a lack of singularity in the problem when it is reduced to practical form, as can be seen in arithmetical form in this instance. In the population defined the mean is 85 and the variance is 3906 to the nearest integer. Let us abolish all differences of environment. We can do this in an infinite number of ways. One would be to culture all flies at 15°C. Result: mean 120.5 and variance 4692. Another is to culture them all at 25°C. Result mean 49.5 and variance 600. Which of these two variances has priority as an estimate of the "contribution" of environment to the observed variance in the fourfold population? Again we eliminate all genetic differences by killing off all ultra bar flies. Result: mean 131.5 and variance 3306. We could alternatively kill off all low bar flies. Result: mean 38.5 and variance 182. Which of these gives the contribution of heredity to the observed variance?

Hogben shoved aside the matter of genotype–environment correlation here: "There is zero correlation between the distribution of environmental and genetic variables." Instead, he focused on the "lack of singularity" which resulted from a variable response of two genotypes to an array of environments. He closed by reemphasizing his lack of interest in genotype–environment correlation and explaining the motivation behind his interest in the "lack of singularity" problem, concluding, "The point I am after is not what assumptions about the distribution of the environment and the distribution of gene differences are made in the mathematical formulation of the problem. Obviously we can make more or less arbitrary assumptions about that. *What I am worried about is a more intimate sense in which differences of genetic constitution are related to the external situation in the process of development*."[83]

Hogben's letter on February 23rd marked the dawn of genotype–environment interactions being utilized as a critical tool to attack

[83] Emphasis added.

the summing of heritable and non-heritable sources of variance.[84] The bar-eye *Drosophila* example also became the empirical backbone of Hogben's last William Withering Memorial Lecture, entitled "The Interdependence of Nature and Nurture" in the published form of these Lectures, and entitled "The Limits of Applicability of Correlation Technique in Human Genetics," published in the *Journal of Genetics* that same year.[85] It was, in short, an all-out attack on Fisher. Fisher's (1918) was noteworthy for human genetics, Hogben claimed, both because of the "thoroughness with which he assailed the mathematical intricacies of a purely genetical theory of correlation" and also because of the "particular conclusions about nature and nurture advanced in his memoir."[86]

Because of the centrality that correlation coefficients played in Fisher's (1918), Hogben devoted his essay to critically assessing the correlation technique. Hogben admitted that the technique of correlation could be "used to detect the existence of differences due to environment and differences due to heredity."[87] Based on correlation coefficients from monozygotic and dizygotic twins, Hogben even conceded that "Few biologists would hesitate to draw the conclusion that intellectual differences may arise because of gene differences."[88] However, moving beyond the detection of such differences, "The difficulties of interpretation begin when we attempt to clarify what is meant by calculating 'the numerical influence…of the total genetic and non-genetic causes of variability.'"[89] Hogben drew on his Cambridge, philosophical hero to make this point: "In his illuminating essay on the *Notion of Cause* Bertrand Russell has pointed out that few words are used with greater ambiguity in scientific discussion."[90] What Hogben

[84] Fisher responded to this letter, and it will be introduced and discussed below. At the moment, however, it will be useful to pause and examine Hogben's position in some detail.

[85] Hogben (1933a, b). Hogben's *Nature and Nurture* (1933a) is much more often cited than his *Journal of Genetics* paper (1933b), so references will be made to his 1933a. However, although the essays are extremely similar, the version that appeared in the *Journal of Genetics* did go into slightly more detail at important points. I will say explicitly when references are being made to those portions uncontained in *Nature and Nurture*.

[86] Hogben (1933a, p. 92).

[87] Hogben (1933a, p. 93).

[88] Hogben (1933a, p. 93).

[89] Hogben (1933a, pp. 94–95).

[90] Hogben (1933a, p. 95). This was not the first time Hogben revealed his philosophical indebtedness to Russell. Hogben's *The Nature of Living Matter* (1931a), a mechanistic critique of vitalism, was dedicated to Russell.

had in mind here was an extension of the critique of Galton and biometry he first made in his *Genetic Principles*. "The biometrical treatment of variability," Hogben argued, "inherited from Galton a tradition of discourse in which the ambiguity of the concept of causation completely obscured the basic relativity of nature and nurture. Since then this relativity has become increasingly recognized through experiments involving the use of inbred stocks in physiological laboratories, especially in connexion with experimental work on diet. It is therefore necessary to examine with great care what we mean when we make measurements of a genetic difference and a difference due to environment."[91]

To drive home this point, Hogben introduced to his reader the same case he introduced to Fisher in correspondence earlier that year, providing both the data and, this time, a reaction norm graph of the differential responses of low-bar and ultra-bar *Drosophila* strains to a variable environment (see Figure 5). The differences between points A and B ($_{16}\delta_H$),[92] and between points E and F ($_{25}\delta_H$) corresponded to what Hogben claimed experimental biologists meant by a genetic difference. Meanwhile, the differences between points B and C ($_B\delta_E$), and between points D and E ($_A\delta_E$) corresponded to what Hogben claimed experimental biologists meant by a difference due to environment. Hogben assessed, "Clearly we are on safe ground when we speak of a genetic difference between two groups measured in one and the same environment or in speaking of a difference due to environment when identical stocks are measured under different conditions of development." But then he continued, questioning, "Are we on equally safe ground when we speak of the contribution of heredity and environment to the measurements of genetically different individuals or groups measured in different kinds of environment?"[93] Hogben asked his reader to consider a low-bar stock kept at 16°C and an ultra-bar stock kept at 25°C, creating the observed differences AC or DF. "How much of AC or DF is due to heredity and how much to environment? The question is easily seen to be devoid of a definite meaning."[94] He then drew for his reader the same conclusion he drew from this data when he wrote to Fisher previously:

[91] Hogben (1933a, p. 95).

[92] Krafka (1920) took measurements at a number of different temperatures including both 15 and 16°C. As a result, it is not necessarily a typographical error that Hogben used 16°C. here but used 15°C. in his correspondence with Fisher.

[93] Hogben (1933a, p. 97).

[94] Hogben (1933a, p. 97).

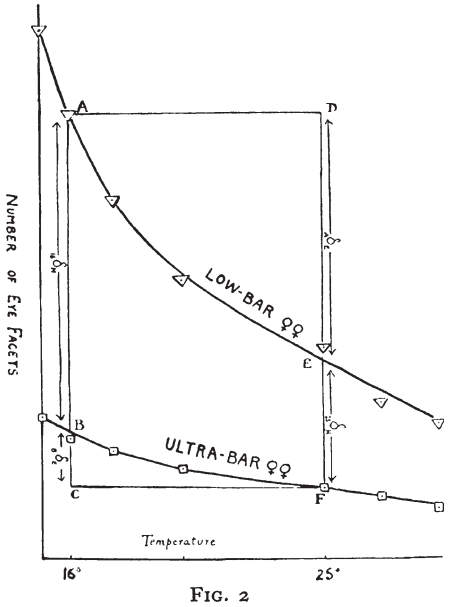

FIG. 2

Figure 5. Hogben's norms of reaction for number of eye facets (*y*-axis) for low-bar and ultra-bar *Drosophila* strains raised at different temperatures (*x*-axis), derived from Krafka (1920). Figure from Hogben (1933a, Figure 2). Reproduced with the permission of Taylor & Francis Books.

> We might be tempted to say that the genetic contribution is the difference which would exist if both stocks had been cultured at the same temperature. This could be done in an infinite number of ways. If they were both cultured at 16°C. heredity would contribute the difference AB. We might be tempted to say that the contribution of environment represents what the difference would be if all the flies belonged to the same stock. Obviously this can be done in at least two ways. Keeping the same difference of environment we might substitute low-bar individuals for the ultra-bar stock at 25°C. The difference between the two sections of the population would then be represented by DE. If we substituted ultra-bar individuals for the low-bar stock at 16°C. the difference would be BC. Either ED or BC is equally entitled to be regarded as the contribution of environment.[95]

Hogben importantly emphasized, "The literature of experimental physiology is not wanting in examples of such divergent curves representing

[95] Hogben (1933a, p. 97).

the measurement of a character and the strength of the environment.''[96] He drew on the research of Norman B. Taylor[97], and Frank R. Winton,[98] his former colleague and co-author from Edinburgh, who respectively examined variation in the sinus beat of *Xenopus* and *Rana* with regards to temperature, and variation in the mortality rate of rats with regards to red squills.[99]

Hogben also explicated the *practical* implications of this variable response by different genotypes to environmental differences. ''The only practical significance which Fisher's analysis of variance seems to admit is that, if it were correct, we could only reduce variance with respect to stature in a human population by 5% or less if the environment were perfectly uniform.''[100] As Hogben pointed out above, though, creating such a uniformity can be done in an infinite number of ways, ''some tending to bring out genetic differences which were not previously measurable, others tending to obscure genetic differences which were measurable before.''[101] Hogben called the calculation devised by Fisher to add up all the sources of variance a ''balance sheet of nature and nurture.'' And he asked, ''Has a balance sheet of nature and nurture any meaning in this sense, unless we assume that the variance of a population, if affected at all, is necessarily diminished when the environment is made more homogenous?''[102] But as he wrote to Fisher before, and as he would repeat in published form, ''Such an assumption is certainly false.'' (ibid) With regard to Krafka's two *Drosophila* populations (low-bar and ultra-bar) exposed equally to the two environments (15 and 25°C), the variance was 3906.5. Creating environmental uniformity by confining both stocks solely to 15°C would *increase* the variance to 4692.25. But creating environmental uniformity by confining both stocks solely to 25°C would *decrease* the variance to 600.25. Hogben asked his reader the same question he asked Fisher: ''Have either of these estimates any special priority as a measure of the contribution of

[96] Hogben (1933a, p. 97).

[97] Taylor (1931).

[98] Winton (1927).

[99] Hogben (1933b, p. 385). These references are not included in the version of this essay which appears in the William Withering Lectures published as *Nature and Nurture* (1933a). There, Hogben only wrote, ''There is no reason to multiply instances in order to show the need for extreme care in formulating the problem of nature and nurture in quantitative terms.'' (Hogben, 1933a, p. 97).

[100] Hogben (1933a, p. 114).

[101] Hogben (1933a, p. 114).

[102] Hogben (1933a, p. 114).

heredity alone to the observed variance?"[103] Likewise, genetic uniformity could be created by substituting low-bar stock for the ultra-bar individuals, generating a variance of 3306.25. Or, genetic uniformity could be created by substituting ultra-bar stock for the low-bar individuals, generating a variance of 182.25. Again, "Which of these two estimates gives the contribution of environment alone?"[104] Hogben concluded:

> In whatever sense Fisher himself intended his balance sheet to be interpreted, there is no doubt that many writers on human biology entertain the belief that biometrical estimates of this kind do entitle us to set such limits. On the basis of such statements as the previous quotation about stature, it is often argued that the results of legislation directed to a more equitable distribution of medical care must be small, and that in consequence we must look to selection for any noteworthy improvement in a population. This is rather like saying that the difference between black and white is negligible because an inkpot thrown into a tank of china clay has very little effect on the latter.[105]

We can only assume that Fisher felt little gratitude when Hogben concluded his *Journal of Genetics* essay by writing, "It is a great pleasure to acknowledge the courtesy with which Dr. Fisher has replied to communications in which some of the issues raised in this discussion have been explored."[106]

From Development to Interaction – the Origin of $G \times E_D$

We have already seen how Fisher came to consider the question of genotype–environment interaction. In developing the analysis of variance, Fisher recognized quite early on that such non-linear interactions would create complications for assessments of the relative contributions of heritable and non-heritable sources of variation.[107] However, in his own empirical research on potato varieties, Fisher found no such interaction.

But how did Hogben come to consider genotype–environment interactions? It was apparently *not* through a familiarity with Fisher's

[103] Hogben (1933a, p. 116).
[104] Hogben (1933a, p. 116).
[105] Hogben (1933a, pp. 116–117).
[106] Hogben (1933b, p. 405).
[107] Fisher and Mackenzie (1923).

own research on the topic. Hogben never mentioned Fisher's "Studies in Crop Variation, II" or his discussion of the topic in *Statistical Methods for Research Workers*. More tellingly, Hogben first introduced the problem to Fisher in correspondence as if it was an issue with which Fisher might have no concern, admitting, "Perhaps you will think the question silly."

Historians who have considered Hogben's criticisms of the eugenicists have tended to explain Hogben's attention to environmental sources of variation by appeal to political motivations. Gary Werskey and Mazumdar both pointed to the influence of the Second International Congress on the History of Science, held in 1931 in London, on Hogben and other left-wing British scientists of the day, such as Haldane, Joseph Needham, Hyman Levy, and J. D. Bernal.[108] At this conference, a Soviet delegation led by Nikolai Bukharin introduced Marxism to the British scientific community. Mazumdar explained, "Hogben's thinking on the problems of social biology did not take a completely new direction following his contact with Marxism, but the Marxist analysis both sharpened his perception of the class-bound nature of the eugenic program, and also provided a theoretical support for his campaign against the over-emphasis of the biological in human society."[109] And Werskey wrote, "Rather than completely sacrifice his outside political interests to the demands of scientific life, he consciously brought his politics to bear on the kind of science he did. As a feminist who was also an experimental biologist, Hogben was drawn in the early twenties to the new field of comparative endocrinology, in order to study the hormonal bases of sex differences. As a socialist, he likewise found himself attracted to the social biology of class and racial differences."[110]

However, while such political analyses may help to explain Hogben's *motivations* for attacking the eugenics movement, they do little to explain the actual *tools* of the attack itself. This point should not be taken as a criticism of these histories; Mazumdar fully admitted, "Marxism helped Hogben to define his problem, but it did not provide him with the tools with which to solve it."[111] Rather, the point is that a closer analysis of Hogben's actual criticisms requires more than an appeal to his political motivations. For Mazumdar, that closer analysis came from assessing the influence of German mathematical genetics

[108] Werskey (1978); Mazumdar (1992).

[109] Mazumdar (1992, p. 161).

[110] Werskey (1978, p. 105).

[111] Mazumdar (1992, p. 161).

(*Vererbungsmathematik*) on Hogben's subsequent research. A familiarity with the work of Wilhelm Weinberg, Fritz Lenz, and Felix Bernstein, Mazumdar revealed, led Hogben to introduce to the English-speaking world new mathematical techniques for analyzing pedigree data. Hogben, in 1931 and 1932, published in the *Journal of Genetics* a series of papers on "The Genetic Analysis of Family Traits" applying the *Vererbungsmathematik* approach to pedigree analyses of traits caused by single gene substitutions, double gene substitutions, and single recessive genes.[112]

But Hogben's discussion of genotype–environment interaction was quite distinct from his discussion of pedigree analyses; the latter was a tool used to reform a methodology employed by eugenicists, while the former was a tool used to critically attack eugenic interpretations of variance analyses. As a result, a familiarity with German mathematical genetics will not suffice to explain the origins of Hogben's consideration of genotype–environment interaction. Fortunately, Hogben left us a revealing clue in the last line he wrote to Fisher: "What I am worried about is a more intimate sense in which differences of genetic constitution are related to the external situation in the process of development." Hogben, here, explained quite clearly what motivated his interest in genotype–environment interaction – an appreciation for the developmental relationship between genotype and environment, and the variation that resulted from that relationship.

Considering the developmental relationship between the genotype and the environment was nothing new for Hogben in 1933. We saw above that his earlier *Genetic Principles* was filled with warnings against only construing phenotypic variation as either a product of genetic differences or of environmental differences. There, Hogben criticized the "false antithesis of heredity and environment."[113] He admitted that some hereditary variability would exist in almost any environment; and, likewise, some variability would be brought about by the environment acting on the same genetic material. However, Hogben also drew attention to a *third class of variability*, which "arises from the combination of a particular hereditary constitution with a particular kind of environment."[114] In 1932, when *Genetic Principles* was published, the only empirical example Hogben gave of this third class of variability came from the "abnormal abdomen" sport of *Drosophila*. If cultured in a dry medium, this sport was indistinguishable from the normal form.

[112] Hogben (1931c, 1932b, c); Mazumdar (1992, pp. 162–169).

[113] Hogben (1932a, p. 201).

[114] Hogben (1932a, p. 98).

However, if cultured in a humid environment, the segmentation of the abdomen was grossly deformed. ''In a culture which progressively dries up,'' Hogben explained, ''a decreasing number of flies manifesting the character appears. The flies which emerge last when the culture is drying up are not different from the wild type, so that in crosses conducted in the usual way any numerical results may be obtained.''[115]

The abnormal abdomen *Drosophila* example provides another important clue in constructing Hogben's path to genotype–environment interaction, acting as something of a bridge between his discussions in 1932 and in 1933. In 1932, Hogben recognized a third class of variability resulting from the combination of a particular genetic constitution with a particular environment; the abnormal abdomen example acted to verify the existence of this class of variability. A year later, in 1933, when Hogben explicated the ''interdependence'' of nature and nurture for his audience at the William Withering Lectures, the abnormal abdomen example joined Krafka's bar-eye example as the two cases revealing the practical limitations of Fisher's analysis of variance. With regard to the practical significance, remember that Hogben claimed, ''A balance sheet of nature and nurture has no meaning in this sense, unless we assume that the variance of a population, if affected at all, is necessarily diminished when the environment is made more homogenous.''[116] Hogben then utilized the abnormal abdomen example as one case showing why ''Such an assumption is certainly false.''[117]

> Imagine a large laboratory with many bottles of culture media, some dry and some moist, providing food for a mixed stock of fruit-flies, a small proportion of which belong to the mutant strain with the gene for vestigial abdomen. Keeping the stock the same, we might make the environment more homogenous in one of two ways, either making all the bottles dry or all the bottles moist. If we make all the bottles dry, the mutant gene will be incapable of manifesting its presence. Variability will be diminished with respect to the difference under consideration. If we make all the bottles moist, a larger proportion of larvae with the mutant gene will hatch out as flies with the mutant deformity. That is to say there will be an increase in variability.[118]

[115] Hogben (1932a, p. 98).
[116] Hogben (1933b, p. 399).
[117] Hogben (1933a, p. 114).
[118] Hogben (1933a, p. 115).

The crucial limitation of the abnormal abdomen example, though, was that it lacked *quantitative* data concerning the phenotype. As a result, Hogben continued, "There will be even less room for misunderstanding if we examine a metrical situation concerning which we have definite experimental knowledge."[119] With that, Hogben introduced Krafka's bar-eye data, displaying genotype–environment interaction quantitatively.

So, for Hogben, attention to individual development actually led him to recognize genotype–environment interaction as a unique, *third* source of variation in a population. He began in *Genetic Principles* by differentiating three different classes of variability: genetic, environmental, and that which "arises from the combination of a particular hereditary constitution with a particular kind of environment."[120] For Hogben, this last source of variation was fundamentally a developmental source of variation, resulting from differences in unique, developmental combinations of genotype and environment. In 1932, Hogben had only a qualitative example to drive this point home; the abnormal abdomen *Drosophila* strain developed quite differently in environments of different humidities in comparison to the wild type's development in these environments. When Hogben came to consider Fisher's summing of variances in 1933, though, he needed quantitative data, and he received that from Krafka. Krafka's investigation of the effect of temperature on *Drosophila* development generated quantitative data revealing that "the number of facets is determined by a specific germinal constitution plus a specific environment,"[121] Hogben's third class of variation. Hogben then used Krafka's data to calculate the variances for the different bar-eye stocks at the different temperatures, displaying the fact that the population variance would increase or decrease depending on which environmental temperature was chosen.

Hogben was operating in the developmental tradition of biology. Since the field of genetics first took shape in the early 20th century, biologists such as Hogben, I. I. Schmalhausen, and Conrad Hal Waddington have focused on unraveling the way in which variation in a population arose from the relationship between genotype and environment during *individual development*.[122] Hogben's focus was on the *causal mechanisms* of individual development. He asked, *how* do differences in genotype and differences in environment relate during

[119] Hogben (1933a, p. 115).
[120] Hogben (1932a, p. 98).
[121] Krafka (1920, p. 419).
[122] Schmalhausen (1949); Waddington (1957).

Table 3. The components of the developmental research tradition

Components	Developmental research tradition
Problem	Individual development
Approach to causation	Causal mechanisms
Causal question	How?
Methodology	Interventionist
Concept of interaction	Developmental – $G \times E_D$

individual development to generate differences in phenotype? And he employed or sought out *interventionist methodologies*, such as those undertaken by Krafka, to manipulate these variables and monitor the phenotypic outcomes. Hogben's route to genotype–environment interaction was in this developmental tradition, and the concept of interaction that he introduced bore the marks of that history. Hogben introduced what will be called the *developmental* concept of genotype–environment interaction, or $G \times E_D$. It was his "third class of variability," and it may be defined as *variation that results from differences in unique, developmental combinations of genotype and environment*. The various components of the developmental tradition, now teased apart, are organized in Table 3.

Fisher versus Hogben: On the Importance of Genotype–Environment Interaction

Fisher responded to Hogben's letter discussing the Krafka data 2 days later.

> Dear Hogben, I think I see your point now. You are on the question of non-linear interaction of environment and heredity. The analysis of variance and covariance is only a quadratic analysis and as such only considers additive effects. Academically one could proceed in theory, though in a theory not yet developed, to corresponding analyses of the third and higher degrees. Practically it would be very difficult to find a case for which this would be of the least use, as exceptional types of interaction are best treated on their merits, and many become additive or so nearly so as to cause no trouble when you choose a more appropriate metric. Thus facet number shows its sweet reasonableness when measured in 'proportional units' or in other words on a logarithmic scale. However perhaps the main point is that you are under no obligation to analyse variance into parts if it does not come apart easily, and its

> unwillingness to do so naturally indicates that one's line of approach is not very fruitful.[123]

Fisher's appraisal of genotype–environment interaction here, along with Hogben's disregard for this appraisal in his William Withering Lectures, reveals much about their divergent views on the importance of genotype–environment interaction. Fisher understood Hogben now to be worrying about the "non-linear interaction of environment and heredity." Fisher, of course, was familiar with the problem, having taken up "Studies in Crop Variation, II" with the sole purpose of testing for such an interaction. With the conclusions of that study in mind, notice how Fisher responded to Hogben: Hogben's concern was written off as "academic," while "Practically it would be very difficult to find a case for which this would be of the least use, as exceptional types of interaction are best treated on their merits…" So while Fisher did acknowledge that "you are under no obligation to analyze variance into parts if it does not come apart easily," his investigation at Rothamsted led him to believe that cases where the variance did not come apart were quite "exceptional." Notice also that Fisher's response bears a striking resemblance to his review of *Genetic Principles* discussed above, where he worried that Hogben's attention to "purely academic considerations" led to an exclusion of "aspects of more practical importance."[124] Fisher explained that the exceptional cases of genotype–environment interaction, such as Hogben's example, could be eliminated by choosing a different scale for measuring the variables (such as a logarithmic scale for the Krafka data).

However, Fisher's *pre*-William Withering congeniality towards Hogben in this correspondence can be contrasted with a letter he wrote to J. A. Fraser Roberts 2 years later, *after* Hogben placed so much emphasis on genotype–environment interactions in his publications. While Fisher was willing to acknowledge to Hogben the limits of analyzing variance into parts "if it does not come apart easily," he wrote to Fraser Roberts on January 18th, 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."[125] Fisher, here, surmised

[123] Fisher to Hogben, 25 February, 1933, R. A. Fisher Papers (Series I, Hogben, L.), University of Adelaide. Quoted with the permission of the University of Adelaide Library.

[124] Fisher (1932, p. 147).

[125] Fisher to Roberts, 18 January 1935, quoted in Bennett, 1983, p. 260.

the weight he placed on genotype–environment interactions much more explicitly: they were of ''possible, but unproved, importance.'' ''Possible'' because, as Fisher recognized in ''Studies in Crop Variation, II,'' the non-linear interactions would complicate the summation of variances. But also ''unproved'' because in ''Studies in Crop Variation, II'' Fisher found no such non-linear interactions. The matter of significance was an open empirical question, and Fisher placed the burden of proof on the ''environmentalists'' seeking such non-linear interactions.

Hogben, not surprisingly, came to quite a different conclusion. Krafka's research was a clear example, and Hogben took full advantage of its implications in the William Withering Lectures and the subsequent publications. Moreover, Hogben felt comfortable claiming that the reaction norm graphs revealing such genotype–environment interaction were standard; remember that he followed the discussion of the bar-eye data with the line, ''The literature of experimental physiology is not wanting in examples of such divergent curves representing the measurement of a character and the strength of the environment.''[126] As evidence, Hogben offered the work of Taylor and Winton.[127]

With limited empirical evidence, Hogben and Fisher were free to attach quite distinct levels of importance to the empirical evidence then accumulated, leading to quite distinct conclusions concerning the importance of genotype–environment interaction. Assessing the importance of limited empirical evidence can involve any number of motivations; and, as a result, Hogben and Fisher's distinct conclusions cannot be pinned to any one motivation. Politically, Hogben's socialism naturally inclined him to favor empirical evidence supporting arguments that might justify the equalization of the environment; while Fisher's disdain for the ''communists and fellow-travelers'' who attacked eugenics, encouraged him to be warier of such evidence and arguments.[128] Turning to eugenics more directly, Hogben and Fisher's opposing perspectives on the British eugenics movement also was a potential factor affecting their respective judgments. Hogben, not surprisingly, welcomed empirical evidence complicating the statistical methodologies of eugenicists, while Fisher, not surprisingly, was critical of such evidence, especially since the methodologies were his own.

But the historical survey of Hogben and Fisher's distinct paths to genotype–environment interaction, traced out in Sections 2 and 3, also revealed an *epistemological* motivation in play, pertaining to how

[126] Hogben (1933a, p. 97).

[127] Hogben (1933b); Taylor (1931); Winton (1927).

[128] Quoted in Mazumdar (1992, p. 211).

the concept of genotype–environment interaction figured into their respective research traditions. Fisher introduced a number of statistical innovations while at Rothamsted as part of his persistent attempts to develop methods for assessing the relative importance of heredity and the environment, the main problem of the biometric tradition. Fisher, focused on the biometric "relative importance" problem, did not take genotype–environment interactions as something to be sought and studied, as if they were something of intrinsic interest. $G \times E_B$ created a potential complication for assessing the relative importance of heredity and the environment, and so it was to be considered and then either dismissed (as with the case in "Studies in Crop Variation, II") or eliminated with a transformation of scale (as with the Krafka data).

Hogben, in contrast, took genotype–environment interactions to be the product of his third class of variability: that resulting from the combination of a particular genetic constitution with a particular kind of environment during the process of development. This third class of variability was, for Hogben, essentially developmental in nature and to be investigated with the tools of the developmental tradition – experimental embryology (as was the case with both the "abnormal abdomen" and bar-eye *Drosophila* studies). Just as experimental embryology was a distinct discipline with its own inherently important results, so too was genotype–environment interaction inherently important. And as experimental embryology continued to grow, Hogben predicted, so too would empirical examples of $G \times E_D$.

The epistemological divide between Fisher and Hogben's concepts can be seen most clearly when their separate research traditions are placed side-by-side, as can be found in Table 4.

Whatever the opposing motivations (political, social, and/or epistemological), the exchange between Fisher and Hogben evidently took its toll on their relationship. In 1932, when reviewing Hogben's *Genetic Principles*, Fisher welcomed Hogben's appointment to the Chair of Social Biology at the LSE. But in an unpublished draft of a review of Hogben's *Nature and Nurture*, Fisher began:

Table 4. The components of the biometric and developmental research traditions

Components	Biometric tradition	Developmental tradition
Problem	Variation in populations	Individual development
Approach to causation	Causes of variation	Causal mechanisms
Causal question	How much?	How?
Methodology	Statistical	Interventionist
Concept of interaction	Biometric – $G \times E_B$	Developmental – $G \times E_D$

> Many of those, who had hopes that the establishment of a Chair of Social Biology at the London School of Economics would lead to a scientific and unbaissed [sic] attack on the social problems in this field, must by now be realising, in various degrees, their disappointment. For the functions of an advocate and of an investigator seem to be incompatible; and though one may be always amused and sometimes stimulated to thought when a brilliant journalist, such as Mr. G. K. Chesterton, sets out to show what a good forensic case can be made in opposition to the weight of scientific evidence and opinion, Professor Hogben lacks the charm of style needed to make confusion of thought seem luminous, or his facetiousness seem penetrating.[129]

Fisher's disdain for Hogben was by no means confined to the years of their debate. Almost 30 years later, when there was some confusion over whether an article in *Nature* was written by A. W. F. Edwards (Fisher's student) or his brother John Edwards (Hogben's student), Fisher wrote of the matter to his former colleague R. R. Race, "It was the thought that it was he [i.e., A. W. F. Edwards] that annoyed me, for the estimates published in *Nature* were manifestly incompetent, and I feared that one of my own pupils was running amok, and adding unnecessarily to darkness and confusion. However, I understand he [i.e., John Edwards] is only one of Hogben's, so all is explained."[130] A. W. F. Edwards, in fact, personally witnessed Fisher's disdain for Hogben upon the arrival of the paperback edition of Fisher's *The Genetical Theory of Natural Selection* (1958), recalling, "I was standing in the departmental office when Fisher opened the parcel of author's copies. 'Hmph,' he said at his first sight of the cover, 'Looks like a book by Hogben.'"[131]

Hogben lost no less love. In discussing the downfall of the Nazi Party in an unpublished portion of his autobiography, Hogben judged, "After the war, the Nuremberg justices of the peace had Rosenberg hanged. If I believed in hanging people for their opinions, the only extenuating circumstances I might enter with a clear conscience as a plan for mercy on behalf of the late Sir R. A. Fisher would be that he did not occupy

[129] R. A. Fisher Papers (Series I, Hogben, L.), University of Adelaide. Quoted with the permission of the University of Adelaide Library.

[130] Fisher to Race, 27 September 1960, R. A. Fisher Papers (Series I, Race, R.R.), University of Adelaide. Quoted with the permission of the University of Adelaide Library.

[131] Edwards (1990, p. 278). I am indebted to Margaret Morrison for bringing this anecdote to my attention.

a government post with responsibility for implementing his convictions."[132] And this from an avowed pacifist.

The Legacies of Fisher and Hogben: $G \times E_B$ and $G \times E_D$

If the Fisher–Hogben debate had been an isolated event, then it would have been interesting in its own right. But it was not an isolated event. And, as a result, there is more than just an interesting story here. The thesis of this section is that the distinct concepts of interaction have had separate legacies of their own in their separate research traditions, and the conceptions have faced off on numerous (sometimes acrimonious) occasions.

Hogben's $G \times E_D$ was carried into the mid-twentieth century most clearly in the work of British developmental geneticist Conrad Hal Waddington. This can be seen in Waddington's *The Strategy of the Gene*.[133] Waddington wanted to explain to his readers what geneticists meant by genetic and environmental influences on the phenotype. To do so, he introduced Hogben's discussion of the Krafka data and, in fact, block-quoted two full paragraphs along with the reaction norm graph from Hogben's *Nature and Nurture* where Hogben discussed the case. Reinforcing the *developmental* nature of the phenomenon, Waddington summed up, "Such a difference of degree in environmental sensitivity to the development controlled by two genotypes is spoken of as 'genotype–environment interaction.'"[134] Like Hogben, Waddington emphasized both the importance of this phenomenon along with the mishandling of it by statistical tabulations of variance, arguing, "…after nearly half a century's development the statistical theory still has to leave out of account the contribution of genotype–environment interactions." And, "Now from the point of view of the theory of evolution such special interactions between genotypes and environments are obviously by no means negligible. In fact, the whole of adaptive radiation, including the formation of local races, turns on the way in which particular genotypes fit into certain environments; that is to say, on this very factor of genotype–environment interaction."[135]

Waddington's emphases on the importance of a developmentally-conceived $G \times E$, however, may be contrasted with the disregard for the concept found in the work of American population geneticist, Jay

[132] Hogben, *LBL*, p. 213. Quoted with the permission of Leslie Hogben.

[133] Waddington (1957).

[134] Waddington (1957, p. 94).

[135] Waddington (1957, p. 100).

Lush, who, working in the biometric tradition, instead adopted Fisher's $G \times E_B$. In his seminal *Animal Breeding Plans*, Lush brushed aside the importance of $G \times E$ in a manner reminiscent of Fisher.[136] "It seems likely," Lush counseled, "that in general the nonadditive combination effects of heredity and environment are small in amount* and that many of those which do occur can be reduced to a negligible remainder by choosing a scale of measurements…which will show the effects of hereditary and environmental on that characteristic in their most nearly additive form."[137] The "*" in Lush's statement directed his readers to a footnote at the bottom of the page where he continued, "For some extreme examples of nonadditive combination effects of heredity and environment consult Chapter 5 of Hogben's *Nature and Nurture*." In contrast to Waddington, then, who introduced Hogben's work as exemplifying what geneticists meant by genetic and environmental influences, Lush relegated Hogben to a footnote, as Hogben offered only "extreme examples," and, like Fisher, simply encouraged a transformation of scale to make the nuisance disappear. Thus, the competing concepts of genotype–environment interaction played out in the separate biometric and developmental traditions even after Fisher and Hogben were no longer the primary participants in the debate.

And the disputes over genotype–environment interaction did not end with Waddington and Lush. As mentioned in the introduction, the IQ Controversy revolved around heritability estimates of IQ and the purported genetic basis of the difference between IQ scores for black and white populations. Critics of this genetic thesis, such as Lewontin and Layzer, pointed to Waddington's research and drew heavily on genotype–environment interaction to fundamentally undermine these heritability estimates.[138] Employing the developmental interpretation, Layzer attacked the very meaningfulness of heritability estimates, arguing, "The information-processing skills assessed by mental tests result from developmental processes in which genetic and nongenetic factors interact continuously. The more relevant a given task is to an individual's specific environmental challenges, the more important are the effects of this interaction."[139]

In stark contrast, Jensen described any discussions of genotype–environment interaction which invoked development as fundamentally

[136] Lush (1937).

[137] Lush (1937, p. 64).

[138] Layzer (1972, 1974); Lewontin (1974).

[139] Layzer (1972, p. 281).

confused. "This position," Jensen countered, "has arisen from a failure to understand the real meaning of the term 'interaction' as it is used in population genetics; but even more it is the result of a failure to distinguish between (a) the *development* of the individual organism, on the one hand, and (b) *differences* among individuals in the population."[140] Jensen, like Fisher and like Lush, employed the biometric interpretation and wrote off genotype–environment interaction as exceptional since the standard biometrical methodologies did not find significant interactions.

$G \times E_B$ and $G \times E_D$, then, have persisted long after the original formulations of Fisher and Hogben. In mid-twentieth century population and developmental genetics, in the IQ Controversy, and in contemporary debates between quantitative behavioral geneticists and developmental psychobiologists, the distinct concepts of interaction have continued to be employed in the biometric and developmental research traditions. Over the last century, members of each research tradition have often butted heads over the appropriate approach to studying variation, and often those quarrels have revolved around $G \times E$. At the center of each of those quarrels, I have argued, rested the biometric and the developmental concepts of genotype–environment interaction.

Conclusion

This essay examined the origins of the concept of genotype–environment interaction. In considering the origins of this concept, it was found that R. A. Fisher and Lancelot Hogben actually came to consider the concept by quite different routes. In developing methods for assessing the relative importance of heredity and the environment as part of the biometric tradition, Fisher came to recognize the possible complications raised by the "non-linear interaction of environment and heredity" for the summing of variances, introducing the *biometric* concept of genotype–environment interaction, or $G \times E_B$. Hogben, meanwhile, began by considering different sources of variability in a population – a standard problem for the developmental tradition of biology. In doing so, he recognized a third class of variability (distinct from genetic or environmental variability) that resulted from the combination of a particular genetic constitution with a particular kind of environment. This source of variation was responsible for cases of genotype–environment interactions and was, for Hogben, a result of development,

[140] Jensen (1973, p. 49), emphases in original.

thus introducing the *developmental* concept of genotype–environment interaction, or $G \times E_D$.

Fisher and Hogben's separate routes to genotype–environment interaction also led to disparate conclusions when it came to considering the importance of genotype–environment interaction. Dedicated to developing methods for assessing the relative importance of heredity and the environment, Fisher took genotype–environment interaction merely to be a potential (but unproved) complication for his statistical techniques. Hogben, meanwhile, understood genotype–environment interaction to be of much more importance. Genotype–environment interactions were a feature of development and, as such, were to be expected in nature despite the fact that experimental embryologists were only beginning to discover them. Finally, these distinct concepts of genotype–environment interaction were traced beyond the work of Fisher and Hogben. The legacy of Fisher's $G \times E_B$ was traced through the biometric tradition in the work of Jay Lush and Arthur Jensen. And the legacy of Hogben's $G \times E_D$ was traced through the developmental tradition in the work of Conrad Hal Waddington, Richard Lewontin, and David Layzer.

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