

1 The Modern Synthesis: a Neo-Darwinian, Genotypic View of Heredity and Evolution

Since around the turn of the century, the idea that mainstream evolutionary theory needs substantial revision has been the subject of vigorous and sometimes vitriolic debate. Some evolutionary biologists maintain that any attempt to radically revise the present view is not only unnecessary and misguided but also dangerous. Any questioning of evolutionary ideas plays into the hands of creationists, they claim.

We are among those who believe that a change in the way we think about evolution is overdue, and in this Element we look at the debate from the perspective of heredity. We argue that what has been learned about genetic, epigenetic, behavioural and symbolic systems of inheritance in the past 50 years requires a substantial revision and extension of the mid-twentieth-century, gene-based ‘Modern Synthesis’ (MS) version of evolutionary theory. We need to return to an earlier, development- and organism-oriented view. As Lenin said, the evolution of a science is ‘a development that repeats, as it were, the stages already passed, but repeats them in a different way, on a higher plane . . . a development, so to speak, in spirals, not in a straight line’ (1914/1930, p. 14). We see the version of evolutionary theory that is being advocated today, commonly called the ‘Extended Evolutionary Synthesis’ (EES), as an updated version of the early twentieth-century organicists’ evolutionary view on a higher plane, growing from, yet also challenging, the Modern Synthesis.

We start here with a historical overview, outlining the origins of the MS and the nature of the challenge to it. In Section 2 we describe the different types of heritable variations that are interacting inputs into the development of phenotypes. Our emphasis will be on epigenetic inheritance, which is found in all forms of life and is the molecular basis of non-genetic inheritance. The evolutionary implications of multiple inheritance systems are discussed in Section 3, and in the final section we explore the implications of this expanded view of heredity and evolution for the philosophy and sociology of biology.

1.1 The Modern Synthesis

In 1942, in the middle of World War II, a book with the title *Evolution, the Modern Synthesis* was published in London. Its author was Julian Huxley. Like his grandfather, the ardent Darwinian Thomas Henry Huxley, Julian Huxley was a zoologist, and as a young man published scholarly work on bird behaviour, experimental embryology and evolution, but he was also a gifted popularizer of science. Through books and articles, broadcasts and films, he introduced lay people to the excitement of the new ideas that were emerging

in biology. One of his most successful projects was *The Science of Life*, a three-volume book that was originally issued in fortnightly parts. This popular work, completed in 1930, was co-authored by the novelist and essayist H. G. Wells and his zoologist son G. P. Wells. It presented a unified view of biology, with evolution as a central theme. Huxley's 1942 book, *Evolution, the Modern Synthesis*, aimed mainly at professional biologists, gave a more focused and academic state-of-the-art account of evolutionary ideas. The title was appropriate – it was modern, and it was a synthesis.

Today, probably very few biologists will have read any of Julian Huxley's writings, but all are familiar with the expression 'the Modern Synthesis' (which we refer to as the MS). This phrase, along with the variants 'the evolutionary synthesis' and 'the synthetic theory of evolution', has entered the lexicon of biology as a summary-term for a view of evolution that was developed in the second quarter of the twentieth century. It had its roots in books written by geneticist Theodosius Dobzhansky, zoologist Ernst Mayr, palaeontologist George Gaylord Simpson and botanist G. Ledyard Stebbins, as well as Julian Huxley and a few other authors. These books, published between 1937 and 1950, vary in the emphasis they put on different aspects of biology, but all acknowledged the significance of the belated marriage of Darwin's theory of natural selection and Mendelian genetics (reviewed in Bowler, 2003; Smocovitis, 1996).

In the late nineteenth and early twentieth centuries, the popularity of Darwin's theory of gradual adaptive evolution through natural selection slumped, but it was revived during the 1920s and 1930s through the work of the population geneticists Ronald Fisher and J. B. S. Haldane in Great Britain and Sewall Wright in the USA (Provine, 2001). They showed mathematically how genetic differences among individuals in a population could lead to adaptation. There was general agreement that evolution usually involves a gradual, cumulative change in gene frequencies in populations, brought about by selection acting on the variation among individuals that results from random gene mutation and recombination. This became the orthodox 'Modern Synthesis' view that dominated evolutionary thinking for most of the rest of the century, a view that hardened as the century progressed.

Not only could gradual selection acting on the abundant variation produced by small random mutations explain adaptedness within populations (microevolution), but the same process could explain the origin, multiplication and diversification of species and higher taxonomic categories (macroevolution). Mayr, in particular, maintained that macroevolution usually occurred through the gradual genetic restructuring of populations during long periods in which

they are biologically (reproductively) isolated from other populations. His summary of the origins and major assumptions of the MS view was:

It was in these years [1936–1947] that biologists of the most diverse subdivisions of evolutionary biology and from various countries accepted two major conclusions: (1) that evolution is gradual, being explicatory in terms of small genetic changes and recombination and in terms of the ordering of this genetic variation by natural selection; and (2) that by introducing the population concept, by considering species as reproductively isolated aggregates of populations, and by analyzing the effect of ecological factors (niche occupation, competition, adaptive radiation) on diversity and on the origin of higher taxa, one can explain all evolutionary phenomena in a manner that is consistent both with the known genetic mechanisms and with the observational evidence of the naturalists. Julian Huxley (1942) designated the achievement of consensus on these points as *the evolutionary synthesis*. It required that the naturalists abandon their belief in soft inheritance¹ and that the experimentalists give up typological thinking and be willing to incorporate the origin of diversity in their research program. It led to a decline of the concept of ‘mutation pressure,’ and its replacement by a heightened confidence in the powers of natural selection, combined with a new realization of the immensity of genetic variation in natural populations. (Mayr, 1982, p. 567, his italics)

Heredity was thus clearly identified with genetics. Dobzhansky, another of the founding fathers of the MS, defined biological heredity not only in terms of genes but in terms of self-serving genes:

Heredity is, in the last analysis, self-reproduction. The units of heredity, and hence of self-reproduction, are corpuscles of macromolecular dimensions, called genes. The chief, if not the only, function of every gene is to build a copy of itself out of the food materials; the organism, in a sense, is a by-product of this process of gene self-synthesis. (Dobzhansky, 1958, p. 21).

1.2 The MS Notion of Heredity

The development of the genocentric notion of heredity, which in the 1970s became integral to Dawkins’ ‘selfish gene’ view of evolution, was strongly influenced by August Weismann’s neo-Darwinian synthesis and Wilhelm Johannsen’s genotype–phenotype distinction. Weismann (1889) combined Darwin’s view of evolution with his own highly speculative theory of heredity

¹ Soft inheritance was the term Mayr used ‘to designate the belief in a gradual change of the genetic material itself, either by use and disuse, or by some internal progressive tendencies, or through the direct effect of the environment. . . . All theories of soft inheritance deny the complete constancy of the genetic material that we now know to exist’ (Mayr, 1980, p. 15). For a brief history of attitudes to soft inheritance, see Jablonka and Lamb (2011).

and development, which involved sets of hierarchically organized hereditary units located in the chromosomes of cell nuclei. According to Weismann, the architectural organization of the units meant that when somatic cells divide, two daughter cells can inherit different sets of units; during development and differentiation, this organization also causes units to move out of the nucleus and take control of the cell's activities. Consequently, during cell division and differentiation, somatic cell nuclei progressively lose hereditary units and their capacity to form all parts of the body. Only germplasm, found mainly in the germline cells that give rise to gametes, retains complete sets of hereditary units. Therefore, any induced or acquired changes that occur in somatic cells during the developmental history of individuals cannot be passed to future generations. This belief became known as 'Weismann's doctrine of the independence and continuity of the germplasm'. 'Weismann's barrier' explained why the inheritance of acquired characters (inappropriately known as 'Lamarckism') is impossible.²

Weismann's view of evolution, with its extreme selectionism and rejection of Lamarckism, was soon dubbed 'ultra-Darwinism' or 'neo-Darwinism' to distinguish it from Darwin's more pluralistic approach. It was widely discussed, but growing knowledge about the behaviour of cells and chromosomes, and the emphasis on experimentation, particularly after the recognition in 1900 of the significance of Mendel's work, led to the rejection of many of Weismann's ideas. His doctrine of the continuity of the germline survived, however.

Wilhelm Johannsen, a Danish botanist, was a critic of the 'morphologico-phantastical speculations of the Weismann school' (1911, p. 133). His work on 'pure lines' – populations of beans and other self-fertilizing plants in which all individuals are descendants of a single parent – led Johannsen to what he called the 'genotype conception of heredity'. Pure lines do not respond to selection, he reasoned, because all individuals are 'genotypically' identical; their 'phenotypes' – their outward appearances – differ, but these differences are the result of environmental effects that are not inherited. Any new selectable variations appearing in pure lines are the outcome of alterations in the constituents of the genotype – of mutations induced by changes in conditions.

Unlike Weismann, Johannsen was unwilling to speculate about the material basis of heredity. In order to distance himself from the mechanistic and deterministic entities that Weismann and others had suggested, he called his abstract

² The inheritance of acquired characters was an almost universal belief among natural philosophers until the late nineteenth century, and was not specific to Lamarck. Weismann's view of the inheritance of acquired characters was more nuanced than is usually assumed. He accepted that the environment could act directly on hereditary elements in the germ cells and that selection within these cells plays a significant role in evolution (Weissman, 2011).

elements ‘genes’. He then defined a genotype as ‘the sum total of all the “genes” in a gamete or in a zygote’ (Johannsen, 1911, pp. 132–3) and concluded: ‘Heredity may then be defined as *the presence of identical genes in ancestors and descendants*’ (p. 159, his italics). Like Weismann, Johannsen concluded that there is a one-way route between an organism’s hereditary endowment and its physical characteristics. Acquired characters cannot be inherited, because there is no mechanism through which developmental modifications can be transmitted to future generations. This was a belief that helped shape the genetic view of heredity that was soon to be incorporated into the MS.

As Mendelian genetics came to dominate thinking about heredity, the meaning of Johannsen’s terms shifted. ‘Genes’ were increasingly thought of as real physical particles located on chromosomes rather than as abstract entities. The meaning of the terms ‘phenotype’ and ‘genotype’ also changed, as increasingly they were applied to a single character and the pair of genes (alleles) associated with it as well as the total genetic constitution and appearance. ‘Mutation’ came to be used for random changes in the material make-up of a gene and for the processes bringing about such changes.

Because they usually studied the inheritance of distinct, alternative, discontinuous characters, many of the early Mendelians thought that evolution occurred in mutational leaps. Other biologists, particularly the naturalists, defended Darwin’s gradualism, insisting that the large differences the Mendelians studied were of little significance in evolution. However, by the 1930s, mutation theories had faded in importance for all but a few diehards like German-American geneticist Richard Goldschmidt, who insisted that ‘systemic’ mutations, which involved a repatterning of the genome, as well as occasional regulatory mutations with large effects, were behind many macro-evolutionary changes. For the quantitative and population geneticists whose mathematical analyses contributed so much to the MS, mutations were the small, rare and random changes in genes that produced new alleles. Evolutionary change had more to do with selection, population size, the system of mating, migration and gene interactions than with rare mutations.

1.3 The MS as a Unifier of Biology

The MS was seen by some of its architects as far more than an updated, Mendelized and mathematized version of neo-Darwinism. This is clear from the title of a book edited by Mayr and Provine (1980), *The Evolutionary Synthesis: Perspectives on the Unification of Biology*, which was based on a conference held in 1974 to discuss the construction of the evolutionary synthesis. As Smocovitis (1996) noted, this title reflects the ambition of the

MS to unify the many branches of biology within a coherent, truly scientific, theoretical framework. Smocovitis suggests that this ambition was comparable to that of the logical positivists of the Vienna Circle, who during the first third of the twentieth century pursued the Enlightenment ideal of unifying all science on the basis of physics. However, evolutionary biologists were not fully satisfied with this. Early twentieth-century philosopher–biologists such as J. S. Haldane (father of geneticist J. B. S. Haldane) and Joseph Henry Woodger also asserted the autonomy of biology. Though based on physics, biology cannot be reduced to physics. It was through evolutionary biology, Huxley, Mayr and others claimed, that the different branches of biology could be unified as an autonomous science.

The MS has always been more of an interpretative framework than a well-defined theory. It has been variously described as ‘a harmonization of ideas’, ‘a coherent set of beliefs’, ‘a disciplinary matrix’ and ‘a treaty’. But however it is described and whatever its aims, population genetics has always been at its core. By building on the concepts of population and quantitative genetics, biologists coming from systematics, biogeography, palaeontology, comparative anatomy and ecology could interpret their findings within a neo-Darwinian framework. Laboratory experiments and studies of natural populations of fruitflies, snails, moths and butterflies confirmed (more or less) some of the predictions of the geneticists’ models. Moreover, as genetics became more molecular, the flexibility of the MS framework allowed it to be updated. Genes were identified with sequences of DNA; heredity was seen in terms of the replication of DNA sequences; mutations were the outcome of unrepaired damage to DNA or errors occurring during its replication; and development could be described in terms of gene expression and its regulation. According to Crick’s ‘central dogma’, information in DNA sequences is transcribed into RNA, and RNA is translated into proteins, but it cannot flow in the opposite direction from protein to RNA or DNA. The central dogma was seen as a molecular version of Weismann’s doctrine and Johannsen’s genotype–phenotype distinction – information flows from germline to soma, genotype to phenotype, or DNA to protein, but never in the opposite direction. Consequently, the inheritance of acquired characters is impossible. According to John Maynard Smith, a leading British evolutionary biologist, ‘The greatest virtue of the central dogma is that it makes it clear what a Lamarckist must do – he must disprove the dogma’ (Maynard Smith, 1966, p. 66). Of course, this would be the case only if DNA could not be directly changed by environmental inputs, and if other inheritance systems, which can transmit developmentally induced variations that are independent of variations in DNA, did not exist. Both of these assumptions can be challenged (see Sections 1.4 and 2).

Today's defenders of the MS constantly claim that new observations and ideas about evolution do not require a change in the fundamental assumptions of the MS. It has been able to absorb the discovery that there is far more DNA variation than had been expected; that many alleles seem to be neutral; and that some DNA seems to be parasitic. By incorporating the notions of kin selection and inclusive fitness, an explanation was provided for aspects of behaviour, such as altruism and cooperation, that had at first been difficult to explain within the MS framework. When Gould and others argued that because the palaeontological record of some groups showed long periods of stasis punctuated by periods of rapid evolution and divergence, something other than gradual adaptive change was occurring, MS adherents responded by saying that no Goldschmidtian systemic mutations or any other special macroevolutionary processes need be invoked. Immense periods of time are involved, they argued, even in periods of rapid change, and most change probably occurred in small populations that were unlikely to have left traces in the fossil record. Genes, gradual selection and random variation can explain everything, they continue to insist. Consequently, current textbooks of evolutionary biology use the same framework as that constructed in the 1930s and 1940s.³ Population geneticists such as Brian Charlesworth and his colleagues, some of today's standard-bearers for the MS view of evolution, use a definition that is almost identical to that given by Dobzhansky 50 years ago:

The core tenet of the MS is that adaptive evolution is due to natural selection acting on heritable variability that originates through accidental changes in the genetic material. Such mutations are random in the sense that they arise without reference to their advantages or disadvantages Because this viewpoint asserts that natural selection acts to increase the frequencies of advantageous variants within populations, it is often referred to as neo-Darwinism. (Charlesworth, Barton and Charlesworth, 2017, p. 1).

1.4 What the MS Excluded

The problem with the MS, particularly after it hardened in the 1960s and 1970s, is that it ruled out or marginalized certain views of heredity and evolution. Mayr was very explicit about which ideas were excluded, or, as he put it, 'misconceptions' that were 'refuted':

³ A comparison of 10 current textbooks of evolutionary biology has shown that only gene selection, genetic drift, gene flow and gene mutation are seen as major evolutionary processes. Inclusive inheritance, plasticity and niche construction are either totally ignored or get only modest treatment (Laland et al., 2015).

In the short run, it was perhaps the refutation of a number of misconceptions that had the greatest impact on evolutionary biology. This includes soft inheritance, saltationism, evolutionary essentialism, and autogenetic theories. The synthesis emphatically confirmed the overwhelming importance of natural selection, of gradualism, of the dual nature of evolution (adaptation and diversification), of the populational structure of species, of the evolutionary role of species, and of hard inheritance. (Mayr, 1982, p. 570)

Mayr and the other subscribers to the MS thus excluded from it certain theories (Lamarckism, orthogenesis), outlooks (essentialism) and mechanisms (soft inheritance). There was no room in the MS for any non-gradual, goal-directed or internally driven processes, and no room for the inheritance of acquired characters or any other type of ‘soft inheritance’. Darwinism was redefined: ‘The term “Darwinism” in the following discussions refers to the theory that selection is the only direction-giving factor in evolution’ (Mayr, 1980, p. 3). This was certainly not Darwin’s Darwinism – it was a version of neo-Darwinism, but labelling this view as ‘Darwinism’ undoubtedly endowed it with more authority.

The MS view of non-human evolution recognizes only the genetic inheritance system. It is assumed that the only mechanisms underlying the patterns and outcomes of evolution that are studied in disciplines such as embryology, systematics and palaeontology are those that lead to changes in gene frequencies in populations. Although the views held by the early promoters of the MS were complex and changed with time,⁴ a genic perspective, a commitment to hard inheritance, and a bottom-up evolutionary population genetic analysis were common to them all and persist today. This is the basis of what we see as the major positive (roman) and negative (italicized) overlapping assumptions of the MS (based on Jablonka and Lamb, 2010):

1. Heredity occurs through the transmission of germline genes, and hereditary variation is caused by variation in DNA base sequence. *There are no inherited non-DNA variations that cannot be explained in terms of DNA variations. The genetic–DNA system is the only source of heritable variation.*
2. New hereditary variation is the consequence of (i) the recombination of pre-existing alleles that are generated during sexual processes and (ii) mutations – the result of accidental changes in DNA. *Hereditary variation is not affected by the developmental history of the individual. There is no soft inheritance.*

⁴ For discussions of differences and changes in evolutionary thinking in the twentieth century, see Jablonka and Lamb, 2011; Lamb, 2011; Mayr and Provine, 1980.

3. The ultimate unit of selection is the gene. Although genes interact, and the interactions are often non-linear, the additive fitness-effects of single genes drive evolution by natural selection. *The phenotype generated by a genetic–developmental network is not heritable and cannot be a unit of evolution.*
4. Developmental canalization and plasticity are products of evolution and affect evolutionary change only by constraining the range of variation on which selection can act. *Developmental plasticity does not drive coordinated developmental changes that can guide adaptive evolution, speciation, evolutionary trends and evolutionary rates.*
5. Evolution is typically gradual, because only variations with small effects are likely to be beneficial. *Variations with large effects are almost always lethal.*
6. Large-scale evolutionary innovations that involve coordination among parts and processes are the results of the accumulation of gene mutations with small effects. *Fundamental physico-chemical processes and processes of developmental accommodation are not a primary generative cause of morphological and physiological innovations. They are merely boundary conditions.*
7. Macroevolution is the outcome of cumulative microevolution. *With few exceptions, macroevolution does not require any extra factors beyond those operating during microevolution.*
8. Conspecifics in groups interact and may coevolve with each other, with their symbionts and parasites, and with their abiotic environment. *The evolutionary effects of transferred ecological legacies that result from these interactions are relatively unimportant.*
9. The individual is a major target of selection. *Somatic selection within the individual, selection among groups, lineage selection, species selection and different forms of community selection occur but are not of major importance.*
10. Evolutionary change occurs mainly during vertical descent from a single common ancestor. *Forms of genetic exchange and sharing such as gene transfer and hybridization have minor significance; they do not alter the basic branching structure of phylogenetic divergence.*

We have no argument with the MS's positive assumptions, but we reject the negative (italicized) ones. For example, we agree that heritable variation, especially at the molecular level, is often blind to function; what we reject is the assumption that there are no developmentally acquired heritable variations (not necessarily genotypic). Similarly, although heritable variations can have

small effects, not infrequently they have very large effects, which can be the basis of saltationary macroevolutionary changes.

1.5 Marginalized Ideas: Waddington's Developmental–Evolutionary Synthesis

One topic that is generally acknowledged not to have been integrated into the MS is developmental biology. This is usually said to be the result of the lack of an adequate theoretical framework and of any empirical evidence that it is important. Yet, in fact, both theory and empirical evidence were in place during the consolidation period of the MS between the 1950s and the 1980s. In the USSR a synthesis between heredity, development and ecology had been made by Ivan Schmalhausen in the late 1930s, but apart from a 1949 translation of one of his books (which was edited by Dobzhansky), it was largely unknown in the West. In Britain, beginning in the early 1940s, Conrad Hal Waddington forged a wide-ranging development-oriented evolutionary synthesis, which, although accessible to evolutionary biologists and initially discussed favourably in Britain, had little impact in the USA, where the MS was hardening. With the rise of molecular biology in the 1960s and 1970s, it came to be seen as out of date, and generated little interest until the last decade of the century. Today, developmental–evolutionary ideas of the type that Waddington put forward are at the core of the EES.

Waddington was an embryologist who turned to genetics to help him solve developmental and evolutionary problems. He began working as a biologist in the 1930s and was strongly influenced by Whitehead's process philosophy and by a group of Cambridge biologists and philosophers who formed the Theoretical Biology Club. The group's 'Biotheoretical Gatherings' took place from 1932 until the outbreak of World War II. One of their main concerns was with the still ongoing arguments between the vitalists and the mechanists, and they attempted to reframe the holistic attitude of the vitalists in materialistic, non-metaphysical terms. They adopted what they called a 'third way', an approach discussed earlier by J. S. Haldane, Lancelot Hogben and others who focused on the dynamic organization and order of living organisms in space and time, and on emergent properties that arise through interactions among parts, with parts determining wholes and wholes determining parts. Process, wholeness, integration and networks of interactions were central to this view (Peterson, 2016).

Waddington developed his biological outlook within this framework. From the 1930s onwards, he was actively experimenting in and theorizing about embryology, genetics and evolution. He worked in Hans Spemann's embryology lab on