Population Genetics and Population Thinking: Mathematics and the Role of the Individual

Margaret Morrison†‡

Ernst Mayr has criticised the methodology of population genetics for being essentialist: interested only in "types" as opposed to individuals. In fact, he goes so far as to claim that "he who does not understand the uniqueness of individuals is unable to understand the working of natural selection" (1982, 47). This is a strong claim indeed especially since many responsible for the development of population genetics (especially Fisher, Haldane, and Wright) were avid Darwinians. In order to unravel this apparent incompatibility I want to examine the possible sources and implications of essentialism in this context and show why the kind of mathematical analysis found in Fisher's work is better seen as responsible for *extending* the theory of natural selection to a broader context rather than inhibiting its applicability.

1. Introduction. In the context of distinguishing essentialism, characterized by an interest in types, from population thinking, which stresses the importance of individuals, Ernst Mayr claims that "he who does not understand the uniqueness of individuals is unable to understand the working of natural selection" (1982, 47). This is a strong claim indeed especially since those who, as a result of their methodology, would seem to fall into the essentialist camp include the early population geneticists, (especially Fisher) many of whom were avid Darwinians. So, what are we to make of this apparent incompatibility? Unravelling Mayr's argument and providing an answer to his charge involves peeling back several layers of concepts and ideas associated with both statistics and biology. Although a complete story is beyond the scope of this paper, I want to at least sketch an account of why Mayr's claim is, to my mind, misdirected.

†To contact the author, please write to: Philosophy Department, University of Toronto, Trinity College, 319 Larkin Bldg, Toronto, ON, M5S 1H8, Canada; e-mail: mmorris@ chass.utoronto.ca.

Much of Mayr's criticism of the essentialist program focuses on the use and interpretation of mathematics in characterizing a population, making it one that is in every sense a 'construct', dealing with the "average man" and variation around mean values. As an alternative Mayr advocates an approach called population thinking that emphasises the uniqueness of biological individuals: an approach that employs mathematics only as a way of representing the aggregate of a natural population where variation differs from character to character. In fact, Mayr goes so far as to say that "Darwin would not have arrived at a theory of natural selection if he had not adopted population thinking" (47). What I want to suggest is that the kind of mathematics Mayr criticises the early population geneticists for using was in fact essential for a biological analysis of populations. Although an initial formulation of the theory of natural selection may have required attention to individuals, in order to fully understand its role in a broader context one *requires* the kind of mathematical analysis that Mayr attempts to eschew. So while Mayr is right to see this work (especially Fisher's) as embodying essentialism, its primary concern is an explanation of variation, something that lies at the heart of the Darwinian program. Consequently the alleged incompatibility between the essentialists and the Darwinians looses much of its significance.

2. Why Population Thinking? I begin by outlining why one might identify a commitment to essentialism with the methods of population genetics. My approach involves paying specific attention to mathematical/statistical techniques rather than examining whether various philosophical accounts of essentialism can be maintained in the face of evolutionary theory.[1] Mayr himself suggests that Galton's recognition that the notion of a 'mean' was a construct helped to loosen the grip of essentialist ways of thinking. While Galton may have differed in certain ways from the essentialist statistics of Quetelet, his *methodology* remained firmly associated with the kind of thinking that Mayr criticizes. My goal is to extend that history to include the methods of Pearson and Fisher, in an attempt to show the ways in which their methodologies were essentialist and why that kind of methodology was necessary in that context.

Although Mayr never *explicitly* says so, one only need look at his characterization of essentialism to see quite clearly that the methods of the biometricians and mathematical population geneticists especially fall squarely within this camp. The essentialist treats biological individuals in the same way that the physicist treats inanimate matter, constructing mathematical representations in order to calculate the characteristics of

1. For a discussion of this issue as it relates to Galton and some earlier figures see Sober 1980.

the average man and thereby determine his essential nature. Variation refers not to individuals but to "errors" around mean values. By contrast, the population thinker stresses the uniqueness of everything in the organic world and claims that we must approach these biological groups in a very different way than groups of inorganic entities. It is differences between individuals in natural populations that are real, not the constructed mean values calculated by the essentialists. Both Pearson (the founder of biometry) and Fisher dealt with large statistical populations, largely neglecting actual populations of living organisms studied in the field or the laboratory.

The other reason why the mathematical geneticists (Fisher, Haldane, and Wright) could be considered essentialists was their focus on the gene as the unit of selection and the attribution of a definite fitness value to each gene. Mayr sees the emphasis on genes as the unit of selection as un-Darwinian, leaving most of evolutionary phenomena unexplained (1982, 588). In that sense then his objections to the essentialism of the population geneticists can be couched in both methodological and ontological terms; that is, he contends that the mathematical populations characterized by the geneticists actually prevent us from understanding the workings of natural selection.

Part of Mayr's criticism rests on the claim that in much of evolutionary biology the contributions of mathematics are very minor (1982, 41). Attempts to translate qualitative biological phenomena into mathematical terms have sometimes proven complete failures because they loose touch with reality (54). For example, he accuses the mathematical population geneticists (specifically Fisher) of oversimplifying, for the sake of mathematical tractability, the factors that entered their formulas. This led to a stress on absolute fitness values of genes, to an overvaluation of additive gene effects, and to the assumption that genes rather than individuals are the target of natural selection. He concludes that this invariably led to unrealistic results (41).

Just what were these unrealistic results? The simple answer of course is that the more simplified the assumptions the less one is able to account for the increasing complexities of the phenomena of population genetics. For instance, Mayr compares, somewhat unfavorably, the different approaches of Fisher and Wright (Mayr 1973, 152). Because Wright emphasized small population size and the interaction of genes, his approach was ultimately more congenial to the true spirit of evolutionary biology than Fisher's. In fact, Fisher's assumptions regarding large populations, the small effects of individual genes, negligible linkage and epistatic effects, together with the unimportance of sampling errors, are all seen by Mayr as serving mathematical rather than biological ends. In what follows I try to show that none of these assumptions was made simply for the sake

of *mathematical* tractability. In fact, at this point in the development of genetics and biology it is very difficult to distinguish, in any determinate way, what is properly biological from what is strictly mathematical. Because the goal was to establish broad general principles of evolution as a genetical process, these kinds of mathematical methods and models, far from being mere calculational devices, were a necessary part of the methodology that gave rise to modern population genetics. Mathematical simplifications were introduced because the methods available to Fisher would not have allowed him to arrive at a satisfactory analysis of variation.

Let me begin then with a brief discussion of Pearson's biometrical Darwinism and the extent to which essentialism is embedded in that approach. From there I go on to discuss the differences between Fisher and Pearson and show why one needed an even more abstract mathematical account of populations than Pearson's to show the compatibility between Mendelism and natural selection.

3. Pearson on Populations. In many senses the origins of biometry (as well as certain aspects of Mendelism) can be found in the work of Francis Galton. Because Pearson, Galton's student, saw the law of ancestral heredity as the starting point for the science of biometry the interesting issue is the extent to which Galton's statistical approach was essentialist; that is, to what extent did it depart from the essentialist approach of Quetelet. That Galton's approach is at odds with individualism is evident from a remark in *Natural Inheritance* that "The science of heredity is concerned with fraternities and large populations rather than with individuals, and must treat them as units" (1889, 37). Galton's use of the law of errors, which later became the cornerstone of biometry, can be traced to Laplace, who showed that if measurement of a phenomenon results from a variety of independent observations then these measures should be roughly distributed according to Gauss' law. Quetelet then used this result to determine whether a group of real objects (as opposed to measures) could be considered homogenous, i.e., whether a Gaussian distribution was a way of detecting groups (populations) of homogenous objects. For Quetelet the distribution revealed an underlying order or ideal type that nature strives to attain; hence variation had no real significance. Differences in characters that have a normal distribution were due to a large number of accidental and independent causes.

Galton took up this methodology and to some extent its underlying ideas but *not* the implication that the individual inheritance of traits was somehow accidental. His conclusion was that the process of heredity must be shown to work harmoniously with the law of errors; in other words, he needed to know *why* organisms typically show Gaussian distributions

for their characters. Galton claimed that selection and heredity both follow the law of errors. The character favored by natural selection is that which represents the best balance between excess and deficiency. Galton's explanation of these processes is not my concern here. Instead I want to point out that for him Darwin's individual differences (continuous variation) were considered unstable deviations from the population mean; they were the object of blending inheritance and generally showed a normal distribution in the population, with the offspring showing a tendency to regression. Hence, these divergences did not contribute to evolutionary progress. What the law of ancestral heredity claimed was that, on average, each child carried an ancestral heritage which pulled them back to the typical center. Both selection and heredity were laws that described the typical character of the population; they explained the fact that most characters showed a Gaussian distribution. In this latter sense Galton was very much in the tradition of Quetelet.

Although Pearson was largely responsible for adopting and extending Galton's work on heredity, he saw it not as a biological hypothesis but rather as the mathematical expression of "statistical variates . . . [which] can be applied . . . to many biological hypotheses" (1930, 21). With the appropriate regression corrections in place Pearson (1898) was able to reconcile Galton's statistical work with his own views about variation, claiming that the ancestral law formed the fundamental principle of heredity from which all the numerical data of inheritance could be deduced, at least to a first approximation. It was this application of statistical tools designed to measure variability and correlation, and the ways in which these influenced various kinds of selection, that defined the new science of biometry.

Pearson's use of biometric methods is intimately connected with his views on science and experience. In his biography of Galton, Pearson (1930, 288) claimed that science could not survive describing only individual experiences; its conclusions are based on average experiences, no two of which exactly agree. When the variability that is characteristic of perceptual experience is removed by a process of averaging, one passes from the perceptual to the conceptual and so from the real world to a "model" world (1911, 153). The process of statistical analysis then involved the construction of models that could, in the case of biometry, be used to predict the inheritance of certain traits from parent to offspring. Using these kinds of techniques one could attain a level of certainty that was impossible using Mendelian schemes. But, it is important to point out that the process of averaging was not carried out solely for epistemic reasons relating to a "smoothing out" of our experiences. What is perhaps more significant, especially with respect to essentialism, is Pearson's beliefs

about the *nature* of individuals and how those beliefs relate to his statistical methods.

His views about the representation of individuals in the context of a statistical analysis are traceable to ideas about homogenous classes, an important element in his notion of a population. In a letter to Galton in 1907 (Pearson 1930, 3A: 288) he described an upcoming lecture to the Oxford Philosophical Club, a lecture which was to start with the claim that no two physical entities are exactly alike; instead they form a class with variation about a mean character. Hence, even in physics the ultimate basis of knowledge is statistical; because we cannot develop a science based on knowledge of individuals we must resort to methods that allow us to represent features of those individuals in a way that is amenable to scientific treatment. This thought was echoed later in the third edition of *Grammar of Science* (1911) where he remarked that the notion of sameness applied to molecules is only statistical sameness (156). He questioned the attempts of Mendelians to replace vital variation with 'unit' characters that are genetically indistinguishable from others of the same kind. He opposed what he saw as the kind of genetic atomism that formed the basis of Mendelism. Although the idea that there were homogenous classes without any degree of variability contravened his *ontological* beliefs, *methodologically* one needed a way of classifying individuals. Hence, the process of averaging took account of both the individuals we are investigating and the experiences we have of them, no two of which exactly agree. Provided we have a large enough sample averaging over the variability allows us to draw general conclusions about the character of the population. But, once this is done we have passed from the perceptual to the conceptual, from the real world to a "model" of that world (Pearson 1911, 154). The important issue here is sample size. Biometrical statistics were designed to apply to large samples drawn from human, plant, and animal populations. If the samples were large enough one could supposedly substitute the sample statistics for the population parameters. As we shall see below it is this concept of a "model population" that would ultimately serve not only to mark the differences between Pearson and Fisher, but ultimately to facilitate the synthesis of Mendelism and biometry.

Although the biometricians were largely Darwinians, part of the power of biometry was its biological neutrality. In other words, its methods did not commit one to a specific theory of the mechanisms of heredity, yet it was capable of providing extremely accurate phenotypic predictions. That task was exemplified in the formulation of the ancestral law, which brought into a single focus all the complex lines of hereditary influence (Pearson 1898, 412). For Pearson the debate between the biometricians and the Mendelians was largely a debate about method; he refused to accept any biological arguments or evidence not grounded in biometrical techniques.

In fact, he (1902) went so far as to claim that one could not even have a coherent notion of discontinuous variation without the employment of biometric methods. Because these methods gave the kinds of phenotypic relations that could be observed in nature, the burden of proof was on the Mendelians to show that a different distribution of variation was the correct one. Without dealing with the vital statistics of large populations it would be impossible to make any progress in the theory of evolution, since no tabulation of individual instances could possibly lead to definite conclusions. Here we see the beginnings of what Pearson, and later Fisher, saw as the importance of mathematics for establishing general conclusions about the role of selection. Empirical work was simply unable to yield the kinds of claims about populations that were necessary if Darwinian theory was to be put on a firm footing.

In a 1909 paper Pearson responded to a report that some Mendelian results contradicted the biometrician's claim that knowledge of ancestry was important in predicting characteristics like stature. He began with a general population and investigated the correlation of the gametic rather than the somatic characters. Using a model based on the Hardy-Weinberg law he showed that the correlation between fathers and sons took the value $\frac{1}{2}$. But crucial to the argument was the fact that this gametic correlation would only hold for somatic or phenotypic characters if one assumed a Mendelian schema with no dominance. Pearson, however, remained unwilling to accept Mendelism, claiming that because it was committed to a law of dominance, the statistical agreement that was reached was in some sense superficial. So, although correlation values could be arrived at using pure gamete theory, no mechanism of particulate inheritance could be inferred from measurements of kinship resemblance and so no assumptions about the causes of inheritance could be proved on the basis of phenotypic data.

By contrast, Fisher's support of Mendelism was rooted in its ability to predict with certainty the possible types of children of given parents. Biometry, however, was preferable as a methodology because its results, although more vague, were capable of wider application. The probable measurement of particular organs of the offspring can be calculated from those of the parents and those of the general population, but large numbers of families of similar parents in that population are required before the prediction is accurate. The fundamental assumption behind biometry is that there are a large number of independent causes acting at random, which is why the results are true only of populations. Variations, which are partially inherited, can take any of an indefinite range of values for each organ. Hence, by taking a sufficient number of measurements (human stature, for example) one can construct a frequency curve that shows the number of individuals per million of the population whose heights lie

within successive inches of the scale. If the measure is determined by a large number of small independent factors, the curve will be a normal one and can be specified by knowing the mean value and the standard deviation (Fisher [1911] 1976, 159). In that sense the methods of biometry allowed for a different kind of certainty than the possibilities generated by Mendelian theory. Since they were based not on any theoretical assumptions and only on the laws and methods of statistical theory, the probability of large errors could be shown to be small.

While Fisher did not object to Mendelism as a *theory* of heredity he nevertheless had well-defined methodological objections to it, such as its preoccupation with detail and accompanying lack of attention to abstract reasoning, which he saw as necessary for arriving at broad coordinating principles of evolution (Fisher and Stock 1915, 60). By focusing on individual natural traits Mendelism was unable to provide a theory upon which to predict and control aspects of the population. The starting point for Fisher's method was a comparison between a biological population and a population of atoms in gas theory. The agencies of selection always act amidst a multitude of random causes, each of which may have a predominant influence if we fix our attention on a particular individual. Yet, these agencies determine the progress or decline of the population as a whole. In the case of the kinetic theory molecules move freely in all directions with varying velocities, yet we can obtain a statistical result that is a perfectly definite measurable pressure. Knowledge of the nature and properties of the atom is inessential and independent of our knowledge of general principles, in the way that eugenics is independent of particular knowledge of individuals. It was this analogical model that would provide the basis for Fisher's methodological approach in his later work. Conceiving of biological populations in this way puts anti-individualism in the predominant role, forming the basis for the kind of mathematical analysis that Mayr finds so objectionable. Yet, as we shall see below, Fisher's main concern is an explanation of variation, its cause, and how it is maintained—all of which were important to the Darwinian picture. What we need to determine then is the extent to which Fisher's techniques were necessary for the kind of results he wanted to achieve. In the remainder of the paper, I want to spell out my reasons for thinking they were, especially when one contrasts his methods with those of Pearson.

4. Fisher's Mathematical Statistics: Abstract Representations. Recall that Pearson's work showed that a normal distribution could be accounted for on the hypothesis that characteristics such as height were controlled by many independent Mendelian loci, yet he rejected any claims about the compatibility between Mendelism and Darwinian biometry. It is in this context that Fisher's work seems most intriguing. What enabled him,

as an advocate of biometric methods, to go beyond the conclusions reached by Pearson? Fisher's (1918) stated goal was the investigation of biometrical properties of a population of a "more general type" than was usually considered, in the hopes that a more exact analysis of the causes of human variability might be given. More specifically, he wanted to determine the extent to which characteristics such as stature were determined by a large number of Mendelian factors (genes). Yule had claimed that the effects of dominance and the environment in reducing correlations between relatives were identical, something that Fisher hoped to disprove by separating how much of the total variance was due to dominance, how much resulted from other environmental causes, and how much from additive genetic effects. If one could resolve observed variance into these different fractions (i.e., expressing these fractions as functions of observed correlations) then one could easily determine the extent to which nature dominated over nurture. Fisher demonstrated that the effect of the dominance in individual effects expressed itself in a single dominance ratio. And, using fraternal correlation he was able to determine the dominance ratio and distinguish dominance from all nongenetic causes such as environment (which might possibly lower correlations). Essentially what Fisher succeeded in doing was distinguishing not only between genetic and environmental variance but also between the different components of genetic variance itself.

Fisher made a number of explicit assumptions that were clearly at odds with Pearson's method, which he claimed was too restrictive with respect to the nature of Mendelian factors. Contra Pearson he did not assume that different Mendelian factors were of equal importance, and allowed that different phases of each could occur in any proportions consistent with the conditions of mating. The heterozygote could take any value between dominant or recessive (and even outside that range) resulting in the terms losing their polarity and becoming simply the means of distinguishing one pure phase from the other. So, all dominant genes did not have a like effect. In order to simplify his calculations random mating as well as the independence of the different factors were also assumed. Finally, and perhaps most importantly, he assumed that the factors were sufficiently numerous so that some small quantities could be neglected; in other words, large numbers of genes were treated in a way similar to large numbers of molecules and atoms in statistical mechanics. As a result Fisher was able to calculate statistical averages that applied to populations of genes in a way *analogous* to calculating the behaviour of molecules that constitute a gas.

Although Pearson was entirely comfortable dealing with large populations (a cornerstone of biometric methods), the idea that the manifestation of a character was the result of an *indefinitely* large number of

Mendelian factors was anathema—something he took to be amenable to neither proper statistical/biometrical analysis (the mathematics was too laborious) nor experimental tests of the kind favored by the Mendelians. But, for Fisher this degree of idealization was essential to guarantee his method, and hence the legitimacy of its conclusions. In other words, he could escape the difficulties associated with detailed Mendelian analyses by focusing on general principles. But in order to do this it was necessary that he assume a large number of factors in order to establish statistically the generality and validity of the principles and his conclusions. In the way that one could have knowledge about the properties of gases without detailed knowledge of the molecules and atoms that make up the gas, one could have knowledge of how a population would evolve without knowing the details of the heredity of all individual characteristics. And, an indefinite number of factors was essential to the process of averaging that yielded such knowledge.

The notion of a population as a way of thinking about groups of organisms was a cornerstone of Darwinian evolutionary theory. According to Pearson, if one was to test the extent to which a Mendelian population accorded with biometrical findings, then it was crucial that that population be properly characterized. That characterization involved assumptions required for the specification of each of the individual Mendelian factors:

1. which allelomorph was dominant
2. to what extent did dominance occur
3. what were the relative magnitudes of the effects produced by different factors
4. In what proportion did the allelomorphs occur in the general population
5. were the factors dimorphic or polymorphic, to what extent were they coupled etc.

If one assumed, as Fisher did, an indefinite number of Mendelian factors then the nature of the population could not be specified in any complete sense, thereby undermining any statistical result that might follow. In addition to these assumptions there were the more general considerations that needed to be taken into account regarding homogamy (preferential mating) as opposed to random mating, selection, and environmental effects, all of which needed to be treated separately if one was to determine the genetic basis of the inheritance of particular characteristics. So, not only did Fisher differ from Pearson with respect to specific assumptions about the *nature* of Mendelian factors (that all were equally important, etc.), but the way in which one characterized or 'modeled' a Mendelian population was also much more general and abstract. By assuming an

indefinite number of factors it was possible to ignore individual peculiarities and obtain a statistical aggregate that had relatively few constants.

What Fisher's analysis does is take the biometric notion of averaging to a greater level of abstraction, by moving even further away from the conception of an individual in order to establish general conclusions about populations. On the view advocated by the biometricians one needs variability at the level of individuals as a basis for blending inheritance, but in order to predict the way in which populations will evolve one begins by averaging over this variability to arrive at a statistical characterization of the population. By contrast, Fisher's model of a Mendelian population was based on the molecular models of statistical mechanics. Knowledge of individuals simply wasn't important; hence the idea that each was a source of variation had no role to play in the general conception of the population. Instead, variation came at the level of Mendelian characters, and if one assumed an indefinite number of such factors then not only did one completely lose sight of any notion of the individual but it became difficult to see how such assumptions could be legitimated using biometric methods. But therein lies both Pearson's problem and Fisher's solution. Pearson's model of Mendelian populations prevented him from calculating the effects of the genetic component of variance; a statistical analysis of anything more than two or three factors was far too cumbersome and beyond the range of calculation. In that sense Mayr is correct to say that particular assumptions were made with mathematical goals in mind. However, these goals were sought in an effort to legitimate the Darwinian project of establishing the role of variation and selection.

What we have seen then are the various ways in which essentialism entered into the statistical methodology of Galton, Pearson, and later Fisher. More so than the others, Pearson was a proponent of the kind of ontological individualism that was characteristic of Darwinism, but for methodological reasons he stressed the necessity of a statistical approach that emphasized averaging and the representation of characteristics using the normal distribution. We have also seen the ways in which Fisher's more abstract characterization of a population seemed crucial for providing the framework for showing that selection operated in Mendelian populations. But, ironically, this wasn't simply the result of idealizing assumptions of the kind that Mayr refers to; instead the focal point of Fisher's essentialism was the anti-individualism inherent in his analogy with the gas model. By assuming an indefinite number of Mendelian factors and focusing on general principles, Fisher was able to synthesize these two traditions in a way that would have been impossible by focusing on either individual variation or the average values produced by biometric methods.

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