Nongenetic Inheritance and Its Evolutionary Implications

Russell Bonduriansky[1] and Troy Day[2]

[1]Evolution & Ecology Research Center and School of Biological, Earth and Environmental Sciences, University of New South Wales, Sydney, Australia; email: r.bonduriansky@unsw.edu.au

[2]Departments of Mathematics and Biology, Queen's University, Kingston, Ontario, Canada; email: tday@mast.queensu.ca

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Abstract

Modern evolutionary biology is founded on the Mendelian-genetic model of inheritance, but it is now clear that this model is incomplete. Empirical evidence shows that environment (encompassing all external influences on the genome) can impose transgenerational effects and generate heritable variation for a broad array of traits in animals, plants, and other organisms. Such effects can be mediated by the transmission of epigenetic, cytoplasmic, somatic, nutritional, environmental, and behavioral variation. Building on the work of many authors, we outline a general framework for conceptualizing nongenetic inheritance and its evolutionary implications. This framework shows that, by decoupling phenotypic change from the genotype, nongenetic inheritance can circumvent the limitations of genetic inheritance and thereby influence population dynamics and alter the fitness landscape. The weight of theory and empirical evidence indicates that nongenetic inheritance is a potent factor in evolution that can engender outcomes unanticipated under the Mendelian-genetic model.

INTRODUCTION

In the early years of the twentieth century, the Danish biologist Wilhelm Johannsen laid the conceptual foundations of modern genetics and evolutionary biology by differentiating the phenotype—the traits expressed by an organism—from the genotype—the "sequestered" library of hereditary information transmitted from parent to offspring (Johannsen 1911). This view of heredity served as a bulwark against Lamarckism—the purported transmission of parental phenotype to offspring[1] —already strongly repudiated by August Weismann in the nineteenth century. Resistance to Lamarckism solidified in the West when Lamarckism congealed into political dogma in Stalin's USSR during the 1940s, and dissenting geneticists faced persecution by the state (Alexandrov & Aronova 2004). In the meantime, a series of important discoveries—Mendel's laws of the segregation of discrete hereditary units (genes), the processes of meiosis and fertilization, the structure and genetic code of DNA—reinforced the concept of the gene as the exclusive agent of heredity, giving rise to a simple and elegant model of inheritance that persists to this day.

The assumption that inheritance is the transmission to one's offspring of DNA sequences received from one's parents—a seamless genetic lineage all but impervious to external influences and perturbed only by rare mutation events—underpins the quantitative- and population-genetic models of modern evolutionary theory (Falconer & Mackay 1996). However, although it captures important elements of biological reality, this model is clearly incomplete. Empirical evidence points to the occurrence of nongenetic mechanisms of inheritance (**Table 1**) in all taxonomic groups, and for a broad range of phenotypic traits (Avital & Jablonka 2000; Jablonka & Lamb 1995, 2005; Youngson & Whitelaw 2008). In plants, researchers have long recognized that environmental influences can be transmitted across generations (Jablonka & Lamb 1995, Johannes et al. 2008). Likewise, in animals, parental influences can be mediated through learning or other mechanisms of developmental plasticity (Avital & Jablonka 2000). Recent discoveries in cell biology and development have revealed that the transfer of epigenetic, cytoplasmic, or somatic factors from parents to offspring can influence offspring phenotype (Cuzin et al. 2008, Youngson & Whitelaw 2008). These phenomena do not involve the modification of germline DNA-sequence by environment (see Steele et al. 1998) but, rather, the vertical transmission of factors other than DNA. At the same time, theoretical analysis of behavioral/cultural transmission (Avital & Jablonka 2000, Boyd & Richerson 1985, Cavalli-Sforza & Feldman 1981, Laland 1994, Richerson & Boyd 2005), transgenerational epigenetic inheritance (Jablonka & Lamb 1995, 2006; Pál 1998; Pál & Miklós 1999), and maternal effects (Kirkpatrick & Lande 1989, Lande & Kirkpatrick 1990, Mousseau & Fox 1998), as well as general treatments of nongenetic inheritance (Gorelick 2005; Jablonka & Lamb 2005; Jablonka et al. 1992, 1995; Lachmann & Jablonka 1996; Maynard-Smith 1990) and related phenomena (Laland et al. 1996, 1999; Odling-Smee et al. 2003; Wolf et al. 1998), has shown that nongenetic inheritance can have important implications for evolution.

Against the current of accumulating empirical evidence and theory, nongenetic forms of inheritance continue to be widely regarded as oddities confined to a few taxa and traits (Jablonka & Lamb 1995, 2005). This is particularly so in relation to higher animals, which are assumed to lack a general mechanism for nongenetic inheritance because (unlike plants and unicellular organisms) they sequester their germline early in ontogeny (Jablonka & Lamb 1995). Doubts about the potential importance of nongenetic inheritance for long-term evolutionary change also reflect the presumed transience or instability of nongenetically transmitted phenotypic states. Continuing

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[1]In the original sense espoused by Jean-Baptiste Lamarck in one of the earliest essays on evolution, the *Philosophie Zoologique*, heritable phenotypic modifications result from differential use or disuse of organs or physiological systems in response to environmental conditions (Lamarck 1809).

Table 1   Mechanisms of nongenetic inheritance and their characteristics

Mechanism	Effecting parent[a]	Mediating factor(s)	Effect of parental extraorganismal environment?	Effect of parental genotype?	Taxa
Transmission of epigenetic state not limited by parent-of-origin	**Mother, Father**	DNA methylation, chromatin structure?	Parental diet, social environment, etc.	Possible	All
Transmission of epigenetic state limited by parent-of-origin (genomic imprinting)	**Mother, Father**	DNA methylation (dependent on parental sex)	Maternal environment	Yes	All
Transmission of cytoplasmic and somatic factors	**Mother,** Father	Hormones, proteins, RNA, etc. provided via gametes, via glandular secretions, etc.	Parental social environment, host, diet, etc.	Possible	All
Transmission of nutrients	**Mother,** Father	Nutrients provided in egg, via nuptial gift, or via other parental investment	Nutrient availability	Possible	All
Transmission of extraorganismal environment	**Mother,** Father	Habitat quality, host type, etc.	Distribution of environments, hosts, etc.	Possible	All
Transmission of behavior or culture through learning	**Mother,** Father	Influence of parental behavior on offspring behavior and development	Ambient/social conditions	Possible	Higher animals

[a]Bold font, opportunity for transmission extensive in most taxa; nonbold font, opportunity for transmission limited in many taxa.

reluctance to accept nongenetic inheritance as an important process in evolution may reflect the lack of a synthetic model of evolution under genetic and nongenetic inheritance, an unfamiliarity with the breadth of empirical evidence, and a lingering association of nongenetic inheritance with Lamarckian heresy.

Here, we outline a general conceptual framework that encompasses all mechanisms of nongenetic inheritance while allowing us to delineate the boundaries of this phenomenon. We also survey the empirical evidence and proximate mechanisms of nongenetic inheritance, focusing on the higher animals, in which the importance of this phenomenon remains especially underappreciated. Finally, we synthesize theory on the evolutionary consequences of nongenetic inheritance and its interaction with genetic inheritance. We show that nongenetic inheritance can not only bring about phenotypic change, but can also alter the fitness landscape (or individual fitness function) and influence long-term evolution.

WHAT IS NONGENETIC INHERITANCE?

By convention, we restrict the concept of inheritance to vertical transmission (that is, effects of ancestors on descendants). Genetic inheritance can be defined as any effect on offspring phenotype brought about by the transmission of DNA sequences from parents to offspring.[2] Conversely, we define nongenetic inheritance as any effect on offspring phenotype brought about by the transmission of factors other than DNA sequences from parents or more remote ancestors.[3] Such nongenetic factors can be regarded as elements of the ancestral environment, considered to encompass all factors external to the DNA sequence, such as extraorganismal ambient conditions, the organismal soma, the intracellular cytoplasm (excluding cytoplasmic DNA), and the proteins and methyl-groups associated with the DNA molecule. Nongenetic inheritance thus comprises mechanisms whereby the environment within which an ancestor's genes reside influences development in descendants (**Table 1**; **Figure 1**). Our definition of nongenetic inheritance is similar to some definitions of parental effects (e.g., Lacey 1998), but we avoid the latter term because it has been used in many different ways in the literature.

Nongenetic inheritance can involve the transfer to offspring of phenotypic traits acquired during the ancestor's lifetime (sometimes called carry-over effects), such as learned behaviors, or environmentally induced variation in condition or epigenetic state. In contrast with Lamarck's (1809) view of inheritance, however, the modern conception of transmission of acquired traits need not involve differential use or disuse of organs in response to environmental change, and is based on well-characterized mechanisms of transmission (**Table 1**). In addition, nongenetic inheritance can involve the transmission to offspring of phenotypic or epigenetic states inherited from ancestors but not modified by environmental input during an individual's lifetime. Moreover, phenotypic variation transmitted to offspring (whether environment-induced or independent of environment) can be either unrelated to parental genotype (**Figure 1**, *blue arrows*), or associated with variation in parental genes (**Figure 1**, *red arrows*). In the latter case, nongenetic inheritance encompasses

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[2]Transmission of RNA viruses, which can reverse-transcribe their genome and introgress it into host DNA, can be regarded as a form of genetic inheritance. Likewise, the possibility that somatic changes such as acquired immunity can be transmitted to the germline via reverse transcription (see Steele et al. 1998) would represent an environmentally influenced form of genetic inheritance under our definition.

[3]Numerous terms have been used to refer to non-DNA-based inheritance, including soft inheritance, Lamarckian inheritance, transgenerational epigenetic effects, non-Mendelian inheritance, parental effects, fetal programming, carry-over effects, and cell memory.
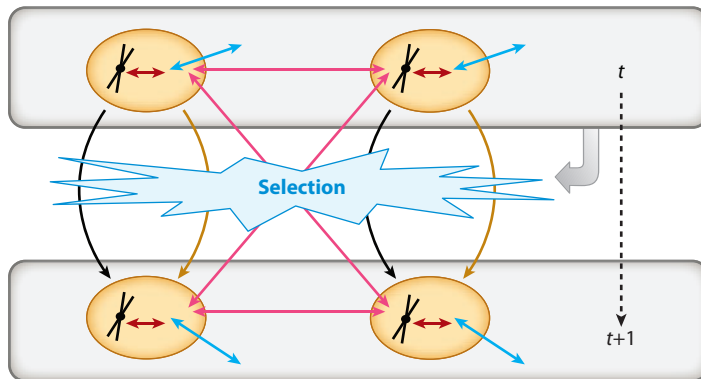
Figure 1

Relationship between nongenetic inheritance and other types of transgenerational effects. Two ancestor-descendant lineages are shown in generations t and $t + 1$. Solid-black chromosomes represent genes, and the solid-black arrow represents genetic inheritance. Yellow ellipses represent the local biotic and abiotic environment of the genes, and the solid-yellow arrow represents the transmission of some component of this environment from parents to offspring (that is, nongenetic inheritance). Oblong gray regions represent the biotic and abiotic environment common to the entire population. Red arrows represent the effects of environment on gene expression and vice versa. Blue arrows represent effects of the population-wide environment on the local environment and vice versa. Pink arrows represent direct horizontal (within-generation) and oblique (between-generation) interactions between individuals that are not ancestor-descendant pairs, and their effects on gene expression. The dotted-black arrow represents transmission of the population-wide environment between generations. The thick gray arrow represents the effect of environment on natural selection (see text).

the influence of an ancestor's genotype on its descendants, mediated by the transmission of factors other than DNA sequences.

The component of the environment that is influenced by the parental genome, and that is transmitted nongenetically to offspring, is a specific kind of indirect genetic effect (IGE) (Wolf et al. 1998). IGEs can arise from horizontal (that is, within-generation) interactions among individuals, or from oblique (transgenerational) interactions between individuals (**Figure 1**, *pink arrows*). However, it is only those IGEs mediated by vertical (that is, ancestor-descendant) interactions that constitute part of nongenetic inheritance (**Figure 1**, *yellow arrows*).

Mother-offspring IGEs, along with transgenerational environmental influences unrelated to maternal genotype, together form a type of nongenetic inheritance called maternal effects (Mousseau & Fox 1998). The definition of nongenetic inheritance used here encompasses maternal effects as well as any other ancestor-descendant IGEs and purely stochastic environmental influences mediated by fathers, grandparents, or more remote ancestors. However, we exclude from nongenetic inheritance the inheritance of mitochondrial and chloroplast DNA, which is maternally inherited and sometimes considered as a maternal effect.

Our definition of nongenetic inheritance is more restrictive than that used in the literature on niche construction (Odling-Smee et al. 2003). Models of niche construction typically consider the transmission of general, population-wide, environmental attributes from one generation to the next (e.g., resource levels, habitat conditions, etc.; **Figure 1**, *dotted-black arrow*) as a form of "inheritance," along with other types of effects (**Figure 1**, *yellow, red, blue arrows*). However, the study of inheritance, as this term is conventionally understood, is concerned with explaining phenotypic variation among individuals within a generation, based on their ancestry (Falconer & Mackay 1996). Any environmentally transmitted material that is common to all individuals is, by

definition, independent of ancestry, and we therefore excluded it from our definition of nongenetic inheritance.

We use the term nongenetic inheritance to refer not only to the transmission of a particular phenotypic state but, more generally, to the vertical, nongenetic transmission of any effect across generations (in contrast with some previous authors: see Lacey 1998). Consequently, nongenetic inheritance may or may not augment offspring-parent resemblance (and heritability), depending on whether the parental environment induces a similar phenotypic state in parents and offspring. For example, transmission of parental condition to offspring may augment heritability of condition-dependent traits (Bonduriansky & Head 2007). However, nongenetic inheritance may have no effect on heritability of any trait, as when diet induces distinct phenotypic effects within and across generations (see Anderson et al. 2006, Cowley & Griesel 1966, Pembrey et al. 2006). In some cases, nongenetic inheritance can even generate negative phenotypic covariance between offspring and parents, as shown by a negative maternal effect on age at maturity in springtails (Janssen et al. 1988).

Nongenetic inheritance can be viewed as a transgenerational form of phenotypic (developmental) plasticity (Jablonka et al. 1995, Uller 2008). Indeed, because variation in the expression of a nonplastic trait can reflect only genetic variation by definition (Falconer & Mackay 1996), only phenotypically plastic traits are susceptible to nongenetic inheritance. This fact may account for apparent intertaxon differences. Nonbehavioral forms of nongenetic inheritance are generally believed to be more important in plants than they are in animals, and this difference has been attributed to the lack of early germline sequestration in plants (see Jablonka & Lamb 1995). However, plants' greater plasticity—perhaps reflecting weaker functional constraints on symmetry, size, and shape—may also make them more prone to the effects of nongenetic inheritance than are most animals.

MECHANISMS AND EXAMPLES OF NONGENETIC INHERITANCE

Below, we provide an overview of mechanisms that can mediate nongenetic inheritance, and the range of possible effects on offspring phenotype. We focus on the higher animals to counter the lingering misconception that some of these phenomena are unimportant in the most complex organisms. We do not aim to review this rapidly growing literature comprehensively. Rather, our intention is to illustrate the range of phenomena comprising nongenetic inheritance.

Transmission of Epigenetic States

Variation in the epigenetic state of the DNA encompasses variation in patterns of DNA methylation, as well as in the histone proteins that bind the DNA, affecting chromatin structure (Henikoff et al. 2004, Cavalli 2006). Differences in epigenetic state between cell types are responsible for tissue differentiation within multicellular organisms. However, some variation in epigenetic state is maintained in the germline and transmitted to offspring, resulting in transgenerational epigenetic inheritance (Jablonka & Lamb 1995, Youngson & Whitelaw 2008). The molecular mechanisms of transgenerational epigenetic inheritance remain poorly understood (Cuzin et al. 2008, Martin & Zhang 2007, Youngson & Whitelaw 2008).

The epigenetic state (epiallele) that is transmitted to offspring may depend on parental genotype, or so-called parental effect genes (Chong et al. 2007, Fitch et al. 1998, Johannes et al. 2008, Youngson & Whitelaw 2008). In mice, mothers transmit the epigenetic state of the *agouti* locus, which affects coat color and susceptibility to obesity, diabetes, and tumors (Morgan et al. 1999). A female's propensity to transmit the epiallele at the *agouti* locus is affected by

methyl-supplementation during her embryonic development (Cropley et al. 2006), although female diet does not appear to engender novel epialleles at this locus (Waterland et al. 2007).

Epigenetic variation can respond to selection, resulting in accumulating phenotypic change over several generations without change in allele frequencies. For example, artificial selection on an epigenetically controlled eye phenotype in *Drosophila* resulted in a large, rapid shift in the phenotypic mean without any genetic change (Sollars et al. 2002).

The mechanisms of transgenerational epigenetic inheritance, and their effects on offspring, may be sex-specific (Chang et al. 2006, Vigé et al. 2008). A phenomenon related to transgenerational epigenetic inheritance is genomic imprinting, whereby transmission of an epigenetic mark is dependent on parental sex. Because parents of only one sex imprint alleles at a given locus, genomic imprinting can result in unequal resemblance of offspring to the mother and father for the imprinted phenotypic trait (Spencer 2002). Recent evidence also suggests that imprinting effects can depend on offspring sex (Hager et al. 2008) and on the external environment provided by the mother (Hager et al. 2009). In mammals, where this phenomenon has been most extensively studied, genomic imprinting affects a variety of traits, including the expression of insulin-like growth factors, behavior, learning ability, and brain structure (Constancia et al. 2002, Goos & Silverman 2001, Swaney et al. 2007, Tycko & Morison 2002). The disruption of normal patterns of imprinting plays a role in the development of cancer and other diseases (Jirtle 1999).

Heritable epigenetic states can also be influenced by extraorganismal environment (Whitelaw & Whitelaw 2006, Youngson & Whitelaw 2008). In animals, such effects appear to be mediated by environment-dependent patterns of methylation established in the germline (e.g., see Chang et al. 2006, Pembrey et al. 2006). In rats, exposure of gestating females to estrogenic and antiandrogenic disruptors during the period of embryonic sex determination resulted in low fertility and high incidence of cancer and other diseases in male offspring, and this phenotype was transmitted through the male line for at least four generations (Anway & Skinner 2006; Anway et al. 2005, 2006). Moreover, female rats whose ancestors were exposed to endocrine disruptors showed altered mate-choice responses (Crews et al. 2007). In humans, transgenerational epigenetic inheritance is implicated in transmission within families of susceptibility to a variety of diseases, and some of these epigenetic states appear to be influenced by the extraorganismal environment (Gluckman et al. 2007). Transgenerational epigenetic inheritance may also mediate some effects of parental age on offspring (Perrin et al. 2007).

Transmission of Cytoplasmic or Somatic Factors

Parental environment can also affect offspring phenotype through the transfer of substances (such as hormones, proteins, lipids, RNA) via the gamete membranes or cytoplasm, or via transfer of parental soma, hormones, food-derived substances, waste-products and even parasites or symbionts. Well-known examples of the influence of cytoplasmic factors come from birds, where mothers can allocate varying quantities of hormones and carotenoids to eggs (Groothuis et al. 2005). Transmission of proteins in egg cytoplasm may also mediate some effects of parental age on offspring (Diaz & Esponda 2004). Although the sperm transmits relatively little material to the zygote, there is evidence that variation in sperm-borne proteins may affect offspring (see Wilson et al. 2006). Transmission of RNA in eggs or sperm can affect offspring phenotype in many ways, and could play a role in transgenerational epigenetic inheritance (Cuzin et al. 2008, Youngson & Whitelaw 2008). For example, in mice, heterozygous individuals carrying a mutant allele exhibit a spotted phenotype, and both mothers and fathers transmit this phenotype to offspring that are homozygous for the wild-type allele through the gametic transfer of RNA (Rassoulzadegan et al. 2006). The offspring then transmit this phenotype to their own offspring.

Parents can also influence their offspring through the transfer of substances to embryos or young. For example, in mammals, offspring diet choice is influenced by maternal diet via the transmission of food-derived substances through the placenta, or via ingestion by offspring of maternal feces containing remnants of maternal food, and gut endosymbionts that facilitate digestion (Avital & Jablonka 2000). Similar effects could be mediated via ingestion of the mother herself by her offspring (e.g., Kupfer et al. 2006). In mammals, mothers transfer acquired immunity through mammary gland secretions (Wheeler et al. 2007). In locusts, the female oviduct secretes a substance that induces migratory morphology and behavior in offspring (Simpson & Miller 2007). This effect occurs in response to exposure of either the female or her mate to crowded conditions. In *Drosophila*, ambient temperature experienced by the mother or grandmother affects viability, temperature tolerance, and morphology of descendants (Gilchrist & Huey 2001, Huey et al. 1995, Magiafoglou & Hoffmann 2003, Watson & Hoffmann 1995), perhaps via egg-borne compounds involved in cold-acclimation (see Watson & Hoffmann 1995). Fathers can also influence their offspring via glandular products. For example, in some blenny fish, males appear to transfer antimicrobial substances to the eggs via specialized anal glands (Giacomello et al. 2006). Paternal effects may also be mediated by accessory gland products in mammals (e.g., Chow et al. 2003, Ying et al. 1998). In some moths, both females and males (via "nuptial gifts" transferred at mating) endow their offspring with defensive compounds (Dussourd et al. 1988, Iyengar & Eisner 1999, Smedley & Eisner 1996).

Transmission of Nutrients

A factor of particular importance in shaping offspring phenotype is variation in parental nutrient provisioning: the quantity and quality of metabolic resources provided to developing offspring. Nutrient provisioning can influence offspring condition and life history. Such effects are well-known in insects (Fox & Czesak 2000, Mousseau & Dingle 1991, Rossiter 1996). For example, in the cockroach *Diploptera punctata*, maternal nutrient investment in embryos affects development rate and body size of male offspring (Holbrook & Schal 2004). Provisioning effects may also occur in rodents (Cowley & Griesel 1966, Zamenhof et al. 1971). In birds, mothers can vary their yolk allocation to eggs (Rutstein et al. 2004).

In some animals, fathers also provision their offspring, and variation in paternal provisioning can affect offspring phenotype. Male insects can transfer nutritious nuptial gifts to females during mating (Gwynne 1988, Vahed 1998), or feed offspring directly (Hunt & Simmons 2000, Rauter & Moore 2002). For example, in the dung beetle *Onthophagus taurus*, large, horned males contribute to the dung balls eaten by larvae and, thus, produce larger offspring and sons with larger horns (Hunt & Simmons 2000).

Transmission of the Extraorganismal Environment

Offspring begin life in the environment where their mother deposited them as eggs or juveniles, and maternal choice of extraorganismal environment can affect offspring phenotype and contribute to offspring-maternal resemblance (see Roitberg 1998). Variation in maternal behavior can reflect variation in maternal genes, inherited nongenetic factors, and stochastic environmental variation, and can affect key parameters of offspring environment such as microclimate, resource abundance and quality, host type, exposure to pathogens and predators, and social environment. For example, mothers can influence offspring larval diet, which affects life history and morphology (Fox 2006, Fox et al. 1995, Rotem et al. 2003). In *Drosophila subobscura*, females inoculate oviposition substrates with yeast, thus increasing the larval viability of their offspring (Rohlfs & Hoffmeister 2005). In

the seed beetle *Callosobruchus maculatus*, females that oviposit on seeds containing eggs from other females produce smaller offspring that, in turn, produce smaller eggs (Fox & Savalli 1998). In some reptiles, females return to the nesting-site used by their mother (Freedberg & Wade 2001). Paternal phenotype can also affect the extraorganismal environment experienced by offspring. In some fish, males build nests into which females deposit their eggs (Giacomello et al. 2006), or brood eggs in their bodies (Peters & Berns 1982, Wilson et al. 2003).

Transmission of Behavior and Culture

In many vertebrates, parental behavior can shape offspring behavior via learning, and exert a powerful influence on offspring brain development (Avital & Jablonka 2000). Such effects are also possible in some arthropods (e.g., Avital & Jablonka 2000, Rauter & Moore 2002).

Cultural variation is especially pronounced in humans (Boyd & Richerson 1985, Cavalli-Sforza & Feldman 1981, Richerson and Boyd 2005) and some other primates (Whiten et al. 1999), but complex behavioral repertoires are transmitted nongenetically to offspring in many mammals and birds (Avital & Jablonka 2000). Many birds learn to sing by listening to parental song, or acquire mate preferences by imprinting[4] on parental traits (Freeberg 2000). Maternal and paternal behavior can influence offspring brain development and behavior in many other ways (Bjorklund 2006, Harper 2005). For example, in the mouse *Peromyscus californicus*, where both parents provide care, experiments show that paternal grooming and retrieval of pups affect the pups' brain chemistry and levels of aggression in adulthood (Frazier et al. 2006). Avital & Jablonka (2000) discuss numerous examples of such effects.

THE ROLE OF NONGENETIC INHERITANCE IN EVOLUTION

In this section, we outline a general conceptual framework for the study of nongenetic inheritance and its implications for evolution. Using this framework, we illustrate how the presence of nongenetic inheritance can overcome some of the limitations of genetic inheritance, and thereby produce phenotypic and evolutionary change that cannot be anticipated under the Mendelian-genetic model. These consequences flow from a crucial property of nongenetic inheritance: the partial decoupling of phenotypic change from genotypic change (Avital & Jablonka 2000; Cavalli-Sforza & Feldman 1981; Jablonka et al. 1992, 1995; Kirkpatrick & Lande 1989; Lachmann & Jablonka 1996; Lande & Kirkpatrick 1990; Pál 1998).

A General Conceptual Framework

Consider the common quantitative genetic model of phenotypic evolution (see Falconer & Mackay 1996). With solely genetic inheritance, the value of a phenotypic trait, z, is partitioned into an additive genetic component, g, and an uncorrelated environmental component, e, whose average value is defined to be zero (that is, e is essentially a stochastic component of the phenotype). Thus, we can write $z = g + e$, and the population average trait value is $\bar{z} = \bar{g}$. As a result, when modeling evolutionary change, we can track either the underlying genetic evolution of $\bar{g}$ or the mean phenotype itself, $\bar{z}$; there is essentially a complete coupling between the two. The commonly used model for evolutionary change in $\bar{g}$ can be expressed as

$$\bar{g}(t+1) = \bar{g}(t) + G\beta, \qquad\qquad 1.$$

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[4]Note the distinction between mate-choice imprinting (a form of learning) and genomic imprinting (a phenomenon related to transgenerational epigenetic inheritance).

where G is the additive genetic variance, and β is the selection gradient arising from the fitness function under consideration. Because there is complete coupling between mean phenotype and mean genotype [that is, $\bar{z}(t) = \bar{g}(t)$], this model is more commonly written in terms of phenotypic evolution as $\bar{z}(t + 1) = \bar{z}(t) + G\beta$. More generally, however, we might write Equation 1 as $\bar{g}(t+1) = \bar{g}(t)+L(W, p_{gz})$, where L is the evolutionary change in mean genotype in one generation, which depends on both the fitness function, W, and on the joint genotypic-phenotypic distribution in the population, p_{gz}.

Nongenetic inheritance provides an additional form of transmission from parent to offspring, so model (1) can be extended to include two equations, each tracking one of the components of inheritance. For example, suppose that the phenotype is now given by $z = g + \delta + e$, where δ is an inherited, nongenetic, component of phenotype (**Figure 1**, *yellow arrow*). In this case the mean phenotype is $\bar{z} = \bar{g} + \bar{\delta}$, and change in the mean phenotype is partially decoupled from the evolution of $\bar{g}$. To model phenotypic change we now need to track the change in both $\bar{g}$ and $\bar{\delta}$:

$$\bar{g}(t + 1) = \bar{g}(t) + M(p_{gz\delta}, \tilde{W}) \qquad \text{2a.}$$

$$\bar{\delta}(t + 1) = \bar{\delta}(t) + N(p_{gz\delta}, \tilde{W}), \qquad \text{2b.}$$

where M is the change in the average genetic composition of the population, and N is the change in the average value of the nongenetic component of inheritance. In general, both M and N will depend on the fitness function, $\tilde{W}$, which itself might be affected by the presence of nongenetic inheritance—hence the distinction between W in Equation 1 and $\tilde{W}$ in Equations 2. For example, the fitness function in Equations 2 might depend on the distribution of the nongenetic component of inheritance in the population. In this case, the presence of nongenetic inheritance would not only affect the expression of the phenotype, but it would alter the way in which selection acts on the genetic and nongenetic components as well (e.g., see Laland et al. 1996, 1999; Odling-Smee et al. 2003). The functions M and N in Equations 2 also depend on the joint distribution of g, z, and δ in the population.

This model captures fundamental attributes of theory developed for particular modes of nongenetic inheritance. As an example, consider the maternal effects model of Kirkpatrick & Lande (1989, also see Lande & Kirkpatrick 1990). In the context of Equations 2, the Kirkpatrick & Lande (K-L) model assumes that the fitness function is independent of the phenotypic composition of the population, and therefore the presence of nongenetic inheritance does not influence the way that selection acts (that is, $\tilde{W} = W$, in the above notation). One can also show that the change in the genetic composition of the population simplifies to $M = (G + C_{g\delta})\beta$ in the K-L model, where $C_{g\delta}$ is the covariance between the genetic and nongenetic components of inheritance. Furthermore, although the K-L model does not explicitly track the nongenetically inherited quantity, δ, separately from the genetically inherited component, one can show that the assumptions of the K-L model imply that the change in the nongenetic composition of the population is given by $N = m\bar{g}(t) - (1 - m)\bar{\delta}(t) + mP\beta$, where m is the effect of maternal phenotype on offspring phenotype, and P is the phenotypic variance of the trait, z. Therefore, Equations 2 simplify to

$$\bar{g}(t + 1) = \bar{g}(t) + (G + C_{g\delta})\beta \qquad \text{3a.}$$

$$\bar{\delta}(t + 1) = m(\bar{g}(t) + \bar{\delta}(t) + P\beta) \qquad \text{3b.}$$

The difference between the formulation of the K-L model given in Equations 3 and that in the original formulation given by Kirkpatrick & Lande (1989) is that Equations 3 explicitly decompose the evolutionary process into the changes that occur in each of the two components of inheritance. The formulation in Kirkpatrick & Lande (1989), however, does not explicitly model the transmission dynamics of the nongenetic inheritance. Rather, it lumps both types of inheritance

together by tracking the phenotypic dynamics. This results in a single equation for the dynamics of $\bar{z}$ that includes a time lag, rather than the two equations for $\bar{g}$ and $\bar{\delta}$ in Equations 3, which have no time lag (Kirkpatrick & Lande 1989).

Equation 3a is the same in form as Equation 1 for evolution in the absence of nongenetic inheritance, but has the additional term $C_{g\delta}$, which reflects the way in which the presence of nongenetic inheritance alters the ability of natural selection to effect change on the genetic composition of the population. Equation 3b reveals that the mean value of the nongenetic quantity in the offspring generation is simply the value of the mean phenotype in the parental generation after selection $[\bar{g}(t) + \bar{\delta}(t) + P\beta = \bar{z}(t) + P\beta]$, weighted by the strength of the maternal effect, m. Equations 3 therefore provide a specific example of the general decoupling of phenotypic and genotypic change across generations seen in Equations 2, for the case of a specific kind of nongenetic inheritance (that is, maternal effects).

Implications for Evolutionary Biology

The decoupling of phenotypic change from genotypic change brought about by nongenetic inheritance can have some interesting consequences for the study of evolution. Generally speaking, all such effects stem from the fact that this decoupling partially removes some limitations of genetic inheritance, and thereby allows the phenotypic distribution of a population to change in ways that might not otherwise be possible. Indeed, strictly speaking, such phenotypic change need not involve evolution at all because the change might be mediated entirely by nongenetic factors. A striking consequence of such decoupling is that the response of the mean phenotype to selection need not always be in the direction of selection (Boyd & Richerson 1985, Cavalli-Sforza & Feldman 1981, Kirkpatrick & Lande 1989, Laland et al. 1996, Lande & Kirkpatrick 1990, Odling-Smee et al. 2003). Furthermore, maternal effects models have revealed a phenomenon (sometimes termed evolutionary momentum) whereby phenotypic change continues even after selection has ceased (Kirkpatrick & Lande 1989, Laland et al. 1996, Lande & Kirkpatrick 1990). As can be seen in Equations 3, however, the phrase evolutionary momentum is somewhat misleading because the cessation of selection (setting $\beta = 0$) does actually lead to the cessation of evolution (that is, change in the genetic composition of the population). Nevertheless, the fact that the resulting phenotypic change is heritable suggests to us that it is still appropriate to consider such nongenetic effects within the purview of evolutionary biology, and to regard them as being evolutionarily significant in a general sense, even if they do not affect evolutionary dynamics *sensu stricto* (that is, the dynamics of gene frequencies).

It is also possible, however, for nongenetic inheritance to affect the evolutionary dynamics of gene frequencies per se. For example, the more general model encapsulated in Equations 2 can produce true evolutionary momentum, whereby the genetic composition of the population continues to change even after externally imposed selection has ceased. This can occur if fitness depends on the phenotypic distribution of the population (Odling-Smee et al. 2003). Under such circumstances, externally imposed selection can leave a signature in the fitness landscape via changes in the transmissible component of the phenotype ($\bar{\delta}$), even after the external source of selection is removed (**Figure 2**). Evolutionary momentum results from a feedback between the genetic and nongenetic inheritance systems, whereby a change in a transmissible component of the environment, brought about by nongenetic inheritance, affects selection on genes (see Boyd & Richerson 1985; Jablonka & Lamb 1995, 2005; Laland et al. 1996, 1999; Odling-Smee et al. 2003; Richerson & Boyd 2005).

Although there are a variety of potential evolutionary implications of nongenetic inheritance, both in a general sense and in the strict sense mentioned above, a great many of these can be
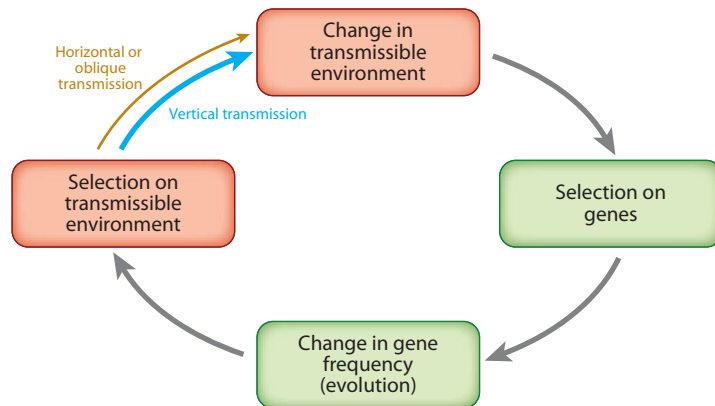
Figure 2

A general representation of the feedback mechanism by which nongenetic inheritance can influence evolution. Selection on a transmissible component of the environment alters the environment within which the genes reside, resulting in a change in the fitness landscape and influencing selection on the genes, leading to evolution (change in allele frequency). This, in turn, alters selection on the transmissible component of the environment. Nongenetic inheritance (that is, vertical transmission) is represented by the blue arrow at top left, whereas horizontal and oblique transmission is represented by the yellow arrow (see text).

understood as arising from one of three general ways in which nongenetic inheritance overcomes some of the limitations of genetic inheritance: (*a*) Although genetic inheritance does not allow for traits acquired during the lifetime, such as high condition or learned behaviors, to be transmitted to offspring, nongenetic inheritance does. (*b*) Genetic recombination breaks up favorable combinations of alleles so that a parent with a high-fitness genotype is usually unable to transmit its full genetic potential to its offspring. In contrast, nongenetic inheritance permits the transmission of favorable trait combinations across generations. (*c*) Selection can deplete additive genetic variation, reducing heritability and the potential for phenotypic change. Through nongenetic inheritance, however, environmental heterogeneity can generate heritable phenotypic variation. Below, we consider some potential implications of the above three properties of nongenetic inheritance. For each property, we first outline examples that are evolutionarily important in a general sense, and then consider cases that have evolutionary implications in the stricter sense of altering gene frequency dynamics.

Transmission of acquired phenotypes. Nongenetic inheritance allows for the transmission of acquired (that is, environmentally induced) traits. This phenomenon extends the concept of phenotypic plasticity (environmental effects on gene expression and development) across generations, allowing for plastic responses in the parental generation to alter development in offspring, even if the offspring themselves do not experience the inducing environmental factor. Although phenotypic plasticity represents purely phenotypic effects rather than evolution, biologists have long recognized its importance in evolution (Baldwin 1896, Lloyd Morgan 1896, Waddington 1942, West-Eberhard 2003). Facultative, plastic responses can permit populations to persist in the face of environmental change that is too rapid for evolutionary (genetic) adaptation (Lloyd Morgan 1896). Plasticity also allows for a degree of fine-tuning of the phenotype that cannot be achieved by genes alone (Hinton & Nolan 1987). However, evolutionary change can follow on the heels of phenotypic change though the eventual assimilation and canalization of optimal phenotypes (Waddington 1942, West-Eberhard 2003). The transmission of acquired

traits can have even greater consequences than within-generation plasticity alone. Although, initially, such changes can be purely phenotypic, they can ultimately affect the course and rate of evolution.

When environmental change is rapid or cyclical, the transmission of adaptive, environmentally induced traits can enhance individual and population-mean fitness by eliminating the lag-time associated with de novo induction of the phenotype in offspring (Jablonka et al. 1992, 1995; Lachmann & Jablonka 1996). Nongenetic transmission over several generations could, in some cases, also result in cumulative phenotypic effects that accentuate the expression of a beneficial phenotype (see Cowley & Griesel 1966, Agrawal et al. 1999). Jablonka et al. (1995) argue that nongenetic inheritance of acquired traits represents "an adaptive mechanism on the ecological timescale that fills the gap between short-term individual adaptations and long-term evolutionary adaptations." Such effects can also influence population dynamics (Ginzburg 1998), and even the associations between species within ecological communities (Jablonka et al. 1995). For example, in many taxa, mothers alter the phenotypes of their offspring (perhaps via transgenerational epigenetic inheritance) in ways that appear to preadapt the offspring to the kinds of parasites that the mothers themselves encountered (Poulin & Thomas 2008). Environmentally induced defenses against herbivores or predators can also be transmitted to offspring (Agrawal et al. 1999). Likewise, some effects of parental or grandparental diet on descendants' physiology (e.g., Anderson et al. 2006) or susceptibility to disease may reflect the effects (or breakdown) of adaptive mechanisms whereby individuals adjust the phenotype of their offspring based on their own diet (Pembrey 2002, Pembrey et al. 2006). Because such effects may tend to flatten the fitness landscape, they could promote population persistence without genetic change (Jablonka et al. 1995, Lachmann & Jablonka 1996, Pál 1998, Pál & Miklós 1999). However, by allowing organisms to thrive in hostile or changing environments, the transmission of acquired defenses or other facultative phenotypes can promote the evolution of new niche-exploitation strategies.

The transmission of acquired traits can also have evolutionary consequences in the strict sense, by altering the fitness landscape and thereby generating a feedback between the genetic and nongenetic inheritance systems. Consider an example adduced by Richerson & Boyd (2005)— the evolution of lactose metabolism in adult humans. Human infants secrete lactase, an enzyme involved in the breakdown of the milk-sugar lactose. In most human populations (as in other mammals), lactase secretion ceases after weaning. However, in some European and African populations that maintain domesticated cattle, the use of milk in the adult diet has spread through cultural transmission. The cultural change generated selection on genes that regulate lactase secretion, favoring an allele that causes continued lactase secretion after weaning. This evolutionary change, in turn, reinforced cultural selection favoring milk use by enabling more adults to digest milk effectively. In other words, nongenetic inheritance brought about a change in selection on genes, causing evolution that, in turn, reinforced nongenetic inheritance.

This example highlights two important caveats, however. First, although we have restricted the definition of nongenetic inheritance to vertical transmission, similar feedback effects can arise through horizontal or oblique transmission (see **Figure 2**, *yellow arrow*), as shown by models of cultural evolution (Boyd & Richerson 1985, Richerson & Boyd 2005). In the above example, dietary preferences could have spread mainly through social interactions between unrelated individuals, within extended families, or within cohorts. Nonetheless, we believe that, in most cases, vertical transmission is far more important in practice than horizontal or oblique transmission for understanding phenotypic variation within generations. It is likely that the greatest share of learning and other modes of nongenetic inheritance are mediated by offspring-parent interactions through the uniquely close contact between offspring and their parents (Avital & Jablonka 2000, Harper 2005). Thus, a preference for milk seems more likely to be shaped by the foods prepared

by one's parents and grandparents than by observing the habits of other households. We argue that the special importance of vertical transmission as a source of phenotypic variation justifies a focus on nongenetic inheritance as a distinct and important phenomenon. Second, it can be argued that any trait could, in principle, evolve in the absence of nongenetic inheritance. However, as the examples discussed here illustrate, many traits are far more likely to evolve, or can evolve much faster, through the agency of nongenetic inheritance. For example, it is unlikely that the domestication of cattle, a preference for milk in the adult diet, and the consequent selection on genes affecting lactase secretion, could have come about in the absence of nongenetic inheritance. Although this example is drawn from the literature on human culture (Richerson & Boyd 2005), such feedback processes are not limited to humans, or to the transmission of learned behaviors. Many traits are influenced by nongenetic inheritance in other animals (e.g., see Avital & Jablonka 2000), and theory suggests that feedback between genetic and nongenetic inheritance systems could play a wide-ranging and fundamental role in evolution. This example also highlights the fact that nongenetic inheritance can influence the evolution of traits that are not themselves subject to nongenetic inheritance.

Maintenance of favorable trait combinations. Nongenetic inheritance can allow for the transmission of favorable trait combinations because it is not subject to the disruptive effects of recombination. The problem of sex-differentiation illustrates the potential evolutionary implications of this property of nongenetic inheritance. When selection favors different phenotypes for homologous traits in females and males, intersexual inheritance (the transmission of alleles from mother to son and father to daughter) can impede the evolution of adaptive sexual dimorphism in response to sex-specific selection because male-benefit alleles are transmitted to daughters and female-benefit alleles are transmitted to sons (Day & Bonduriansky 2004). Because nongenetic inheritance can function in a sex-specific manner (Badyaev 2005, Vigé et al. 2008), it can potentially mitigate the severity of such conflicts. In particular, genomic imprinting could, in theory, contribute to the maintenance of favorable sex-specific trait combinations for such traits by allowing males (females) to express only the alleles inherited from their fathers (mothers). Such offspring-sex-dependent imprinting (see Hager et al. 2008) can permit both sexes to more closely match their optimal phenotype (Day & Bonduriansky 2004). Genomic imprinting could thereby influence sexually antagonistic coevolution (Bonduriansky & Chenoweth 2009).

Genomic imprinting could also play a role in other situations where offspring may benefit from greater resemblance to one parent. For example, if offspring fitness is enhanced by maximizing the fit with maternal phenotype, then selection will favor enhanced offspring-maternal resemblance via the silencing of paternally inherited alleles (Wolf & Hager 2006).

By allowing for the transmission of favorable trait combinations, nongenetic inheritance can also influence evolution in the strict sense. For example, nongenetic inheritance can interact with genetic inheritance to promote the evolution of reproductive isolation between populations (Jablonka & Lamb 1995, 2006; Bossdorf et al. 2008). It has been suggested that phenotypic divergence in plastic traits can facilitate the evolution of reproductive isolation (West-Eberhard 2003). Nongenetic inheritance can strengthen such effects by bolstering both pre- and postmating barriers to gene flow. Behavioral imprinting on plastic or population-specific components of parental phenotype can result in discrimination against phenotypically distinct migrants as potential mates (Laland 1994, Verzijden et al. 2005). Moreover, nongenetic transmission of local variations in chromatin structure might reduce hybrid viability and, thus, favor premating barriers to gene flow (Jablonka & Lamb 2006). Here, once again, nongenetic inheritance can bring about a change in a transmissible component of the environment (mate preference or hybrid viability) that, in turn,

alters selection on genes (e.g., alleles affecting traits involved in species-recognition), promoting evolution and speciation.

Maintenance of heritable variation.   Through nongenetic inheritance, environmental effects on the phenotype can contribute to heritable variation. Such variation can result from random and potentially environment-independent processes analogous to genetic mutation (e.g., epimutation), as well as from facultative, plastic responses to ambient conditions.

Experiments with *Drosophila* have shown that rapid and relatively stable phenotypic change can occur via selection on heritable epigenetic variation that appears to arise randomly (that is, nonfacultatively) with respect to the fitness landscape (see Sollars et al. 2002). Through such effects, adaptive phenotypic change can occur without genetic change. Like the transmission of environmentally induced phenotypes, such effects may promote population persistence in rapidly changing environments, particularly when the mean phenotype is far from the optimum (Pál 1998, Pál & Miklós 1999), and ultimately facilitate genetic adaptation and promote reproductive isolation.

The maintenance of heritable variation through nongenetic inheritance can also influence evolution in the strict sense. Consider variation in condition, an important trait that reflects both environmental and genetic variation in the total quantity of metabolic resources available to an individual, and the efficiency with which these resources can be converted into fitness. Condition is a key determinant of fitness, but much of the variation in condition is determined by environmental variables such as diet quality (Bonduriansky 2007). Empirical evidence shows that mothers and fathers transmit environmentally acquired condition nongenetically to offspring in many species (Qvarnström & Price 2001, Bonduriansky & Head 2007), and this can contribute to heritable variation for fitness. One interesting consequence of this phenomenon can be seen in sexual coevolution. Classic theory has suggested that indirect selection (or so-called good genes processes) may be too weak to maintain costly female mate preferences because the necessary genetic variation in male quality will ultimately be depleted through directional selection (Kirkpatrick & Ryan 1991, Qvarnström & Price 2001). This is the so-called paradox of the lek. The fact that female preferences nonetheless evolve and persist suggests that indirect selection is, in fact, sufficiently strong, but it remains unclear by what mechanism heritable variation is maintained, and whether it be sufficiently important to drive sexual coevolution. However, if a male's condition (that is, viability and attractiveness) depends on both its own and its father's environment (that is, paternal condition is transmitted to offspring), then a costly female preference for high-condition males can spread because it will enhance offspring condition (Bonduriansky & Head 2007; T. Day & R. Bonduriansky, unpublished). Low-condition males will, of course, also transmit their condition to their offspring. However, as with any other fitness-enhancing trait, the transmission of condition will have a net benefit because it will enhance the fitness of high-condition individuals, which contribute disproportionately to the next generation. Heritable variation in male condition will be maintained because part of the variation is generated by environmental heterogeneity. Thus, nongenetic inheritance (transmission of male condition) alters selection on genes (female preferences), influencing evolution (see **Figure 2**).

Besides the transmission of condition to offspring, nongenetic inheritance can contribute to heritable variation in male quality in several other ways. Indirect genetic effects of maternal care on male attractiveness can augment heritable variation in male quality by allowing males to signal good genes for maternal care (Wolf et al. 1999, Qvarnström & Price 2001). Likewise, heritable epigenetic variation in the competitive ability of sperm can contribute to heritable variation in male quality (Zeh & Zeh 2007). All of these phenomena can influence the evolution of female mating preferences.

THE EVOLUTION OF NONGENETIC INHERITANCE

In the previous section, we outlined some potential consequences of the existence of nongenetic inheritance for evolution, but how did nongenetic inheritance arise in the first place? Is it adaptive, and if so, what selective factors were likely involved in its evolution? Although theoretical analyses have explored the consequences of nongenetic inheritance for the evolution of other traits, surprisingly little theory has been developed to explore the evolution of the molecular machinery that gives rise to nongenetic inheritance itself (although see Burt & Trivers 1998, Day & Bonduriansky 2004). Nonetheless, like previous authors (Boyd & Richerson 1985; Cavalli-Sforza & Feldman 1981; Jablonka & Lamb 1995, 2005; Richerson & Boyd 2005), we believe that nongenetic inheritance systems combine adaptive and nonadaptive features. Although nongenetic inheritance may inevitably occur as a transgenerational form of developmental noise, selection is expected to favor genes that hone nongenetic inheritance mechanisms as strategies to enhance genetic fitness (Jablonka & Lamb 1995, 2005).

A number of adaptive hypotheses have been proposed for the evolution of nongenetic inheritance and, as the examples discussed above show, such effects clearly have the potential to enhance fitness. For example, mechanisms involving the transmission of epigenetic marks might have evolved to silence transposable elements (Bestor 2003), facilitate pairing of homologous chromosomes during cell division (de la Casa-Esperon & Sapienza 2003), or allow organisms and populations to respond to rapid fluctuations in environmental conditions (Jablonka et al. 1995, Lachmann & Jablonka 1996). In the case of adaptation to environmental change, the lability of nongenetically transmitted phenotypes is an essential feature of their utility, and genes that affect the rate of attenuation of environmentally induced phenotypes over multiple generations are likely to be under strong selection (Jablonka et al. 1995). Nongenetic inheritance may also enhance fitness by allowing parents to pass on learned behaviors, or other beneficial acquired traits such as high condition, to their offspring (Avital & Jablonka 2000, Bonduriansky & Head 2007). Effects of this type may evolve as integral components of the reproductive strategy.

Nonetheless, there is considerable potential for parent-offspring conflicts over nongenetic inheritance (Lacey 1998, Marshall & Uller 2007, Uller 2008). Nongenetically transmitted factors may have differential consequences for the fitness of parents and their offspring, particularly where the transmission and/or expression of such factors is costly. Nongenetic inheritance of particular traits may therefore be maladaptive for parents, offspring, or both. The evolutionary dynamics and outcomes of such conflicts remain poorly understood.

Regardless of their current function, however, the evolutionary origins of nongenetic inheritance mechanisms may be largely nonadaptive. Nutritional, somatic, environmental, and behavioral mechanisms of transmission may have originated as inevitable by-products of the interaction of parental phenotypic variation with plastic traits in developing offspring. Likewise, epigenetic and cytoplasmic transmission may occur as an incidental by-product of the imperfect fidelity of cytological mechanisms that reset the epigenetic and cytoplasmic state between generations. This view is supported by the maladaptive consequences of nongenetic inheritance. For example, nongenetic transmission of disease susceptibility (Gluckman et al. 2007, Youngson & Whitelaw 2008) probably represents a transgenerational symptom of ancestral disease states, much as some nongenetic effects of parental age (see Diaz & Esponda 2004) might be viewed as transgenerational manifestations of senescence. All nongenetic inheritance mechanisms are likely to function nonadaptively, however, in environments very different from those where they evolved. For example, strategies whereby ancestors adjust descendants' physiology and metabolism for optimal functionality in the anticipated dietary environment may malfunction when confronted with rapid

and unprecedented changes of environment and life-style, like those experienced by modern humans (see Pembrey 2002, Pembrey et al. 2006). Similar reasoning applies to the transmission of behavioral variation (Avital & Jablonka 2000). Indeed, in such circumstances, nongenetic inheritance may interfere with the potential for adaptive plasticity in descendants encountering novel conditions.

Theory also suggests that nongenetically transmitted factors that promote their own transmission may spread within populations, even if they reduce individual and population-mean fitness (see Freedberg & Wade 2001). This is possible because the rate of spread is a function of transmission probability as well as selection (Cavalli-Sforza & Feldman 1981). The evolution and fitness consequences of such factors pose interesting problems for future research.

FUTURE DIRECTIONS

Empirical evidence shows that nongenetic inheritance can contribute to variation in phenotype and fitness. However, despite the many fascinating results produced by laboratory studies, few ecologically relevant traits have thus far been explicitly examined for nongenetic inheritance, particularly in natural environments (Bossdorf et al. 2008). The extent to which some of the effects identified in the laboratory carry over to natural settings thus remains unknown. Natural environments also contain a much greater variety of environmental variation that can potentially result in nongenetic inheritance, including variation from interspecific interactions (e.g., Jablonka et al. 1995, Poulin & Thomas 2008). Consequently, although the potential for nongenetic inheritance to influence phenotypic variation and fitness is no longer in doubt, its actual role and importance in natural populations remains uncertain. This knowledge gap must be addressed through experimental studies on nongenetic inheritance of ecologically relevant traits, using tractable laboratory and field models.

Theory clearly shows that nongenetic inheritance can have wide-ranging consequences for long-term phenotypic change and evolution. Nonetheless, most past theoretical treatments have focused on particular mechanisms or examples of nongenetic inheritance, such as cultural transmission and maternal effects. Perhaps because of its presumed limitation to certain taxa and traits, this work has had relatively little influence on fundamental evolutionary theory. There is a need to develop a general, synthetic theory of evolution encompassing both genetic and nongenetic inheritance.

We have outlined a general conceptual framework for understanding the evolutionary implications of nongenetic inheritance, but have not considered the potential structure of a statistical model for estimating the contributions of nongenetic inheritance to observed phenotypic variation. The standard quantitative-genetic model (Falconer & Mackay 1996) can, in principle, be extended to incorporate all distinct sources of variation due to parental environment and genotype, and its interaction with offspring genes and environment (see Bossdorf et al. 2008, Gorelick 2005, Santure & Spencer 2006). A complete model would thus include additive and nonadditive genetic effects, environmental effects, and separate terms describing maternal and paternal nongenetic and indirect genetic effects, genomic imprinting effects, and a complete set of interaction terms. However, the enormous complexity of such a model may limit its utility as a tool for empirical analysis of phenotypic variation. Manipulative approaches designed to test specific hypotheses may be more tractable (see Johannes et al. 2008).

As Jablonka & Lamb (1995, 2005) have been arguing for over a decade, an understanding of the implications of nongenetic inheritance will lead to a more powerful model of evolution. We see the development of such a model as a key challenge for biology.

> **SUMMARY POINTS**
>
> 1. We define nongenetic inheritance as an effect on offspring phenotype brought about by vertical transmission of factors other than DNA sequences. Nongenetic inheritance can have wide-ranging phenotypic effects in animals, plants, and simple organisms.
>
> 2. Nongenetic inheritance encompasses a diversity of mechanisms, including transgenerational epigenetic inheritance and genomic imprinting, the transmission of substances via the gametes or the transfer of parental soma to embryos or juveniles, and the transmission of behavior and culture through learning. These mechanisms can convey influences of the parental phenotype (including effects of the extraorganismal environment), as well as influences of parental genes.
>
> 3. Nongenetic inheritance can be conceptualized as an extension of the Mendelian-genetic model of inheritance.
>
> 4. The evolutionary implications of nongenetic inheritance flow from the fact that nongenetic inheritance decouples phenotypic change from genotypic change and, in so doing, can overcome some of the limitations of genetic inheritance. As a result, nongenetic inheritance can not only bring about phenotypic change, but also alter the fitness landscape and influence long-term evolution.
>
> 5. We need a synthetic theory of evolution that integrates genetic and nongenetic inheritance systems. Research must also address the evolution of nongenetic inheritance mechanisms themselves, and the role of parent-offspring conflicts and the interplay of multiple levels of selection in shaping the nature and fitness-consequences of such mechanisms. Empirical research must explore the ecological importance of nongenetically transmitted phenotypic variation.

DISCLOSURE STATEMENT

ACKNOWLEDGMENTS

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