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# The Extended Evolutionary Synthesis and the role of soft inheritance in evolution

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# The Extended Evolutionary Synthesis and the role of soft inheritance in evolution

## *Abstract*

In recent years a number of researchers have advocated extending the modern synthesis in evolutionary biology. One of the core arguments made in favour of an extension comes from work on soft inheritance systems including transgenerational epigenetic effects, cultural transmission, and niche construction. In this paper we outline this claim and then take issue with it. We argue that the focus upon soft inheritance has led to a conflation of proximate and ultimate causation, which has in turn obscured key questions about biological organization and calibration across the life-span to maximize average lifetime inclusive fitness. We illustrate this by presenting hypotheses that we believe incorporate the core phenomena of soft-inheritance and will aid in understanding them.

**Keywords:** Soft inheritance; Extended Evolutionary Synthesis; Epigenetic inheritance; Proximate and Ultimate causation

## 1. Introduction

By the 1940s the Darwinian view of evolutionary change was married with Mendelian genetics to produce what has come to be known as the modern synthesis (MS) [1-3]. Recently, some researchers have argued that a new extended evolutionary synthesis (EES) is necessary [4] in order to account for specific phenomena. These phenomena come from several different areas of enquiry, but many can be grouped under the banner of 'soft inheritance' [5]. This term, coined by Mayr [6], refers to the inheritance of variations that are the result of non-genetic effects. Those arguing for an EES draw upon examples of soft inheritance coming from evolutionary developmental biology, epigenetics, niche construction, and learning and cultural transmission [7-11].

Each of these fields describe non-genetic processes that introduce phenotypic variation, which has some utility and can be inherited. For instance, Jablonka and Lamb [5] point to the fact that there is heritable variation that is developmentally induced and not caused by underlying DNA sequence. A classic example of this comes from the licking and grooming literature in rats, which shows that the level of licking and grooming experienced by a pup becomes an epigenetically inherited part of their own maternal behavioural phenotype and is passed on across a number of generations [12] . This is associated with other phenotypic changes, and is discussed in detail below (§5). The key point is that no new mutation is required to lead to a significant, inherited change.

Examples such as this are sometimes presented as an expansion of focus for the MS, but on occasion advocates of an EES have argued that they illustrate the need for more fundamental conceptual change, on the grounds that the MS is simply unable to account for them in a satisfactory way. For example:

> Evolutionary biology today has to incorporate soft inheritance, saltational changes due to systemic mutations, and various types of genetic exchange and cooperation. These all challenge the assumptions of the Modern Synthesis. We believe that rather than trying to continue to work within the framework of a Synthesis that was made in the middle of the last century, we now need a new type of evolutionary theory, one that acknowledges Darwinian, Lamarckian and saltational processes [5]. (p. 394)

> [When] niche construction is added to the [MS] it extends the "Synthesis." The evolution of organisms now depends on natural selection and niche construction' [13]. (p. 176)

If such claims are correct, they potentially cast doubt on the theoretical foundations of several areas of biology. Yet despite this, there have been few explicitly critical analyses of the claims made for an EES [14,15].

Our aim is to review the EES argument from soft inheritance. We will focus in particular on epigenetic inheritance and will conclude that the term 'soft inheritance' refers to a kind of proximate mechanism, with the ultimate function of calibrating behaviour in the face of environmental uncertainty. This poses no challenge to the explanatory and conceptual resources of the MS, which are sufficient.

We begin with a brief historical overview of the MS and its central commitments. Following this we detail the soft inheritance claims, presenting our argument that, when seen as a proximate mechanism, soft inheritance fits straightforwardly within the MS. This failure to recognise the proximate character of soft inheritance means that there is a set of novel hypotheses about ultimate function that are presently unaddressed. We conclude by outlining examples of these hypotheses. Our overall goal is not to defend or promote a particular view of the MS, but rather to analyse the coherence of one of the central elements of the putative EES.

## 2. The Modern Synthesis

The epithet, the modern synthesis, was coined in the subtitle of Huxley's 1942 book *Evolution: The Modern Synthesis*. Huxley regarded the synthesis as a two-stage process beginning with marriage and then moving onto the application of this framework to various sub-disciplines in biology.

At the beginning of the twentieth century the particulate views of inheritance promoted by Mendelians were seen as incompatible with the models of gradual, incremental change proposed by the Darwinians. Thanks to the mathematical modelling of the population dynamics of gene pools by Fisher, Haldane and Wright this impasse was resolved. Thus the first stage of the MS was the use, or invention of population genetics to bring Mendel and Darwin conceptually together such that evolutionary forces could now account for changes in gene frequencies within populations. This stage can be read as one of restriction [2] as it also led to the removal of Lamarckianism, saltationism and orthogenesis, which were not compatible with a particulate model of gradual evolution driven by external forces. What this stage of the synthesis did not do was enforce a particular focus upon levels of selection, nor upon natural selection as the predominant force in evolutionary change. In particular, drift could still be seen as a significant, if external force.

According to Gould [2], the second stage of the synthesis saw the emergence of a much narrower and more dogmatic focus upon natural selection as the predominant evolutionary force. This is the stage Gould is most critical of and he can be seen as an early pioneer of the EES movement. Gould describes the transition from stage one to two as one from a pluralist view that simply saw that everything must be consistent with genetics to a conception that natural selection is a sufficient cause of all evolutionary change. To support this Gould cites Mayr's definition of the MS, some twenty years after Huxley:

> The proponents of the synthetic theory maintain that all evolution is due to the accumulation of small genetic changes, guided by natural selection, and that transpecific evolution is nothing but an extrapolation and magnification of the events that take place within populations and species [16]. (p.586)

Embodied within this quotation are the core ideas that natural selection operating over genes within populations is the predominant force of micro-evolutionary change and that these micro-evolutionary changes can also account for macro-evolutionary change. But, a further 23 years down the line a leading textbook summarizes the situation more subtly, and in a slightly more pluralistic vein than Gould and Mayr implied:

> The major tenets of the evolutionary synthesis, then, were that populations contain genetic variation that arises by random (i.e. not adaptively directed) mutation and recombination; that populations evolve by changes in gene frequency brought about by random genetic drift, gene flow, and especially natural selection; that most adaptive genetic variants have individually slight phenotypic effects so that phenotypic changes are gradual (although some alleles with discrete effects may be advantageous, as in certain color polymorphisms); that diversification comes about by speciation, which normally entails the gradual evolution of reproductive isolation among populations; and that these processes, continued for sufficiently long, give rise to changes of such great magnitude as to warrant the designation of higher taxonomic levels (genera, families, and so forth) [17]. (p.12)

Natural selection is still predominant, but not regarded as the sole cause. But within this quotation we can see a commitment to gradualism, micro-evolutionary changes accounting for all, and, as with Mayr, a focus on genes [18].

While Gould and others read this second stage of the synthesis as a process of increasing dogmatism, we would not see it like this. Instead, the explanatory successes of the application of stage one across the biological sciences were enormous and naturally led to the increased use of gene-level hypotheses. This is an instrumental strategy (an 'adaptationist stance' [19]) that allowed researchers to employ a fairly Popperian process of conjecture and refutation. From a Kuhnian perspective [20], we can regard the MS as a period of scientific revolution leading to many years of normal scientific activity exploring the hypothesis-space that it

created. The MS is now a commonly agreed framework adhered to by many biologists. But one might expect a gradual accumulation of glitches, of findings that do not quite fit with the common framework, and as this accumulation increases more suitable theories will begin to be sought, theories that might encompass the glitches as well as reorganize our previously accepted facts. We would anticipate a paradigm shift.

It is this form of analysis that informs those seeking an extended synthesis. The foremost proponents of this extension are Pigliucci and Müller who have published much on this topic but have recently convened a number of scholars under the title *Evolution: The Extended Synthesis* [4]. This book is clearly a nod to Huxley and an attempt to anthologize new science. It is also an attempt to document the shifting sands of the current paradigm, the things that do not quite fit or were never included, but nothing so bold as a new alternative theory. As such they are more in line with Lakatos, steering a course between a Popperian refutation and a Kuhnian revolution. Indeed, Pigliucci and Müller [4] refer to the extended thesis as a multi-faceted research programme, hinting at their navigational task. The following quote captures their enterprise:

> The commonest reaction to our explanations is something along the lines of "But that is already understood as part of the Modern Synthesis anyway." We beg to differ. Many of the empirical findings and ideas discussed in this volume are simply too recent and distinct from the framework of the (Modern Synthesis) to be reasonably attributed to it without falling into blatant anachronism [4]. (p.4)

Pigliucci and Müller's volume presents a wealth of interesting phenomena, as do the majority of papers that support an EES, and one particular area of focus is epigenetic inheritance.

## 3. Epigenetic Inheritance

Transgenerational epigenetic effects are those where DNA sequence remains unchanged but higher-level systems are altered that lead to differences in phenotypic expression in the next generation. These systems can include DNA methylation and histone modification. In particular, the inheritance of the epigenetic modification of gene expression through processes such as methylation has been a focal interest for advocates of an EES, because they are regarded as a challenge to the hard inheritance at the core of the MS [8,9,12,15,21,22]. In this section, we will argue that epigenetic inheritance requires no extension of the MS. This argument rests on two points. The first is that we can straightforwardly interpret epigenetic processes as proximate mechanisms designed to calibrate organisms to stochastic environments. The related empirical point is that epigenetic variation is itself under genetic control.

### *3.1 The central epigenetic argument from the EES*

A key element of the EES is the concept of inclusive inheritance, where soft and hard forms of inheritance are at least equal partners. For example:

> (T)he merging of Darwinism with genetics into the modern synthesis has led to a semantic shift, resulting in the tendency to assume that only the DNA sequence is inherited across generations. However, evolution acts on any phenotypic differences that are stable across generations. According to this view, phenotypic variation should be partitioned into its transmitted versus non-transmitted components rather than into its classical genetic and environmental components [8]. (p. 475)

This use of the term evolution is odd. Evolution does not act on anything; 'evolution' describes a kind of change, change that can be caused by natural selection, drift etc. More precisely, a distinction can be drawn between a general theory of evolution and a special theory [23]. The general theory captures the basic Darwinian dynamics of variation, inheritance, competition and selection. This is potentially applicable across a large number of classes of system and constitutes a basic definition of the kind of change referred to by the term evolution. The MS is an example of a special theory, perhaps our only one, which includes competition and selection, as well as inheritance, and sees new genetic variation emerge at random, thereby affecting the phenotype. It is a mature theory with clear defined parameters of operation.

The inclusive inheritance claim is that evolution is something that operates on phenotypes and that phenotypes can be inherited by genetic and non-genetic means, such as epigenetic processes. As a consequence, advocates say, we must consider moving beyond the MS. This is neither a formal nor an empirical argument. At best it is an argument stating that phenotypic change as a consequence of epigenetic processes appears to conform to the general theory of evolution. If this is so it is of no consequence to the MS, which already has that quality as a special theory of evolution, and focuses upon a different level of biological organization (see §4).

To be clear, this is an issue of what is to be explained. Those seeking an EES, through inclusive inheritance, wish to explain changes in phenotypic frequency within populations as a consequence of epigenetic (and other soft) processes. We do not deny those processes but we do claim that any account of evolutionary change that relies upon them is not the same order of account as that of the MS. If the change through soft inheritance can be seen to conform to the general theory of evolution then this leaves open the possibility of a second special theory of evolution, that relying upon epigenetic processes. Indeed, no one from the EES position denies hard inheritance but they wish to distinguish between hard and soft contributions

because they claim that they differently affect the evolutionary dynamic [5]. But should this be established there is no logical reason to see this as a refutation or an extension of the MS, let alone a problem for it. As we shall argue (§ 3.2), epigenetic processes rely upon mechanisms that are genetically inherited. Therefore, at most these colleagues are simply focusing upon a different level of explanation and the question becomes one of how these levels relate to one another.

### 3.2 Epigenetic variation is under genetic control

A number of researchers equate phenotypic variation as a consequence of DNA sequence variation with phenotypic variation as a consequence of variation in DNA expression; epigenetic processes affecting the latter [8,9,24] . Both systems affect the phenotype, and as such epigenetic processes have a second order effect upon DNA expression. So, the inclusive inheritance model sees phenotypic variation as the *explicandum* and inclusive inheritance as the *explicans*.

Epigenetic mechanisms are also invoked to address the "missing heritability" problem in genome-wide association studies (GWAS), which show that most traits with high heritabilities (such as height, IQ, personality traits, and many common diseases) cannot be explained by association with common genetic variants [25] . This could be seen as evidence in favour of the inclusive inheritance position, however there are several possible explanations for the poor link between DNA sequence variants and heritability; including imprecise heritability estimates, statistical power in GWAS, and the ambiguity in modern behaviour genetics about the sources of non-genetic influence, particularly the concept of the "non-shared environment" [26-28] .

Epigenetic processes are a potential answer to this problem because they allow non-genetic information to be inherited across generations. But, there is a great deal of variation in epigenetic mechanisms. They are present in many taxa and multiple epigenetic mechanisms are proposed to affect development and disease; including DNA methylation, histone modifications, and non-coding RNA.  The erasure of epigenetic marks at the germline and embryogenesis in vertebrates is quite extensive and makes it a difficult topic to study (although this resetting of epigenetic profiles is uneven across taxa [29-31]).  At the very least, the potential for epigenetic transgenerational inheritance appears limited.  Moreover, quantitative genetic evidence shows that epigenetic variation itself is influenced by genetic variation. This evidence comes from twin studies of epigenetic variability, offering a reliable way of estimating heritability as a proportion of phenotypic variation. They compare similarity between MZ and DZ twins and are unbiased by age effects. The twin approach has a very

narrow definition of heritability and includes anything that does not involve DNA sequence variation in its broad definition of 'environment' (including random or stochastic processes as well as measurement error).  Thus twin studies apportion variance in a phenotype (e.g., epigenetic profiles) into their genetic and non-genetic variance components.

Twin comparisons of genome-wide epigenetic marks show that epigenetic marks are heritable on a genome-wide level [32]. Locus-specific studies of age-matched twins using multiple tissues (e.g. in 182 newborn MZ and DZ twins [33]) and blood sampling (e.g. in 196 adolescent and 176 middle-age MZ and DZ pairs [34]) report high epigenetic heritability estimates. The largest study to date, using high-resolution DNA methylation assays across buccal, gut and white blood cells, reported similar methylation profiles in MZ compared to DZ pairs (the estimates were highest for buccal samples [35]). Importantly, this study demonstrated that the most heritable epigenetic sites were those correlated with functional genome regions indicating that function-specific epigenetic indicators were under the strongest genetic control.

This evidence for genetic control of epigenetic signals is consistent with several other family-based approaches including population-level findings from quantitative trait loci studies [36,37] and familial clustering of methylation profiles [38,39]. Furthermore, heritable effects are now documented for other epigenetic process such as individual-and allele-specific chromatin signatures [40]. Given this it is hard to understand epigenetic processes as a challenge to the MS.  This evidence suggests that epigenetic systems are themselves phenotypes and their genes are subject to natural selection, drift and all else. This immediately presents the instrumentally minded evolutionist with a set of adaptationist questions.  Twin and family studies do not claim that all epigenetic variation can be accounted for by genetic variation.  Animal studies also report that epigenetic variation can be separated from genetic variation [41, 42].  This observation brings us to the issue of levels of organization.

## 4. Causation and levels of organization

If epigenetic specializations are adaptations it means that discussion within the extended synthesis has overly focused upon accounts of how epigenetic inheritance works at the expense of discussion about function. This dichotomy is typically understood as the ultimate-proximate distinction [43,44].

Mayr [43] gives the example of the causes of bird migration. He claims that causality contains three elements – an explanation of past events, prediction of future events and an interpretation of goal-directed phenomena -and then lists four causes for migration: 1) an ecological cause, as the bird must track food resources which are seasonal; 2) a genetic cause, as the bird has inherited a disposition to respond to particular cues at particular times in particular ways; 3) an intrinsic physiological cause, as the bird responds to reductions in daylight; and, 4) an extrinsic physiological cause, as the temperature dropped significantly on the day of migration, stimulating an already prepared bird to leave. Mayr labels 3 and 4 proximate and 1 and 2 ultimate causes. The proximate accounts are about how a trait works and ultimate are about the evolutionary history and function of a trait – why the trait is as it is – and are understood in terms of their effect upon inclusive fitness [45].

Jablonka and Lamb [9], in their comprehensive case for soft inheritance, argue that there are four dimensions or sources of evolutionary change – genetic inheritance and then three sources of soft-inheritance: epigenetic, behavioural and symbolic inheritance systems. They regard soft inheritance as providing phenotypic tailoring during the lifetime development of an organism. This is a position we have some regard for and will return to below (§ 4.1 & 5). However, Jablonka and Lamb [9] do not provide any account of how these soft-inheritance systems are orchestrated in order to provide this service [46]. Nor do they directly discuss tailoring in terms of inclusive fitness. Indeed, all that is provided is much proximate detail. None the less, they claim [5,21] that soft inheritance systems play a Lamarckian role in the overall evolutionary dynamic such that epigenetic processes allow for the inheritance of acquired characteristics [15]. So, on the one hand epigenetic, behavioural and symbolic systems are seen as proximate mechanisms that provide a phenotypic tailoring service across the lifespan and on the other this very action introduces new variation into the phenotype, changing frequencies at the population level, being transmitted across generations and looking like evolutionary change. In doing this they have conflated proximate and ultimate causation.

To understand this conflation one must realize that genetic inheritance systems are also proximate mechanisms. Mayr's [43] distinction made reference to ultimate causes understood in terms of the interaction between organismic traits and their ecology and the evolutionary history of that relationship as embedded within DNA sequences (causes 1 and 2 above). However, the details of how particular DNA sequences operate to control other gene expression or to build particular proteins are proximate causes, in just the same way as the physiological causes referenced as 3 and 4 above. Crucially, genetic inheritance is not natural selection. Natural selection is the outcome of trait variation, inheritance, and competition. According to the MS, trait variation is a consequence of genetic mutation, inheritance is a result of genes being passed on during reproduction and competition is endemic where

resources are finite. Any trait variation that increases the differential in accessing those resources will be selected and the genes underpinning this will increase in relative frequency. This is the essence of ultimate causation, how genes work is not. So to simply outline other inheritance systems and describe how they work is not to provide an account at the ultimate level, and to claim otherwise is at best a conflation.

This situation is perhaps not surprising as the target is the MS and EES advocates may reject the ultimate-proximate distinction as a part of their effort [24]. But if this distinction is denied we find it hard to understand how any meaningful questions about evolutionary biology could be framed, and how there could be any hope of synthesis, let alone an extended synthesis, between proximate and evolutionary biology. This is because the MS of Mendelian genetics and Darwinian evolution was precisely a synthesis of proximate genetic concerns with ultimate evolutionary ones – the how of genetic transmission with the why of evolution. As we have seen this required the invention of population genetics and to date no one from the EES movement has proposed a similar theoretical structure. Indeed, those working on soft cultural inheritance have had to directly borrow population genetic models in order to hypothesize cultural dynamics [47], effectively treating the mathematics as substrate neutral.  On the surface this may appear to support the EES position, as surely the mathematics is reflecting a deeper truth about nature, but these models rely upon the assumption that cultural variants are inherited in a manner equivalent to genes, and in so doing simply model cultural change as if it were directly tied to genetic variation.  This is clearly not a distinct conceptual departure.  The only available counterpoint for the EES community would be to argue that they simply see their soft inheritance systems as fitting into the synthesis as already described – theirs are alternative mechanisms to the genetic, introducing variation through developmental induction and being open to the same competition. This requires a certain view of biological organization and is to this that we next turn.

### 4.1 Integration across levels

Bolhuis et al. [7] note that neuroscientists have 'been aware since the 1980s that the human brain has too much architectural complexity for it to be plausible that genes specify its wiring in detail; therefore developmental processes carry much of the burden of establishing neural connections' (p.2). This statement must be true in its detail [48] and it is very much in keeping with the general thrust of the soft inheritance theorists who think that genes cannot account for everything. Exact connections are established after exposure to critical inputs from the environment, and as a consequence of other organizing events downstream. These processes would seem to be a consequence of core properties of neurons – which might imply an evolutionary history. But Bolhuis et al. lump together developmental systems theory,

epigenetic inheritance and niche-construction theory and argue that organisms are to be seen as constructors of their own environments. We are told that the final neurological product, a human brain, is the result of a complex interaction between genes and these processes. However, this argument is crucially different from those previously outlined, for here there is a direct claim for interaction across organizational levels. Developmental processes take off where genetics stops, and new design is introduced almost as an emergent property of the initial complexity. This view of total phenotypic variation implies some orchestration.

This orchestration need not be internally sourced; there is no implication of orthogenesis. It could all be entirely externally sourced, as it possibly is in each of Jablonka and Lamb's four dimensions. For those focusing upon genetic systems it is a basic principle that genes rely on inputs from other genes and the environment external to them to function [49]. However a key organizational point, which was recognized during the MS, is that the level of the gene is where the conceptual buck stops [18]. More precisely, it is at the level of the genes that the first effects of a system that can organize environmental inputs and respond to them, by building more complex systems, begins. This is another element of its special theory status. There is no suggestion in the soft inheritance literature that theorists see epigenetic mechanisms etc. as the lowest level of such organization. Moreover, given the heritability claims made above, this would be empirically hard to sustain.

Instrumentally minded biologists would think about a possible role for natural selection in building the proximate machinery for epigenetics and learning. So the question becomes: has natural selection led to changes in relative gene frequencies due to the effectiveness of particular genes at coordinating higher levels of organization? They will regard cultural learning, individual learning and epigenetic inheritance as an intricately nested hierarchy of adaptations that are 'designed' to calibrate organisms to their ecology, as proximate mechanisms with an evolutionary history [44]. Where the soft inheritance theorists have failed to formally account for function and cannot explain why a particular inheritance mechanism is structured in the way it is, someone schooled in the MS can begin to ask fruitful, falsifiable questions. Because of the conflation of ultimate with proximate causation, advocates of the EES consistently fail to understand biological organization and its provenance. They have a general theory of evolutionary change and the conceptual tools of proximate biology, not evolutionary biology at their disposal. By insisting on the causal parity of different levels of biological organization, and mapping the dynamics of inheritance using a general theory of evolution, the soft inheritance theorists fail to say something more meaningful about inheritance, something that classifies and denotes differences, something that is usefully limiting.

## 5. Hypotheses about calibration

If we are correct, several hypotheses about experience dependent epigenetic inheritance should follow. In this section we develop two examples. Our aim is to more clearly expose the kind of thinking that the MS permits through clear sight of proximate and ultimate causation. The hypotheses may prove to be false, but that would not be an indictment of the framework.

### 5.1 Licking and grooming: adapted parental effect

Within rodents there are stable and heritable individual differences in the amount of grooming offered by mothers. Cross-fostering experiments have shown that this inheritance is not genetic but that it is modified by behaviour. A number of integrated proximate mechanisms are involved [50].

Relatively low levels of oxytocin receptor binding in the medial preoptic area of the hypothalamus have been associated with low levels of grooming. Oxytocin is implicated in facilitating bonding [51]. In high grooming females, dopamine levels in the nucleus acumbens increase evenly before grooming. The amount released directly predicts how long the mother will engage in grooming. When grooming stops the dopamine level returns to baseline. This effect is not seen in low grooming mothers. Champagne [50] argues that the hypothalamic oxytocin neurons mediate this mesolimbic response, which in turn leads to behavioural differences between mothers. Furthermore, pups of mothers who are low in grooming have a relatively prolonged passive stress response after the stressor has been removed. This order of response has well-documented behavioural effects such as a reduction in exploratory behaviour and an increase in inhibition, sometimes classed as behavioural depression.

The pups of low grooming mothers have low oestrogen sensitivity. Oestrogen has an epigenetic effect in that it increases the expression of the oxytocin receptor gene. Birth is normally associated with high oestrogen exposure for pups, which in turn should lead to increased oxytocin receptor binding in the hypothalamus. Low oestrogen sensitivity is equivalent to that of mice lacking a functioning copy of the oestrogen receptor alpha, which affects gene expression, thus causing a reduction in the ability of oestrogen to affect expression. In the offspring of low grooming mothers the expression of oestrogen receptor alpha is reduced relative to that of high grooming mothers, which potentially will affect the oxytocin activity in the medial preoptic area. Fostering experiments have revealed that this alteration to gene expression is affected by postnatal maternal care – low grooming mothers cause a reduction in the level of oestrogen receptor in the medial preoptic area of the

hypothalamus. This has been linked to high levels of methylation at a number of sites in the promoter region of oestrogen receptor alpha.

This example presents a complex and highly integrated set of proximate mechanisms. It appears that low levels of grooming set in motion a particular stress response and inhibition of bonding that in turn leads to subsequent low grooming investment when those pups become mothers. Stressing high grooming females can lead to a reduction in their grooming and this is then epigenetically inherited. If external stressors diminish then the level of grooming rises after a few generations to a higher level.

This order of epigenetic effect appears facultatively responsive to key ecological factors. The inherited trait is not invariant over time, but changes in the presence or absence of stressors. A reasonable hypothesis for such patterned change is to assume that there is a fitness benefit for the mother in reducing her grooming under stress and that this behaviour will track particular ecological cues, or stressors, and not others.  For example, food stress and local predation rates should predict low licking and grooming in rodent mothers.   This can be experimentally tested.

This hypothesis can be captured by life-history theory that frames development and behaviour as fitness maximizing strategies over a lifetime [52, 53], those strategies being seen as reaction norms. To this end, licking and grooming behaviour will be seen as an adaptation that acts to maximize the average lifetime inclusive fitness of the mother. This idea is given weight by the fact that in rats the pups of low grooming mothers reach sexual maturation faster and display more indiscriminate sexual behaviour than those under high licking and grooming regimes [54]. The paracopulatory behaviours of female Long Evans rats raised under low licking and grooming regimes also appear to make them more sexually attractive to males [55], so a lack of discrimination will pay off. Maestripieri [56] has shown that poor maternal care in rhesus macaques leads to an increased interest in infants. Belsky et al.[57] have recently demonstrated a relationship in humans between maternal harshness, early sexual maturation and sexual risk taking that fits with this order of life-history prediction and makes sense of recent findings in the literature on early reproduction in humans [58].

All told, there is evidence for an epigenetic calibration to harsh, yet changeable environments that can hasten reproduction. This makes intuitive and evolutionary sense. If an organism is under stress delaying reproduction could carry significant fitness costs, for there is no guarantee the stressors will be removed and endogenous resource will continue to be used making it harder in the future to successfully reproduce under stressed conditions. In effect these proximate mechanisms are designed to hedge bets [59] and thereby maximize lifetime

inclusive fitness. In the case of stressed rat mothers calibrating your pups for a more rapid development and earlier reproduction makes sense for your own inclusive fitness, as each pup is an investment. Such maternal decisions are also seen operating *in utero* and directly affecting birthweight and future development in a number of species in order to produce smaller, more rapidly developing offspring [60].

It is worth noting in passing that the kind of induced phenotypic variation seen in the licking and grooming work is entirely non-random, a response to specific inputs [49], and should be contrasted with the introduction of new variation through mutation at the heart of the MS.

### 5.2 Learning biases

Epigenetic modification of genes that are expressed in the brain have an effect upon learning and memory [61]. This suggests that specific learning biases should emerge under particular developmental conditions. It is also worth noting that not all organisms calibrate using epigenetic mechanisms. For example, birds deposit hormones in egg yolk, which in turn affects chick development and adult reproductive success [62]. This presents a question about the fit of epigenetic calibration to specific ecologies, as well as one of the phylogeny of such mechanisms. The existence of calibrating mechanisms is evidence that an organism lives in a stochastic ecology, moves between a variety of environments, or both. If they move from environment to environment then they are some order of generalist. Selection will shape the calibration accordingly.

Generalist strategies present a lot of moment-to-moment and day-to-day change that would be well served by learning mechanisms. Learning is itself parametized [63], and could not possibly function as a general association architecture, such that particular learning biases have been selected. This is something we have known since at least Garcia and Koelling [64]. The extended synthesis has packaged learning as soft-inheritance at the cultural level but paid little attention to individual learning. But even cultural learning processes are situated within individuals and there is variation in how well individuals learn and teach in such situations. One might predict the emergence of stable strategies within such scenarios that are effectively under frequency dependent selection, and more interestingly still some of these strategies might be facultative responses to particular local conditions.

As a thought experiment we can imagine selection building a learning mechanism that is biased to make certain associations. The Garcia Effect showed that rats associated nausea with taste but not other stimuli. This is a candidate adaptation as the fitness consequences are clear. But we might imagine a rat living under food stress needing to relax the associative grip such that a single exposure to a pairing of taste and nausea might be too strict: one instance

of food being off should not deter future tasting in a food stressed environment. Under no food stress then a strong learning bias in this direction makes sense as it is easy to avoid that food in the future without compromising fitness. Epigenetic mechanisms would be a candidate solution to introducing shifts in learning bias across such situations, as would endocrine functioning. Thus one hypothesis would be that under protracted food stress mothers would have less exposure to food, making them more hungry, such that when they do encounter food the benefits are increased relative to a constant negative value associated with nausea. In effect the strength of the taste aversion association would be diminished. This learning effect could come under internal epigenetic control. The mother potentially bears some learning costs, in spite of this shift in relative salience, that could be time expensive and detrimental to fitness. An epigenetically transmitted change in the strength of taste aversion learning would significantly benefit the pups of such mothers and could be seen across subsequent generations to a point beyond the removal of food stress.

What this imagined scenario brings is the view that increased ecological complexity, or large ecological bandwidth, brings with it an increased need for highly integrated calibrating mechanisms. These mechanisms are dealing with various sources of information and fine-tuning the organization of the phenotypic response to factors that are at best described as exogenous to the genes that build them. This is plasticity, this is development and this does lead to changes in the frequencies of available phenotypes in the population. Genetically encoded capacities for generating epigenetic variation may drive part of this phenotypic plasticity. This might be captured by a general theory of evolution, to some limited extent, but it is quite clearly not biological evolution. It is instead a consequence of it.

## 6. Summary

In this paper we have taken issue with a core component of recent claims for an EES, that of soft-inheritance, and in particular epigenetic inheritance. Specifically, we have sought to demonstrate that there is a conflation in the EES literature between ultimate and proximate causation, and, as a consequence, a failure to address the issues of levels of organization within biology in ultimate terms. Some researchers have discussed the functional utility of soft inheritance, seeing epigenetic, behavioural and symbolic learning systems as means to tailoring organismic response to the environment across lifespan, but at no point has an account of how these levels of organization might be orchestrated been provided. Instead, each inheritance system has been afforded equal causality in a general evolutionary dynamic, a dynamic that does little to account for the apparent design we see in biology.

We have attempted to demonstrate how the MS enables such questions to be framed and potentially answered. Those seeking to defend an extended synthesis would have to find some evidence that would undermine the wealth of data pointing to a high level of integration between development and behavioural outcomes. As it stands, the supporters of the extended synthesis merely point to soft inheritance and trait variation as a consequence of this, without fully accounting for why such trait variation is patterned and persists.

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## 8. References

1. Huxley, J. (1942). *Evolution: The Modern Synthesis*. London: Allen and Unwin.

2. Gould, S.J. (2002). *The Structure of Evolutionary Theory*. Cambridge MA: Belknap: Harvard University Press.

3. Ruse, M. (2003). *Darwin and Design: Does Evolution Have a Purpose?* Cambridge MA: Harvard University Press.

4. Pigliucci, M., & Müller, G.B. (2010). *Evolution: The Extended Synthesis*. Cambridge MA: MIT Press.

5. Jablonka, E., & Lamb, M.J. (2008). Soft inheritance: Challenging the Modern Synthesis. *Genetics and Molecular Biology*, *31* (2), 389-395.

6. Mayr, E. (1982). *The Growth of Biological Thought*. Cambridge MA: Belknap: Harvard University Press.

7. Bolhuis, J.J., Brown, G.R., Richardson, R.C., & Laland, K.N. (2011). Darwin in Mind: New Opportunities for Evolutionary Psychology. *PLoS Biology*, *9* (7), e1001109. Doi:10.1371/journal.pbio.1001109

8. Danchin, E., Charmantier, A., Champagne, F.A., Mesoudi, A., Pujol, B., & Blanchet, S. (2011). Beyond DNA: integrating inclusive inheritance into an extended theory of evolution. *Nature Genetics*, *12*, 475-486.

9. Jablonka, E., & Lamb, M.J. (2005). *Evolution in Four Dimensions: Genetic, Epigenetic, Behavioral, and Symbolic Variation in the History of Life*. Cambridge MA: MIT Press.

10. Odling-Smee, F.J., Laland, K.N., & Feldman, M.W. (2003). *Niche Construction: The Neglected Process in Evolution*. Princeton: Princeton University Press.

11. Pigliucci, M., Murren, C.J., & Schlichting, C.D. (2006). Phenotypic plasticity and evolution by genetic assimilation. *Journal of Experimental Biology*, *209*, 2362-2367.

12. Youngson, N.A., & Whitelaw, E. (2008). Transgenerational Epigenetic Effects. *Annual Review of Genomics and Human Genetics*, *9*, 233-257.

13. Odling-Smee, J. (2010). *Niche Inheritance*. In: M. Pigliucci & G.B. Müller, (Eds.) Evolution: The Extended Synthesis. Cambridge MA: MIT Press. Pp. 175-207.

14. Craig, L.R. (2010). The So-Called Extended Synthesis and Population Genetics. *Biological Theory: Integrating Development, Evolution and Cognition*, *5* (2), 117-123.

15. Haig, D. (2007). Weismann Rules! OK? Epigenetics and the Lamarckian temptation. *Biology and Philosophy*, *22*, 415-428.

16. Mayr, E. (1963). *Animal Species and Evolution*. Cambridge MA: Harvard University Press.

17. Futuyma, D.J. (1986). *Evolutionary Biology*. Sunderland MA: Sinauer.

18. Williams, G.C. (1966). *Adaptation and Natural Selection: A Critique of Some Current Evolutionary Thought*. Princeton: Princeton University Press.

19. Dennett, D.C. (1995). *Darwin's Dangerous Idea*. London: Allen Lane.

20. Kuhn, T.S. (1962). *The Structure of Scientific Revolutions*. Chicago IL: University of Chicago Press.

21. Jablonka, E., & Lamb, M.J. (2010). *Transgenerational Epigenetic Inheritance*. In: M. Pigliucci & G.B. Müller, (Eds.) Evolution: The Extended Synthesis. Cambridge MA: MIT Press. Pp. 137-174.

22. Pigliucci, M. (2007). Do we need an extended evolutionary synthesis? *Evolution*, *61* (12), 2743-2749.

23. Webb, R.H. (2011). If evolution is the answer, what is the question? *Journal of Evolutionary Psychology*, *9*, 91-107.

24. Laland, K.N., Sterelny, K., Odling-Smee, J., Hoppitt, W., & Uller, T. (2011). Cause and Effect in Biology Revisited: Is Mayr's Proximate-Ultimate Dichotomy Still Useful? *Science*, *334*, 1512-1516.

25. Maher, B. (2008). Personal genomes: the case of missing heritability. *Nature*, *456*, 18-21.

26. Hunter, D. J., & Kraft, P. (2007). Drinking from the fire hose – statistical issues in genome wide association studies. *New England Journal of Medicine*, *357*, 436-439.

27. Plomin, R. (2011). Why are children in the same family so different? Non-shared environment three decades later. *International Journal of Epidemiology*, *40*, 582-592.

28. Turkheimer, E., & Waldon, M. (2000). Nonshared environment: a theoretical, methodological, and quantitative review. *Psychological Bulletin*, *126*, 78-108.

29. Morgan, H. D., *et al*. (2005). Epigenetic reprogramming in mammals. *Human Molecular Genetics, 14*, R47-R48.

30. Feng, S. E., *et al*. (2010). Epigenetic reprogramming in plant and animal development. *Science, 330*, 622-627.

31. MacKay, A. B., *et al*. (2007). Immunological detection of changes in genomic DNA methylation during early zebrafish development. *Genome, 50*, 778-785.

32. Fraga, M. F., et al. (2005). Epigenetic differences arise during the lifetime of monozygotic twins. *Proceedings of the National Academy of Science*, USA, *102*, 10604-10609.

33. Heijmans, B.T., Kremer, D., Tobi, E. W., Boomsma, D. I., & Slagboom, P. E. (2007). Heritable rather than age-related environmental and stochastic factors determine variation in DNA methylation of the human IGF2/H19 locus. *Human Molecular Genetics*, *16*, 547-554.

34. Ollikainen, M., et al. (2010). DNA methylation analysis of multiple tissues from newborn twins reveals both genetic and intrauterine components to variation in the human neonatal epigenome. *Human Molecular Genetics*, *19*, 4176-4188.

35. Kaminsky, Z. A., et al. (2009). DNA methylation profiles in monozygotic and dizygotic twins. *Nature Genetics*, *41*, 240-245.

36. Boks, M. P., et al. (2009). The relationship of DNA methylation with age, gender and genotype in twins and healthy controls. *PLoS ONE*, *4*, e6767

37. Gibbs, J. R., et al. (2010). Abundant quantitative trait loci exist for DNA methylation and gene expression in human brain. *PLoS Genetics*, *6*, e1000952.

38. Bjornsson, H. T., et al. (2008). Intra-individual change over time in DNA methylation with familial clustering. *JAMA*, *299*, 2877-2883.

39. Johannes, F., et al. (2009). Assessing the impact of transgenerational epigenetic variation on complex traits. *PLoS Genetics*, *5*, e1000530.

40. McDaniell, R., et al. (2010). Heritable and individual-specific and allele-specific chromatin signatures in humans. *Science*, *328*, 235-239.

41. Anyway, M. D., *et al* (2005). Epigenetic transgenerational actions of endocrine disruptors and male fertility. *Science, 308*, 1466-1469.

42. Sollars, V., *et al*. (2003). Evidence for an epigenetic mechanism by which Hsp90 acts as a capacitor for morphological evolution. *Nature Genetics, 33*, 70-74.

43. Mayr, E. (1961). Cause and Effect in Biology. *Science*, *134*, 1501-1506.

44. Scott-Phillips, T.C., Dickins, T.E., West, S.A., (2011). Evolutionary Theory and the Ultimate-Proximate Distinction in the Human Behavioral Science. *Perspectives on Psychological Science*, *6*, 38-47.

45. Ariew, A. (2003). Ernst Mayr's "ultimate/proximate" distinction reconsidered and reconstructed. *Biology and Philosophy*, *18*, 553-565.

46. Dickins, T.E., & Dickins, B.J.A. (2007). Designed calibration: Naturally selected flexibility, not non-genetic evolution. *Behavioral and Brain Sciences*, *30* (4), 368-369.

47. Boyd, R., & P. J. Richerson (1985). *Culture and the Evolutionary Process*. Chicago: University of Chicago Press.

48. Dickins, T.E. & Levy, J. (2001). *Evolution, development and learning -a nested hierarchy?* In: R.M. French & J.P. Sougné (Eds.) Connectionist Models of Learning, Development and

Evolution: Proceedings of the Sixth Neural Computation and Psychology Workshop. London: Springer-Verlag

49. Dickins, T.E. & Dickins, B.J.A. (2008.) Mother Nature's Tolerant Ways: Why non-genetic inheritance has nothing to do with evolution. *New Ideas in Psychology*, *26*, 41-54

50. Champagne, F.A. (2008). Epigenetic mechanisms and the transgenerational effects of maternal care. *Frontiers in Neuroendocrinology*, *29* (3), 386-397.

51. Campbell, A. (2007). Attachment, aggression and affiliation: the role of oxytocin in female social behavior. *Biological Psychology*, *77* (1), 1-10.

52. Stearns, S.C. (1976). Life history tactics: A review of the ideas. *Quarterly Review of Biology*, *51*, 3-47.

53. Ellis, B.J. (2011). *Toward an evolutionary-developmental explanation of alternative reproductive strategies: The central role of switch-controlled modular systems*. In: D.M. Buss & P.H. Hawley (eds.) The Evolution of Personality and Individual Differences. New York: Oxford University Press. Pp. 177-209.

54. Cameron, N.M., et al. (2008). Epigenetic Programming of Phenotypic Variations in Reproductive Strategies in the Rat Through Maternal Care. *Journal of Neuroendocrinology*, *20*, 795-801.

55. Sakhai, S.A., Kriegsfeld, L.J., & Francis, D.D. (2011). Maternal programming of sexual attractivity in female Long Evans rats. *Psychoneuroendocrinology*, *36* (8), 1217-1225.

56. Maestripieri, D. (2005). Effects of early experience on female behavioural and reproductive development in rhesus macaques. *Proceedings of the Royal Society B*, *272*, 1243-1248.

57. Belsky, J., Steinberg, L., Houts, R.M., & Halpern-Felsher, B.L. (2010). The Development of Reproductive Strategy in Females: Early Maternal Harshness -> Earlier Menarche -> Increased Sexual Risk Taking. *Developmental Psychology*, *46* (1), 120-128.

58. Nettle, D., Coall, D.A., & Dickins, T.E. (2011). Early life conditions and age at first pregnancy in British women. *Proceedings of the Royal Society, B*, *278*, 1721-1727

59. Ellis, B.J., Figueredo, A.J., Brumbach. B.H., & Schlomer, G.L. (2009). Fundamental Dimensions of Environmental Risk: The Impact of Harsh versus Unpredictable Environments on the Evolution and Development of Life History Strategies. *Human Nature*, *20* (2), 204-268.

60. Wells, J.C.K. (2003). The Thrifty Phenotype Hypothesis: Thrifty Offspring or Thrifty Mother? *Journal of Theoretical Biology*, *221* (1), 143-161.

61. Zhang, T-Y. & Meaney, M.J. (2010). Epigenetics and the Environmental Regulation of the Genome and Its Function. *Annual Review of Psychology*, *61*, 439-466.

62. Groothuis, T.G.G., Eising, C.M., & Müller, W. (2005). Balancing between costs and benefits of maternal hormone deposition in avian eggs. *Biology Letters*, *1* (1), 78-81.

63. Gallistel, C.R. (1990). *The Organization of Learning*. Cambridge MA: MIT Press.

64. Garcia, J. & Koelling, R.A. (1966). Relation of cue to consequence in avoidance learning. *Psychological Science*, *4*, 123-124