Weldon's Search for a Direct Proof of Natural Selection and the Tortuous Path to the Neo-Darwinian Synthesis

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W F R Weldon first clearly formulated the principles of natural selection in terms of what would have to be observed in natural populations in order to conclude that natural selection was, indeed, acting in the manner proposed by Darwin. The approach he took was the statistical method developed by Galton, although he was closer to Darwin's conception of selection acting on small individual variations than Galton was. Weldon, together with Karl Pearson, who supplied the statistical innovations needed to infer the action of selection from populational data on trait distributions, laid the foundations of biometry and provided the first clear evidence of both stabilizing and directional selection in natural populations.

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To fully appreciate W F R Weldon's contribution to evolutionary biology, it is necessary to understand the state of the subject around the time he was embarking upon an academic life as a researcher in 1882. It is often believed that between the publication of Charles Darwin's *Origin of Species* in 1859, and the welding together of Mendelian genetics and the principle of natural selection in the Neo-Darwinian Synthesis of the 1930s, there was a smooth progression of evolutionary thinking towards the elaboration of Darwin's well-received thoughts. That is, however, far from the truth. For the first fifty years or so after Darwin's *Origin of Species* and the two-volume *The Variation of Animals and Plants under Domestication* in 1868, there was considerable disagreement about whether natural selection could indeed work the way Darwin had suggested and be the driving engine of adaptive evolution. Evolution, in the sense of descent with modification, was widely accepted, but natural selection as its main driver

was not. In order to place Weldon's evolutionary contributions in context, I first briefly summarize the very mixed, often confused, reception to Darwin's principle of natural selection in the late nineteenth century.

Darwin derived his concept of natural selection from the experiences of plant and animal breeders, who were routinely able to modify varieties by choosing individuals with certain desired traits to breed from. He realized that the natural analogue of the breeder selecting which individuals get to reproduce, based on whether they have the desirable trait(s) or not, would be the ecological struggle for existence in nature as a result of competition for limiting resources. Thus, individuals that happened to possess traits that enabled them to function well in the environment they inhabited, would tend to be more successful at surviving to breed, and eventually leave more offspring than their counterparts with traits less suited to the environment. Linking this success in the struggle for existence to longer term evolutionary change was what Darwin referred to as the "powerful principle (or, sometimes, force) of heredity". Of course, Darwin did not know how variations in traits were generated or how they were inherited. Yet, he made the conceptually important point that, given that offspring would be relatively more likely to carry trait variations of their parents, if individuals with certain trait variations were to routinely produce more offspring than others, then eventually those 'favourable' trait variations would become more common in the population. In doing so, Darwin subtly recast the focus of heredity from the 'inheritance of similarity of type' to the inheritance of 'individual trait variations' (see *Box* 1).

The first major critique of Darwin's proposed mechanism for evolutionary change – natural selection – came within a few years of the publication of the *Origin*. A professor of engineering, Henry Charles Fleeming Jenkin, raised several very prescient questions about the nature of variations and their inheritance, and the implications thereof for the proposed mechanism of natural selection, in a review of Darwin's book published in 1867.

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Box 1. The Changing Conceptions of Heredity.

Science is ultimately more about the concepts we invent to explain the facts we observe than about the facts themselves, a distinction not often brought out during one's education. Today, when most of us have grown up in the 'era of genetics', and when genetic phrases have even made their way into political discourse, it is difficult to appreciate how recent our dominant conceptions of heredity are. In a way, any science of heredity has to explain, in a unified and coherent manner, two seemingly opposite phenomena: similarity and difference. Reproduction at one level is a conservative phenomenon – offspring resemble their parental types. At another level, reproduction allows for variation between parents and offspring, and among offspring of the same parents. Heredity must explain why the offspring of a crow are invariably crows, and not mynas, and also why all offspring of a given mating pair of crows differ among one another, while remaining crows. Also tied up with reproduction is the question of how a fertilized egg eventually gives rise to an adult organism. From the 1700s through to the late 1800s, embryology was one of the central disciplines within biology, trying to answer fundamental questions about reproduction and development. As such, the study of heredity was a sub-discipline of embryology, and its focus was on the 'similarity' aspect: how do parent crows make baby crows? One consequence of this, conceptually, was a focus on mechanisms and materials of heredity. Especially from the mid-1800s onwards, once it had been generally recognized that development consisted of not only growth but differentiation of tissue types (the epigeneticists' position, as opposed to the preformationist view), embryologists grappling with the question of heredity were focused on how 'form' arose during development and how the 'instructions' for form would be transmitted from parents to offspring.

Darwin amended this focus to a large degree by recognizing that the mechanisms of heredity had to account for not only large-scale similarity of parents and offspring but also, on a much smaller phenotypic scale, the generation and inheritance of the variants on which natural selection would then act. In doing so, he introduced two important conceptual innovations into the study of heredity, especially as it impinged upon evolution. One was to focus on the outcome of heredity rather than its mechanism. Thus, Darwin empha-sized that from an evolutionary perspective, what mattered about heredity was that it implied some degree of similarity between trait variations exhibited by parents and their offspring greater than that expected between the offspring and the population as a whole. This insight was subsequently elaborated by Galton and Pearson and became the foundation for the statistical depiction of heredity in terms of parent-offspring correlations in phenotypic traits. This conceptualization of heredity as parent-offspring correlation also side-lined the details of development (the ontogeny) from the role of heredity in explaining adaptive evolution, a point implicit in Darwin and subsequently made explicit by Galton. The second conceptual innovation of Darwin's view of heredity in the context of evolution was to imagine that the individual organism could be treated as a mosaic of traits, each of which, at least to a degree, could be independently modified by selection. Here, of course, the analogy to breeding is clear. This dovetailed neatly with the first innovation in the sense that instead of considering the inheritance of holistic organismal types, one could focus on the parent-offspring similarity for one or a few traits at a time.

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Box 1. *Contd*.

Darwin, however, also had to grapple with the role of heredity in the generation and transmission of variations. This was the context in which he developed a particulate theory of heredity – 'pangenesis'. He imagined that all parts of the body produced gemmules that collected in the reproductive organs and these gemmules carried the 'information' regarding the corresponding characteristics that would be shown by the offspring with regard to those specific traits. In this schema, Darwin allowed for gemmules to get modified by environmental effects experienced within the individual's lifetime. In this sense, Darwin was very Lamarckian for he believed in the inheritance of acquired variations. This was crucial for him as it provided a mechanism for the generation of new variations. The theory of pangenesis was soon discredited experimentally by Galton, who then switched to a purely statistical conception of heredity, but continued to influence subsequent workers interested in particulate mechanisms of inheritance, most notably Hugo de Vries.

The notion of the inheritance of acquired variations was severely discredited in 1883 by August Weismann's insistence on the sequestration of germplasm early in the ontogeny. This lead to the germ-soma dichotomy, foreshadowing the later genotype-phenotype distinction of Johannsen in the early 20th century. However, Weismann's germ-soma distinction was actually a byproduct of his embryological theory, along with Wilhelm Roux, about the mechanism of differentiation. In their view, various cells destined to become different tissue types gradually lost 'hereditary determinants' over multiple cycles of cell division in the developing embryo. Thus, only the fertilized egg had all the 'hereditary determinants'. Therefore, some cells carrying the full array of determinants needed to make the organism with all its different tissue types would have to be sequestered away early on in embryonic development, becoming the germline cells. This view was criticized by de Vries in 1889, based on the observation in many plants that almost any differentiated cell could regenerate a whole plant. The role of the nuclei (fusion of sperm and egg nuclei) in fertilization had been demonstrated in 1874, and de Vries extended the gloriously prescient 1866 proclamation of Ernst Haeckel's that "heredity resided in the nucleus" to a view that placed the hereditary determinants in the nuclei of cells, whereas their actions were carried out in the cytoplasm. The germ-soma (or genotype-phenotype) distinction thus got redefined on to each cell, a view much more in line with present understanding.

Thereafter, following the independent rediscovery of Mendelian laws by de Vries, Erich von Tschermak, and Carl Correns, particulate inheritance gradually won over most biologists and by 1918, the great conceptual reconciliation of particulate Mendelian inheritance and the statistical descriptions of parent-offspring similarity for continuously varying phenotypes had been completed by Ronald A Fisher. It should be noted that many people, including Mendel himself, as well as Udney Yule and Karl Pearson, had pointed out that Mendelian inheritance was not incompatible with continuous variation of phenotypes. Also in the early decades of the 20th century, the hereditary determinants that resided presumably in the nuclei of cells were identified with chromosomes and eventually in the 1940s and 1950s, with DNA.

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Interestingly, after almost half a century of an increasingly molecular level mechanistic characterization of heredity, the statistical approach of treating heredity as parent-offspring similarity, at least for understanding the role of heredity in evolution, is making a comeback. Contemporary attempts to incorporate non-genic modes of inheritance (epigenetic, cultural, ecological) into broader conceptualizations of the evolutionary process, often referred to as the 'extended evolutionary synthesis,' have led to a renewed interest in conceptualizing heredity as parent-offspring phenotypic correlations.

Jenkin's major criticism related to what he termed the 'phenomenon of reversion' that was to later also occupy Francis Galton as well as the biometricians Karl Pearson and W R F Weldon. In modern terms, Jenkin believed that a species had a fixed range of variations it could show, i.e., a species was a well-defined subspace of phenotypic space, whose boundaries were immutable. Therefore, if variations arose randomly (of course, Jenkin, like Darwin, had no idea about how or why they arose), then variations arising from parents close to the species boundaries in phenotypic space would be more likely to comprise of phenotypes closer to the species type, or mean phenotype.

This would automatically result in a conservative tendency towards reversion, i.e., offspring of phenotypically deviant parents would tend to be more similar to the population mean. Jenkin also noted that if inheritance were such that offspring phenotypes were intermediate between the two parents (blending inheritance), then variations could not be maintained for long in any population. Very presciently, and foreshadowing the concept of random genetic drift in population genetics by several decades, he also noted that a rare variant, however beneficial, would be likely to be lost from the population merely by the sampling error associated with the survival of a finite number of individuals out of a potentially almost infinite number of zygotes. Basically, Jenkin pointed out that natural selection would work only under a set of very specific assumptions about how variations arose, how common they were in populations, how they were inherited, and what the mating system was. He also clearly differentiated be-

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tween what we would today call stabilizing and directional selection – the selection that results in maintaining the existing trait distribution *versus* causing its mean to shift in one direction over generations, respectively. Jenkin's critique was made from the somewhat backward-looking position of someone who believed in the fixity of species. Yet, the questions he raised were conceptually sophisticated and spot on. Essentially, his work pointed to a disconnect between Darwin's conception of adaptive evolution involving a sort of diffusion process in which the relative abundances of discrete variants got altered by selection, and his simultaneous insistence that evolution proceeded by gradually altering the distribution of traits that varied continuously. Darwin confounded the two and did not clearly appreciate either that they were different or how to reconcile them. Jenkin's critique, thus, focussed subsequent attention to a proper statistical description of both variation and selection, as well as to issues of whether inheritance was particulate or blending. It also focussed on whether mating was assortative (like mates with like) or at random with respect to phenotype, and the effects of population size on the relationship between the rarity of a favourable variant, and the likelihood that it would become common in the population under selection. His critique set the agenda for evolutionary genetics even before the field actually existed, and the disconnect he had first pointed out between the replacement of discrete variants and the gradual shift of trait distributions got resolved only with the work of Ronald A Fisher from 1918 onwards (see *Box* 2). Jenkin's critique is an excellent example of how one can raise very valid and important points, even though the motivations may be completely wrong in the sense of being based on anachronistic beliefs. This often happens in science and is a good reason for always following and debating the actual arguments rather than the position or 'camp' espoused by the person putting them forward.

Box 2. Continuous Phenotypic Change *via* the Replacement of Discrete Hereditary Variants Through Selection.

In the writings of Darwin, and of evolutionists in the following few decades, there is considerable terminological confusion about what types of trait variants are being referred to. Darwin himself typically used the terms 'variations', 'individuals', and 'races' or 'varieties'. His use of variations was with regard to small differences in traits among individuals that could be transmitted to offspring. He was quite clear that he conceived of natural selection as occurring due to competition among individuals, resulting in the preferential transmission of variations useful to the individual in its particular ecological context, ultimately resulting in a change of the composition of the variety or race. Thus, Darwin treated individuals as mosaics of different traits whose evolution could be tracked independently. Wallace viewed selection as largely being due to competition between varieties or races, rather than among individuals within a variety. Herbert Spencer differed from Darwin in considering the individual organism as a holistic entity. He, therefore, thought of selection as acting on entire individuals, not on small variants of specific traits. Both Wallace and Spencer, therefore, were implicitly thinking in terms of slightly larger-scale variations than Darwin's small individual variations, and in terms of types defined by specific constellations of these larger-scale variants at multiple traits defining either distinct varieties (Wallace) or individuals (Spencer).

After the initial work on selection by these three pioneers, the situation became even murkier. Many evolutionists, including Jenkin, and the very influential Galton and Weismann, thought that small individual variations actually represented environmentally induced noise and were either not heritable, or subject to hereditary reversion to type, and could not, therefore, be effectively acted upon by selection. Thus, although Darwin's notion of descent with modification was widely accepted very rapidly after the publication of the *Origin*, his mechanism of natural selection remained under a huge shadow of doubt for many decades. Basically, there was an ambiguity in Darwin's formulations that could not be clarified in the absence of any knowledge of the mechanisms of inheritance. The ambiguity was about whether selection acted through a sort of a diffusion process in which alternative (discrete) trait variants replaced one another over time, or whether selection somehow directly modified the frequency distribution of a continuously varying quantitative trait. While Darwin favored the latter view, some passages in his writings lean toward the former, too. This ambiguity remained the basis for the bitter biometrician-Mendelian debates of the early 20th century.

The confusion about how exactly selection was mediating evolutionary change was finally cleared up only after Fisher's reconciliation of Mendelian genetics and biometry in his masterful 1918 paper entitled 'The Correlation Between Relatives on the Supposition of Mendelian Inheritance'. As often turns out to be the case in long-standing scientific debates, both sides of the biometrician-Mendelian debate were correct, at least in some ways. Fisher pointed out that continuously varying quantitative traits were consistent with Mendelian genetics if one assumed that the phenotype in such cases was the result of the cumulative effects of alleles at very large numbers of loci, each exerting but a small effect on the phenotype. This had actually been pointed out by Mendel himself but was somehow ignored in the excitement following the rediscovery of his work, perhaps because those involved in the rediscovery and its championing were so committed to the importance of discontinuous variations in evolution.

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Box 2. *Contd*.

The same point was also made by Yule and even Pearson in the first decade of the 20th century, but their treatment was relatively perfunctory and, coming right at the most heated period of the biometrician-Mendelian debates, did not make much impact. Fisher's treatment was far more detailed, and unlike Pearson, he derived his results for a very general case, rather than for one example with somewhat arbitrary and restrictive assumptions. Moreover, the debate had largely subsided by 1918, partly due to the rapidly increasing evidence for Mendelian genetics, including the chromosome theory of inheritance and the discovery that genetic recombination was accompanied by crossing over of chromosome segments.

The essence of Fisher's resolution of the confusion lay in realizing that, at the level of alleles at a locus, directional selection is indeed best viewed as a diffusion process involving the gradual replacement of one discrete entity (an allele) by another. Yet, this allelic diffusion process, when integrated over large numbers of loci and projected onto the continuous phenotype that those loci affect, will result in smooth, gradual changes in the phenotypic distribution, resulting in a shift of the mean over generations. The debate was thus, not so much resolved as dissolved, and this appreciation became the basis for the rapid development of evolutionary genetics, which remains an important and foundational part of our understanding of the process of adaptive evolution *via* natural selection in a manner that is in many ways, very close to that envisaged by Darwin even in the absence of any knowledge of the mechanisms of heredity.

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In the first few decades after Jenkin's criticisms, evolutionary biologists were groping in the dark at least as far as mechanisms governing variations and their inheritance were concerned. Not surprisingly, the early attempts to empirically support the principle of natural selection were based on a strategy of indirect corroboration. Darwin himself had taken this approach, especially in second half of the *Origin*. Lacking direct evidence for natural selection, Darwin built his case largely upon two pillars. One was to deduce the principle of natural selection from generally accepted observations such as the fact that there was indeed a struggle for existence, based on the fact that more offspring are typically produced than can possibly survive, given the resources available, and that offspring tend to resemble their parents more than they resemble the population average phenotype. This deductive argument was supported by the analogy of natural selection to what breeders did while selecting for enhanced traits they were interested in: they would choose individuals showing the desired trait variations and selectively breed from them. The second pillar on

which the case rested was the detailed exposition of how natural selection could be used to explain so many, seemingly independent, phenomena in the real world of natural history. This second approach was also taken by Alfred Russell Wallace, August Weismann, and Ernst Haeckel. Some of the most striking indirect evidence for natural selection in the late 1800s came from careful field studies of the phenomenon of mimicry by Henry Bates and Fritz Müller. This line of work was the forerunner of modern day evolutionary ecology and attempted to interpret and explain natural history in terms of natural selection by trying to develop adaptive explanations for various observed traits of animals and plants.

An alternative approach, inspired in part by Jenkin's critique, that was taken by many scientists in the decades following Darwin's book was to investigate the mechanisms by which variations arose and were inherited and thereby try to examine the process of natural selection directly. This approach was rooted initially in Darwin's theory of pangenesis (*Box* 1) but rapidly split into two distinct modes of thought, following Francis Galton's experimental refutation of pangenesis. One line of thought was more mechanistic, the other more statistical.

Like Galton, Weismann also rejected pangenesis, replacing it with his notion of the germline cells, containing all hereditary determinants, sequestered away early in embryonic development. He also completely rejected the inheritance of acquired characters and believed that natural selection was both a conservative and transforming principle in that it was solely responsible for both maintaining the 'type' and altering the 'type'[1]. Thus, Weismann gave selection more importance than even the principle of heredity, and this led to his position initially being called Neo-Darwinism or sometimes, Ultra-Darwinism[2]. Weismann believed that in the absence of selection, there would be a complete breakdown of the integrity of a type. This was based partly on the observation by breeders that, once selective breeding was stopped, often the variety under selection would degenerate and start exhibiting all kinds of variations and often lose the selected variants altogether. To-

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[1] Today, we would call these two roles stabilizing *versus* directional selection.

[2] Today, Neo-Darwinism refers to the synthesis of the principle of selection and Mendelian genetics, that occurred in the 1920s–40s.

day, we would attribute this to the selected variants having higher mortality or reduced reproductive output than others. Thus, as long as we are breeding only from them, the selected variant is increasing in frequency within the bred variety. However, once we stop selection, the other variants are favored by natural selection, and the selected variants begin to decrease in frequency. Although we do recognize today that selection has both a conservative (stabilizing) role, especially if environments are relatively unchanging for long periods of time, as well as a role in promoting rapid change in response to a changed environment, Weismann pushed this idea to an extreme. He almost denied any role of heredity in the evolutionary process, invoking the absence of natural selection to explain even vestigial organs or the loss of traits in some lineages. He also completely neglected the counterfact that long-established varieties often did breed true to type even after selection ceased.

Partly, as a consequence, this line of thought did not lead to major breakthroughs, except convincing many people, especially in Germany, that selection was indeed a very important and powerful force. This foreshadows the later 'hyper-adaptationism', much criticized in the late 20th century by Stephen Jay Gould and Richard Lewontin, that sought to find an adaptive explanation for everything. The more enduring part of Weismann's thought was his departure from Darwin's emphasis on natural selection acting on small individual variations[3]. Weismann seems to have thought that small individual variations were likely to be restricted to the somatic tissues and, thus, would not be inheritable. Consequently, his work focused on discrete phenotypic variants, eventually leading through the work of Hugo de Vries and others to the rediscovery of Mendel's laws. Ironically, given Weismann's all-powerful conception of selection, the role of selection in evolution was eventually downplayed in this tradition, particularly as it developed in the work of de Vries, Wilhelm Johanssen, and William Bateson. These ideas, often introduced in textbooks as the 'mutation theory of evolution', held that the major 'creative' force shaping evolutionary change was non-randomness in which

[3]Continuously varying phenotypes, in today's terminology.

kinds of discrete variants actually arose in a population, and that selection, at best, served to trim out deviants from the population. In other words, selection was purely stabilizing, with directionality in evolution coming from biases in the generation of discrete phenotypic variants. As it often happens in the history of science, this idea, after being eclipsed for many decades by the dramatic rise of formal genetics since the 1920s, has now come back under a new label called 'developmental bias'. The focus on discrete traits and Mendel's laws, along with a downgradation of selection to a purely stabilizing role, became the essence of the 'Mendelian' position in the Mendelian-biometrician debates of the early 20th century.

Galton, once he had demolished the theory of pangenesis in the early 1870s, took the more statistical route to understanding both heredity and evolution. In a dramatic counterpoint to Weismann, he actually argued that heredity would successfully act against selection and prevent it from operating on small individual variations in the manner that Darwin had envisaged. Almost paradoxically, Galton was thus the motivator, especially in England, for both the biometricians, through his statistical approaches to selection and heredity, and the Mendelians, through his insistence on discrete variations rather than continuous ones being the mediators of evolutionary change. The essence of Galton's statistical approach to heredity and evolution lay in two observations. The first was that continuously distributed traits in plant and animal populations typically followed, more or less, a normal or Gaussian distribution. The second was the phenomenon of reversion, though more in the sense of Jenkin's idea of an inherent or hereditary tendency of traits to revert to the mean of the distribution, rather than Weismann's notion that, in the absence of selection, traits would revert to ancestral forms or be lost altogether. Galton, incidentally, was the first major figure after Jenkin to explicitly emphasize that the problems of heredity and evolutionary change were, in essence, statistical or populational problems. Although Darwin has often been credited with replacing typological thinking with populational thinking, especially by Ernst Mayr,

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From the depiction of the normal distribution as the 'law of errors', Galton drew the inference that if in a collection of individuals some trait varied normally, then it was an indication that one was looking at a distinct biological population or type, with the individual deviations from the type mean representing the random effects of various vagaries of biological existence.

[4]Incidentally, Galton referred to the tendency of offspring to regress towards the population mean, and this is why a technique for finding the best-fitting straight line is known as regression or going backward.

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Galton was familiar with the normal distribution as the 'law of errors'. This was the idea that quantities, all of which represent one basic underlying value but are subject to small and random sources of error that cumulatively cause individual observations to depart from the underlying value, would follow a normal distribution. From this, Galton drew the inference that if in a collection of individuals some trait varied normally, then it was an indication that one was looking at a distinct biological population or type, with the individual deviations from the type mean representing the random effects of various vagaries of biological existence. The other consistent observation that Galton made was that if one looked at the phenotypes of offspring from a mating pair with phenotypes very deviant (above or below) from the population mean, then the mean offspring phenotype was always less deviant from the population mean than its parents had been. In the course of studying this phenomenon, Galton invented the technique of linear regression[4], eventually put on a sound mathematical footing by Pearson. In terms of regression, if one depicts the average phenotype of parents making up the mating pairs on the x-axis, and the mean phenotype of offspring resulting from those matings on the y-axis, then what Galton saw was that the slope of the regression line through these data points was always positive, and always less than unity.

These two findings were what led Galton to reject Darwin's idea of evolutionary change happening through natural selection acting on small individual variations. In his view, the small individual variations (continuously distributed variants) mentioned by Darwin represented mere environmentally or otherwise induced 'noise' around the type or population mean. He further argued that the tendency of offspring to regress to the population mean implied that heredity was a conservative force that tended to bring the offspring of individually varying parents back towards the population mean. Heredity, in this view, was a force maintaining the stability of the type, with each generation showing

small individual variations due to extrinsic factors like the environment. Therefore, Galton rejected the role of natural selection acting upon small individual variations specifically because he thought that heredity would oppose it. He also articulated a vision of heredity which was similar to Weismann's in that he postulated that organisms had latent characters (analogous to the germ-line) and patent characters that were what we could observe (analogous to somatic tissue). It was the latent characters from the parents that came together upon fertilization to form an offspring's latent characters, which the ontogeny, modified by the environment and inherent aspects of heredity, rendered patent. This view of Galton's had shades of the later genotype-phenotype dichotomy, and also the notion of dominance/recessiveness. It is, therefore, not surprising that the English Mendelians in the early 20th century claimed intellectual descent from Galton. Galton's view of evolutionary change arose directly from his views on the normal distribution of traits and the tendency to regress. He believed that discrete variations arose by some unknown underlying mechanisms of development and resulted in the formation of a new type or population mean in one step. Around this new mean would still arise small individual variations, but the mechanism of evolutionary change would have to be through selection acting between these two new types rather than between individual variations of any given type. Interestingly, this was very close to Wallace's conception of selection as primarily occurring between varieties rather than individuals, as Darwin thought.

It was against this backdrop of thinking about variation, heredity, and evolution in the 1870s and 1880s that Weldon and Pearson developed their biometrical approach. While inspired by Galton's emphasis on statistically analyzing problems of heredity and evolution, they departed from Galton in not rejecting the significance of small individual variations to evolutionary change. Indeed, the work of Weldon and Pearson is best seen as a rigorous attempt to uphold the Darwinian conception of selection acting on small continuous variations among individuals within populations, rather than between sub-populations representing different

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Despite their misconception of heredity, the statistical reframing of Darwinian questions of variation, heredity, and selection that Weldon and Pearson achieved, was to have effects on the development of evolutionary thought that far outlived the biometrician-Mendelian debate.

types. In this sense, Weldon and Pearson were actually the truest intellectual heirs of Darwin. Their work contributed a great deal to the eventual reconciliation of continuous phenotypic variation with discrete heredity (see *Box* 2), even though their views on heredity, based on Galton's early work but increasingly departing from his own changing views, turned out to be completely wrong.

One of the conclusions that Galton had erroneously drawn from his empirical observation that offspring phenotypes were correlated not only with parental phenotypes but also with those of grandparents and more distant ancestors was that heredity was affected by multiple generations of ancestry. This became the basis for his 'law of ancestral heredity', which was further elaborated by Pearson. This view seemed to dovetail well with regression, in that the multi-generational ancestral heritage was thought to be the force that tended to pull traits back towards the ancestral or type mean. Both Weldon and Pearson deeply and fervently believed in the law of ancestral heredity, and it was largely this that drove their strident opposition to Mendel's laws when they were rediscovered in 1900. Mendelian genetics restricted the ancestral effects on offspring phenotypes to parental genotypes; there was no room there for previous generations to affect offspring phenotypes. Yet, despite their misconception of heredity, the statistical reframing of Darwinian questions of variation, heredity, and selection that Weldon and Pearson achieved, was to have effects on the development of evolutionary thought that far outlived the biometrician-Mendelian debate which, in a sense, the biometricians lost, at least with respect to their opposition to Mendelian genetics.

In particular, Pearson's formulation of both heredity and selection in terms of statistically describable factors affecting trait distributions laid the foundations for Fisher's breakthrough in 1918. Pearson formalized different modes of action of selection as those that could affect the variance of a trait distribution in a population while leaving the mean unaltered, or those that would alter both the mean and the variance. Alternatively, there could be situations in which the population was heterogeneous, consisting of

different types, each characterized by a different normal distribution. In such cases, selection could be conceptualized as acting between the types, rather than among individuals within a population represented by a single normal distribution of variants for that trait. He also clarified and formalized the distinctions between, and consequences of, natural selection acting through differential mortality and differential reproduction, and in the process, also clearly distinguished between mate-choice and assortative mating, a distinction not very clearly made in Darwin's writings. Pearson was also the first to formalize the now widely-used concept of Darwinian fitness. In the first few decades after Darwin's *Origin*, most evolutionists thought of selection primarily in terms of differential mortality, even though Darwin had clearly recognized that differences in both reproduction and survival constituted selection. Pearson actually developed the formalism that emphasized that fitness, in the sense of the attribute or quality that was the focus of selection, was composed of both the propensity to survive and to produce offspring and that the two might interact in complex ways to affect overall fitness. However, although it was Pearson who supplied the mathematical acumen and rigor in their scientific partnership, Weldon's contributions were crucial. It was Weldon who first posed the relevant biological questions in statistical terms, thus drawing Pearson into the enterprise. And in science, a well-posed question is half the job done. Moreover, Weldon established a methodology for identifying selection in action on a natural population that essentially has not been bettered till today.

Around 1888–89, Weldon, then in his late twenties, began to depart from the evolutionary concerns of classical embryologists, then dominated by the principle of recapitulation. This was a pre-Darwinian but vaguely evolutionary speculation, made independently by Johann Friedrich Meckel (in 1808) and Ètienne Reynaud Augustin Serres (in 1821), later interpreted in terms of descent with modification by Darwin, and championed with characteristic vigor by Haeckel *via* the slogan "ontogeny recapitulates phylogeny". The principle of recapitulation held that evolution-

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ary modifications tend to occur in the later stages of development, implying that natural selection predominantly shapes adult characteristics, leaving earlier larval characters largely unchanged. In an unpublished note written in 1888, the young Weldon observed that the evolution of new adult characters was always accompanied by new characters in the larvae and *vice versa*. Weldon developed the implications of this observation in the light of Darwin's concept of 'growth correlations', namely the correlations between the same trait expressed at different life-stages, suggesting that the phenotypic values of a trait observed at different life-stages were not independent of one another, being linked *via* ontogenetic connections. He then articulated with exemplary clarity the implication of these 'growth correlations' for the empirical study of natural selection.

An obvious way to demonstrate natural selection, Weldon argued, would be to establish that variations among individuals for a given trait actually had effects on the mortality suffered by those individuals. In natural populations, it would typically be difficult to obtain direct estimates of mortality rates suffered by individuals sharing a particular trait variant as it would not be possible to record the phenotypes of every individual that survived or died in a given period. However, Weldon suggested, it would be possible to compare the trait variant distribution in the same population at two different time points. If one could then observe changes in the mean or reductions in the variance of the trait distribution over time, it would provide a demonstration of directional or stabilizing selection acting on that population. One problem identified by Weldon in this approach was that it could be that any such observed changes in the trait distribution were merely a reflection of the manner in which trait values were correlated across life-stages. Thus, it became important to also establish how the same trait was correlated across life-stages, referred to by both Darwin and Weldon as the 'law of growth' of that character, such that the effects of selection on the alteration of trait distributions with age could be teased apart from the manifestations of the law of growth. Similarly, Weldon also argued that it would be im-

portant to establish how different characters were correlated with each other, giving rise to a constellation of phenotypes reflecting the type, and how these correlations might themselves change with life-stage or age. Around this time, Weldon also became acquainted with Galton's statistical approach to heredity and selection, and realized that the key information to be sought empirically was that pertaining to these various correlations. Weldon also realized that the statistical approach provided an avenue to rigorously examine Darwinian principles in natural populations in a manner just not possible through the classical approach of qualitative comparative embryology and morphology. This realization was the inspiration for his empirical work on the common grey shrimp *Crangon vulgaris*, the shore crab *Carcinus moenas*, and the gastropod *Clausilia laminata* , between 1890–1901.

Weldon's first studies on *C. vulgaris* were aimed at refuting Galton's notion that evolutionary change through gradual selection on small individual variations could not be effective. These studies were the first to examine whether various traits in natural populations, as opposed to humans or domesticated species of plants and animals, were distributed normally. They were also the first studies in which correlations among different traits were compared across populations, an issue that had a bearing on Galton's view that organisms were holistic and thus would be characterized by similar among-trait correlations across populations, reflecting the stability of type. In the first paper, in 1890, Weldon looked at various quantitative morphological traits in five populations of *C. vulgaris*, from northern and southern England, Scotland, Brittany, and the Netherlands, and observed that all traits appeared to be more or less normally distributed in each population. This confirmed Galton's prediction about small individual variations being normally distributed, with data from a natural population. However, Weldon also noticed that the parameters of the normal distribution for a given trait varied among populations and he interpreted this result in a distinctly anti-Galtonian manner, though the language he used suggested otherwise: "Since the variations observed in adult individuals depend not only on the variability

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of the individuals themselves (which is possible nearly alike in all races), but also upon the selective action of the surrounding conditions – an action which must vary in intensity in different places – the result here obtained is precisely that which might be anticipated, and it is precisely that predicted by Mr. Galton" (*Proc. R. Soc.*, Lond., Vol.47, pp.445–453, 1890.). This interpretation of the trait distribution in various populations being shaped differently by natural selection was very different from Galton's view that continuous variation was mere noise about a type and would not be shaped by selection. Despite the somewhat misleading statement that this was as predicted by Galton, the quote actually represents the beginning of Weldon and Pearson's attempt to rehabilitate Darwin's idea of selection acting on small individual variations. Weldon's second 'shrimp paper', also published in the *Proceedings of the Royal Society*, in 1892, was more Galtonian in its message. Weldon observed that pairwise correlations between traits were pretty similar across the five populations sampled, supporting the view of a certain holistic similarity of type across populations, despite the individual trait distributions being different. Incidentally, Pearson later argued in 1896 that the small differences between populations of correlations among traits were significant, supporting the view that natural selection might be able to shape even the ontogenetic relationship between different traits.

In 1893, Weldon published his first study on *C. moenas*, measuring 11 morphometric traits of the carapace in female crabs from Naples and Plymouth. He took exemplary care to scale each measurement by the total carapace length, in order to account for variation arising from size differences among animals!

In 1893, Weldon published his first study on *C. moenas*, measuring 11 morphometric traits of the carapace in female crabs from Naples and Plymouth. He took exemplary care to scale each measurement by the total carapace length, in order to account for variation arising from size differences among animals! For ten of the traits, and for 23 pairwise correlations among traits, the results were the same as observed in the two shrimp studies: traits were normally distributed within populations, and trait correlations were similar across populations. One trait (frontal breadth of the carapace) in the Naples population, however, had a strongly right-skewed distribution that was clearly non-normal. This was the finding that led to Weldon approaching Pearson for statistical

help, wondering whether it could be shown statistically that the skewed distribution actually arose due to the population being a mixture of two normal distributions with different means and variances. Pearson invented the necessary statistical techniques for dissecting the distribution into components, and it turned out that this was indeed the case, and the population was thus found to be 'slightly dimorphic for frontal breadth'. Weldon interpreted this result cautiously as implying that the Naples population consisted of two coexisting races, each of which was a homogenous type, subject to the usual, normally distributed, small individual variations. Pearson, when he wrote up his statistical work a year later, argued more strongly that the situation indicated 'real evolution' taking place in the population, as one, presumably ancestral, trait distribution was seen to be splitting up into two, although the data could also be interpreted as simply an admixture of two types in that location. Nevertheless, the holy grail of catching Darwinian evolution in the act, and explaining it through natural selection, was almost within grasp!

In the same paper of 1893, Weldon laid out his approach to what he believed to be the central issue in evolution – the empirical observation of selection. He wrote, in a passage that pretty much constituted the foundational statement of the biometricians' approach: "It cannot be too strongly urged that the problem of animal evolution is essentially a statistical problem: that before we can properly estimate the changes at present going on in a race or species we must know accurately (a) the percentage of animals which exhibit a given amount of abnormality with regard to a particular character; (b) the degree of abnormality of other organs which accompanies a given abnormality of one; (c) the difference between the death rate percent in animals of different degrees of abnormality with respect to any organ; (d) the abnormality of offspring in terms of the abnormality of parents, and *vice versa*. These are all questions of arithmetic; and when we know the numerical answers to these questions for a number of species we shall know the direction and the rate of change in these species at the present day – a knowledge which is the only legiti-

Weldon was able to show evidence for selective mortality of individuals that deviated from the mean trait value, with mortality increasing exponentially with departures from the mean, essentially an example of what we call stabilizing selection.

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mate basis for speculations as to their past history and future fate" (*Proc. R. Soc. Lond.*, Vol.54, pp.318–329, 1893). The hereditary theories of the biometricians may well have been buried under the triumphs of modern genetics in its formal, cytological, physiological and, eventually, molecular avatars, but this statement of Weldon's still accurately and succinctly describes how all of us study natural selection in action!

Following the first crab study, Weldon was keen to use the technique of dissecting non-normal distributions to catch selection in action in other species. To this end, he did a similar, much larger, study on herrings. This study, however, did not yield clean results and the skewed distribution of the herring populations resisted all attempts at decomposition into two or more normal distributions. This, in part, led Weldon to adopt an even more direct strategy to examine natural selection in wild populations. In 1895, he published another study on *C. moenas* that tried to link variations in the frontal breadth of the carapace, the trait that the earlier study indicated might be evolving in the dimorphic Naples population, to differential mortality. He studied the Plymouth population of *C. moenas*, and examined the distribution of this trait in about 8000 crabs from 36 different age-classes, inferred by size. In very young crabs, the distribution was relatively narrow, then increased substantially in variance and, finally, narrowed again in adult crabs. Weldon argued that non-selective mortality that was not due to variation in frontal breadth would not change the variance of the trait distribution, but merely reduce the area under the curve. On the other hand, if mortality was associated with frontal breadth (i.e., the selection was acting on the trait), the variance of the trait distribution would reduce with age. Weldon was able to show evidence for selective mortality of individuals that deviated from the mean trait value, with mortality increasing exponentially with departures from the mean, essentially an example of what we call stabilizing selection. This was a huge moment in the history of evolutionary biology as it pertained to empirically nailing down an example of natural selection in action in the wild. Weldon wrote, in summation, "By purely statistical methods, with-

out making any assumption as to the functional importance of frontal breadth, the time of life at which natural selection must be assumed to act, if it acts at all, has been determined, and the selective death-rate has been exhibited as a function of the abnormality" (*Proc. R. Soc. Lond.*, Vol.57, pp.360–379, 1895). A very similar later study by Weldon on the gastropod *C. laminata*, published in 1901, also provided clear evidence for stabilizing selection, in this case on the radius of the peripheral spiral of the animal's shell.

Weldon followed up this demonstration of stabilizing selection with another study on *C. moenas* in 1898. In this paper, he analyzed data on the frontal breadth of adult crabs from the Plymouth population collected during 1893–1898. He observed that in crabs of any age-class, collected at similar seasons in different years, average frontal breadth seemed to have monotonically decreased over those five years – an observation clearly suggesting the possibility of directional selection for reduced frontal breadth. This time, instead of a purely statistical approach, Weldon adopted an even more direct experimental strategy by seeking to identify an ecological cause for greater mortality in crabs with greater frontal breadth. He noted that the recent construction of a large dyke that partly closed off Plymouth Bay, and greater sewage flow into the bay due to an increasing human population, had led to an increase over the study years of suspended clayey particles in the waters of the bay. Also, during these study years, some invertebrate species had disappeared from the coastal waters of Plymouth Bay altogether. These observations led Weldon to speculate that the increased muddiness and pollution of the water might be what was causing selective mortality of larger crabs. He tested this hypothesis by keeping large numbers of crabs in a tank with seawater containing considerable suspended fine clay particles. The experiment was replicated multiple times, including with mud from the actual bay instead of clay. Over time, in all runs of the experiment, many of the crabs died, and Weldon compared the distributions of frontal breadth in those that died with the distributions in the survivors. He found that mean

These studies of Weldon on shore crabs remain exemplars of how to study natural selection empirically, and seamlessly weld together formal statistical, ecological, experimental and functional approaches in a manner not bettered in the more than a century that separates us from him.

frontal breadth in the survivors was invariably less than that in the crabs that died. Weldon then followed up with another experiment in which crabs were reared in seawater free of suspended particles. In these crabs, mean frontal breadth indeed turned out to be greater than that in wild caught crabs of the same age from the waters of the bay. Weldon wrote, "I see no shadow of reason for refusing to believe that the action of mud upon the beach is the same as that in an experimental aquarium; and if we believe this, I see no escape from the conclusion that we have here a case of Natural Selection acting with great rapidity because of the rapidity with which the conditions of life are changing" (*Report of the British Association for the Advancement of Science*, pp.887–902, 1898). If this were not enough, Weldon also moved from identifying the ecological factor mediating selection on frontal breadth towards a functional explanation. In the same paper, he observed that "The gills of a crab which has died during an experiment with china clay are covered with fine white mud, which is not found in the gills of the survivors. In at least ninety percent. of the cases this difference is very striking, and the same difference is found between the dead and the survivors in experiments with mud". It appeared, thus, that the rapid changes in the levels of suspended particulate matter in the waters of the bay resulted in larger crabs being more susceptible to getting their gills clogged with clay and therefore suffering higher mortality than smaller ones. These studies of Weldon on shore crabs remain exemplars of how to study natural selection empirically, and seamlessly weld together formal statistical, ecological, experimental, and functional approaches in a manner not bettered in the more than a century that separates us from him.

Concluding Note

In writing this article, I have leaned heavily on four of the five books mentioned in the Suggested Readings. The reprint of Pearson's obituary memoir is useful for a detailed personal and professional appreciation of Weldon, the man and scientist, by one who knew him the best. The other four books deal in some depth

and detail with the historical development of evolutionary and genetic thinking, albeit with different focuses and perspectives. Amundson's book deals with the rich roots of much of evolutionary thought in systematics and embryology, especially in the 18th and 19th centuries. His perspective is that of today's evolutionary developmental biologists who believe that the black-boxing of development in the Neo-Darwinian Synthesis left out many important dimensions of the evolutionary process, especially those pertaining to the gross evolutionary changes in organismal form. Gayon's book is a magisterial treatment of the historical development of the concept of natural selection from Darwin to the Neo-Darwinian synthesis, especially in the face of the challenge posed by the widespread belief that heredity would swamp out the effects of selection, a point of view that persisted for almost 60–70 years after Darwin's *Origin*. Henig's book is more closely focused on understanding Mendel's work in its proper historical and conceptual context, whereas the book by Schwartz is a very readable account of the history of thinking about heredity from Darwin till the nailing down of DNA as the hereditary material in the mid-20th century. Together, these books emphasize how the historical development of fields of study is not linear, the way it is often presented in textbooks. There are digressions, dead-ends, wrong paths, and circuitous paths that meander and then, almost miraculously, come back to the main trail. Thus, the history of any set of ideas is as much a bushy rather than a ladder-like structure as the so-called 'tree of life' is. What I find most impressive, in fact awe-inspiring, is how these scientists in decades past, were not afraid to be spectacularly wrong when they made their great leaps of imagination. Trying hard to make sense out of what were then deeply mysterious phenomena, they came up with dazzlingly imaginative hypotheses and often developed equally amazing methodological and conceptual tools to test them. That level of imagination and creativity is much rarer in biology today.

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Suggested Reading

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[3] R M Henig, *The Monk in the Garden: The Lost and Found Genius of Gregor Mendel, the Father of Genetics*, Houghton Miflin Co., New York, USA, 2000.

[4] K Pearson, *Walter Frank Raphael Weldon: A Memoir* Reprinted from *Biometrika* (1906), Cambridge Univ. Press, Cambridge, UK, 2011.

[5] J Schwartz, *In Pursuit of the Gene: From Darwin to DNA*, Harvard Univ. Press, Cambridge MA, USA, 2008.