Opinion

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Rethinking heredity, again

R. Bonduriansky

Evolution and Ecology Research Centre and School of Biological, Earth and Environmental Sciences, University of New South Wales, Sydney, NSW, Australia

The refutation of 'soft' inheritance and establishment of Mendelian genetics as the exclusive model of heredity is widely portrayed as an iconic success story of scientific progress. Yet, we are witnessing a re-emergence of debate on the role of soft inheritance in heredity and evolution. I argue that this reversal reflects not only the weight of new evidence but also an important conceptual change. I show that the concept of soft inheritance rejected by 20th-century genetics differs fundamentally from the current concept of 'nongenetic inheritance'. Moreover, whereas it has long been assumed that heredity is mediated by a single, universal mechanism, a pluralistic model of heredity is now emerging, based on a recognition of multiple, parallel mechanisms of inheritance.

A scientific revolution undone?

A fundamental assumption of classical Mendelian genetics and the evolutionary Modern Synthesis is that heredity is 'hard' – that is, mediated by the transmission of gene alleles that are impervious to environmental influence. By the standard historical narrative, the exclusive validity of the Mendelian model of heredity was established through the culmination of a lengthy scientific debate [1–3]. According to Mayr's authoritative history [3], the possibility of 'soft' or 'Lamarckian' inheritance, whereby traits acquired during an individual's lifetime could be passed on to its offspring, had been firmly refuted by the 1930s, and the discovery of the structure of DNA in 1953 was its 'death knell'. This narrative is repeated in most contemporary evolutionary biology textbooks (Box 1). The triumph of hard, Mendelian heredity has all the hallmarks of a scientific revolution [4].

However, the empirical evidence now points to the existence of a variety of inheritance mechanisms (collectively called 'nongenetic inheritance') that operate alongside Mendelian inheritance and allow for the inheritance of acquired traits (see Glossary), and a number of authors are calling for the Mendelian model of heredity to be extended to incorporate these phenomena [5–10]. How can the current challenge to the established model of heredity be reconciled with the unequivocal rejection of soft inheritance by 20th-century genetics?

In this paper, I trace changes over the past century in the core issues at stake in the inheritance debate – the politically charged scientific controversy over the nature of heredity – and show that the concept of soft inheritance that was rejected by 20th-century genetics differs fundamentally from the one at the center of current debate. Although the empirical evidence was equivocal [1,2,11], soft inheritance was rejected by influential geneticists as a corollary of a new, narrowed concept of heredity that emerged by the second decade of the 20th century – a concept that is now being challenged on both conceptual and empirical grounds [6]. This conceptual shift means that the conventional narrative of the inheritance debate is a misleading guide to current developments in the study of heredity. I sketch out the nature of the emerging 'pluralistic' model of heredity [7–10,12], which recognizes the diversity of inheritance mechanisms.

Glossary

Acquired trait: a phenotypic character (trait) induced by the environment or arising spontaneously during an individual's lifetime.
Behavioral/cultural inheritance: the transmission from parents to offspring of variation in behavior or culture via imitation or learning by offspring (and, in some cases, teaching by parents).
Biased mutation: mutation that is non-random in that particular environmental factors tend to induce particular changes in the DNA sequence.
Environmental inheritance: the transmission from parents to offspring of variation in the ambient environment, such as a tendency to encounter particular chemicals or micro-organisms, or a tendency to develop at a particular range of temperatures.
Genetic encoding: the term used here to denote a hypothesized process whereby an acquired trait is 'encoded' in the germ-line DNA sequence, thereby giving rise to a new, transmissible gene allele. The term 'somatic induction' is sometimes used to denote a similar process.
Hard heredity: a model of heredity based on the transmission from parents to offspring, at conception, of a set of factors whose nature is unaffected by the environment or phenotype of the parents.
Heredity: the tendency for offspring to be influenced by and to resemble their parents and for biological characters (traits) to 'run in families'. Heredity is mediated by one or more mechanisms of inheritance.
Inheritance: the process or mechanism mediating the passing of influences and characters (traits) from parents to offspring (i.e. heredity).
Mendelian/genetic inheritance: the transmission from parents to offspring, at conception, of factors (gene alleles) that are not subject to modification by the parental environment or soma, and that segregate in accordance with the Mendelian model.
Niche construction: the process whereby organisms modify their environment and thus alter patterns of natural selection (i.e. the ecological niche) – a feedback process between organisms and their environment that can influence evolution.
Nongenetic inheritance: inheritance mediated by the transmission to offspring of elements of the parental phenotype or environment, such as glandular secretions, nutrients, components of the gametes, epigenetic marks, or behavioral variation, but excluding DNA sequences (gene alleles).
Soft/Lamarckian heredity: a model of heredity based on the transmission from parents to offspring of factors whose nature can be influenced by the environment or phenotype of the parents. Note that the term 'Lamarckian' can also refer to J-B. Lamarck's theory of evolution, but is not used here in this sense.
Somatic inheritance: the transmission from parents to offspring of variation in phenotypic traits via the transfer of elements of the parental soma (e.g. glandular secretions) to the offspring.
Transgenerational epigenetic inheritance: the transmission from parents to offspring of variation in phenotypic traits via the transfer of variations in DNA-methylation patterns or chromatin structure, which affect patterns of gene-expression in the offspring.

Corresponding author: Bonduriansky, R. (r.bonduriansky@unsw.edu.au).

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Box 1. Soft inheritance in evolutionary biology textbooks

Evolutionary biology textbooks typically present soft inheritance as an antiquated and refuted idea. One of the few texts to treat the subject in a more nuanced way is Futuyma's *Evolution* [69]. Representative quotations from major contemporary texts are given below (Landman [2] documents similar statements in older texts).

Futuyma 1986 [70]	"...the theory of the inheritance of acquired characteristics...is contradicted by fact."
Ridley 1996 [71]	"...acquired characters are, as a matter of fact, not inherited."
Stearns and Hoekstra 1997 [72]	"...Lamarck [expressed the idea] that an adaptation acquired by an organism during its lifetime can be transmitted to its offspring. This would be the case, for example, if an animal could transmit to its offspring the immunity to a disease that it had developed through an immune response; but it cannot."
Freeman and Herron 2006 [73]	"...offspring do not inherit phenotypic changes acquired by their parents. If people build up muscles lifting weights, their offspring are not more powerful; if giraffes stretch their necks reaching for leaves in treetops, it has no consequence for the neck length of their offspring."
Barton *et al.* 2007 [74]	"...inherited characteristics cannot be influenced directly by the environment..."
Futuyma 2009 [69]	"There is no evidence yet that epigenetic variation contributes to evolutionary change, and considerable difference of opinion on whether or not it is likely to do so."

The refutation of soft inheritance

The hard/soft dichotomy

The roots of the scientific study of heredity, the attempt to understand why and how traits such as personality, facial features and certain diseases run in families, can be traced back to the 18th century [13]. Of the many competing ideas from this early period, two views of heredity – hard versus soft [14] – crystallized, by the late 19th century, into a dichotomy that has been at the center of the inheritance debate ever since (Box 2). Proponents of hard heredity believed that parents transmit a developmental blueprint (whose elements are impervious to environmental and somatic influences) to offspring at the moment of conception. Hard heredity triumphed during the 20th century in the guise of Mendelian genetics [3,14,15]. Proponents of soft heredity believed that parents transmit their features (i.e. phenotypic traits) to their offspring, including features acquired during their lifetime, and that transmission can occur not just at conception but also via subsequent interactions between parent and offspring [14–17].

Soft inheritance as 'genetic encoding'

Prior to the 20th century, heredity was typically conceptualized as the transmission of parental features or influences to offspring [15,17]. During the first decades of the 20th century however, influential proponents of hard heredity came to redefine heredity more narrowly as the transmission of genes or 'the presence of identical genes in ancestors and descendants'[18]. The gene, originally a purely theoretical entity, eventually acquired a material basis in the DNA molecule, and inheritance came to be understood as the transmission of germ-line DNA sequences (gene alleles) [9,15]. However, once this new definition of inheritance was accepted, it necessitated a change in how soft inheritance was conceptualized also. As their writings make clear, leading geneticists and evolutionary biologists assumed that, if heredity is mediated by the transmission of DNA sequences, then soft inheritance, if it exists, must also occur via this mechanism of transmission. In other words, it must be possible for the environment or soma to modify the germ-line DNA sequence so as to produce an inheritance of acquired traits – a mechanism that I will refer to as 'genetic encoding' (Box 3). As Huxley [19] stated, "...any Lamarckian theory whatsoever must come to terms with the facts concerning the physical basis of heredity." However, because no mechanism for genetic encoding was known or could be imagined, soft inheritance was deemed impossible. This idea was ultimately enshrined in the Central Dogma of molecular genetics, the exclusive one-way passage of information from DNA sequence to RNA to protein [20]. Consequently, the possibility that an individual's experiences during its lifetime could have predictable effects on the phenotype of its offspring was deemed to be conclusively refuted and research on such effects was increasingly relegated to the margins of respectable biology [1,2,11].

The (sole) physical basis of heredity

The idea that any form of inheritance, whether hard or soft, must occur via the transmission of DNA sequences also reflects the belief, held by influential Mendelian geneticists, that heredity is mediated by a single, universal mechanism [9]. On the basis of compelling empirical support for hard, Mendelian inheritance, as well as a lack of incontrovertible evidence of soft inheritance, many influential geneticists concluded not only that the transmission of DNA sequences was a mechanism of heredity, but also that it was the sole mechanism of heredity [21–24]. As early as 1919, Morgan titled his book on Mendelian genetics *The Physical Basis of Heredity* [23]. Subsequent authors typically followed suit, equating the Mendelian transmission of alleles with heredity [3,25]. The idea that multiple mechanisms of heredity could operate in parallel was, by the 1930s, a heterodox position within mainstream genetics [11].

Interestingly, some researchers have argued that inheritance via genetic encoding is indeed possible. According to E.J. Steele and coworkers, acquired somatic changes that are amplified by somatic selection (e.g. acquired immunity) can be encoded in the germ-line DNA through the agency of reverse transcriptase enzymes, which catalyze the synthesis of DNA from an RNA template [26,27]. This mechanism remains controversial [28]. As I explain below, however, the emerging pluralistic model of heredity is based on a very different concept.

Heredity reconsidered

Nongenetic inheritance

Over the past three decades, several research programs have explored various nongenetic mechanisms of inheritance

Box 2. The inheritance debate and the triumph of hard heredity

For centuries, it was widely assumed that an individual's actions and experiences could influence the body and mind of offspring [13,15,16,75]. The concept of heredity was not clearly differentiated from individual development until the second half of the 19th century, and belief in the inheritance of acquired traits simply reflected the idea that parents manufacture their offspring from parts of themselves, and must thereby transmit their bodily features to their offspring [15–17]. Belief in the inheritance of acquired traits eventually became associated with the name of Jean-Baptiste Lamarck, who based his theory of evolution on this idea [15].

However, Mameli [12] has argued that, since antiquity, it was also widely believed that parental influences on offspring are mediated by the transmission of a 'developmentally privileged material' at conception. In the second half of the 19th century, a number of authors began to promote the idea that offspring development is autonomously guided by a chemical blueprint transmitted at conception, and that this blueprint is largely impervious to environmental or somatic influences (hard) [15]. From the 1860s, Francis Galton, father of the eugenics movement, advocated a hard model of heredity based on evidence of the inheritance of achievement in British families [76,77]. Galton influenced August Weismann, who argued that heredity reflects the developmental effects of a 'germ-plasm' comprised of independently-segregating elements that are transmitted unaltered across generations, thereby precluding the inheritance of acquired traits [78]. Bowler [15] has argued that ideology and world view influenced the views of early researchers on the nature of heredity.

By the second decade of the 20th century, proponents of hard heredity incorporated Mendel's model of discrete hereditary units into their theory [15], the 'genotype' was distinguished from the 'phenotype' [18], and T.H. Morgan and others demonstrated Mendelian inheritance of mutations in *Drosophila* and other organisms [23,79]. Classical genetics was well established by the 1930s [15]. At the same time, evolutionary biologists reconciled Darwinian natural selection with the Mendelian model of heredity, resulting in the evolutionary Modern Synthesis [3]. By the middle of the 20th century, the physical vehicle of Mendelian inheritance was definitively established as the DNA molecule [20].

Alongside these developments (Figure I), the study of soft inheritance was increasingly marginalized [6], although it continued to play a prominent role well into the 20th century outside the English-speaking world [11]. The decline of soft inheritance was also spurred by a reaction in the West to developments in the USSR under Stalin, where a pseudoscientific view of heredity based on soft inheritance (promulgated by agronomist T.D. Lysenko) became state-sponsored dogma, and Mendelian geneticists were persecuted [19,80]. For further discussion of reasons for the exclusion of soft inheritance from the Modern Synthesis, see [81–83].

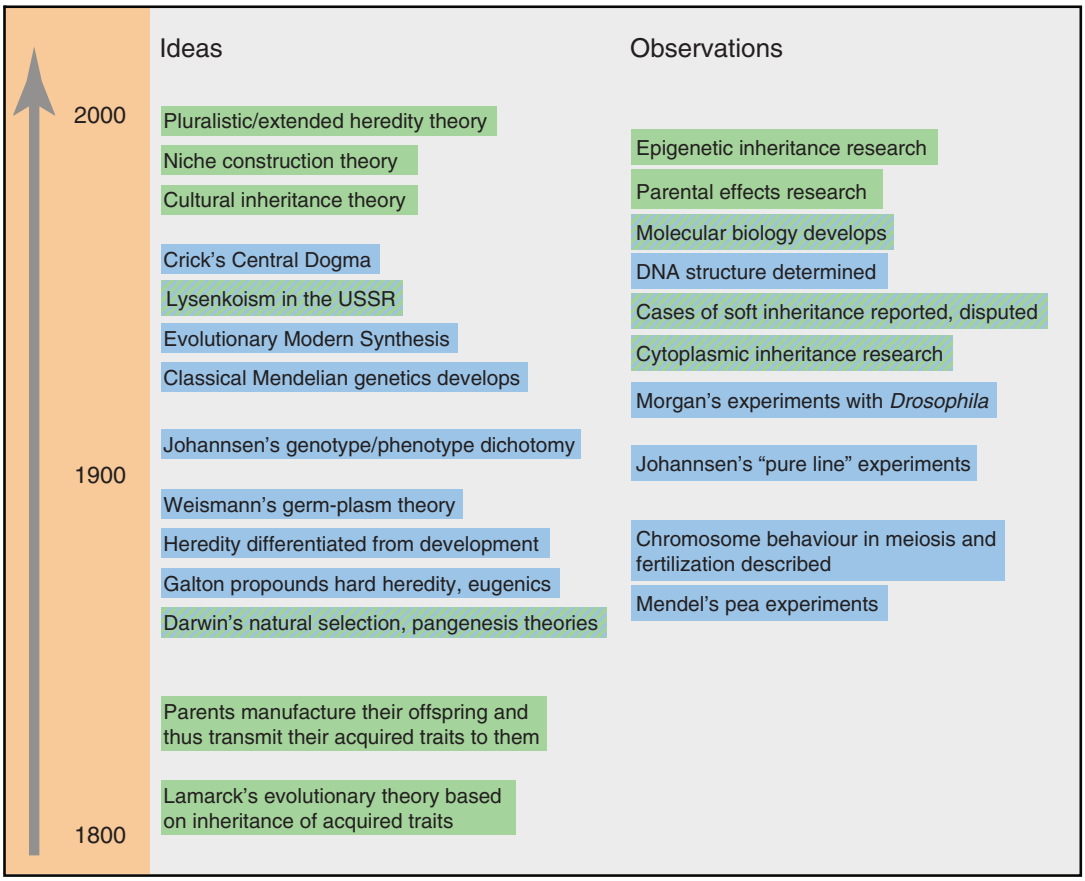

Figure I. A time-line of the development of heredity theories since 1800. Major theoretical or conceptual developments (ideas) are shown on the left, and some key empirical advances (observations) are shown on the right, with developments that bolstered hard heredity shown in blue, developments that bolstered soft heredity shown in green, and developments with equivocal consequences for heredity concepts represented by a striped pattern. For further details and discussion of the history of heredity theories, see [1–3,9–11,13,15–17,48,75,80–83].

Box 3. The 'genetic encoding' concept of inheritance

Influential 20th-century geneticists and evolutionary biologists typically assumed that soft inheritance, if it occurs, must involve somatic or environmental influences on germ-line DNA sequences ('genetic encoding'). The quotations below illustrate the development of this view.

Weismann 1893 [78]	"At the present day I can therefore state my conviction…that neither injuries, functional hypertrophy and atrophy, structural variations due to the effect of temperature or nutrition, nor any other influence of environment on the body, can be communicated to the germ-cells, and so become transmissible."
Johannsen 1911 [18]	"Personal qualities are then *the reactions of the gametes* joining to form a zygote; but the nature of the gametes is not determined by the personal qualities of the parents or ancestors in question."
Morgan 1926 [79]	"…the Lamarckian theory of the inheritance of acquired characters…postulates [that] the germ-cells are affected by the body in the sense that a change in a character may bring about corresponding alterations in specific genes."
Haldane and Huxley 1934 [84]	"All acquired characters…affect the soma. But how is a change in the soma to alter the germ-plasm?"
Huxley 1949 [19]	"…the observed facts about reproduction and the chromosome mechanism of inheritance make it extremely difficult to see how a somatic effect (say of sunlight on the colour of our skins) could find its way into the elaborately self-regulating system of self-reproducing genes."
Dobzhansky 1951 [25]	The error of the Lamarckian belief in the inheritance of acquired characters is due to a failure to recognize that the phenotype…is a by-product of the gene reproduction…, and not vice versa."
Crick 1966 [20]	"Notice that as far as we know the cell can translate in one direction only, from nucleic acid to protein, not from protein to nucleic acid. This hypothesis is known as the Central Dogma. …detailed work on the genetic code…illuminates such concepts as the absence of the inheritance of acquired characteristics."
Dobzhansky 1970 [85]	"Consider such an acquired trait as big muscles strengthened by exercise. Its inheritance would require that some product secreted by the muscles changed the nucleotide sequence or number in the DNA chains of some genes. Such changes are unknown and seem quite improbable."
Mayr 1982 [3]	"The proteins of the body cannot induce any changes in the DNA. An inheritance of acquired characters is thus a chemical impossibility."

that operate in parallel with Mendelian-genetic inheritance. Nongenetic inheritance comprises all vertical (i.e. parent–offspring) mechanisms of inheritance (other than the transmission of DNA sequence variation), including transgenerational epigenetic inheritance, somatic inheritance, environmental inheritance, and behavioral or cultural inheritance [6–8,10]. A common feature of these nongenetic mechanisms is that they are mediated by the transmission to offspring of elements of a parent's 'extended phenotype' – that is, components of the parent's body, behavior or ambient environment. Nongenetic inheritance is soft, in that some traits acquired by parents during their lifetime can be transmitted to offspring via these mechanisms. Some nongenetic inheritance mechanisms (such as transgenerational epigenetic inheritance) function via factors transmitted in the gametes at conception, whereas other mechanisms (such as somatic or behavioral inheritance) can operate via post-conception interactions. Recent interest in the role of soft inheritance as a general factor in evolution was primarily inspired by the work of Jablonka and Lamb [9,10].

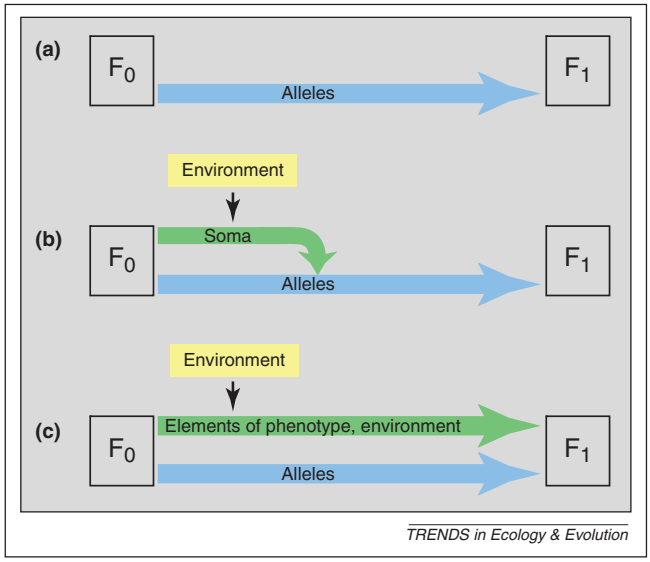

Figure 1. Contrasting models of heredity. **(a)** Mendelian heredity, whereby inheritance is mediated by the transmission (blue arrow) of gene alleles (DNA sequence variants), unaffected by environment (hard), from parents (F_0) to offspring (F_1). **(b)** The 'genetic encoding' model of 'soft'/'Lamarckian' heredity, whereby inheritance is mediated by the transmission of gene alleles, but those alleles are subject to modification in the germ-line by factors originating in the soma (green arrow), thereby allowing for the inheritance of acquired traits. **(c)** A pluralistic model of heredity, whereby inheritance is mediated by the transmission of gene alleles ('genetic inheritance', blue arrow) alongside a set of other factors (elements of the parental phenotype or environment), including some acquired traits ('nongenetic inheritance', green arrow).

Nongenetic inheritance differs in important ways from the hypothetical mechanism of genetic encoding. Whereas genetic encoding involves the transmission of DNA sequence (allelic) variation, and can thus be viewed as a form of biased mutation [26], nongenetic inheritance involves the transmission of other factors alongside alleles (Figure 1).

The extension of the Mendelian model of heredity to encompass nongenetic inheritance represents a synthesis of the 19th-century idea that parents 'manufacture' their offspring with the 20th-century belief that offspring develop autonomously by following a genetic blueprint (Box 2). The pluralistic model of heredity reflects the belief that both of these hitherto antithetical positions capture elements of the complex process of development: the offspring genome guides development, although many facets of this process are influenced by the developmental environment and resources determined by parental phenotypes.

A diversity of inheritance mechanisms

Nongenetic inheritance comprises both long-recognized and recently discovered mechanisms of inheritance that operate in parallel with genetic inheritance. It is clear that human cultural and linguistic variation is transmitted from parents to offspring via non-Mendelian mechanisms (cultural inheritance) and, beginning in the 1970s, these ideas developed into a theory of cultural evolution and, ultimately, gene–culture coevolution [29–33]. It was further recognized that cultural inheritance could occur in other animals [5,30,34,35]. Moreover, niche construction theory proposed that any species can undergo analogous processes, whereby the activities of organisms lead to a modification of their environment which, in turn, affects selection and influences evolution [36,37]. Furthermore, experiments on diverse animals, plants and unicellular organisms showed that parental environment, phenotype or genotype, sometimes affects offspring phenotype, a phenomenon called 'parental effects'[38] or 'indirect genetic effects' [39]. Recent discoveries in molecular and cell biology have revealed novel mechanisms, such as transgenerational epigenetic inheritance [6,40–42], that could account for a variety of parental effects. Empirical studies are now providing evidence that parental effects can be mediated by a range of substances in the gametes, and also parental glandular and other somatic donations, behavior and environment, and can affect a range of offspring traits [7]. Although it was long thought that maternal effects were far more common than paternal effects because of the greater opportunity for maternal influence on offspring development, this view is being challenged by the increasing number of examples of paternal effects [43]. Nongenetic inheritance is attracting increasing attention in medicine [44,45], ecology [46] and evolutionary biology [7,8,10,47].

The new debate

Efforts to extend the Mendelian model of heredity to encompass nongenetic inheritance represent an important change in the nature of the inheritance debate. Throughout much of the past century debate centered on the existence of soft inheritance (Box 2). By contrast, nongenetic inheritance, as defined by current authors [7,8], is a phenomenon whose existence is established beyond reasonable doubt by diverse programs of empirical research [48], although some putative mechanisms of nongenetic inheritance remain poorly understood [49]. However, debate continues about the importance of nongenetic inheritance for phenotypic variation and evolution [48]. According to a widely-held view, the Mendelian-genetic model is adequate in most contexts and does not need to be replaced by a more complex pluralistic model. Proponents of this view argue that, outside of some specialized domains such as human culture, the importance of nongenetic inheritance has not been demonstrated [50–52]. This position is reinforced by the practical difficulties involved in extending population – and quantitative – genetic approaches to encompass the diverse array of nongenetic mechanisms of inheritance [53–55]. The alternative position is that it is no longer tenable to ignore nongenetic inheritance. Proponents of this view point out that empirical studies have provided numerous examples of large effects of nongenetic inheritance on offspring phenotype [7–10], and theoretical studies have shown that such effects can influence the dynamics and course of evolution [37,47,56–59]. Debate on the importance of nongenetic inheritance will ultimately be resolved empirically.

A pluralistic model of heredity

The model of heredity now emerging is pluralistic [12], or 'inclusive' [8] or 'extended' [60], in that it combines genetic and nongenetic mechanisms of inheritance [7,8,10]. The pluralistic model therefore recognizes the reality of both hard and soft inheritance, and the potential for a range of intermediate phenomena.

A corollary of the pluralistic model is variation in the nature of inheritance among different traits and taxa, spanning a continuum from purely genetic to purely nongenetic. Variation in the relative importance of genetic and various nongenetic mechanisms of inheritance is likely to have important implications for evolution. Two human traits – eye color and language – serve to illustrate opposite ends of the continuum. Eye color may be determined largely by allelic variation [61–63], whereas mother tongue is determined by nongenetic (cultural) factors. Both traits are transmitted from parents to offspring, and might be expected to respond to natural selection, although the dynamics and endpoints of change in mean phenotype over generations may be substantially different [29,31,33]. Many traits may fall in between these extremes. For example, both genetic and nongenetic inheritance may influence life history [64], physiology [65–67] and even morphology [43,68]. The relative importance of nongenetic inheritance may also be greater in some taxonomic groups than in others. For example, transgenerational epigenetic inheritance may play a particularly important role in plants and unicellular organisms [9]. Conversely, most animals are highly plastic in behavior and, in some species, variation in behavioral traits may be shaped to a considerable degree by parental behavior [5]. Variation among traits and taxa in the nature of inheritance presents an important, novel research problem arising from the pluralistic model of heredity.

Concluding remarks

I argue that the rejection of soft inheritance by influential 20th-century geneticists reflected two key ideas: a narrowed definition of heredity as the transmission of DNA sequences at conception, and the belief that heredity is mediated by a single, universal mechanism of transmission. As a corollary of these ideas, many leading geneticists assumed that soft inheritance, if it occurs, must involve the modification of germ-line DNA sequences by environmental or somatic factors – a process that they rejected as a 'chemical impossibility' (Box 3). In contrast, recent challengers of the established view of heredity propose a pluralistic model, whereby heredity reflects the transmission of gene alleles (genetic inheritance) alongside a variety of other factors that influence offspring phenotype (nongenetic inheritance) [6–8,10,12]. The pluralistic model of heredity points to the existence of variation in the nature of inheritance among taxa and traits. Although the existence of nongenetic inheritance is not in doubt, some putative mechanisms of nongenetic inheritance remain poorly understood, and

controversy persists over the role and importance of nongenetic inheritance in shaping phenotypic variation and influencing the dynamics and course of evolution.

References

1 Cook, G.M. (1999) Neo-Lamarckian experimentalism in America: origins and consequences. *Q. Rev. Biol.* 74, 417–437
2 Landman, O.E. (1991) The inheritance of acquired characteristics. *Ann. Rev. Genet.* 25, 1–20
3 Mayr, E. (1982) *The Growth of Biological Thought: Diversity, Evolution, and Inheritance*, Belknap, (Harvard)
4 Kuhn, T.S. (1970) *The Structure of Scientific Revolutions*, University of Chicago Press
5 Avital, E. and Jablonka, E. (2000) *Animal Traditions: Behavioural Inheritance in Evolution*, Cambridge University Press
6 Jablonka, E. and Lamb, M.J. (2010) Transgenerational epigenetic inheritance. In *Evolution – the Extended Synthesis* (Pigliucci, M. and Müller, G.B., eds), pp. 137–174, The MIT Press
7 Bonduriansky, R. and Day, T. (2009) Nongenetic inheritance and its evolutionary implications. *Annu. Rev. Ecol. Evol. Syst.* 40, 103–125
8 Danchin, E. *et al.* (2011) Beyond DNA: integrating inclusive inheritance into an extended theory of evolution. *Nat. Rev. Genet.* 12, 475–486
9 Jablonka, E. and Lamb, M.J. (1995) *Epigenetic Inheritance and Evolution*, Oxford University Press
10 Jablonka, E. and Lamb, M.J. (2005) *Evolution in Four Dimensions*, The MIT Press
11 Sapp, J. (1987) *Beyond the Gene: Cytoplasmic Inheritance and the Struggle for Authority in Genetics*, Oxford University Press
12 Mameli, M. (2005) The inheritance of features. *Biol. Philos.* 20, 365–399
13 López-Beltrán, C. (2007) The medical origins of heredity. In *Heredity Produced: at the Crossroads of Biology, Politics, and Culture, 1500–1870* (Müller-Wille, S. and Rheinberger, H-J., eds), pp. 105–132, The MIT Press
14 Mayr, E. (1998) Prologue: some thoughts on the history of the evolutionary synthesis. In *The Evolutionary Synthesis: Perspectives on the Unification of biology* (Mayr, E. and Provine, W.B., eds), pp. 1–48, Harvard University Press
15 Bowler, P.J. (1989) *The Mendelian Revolution: the Emergence of Hereditarian Concepts in Modern Science and Society*, The Athlone Press
16 Churchill, F.B. (1976) Rudolf Virchow and the pathologist's criteria for the inheritance of acquired characteristics. *J. Hist. Med.* 31, 117–148
17 Churchill, F.B. (1987) From heredity theory to vererbung: the transmission problem, 1850–1915. *ISIS* 337–364
18 Johannsen, W. (1911) The genotype conception of heredity. *Am. Nat.* 45, 129–159
19 Huxley, J. (1949) *Soviet Genetics and World Science*, Chatto and Windus
20 Crick, F.H.C. (1966) The Croonian Lecture: The Genetic Code. *Proc. R. Soc. Lond. B* 167, 331–347
21 Chetverikov, S.S. (1926) O nekotrikh momentakh evolutsionnovo protsessa s tochki zrenija sovremennoj genetiki (On certain aspects of the evolutionary process from the perspective of modern genetics). *Zhurnal Eksperimentalnoj Biologii (A)* 2, 3–54
22 East, E.M. and Jones, D.F. (1919) Inbreeding and outbreeding: their genetic and sociological significance. In *Monographs on Experimental Biology* (Loeb, J. *et al.*, eds), p. 285, J.B. Lippincott
23 Morgan, T.H. (1919) *The Physical Basis of Heredity*, J.B. Lippincott
24 Wright, S. (1921) Systems of mating. I. The biometric relations between parent and offspring. *Genetics* 6, 111–123
25 Dobzhansky, T. (1951) *Genetics and the Origin of Species*, Columbia University Press
26 Steele, E.J. (1979) *Somatic Selection and Adaptive Evolution: on the Inheritance of Acquired Characters*, Williams and Wallace
27 Steele, E.J. *et al.* (1998) *Lamarck's Signature: How Retrogenes are Changing Darwin's Natural Selection Paradigm*, Allen & Unwin
28 Parascandola, M. (1995) Philosophy in the laboratory: the debate over evidence for E.J. Steele's Lamarckian hypothesis. *Stud. Hist. Philos. Sci.* 26, 469–492
29 Boyd, R. and Richerson, P.J. (1985) *Culture and the Evolutionary Process*, The University of Chicago Press
30 Mesoudi, A. (2011) *Cultural Evolution: How Darwinian Theory can Explain Human Culture and Synthesize the Social Sciences*, The University of Chicago Press
31 Cavalli-Sforza, L.L. and Feldman, M.W. (1981) *Cultural Transmission and Evolution: a Quantitative Approach*, Princeton University Press
32 Feldman, M.W. and Cavalli-Sforza, L.L. (1989) On the theory of evolution under genetic and cultural transmission with application to the lactose absorption problem. In *Mathematical Evolutionary Theory* (Feldman, M.W., ed.), pp. 145–173, Princeton University Press
33 Richerson, P.J. and Boyd, R. (2005) *Not by Genes Alone: How Culture Transforms Human Evolution*, The University of Chicago Press
34 Grant, P.R. and Grant, R. (2009) The secondary contact phase of allopatric speciation in Darwin's finches. *Proc. Natl. Acad. Sci. U.S.A.* 106, 20141–20148
35 Danchin, É. *et al.* (2004) Public information: from nosy neighbors to cultural evolution. *Science* 305, 487–491
36 Laland, K.N. *et al.* (1999) Evolutionary consequences of niche construction and their implications for ecology. *Proc. Natl. Acad. Sci. U.S.A.* 96, 10242–10247
37 Odling-Smee, F.J. *et al.* (2003) *Niche Construction: The Neglected Process in Evolution*, Princeton University Press
38 Mousseau, T.A. and Fox, C.W. (1998) The adaptive significance of maternal effects. *Trends Ecol. Evol.* 13, 403–407
39 Wolf, J.B. *et al.* (1998) Evolutionary consequences of indirect genetic effects. *Trends Ecol. Evol.* 13, 64–69
40 Richards, E.J. (2006) Inherited epigenetic variation – revisiting soft inheritance. *Nat. Rev. Genet.* 7, 395–401
41 Seong, K-H. *et al.* (2011) Inheritance of stress-induced, ATF-2-dependent epigenetic change. *Cell* 145, 1049–1061
42 Youngson, N.A. and Whitelaw, E. (2008) Transgenerational epigenetic effects. *Annu. Rev. Genomics Hum. Genet.* 9, 233–257
43 Bonduriansky, R. and Head, M. (2007) Maternal and paternal condition effects on offspring phenotype in *Telostylinus angusticollis* (Diptera: Neriidae). *J. Evol. Biol.* 20, 2379–2388
44 Gluckman, P.D. *et al.* (2007) Non-genomic transgenerational inheritance of disease risk. *Bioessays* 29, 145–154
45 Gluckman, P.D. *et al.* (2009) Epigenetic mechanisms that underpin metabolic and cardiovascular diseases. *Nat. Rev. Endocrinol.* 5, 401–408
46 Bossdorf, O. *et al.* (2008) Epigenetics for ecologists. *Ecol. Lett.* 11, 106–115
47 Day, T. and Bonduriansky, R. (2011) A unified approach to the evolutionary consequences of genetic and nongenetic inheritance. *Am. Nat.* 178, E18–E136
48 Sterelny, K. (2007) Rethinking inheritance. *Biol. Theory* 2, 215–217
49 Daxinger, L. and Whitelaw, E. (2010) Transgenerational epigenetic inheritance: more questions than answers. *Genome Res.* 20, 1623–1628
50 Dickins, T.E. and Dickins, B.J.A. (2008) Mother nature's tolerant ways: Why non-genetic inheritance has nothing to do with evolution. *New Ideas Psychol.* 26, 41–54
51 Haig, D. (2007) Weismann rules! OK? Epigenetics and the Lamarckian temptation. *Biol. Philos.* 22, 415–428
52 Various (1998) Commentary on "Epigenetic inheritance in evolution" by E. Jablonka and M.J. Lamb. *J. Evol. Biol.* 11, 185–242
53 Johannes, F. and Colome-Tatche, M. (2011) Quantitative epigenetics through epigenomic perturbation of isogenic lines. *Genetics* 188, 215–227
54 Santure, A.W. and Spencer, H.G. (2006) Influence of mom and dad: Quantitative genetic models for maternal effects and genomic imprinting. *Genetics* 173, 2297–2316
55 Tal, O. *et al.* (2010) Epigenetic contribution to covariance between relatives. *Genetics* 184, 1037–1050
56 Jablonka, E. *et al.* (1995) The adaptive advantage of phenotypic memory in changing environments. *Philos. Trans. R. Soc. Lond. B* 350, 133–141
57 Lachmann, M. and Jablonka, E. (1996) The inheritance of phenotypes: an adaptation to fluctuating environments. *J. Theor. Biol.* 181, 1–9
58 Pál, C. (1998) Plasticity, memory and the adaptive landscape of the genotype. *Proc. R. Soc. B: Biol. Sci.* 265, 1319–1323
59 Pál, C. and Miklós, I. (1999) Epigenetic inheritance, genetic assimilation and speciation. *J. Theor. Biol.* 200, 19–37

60 Helanterä, H. and Uller, T. (2010) The Price equation and extended inheritance. *Philos. Theory Biol.* 2, e101
61 Bräuer, G. and Chopra, V.P. (1980) Estimating the heritability of hair colour and eye colour. *J. Hum. Evol.* 9, 625–630
62 Larsson, M. *et al.* (2003) Importance of genetic effects for characteristics of the human iris. *Twin Res.* 6, 192–200
63 Sturm, R.A. and Larsson, M. (2009) Genetics of human iris colour and patterns. *Pigment Cell Melanoma Res.* 22, 544–562
64 Greer, E.L. *et al.* (2011) Transgenerational epigenetic inheritance of longevity in *Caenorhabditis elegans*. *Nature* 479, 365–371
65 Anderson, L.M. *et al.* (2006) Preconceptional fasting of fathers alters serum glucose in offspring of mice. *Nutrition* 22, 327–331
66 Carone, B.R. *et al.* (2010) Paternally induced transgenerational environmental reprogramming of metabolic gene expression in mammals. *Cell* 143, 1084–1096
67 Ng, S.F. *et al.* (2010) Chronic high-fat diet in fathers programs beta-cell dysfunction in female rat offspring. *Nature* 467, 963–967
68 Vijendravarma, R.K. *et al.* (2010) Effects of parental larval diet on egg size and offspring traits in *Drosophila*. *Biol. Lett.* 6, 238–241
69 Futuyma, D.J. (2009) *Evolution*, Sinauer Associates
70 Futuyma, D.J. (1986) *Evolutionary Biology*, Sinauer Associates
71 Ridley, M. (1996) *Evolution*, Blackwell Science
72 Stearns, S.C. and Hoekstra, R.F. (2005) *Evolution, an Introduction*, Oxford University Press
73 Freeman, S. and Herron, J.C. (2007) *Evolutionary Analysis*, Pearson, Prentice Hall
74 Barton, N.H. *et al.* (2007) *Evolution*, Cold Spring Harbor Laboratory Press
75 Zirkle, C. (1946) The early history of the idea of the inheritance of acquired characters and of pangenesis. *Trans. Am. Philos. Soc.* 35, 91–151
76 Galton, F. (1865) Hereditary character and talent. *Macmillan's Mag.* 12, 157–166
77 Galton, F. (1873) Hereditary improvement. *Fraser's Mag.* 116–130
78 Weismann, A. (1893) *The Germ-plasm: a Theory of Heredity*, Charles Scribner's Sons
79 Morgan, T.H. (1926) *The Theory of the Gene*, Yale University Press
80 Soyfer, V.N. (1994) *Lysenko and the Tragedy of Soviet Science*, Rutgers University Press
81 Gissis, S.B. and Jablonka, E. (2011) Introduction: the exclusion of soft ("Lamarckian") inheritance from the Modern Synthesis. In *Transformations of Lamarckism: From Subtle Fluids to Molecular Biology* (Gissis, S.B. and Jablonka, E., eds), p. 103, Massachusetts Institute of Technology
82 Gilbert, S. (2011) The decline of soft inheritance. In *Transformations of Lamarckism: From Subtle Fluids to Molecular Biology* (Gissis, S.B. and Jablonka, E., eds), p. 121, Massachusetts Institute of Technology
83 Wilkins, A. (2011) Why did the modern synthesis give short thrift to "soft inheritance"? In *Transformations of Lamarckism: From Subtle Fluids to Molecular Biology* (Gissis, S.B. and Jablonka, E., eds), p. 127, Massachusetts Institute of Technology
84 Haldane, J.B.S. and Huxley, J. (1934) *Animal Biology*, Clarendon Press
85 Dobzhansky, T. (1970) *Genetics of the Evolutionary Process*, Columbia University Press