From Replicators to Heritably Varying Phenotypic Traits: The Extended Phenotype Revisited

Article *in* Biology and Philosophy · January 2004

DOI: 10.1023/B:BIPH.0000036112.02199.7b

1 author:

Eva Jablonka
Tel Aviv University
128 PUBLICATIONS **7,911** CITATIONS

Biology and Philosophy **19:** 353–375, 2004.

From Replicators to Heritably Varying Phenotypic Traits: The Extended Phenotype Revisited

E. JABLONKA
The Cohn Institute for the History and Philosophy of Science and Ideas, Tel-Aviv University, Ramat-Aviv, Tel-Aviv 69978, Israel

Received 2 August 2003; accepted in revised form 6 August 2003

It may seem somewhat odd to write about a book that was published 21 years ago, and when Kim Sterelny first suggested that I review again Dawkins' *Extended Phenotype* I was dubious. It has been a very influential book, and although not as widely read as *The Selfish Gene*, it has had, I think, as great an impact on biologists' work as its older sibling. Many reviews of the book have been written, and many scholars have referred to this book directly and indirectly. The point of view advocated in it – and it was, as Dawkins asserted at the very beginning of the book, openly a work of advocacy – has become mainstream among evolutionary theorists. There has been, as Dawkins hoped, a shift in perspective from the organism to the replicator as a unit of selection, and we are living in an intellectual atmosphere that is dominated by genetic and cultural replicators. Although this dominance has been challenged many times, it is today the most influential approach to evolution. Revisiting the book is therefore a daunting task, but it is also something that may be timely, for new ideas and new discoveries have emerged during the last 20 years, and some arguments have acquired a new significance (or insignificance).

It is quite impossible to cover all the ground discussed in *The Extended Phenotype*, but it is possible to scrutinize the central idea – the superiority of the replicator-oriented perspective and its implications. I shall first examine the basis for choosing the single gene variant as the fundamental unit of genetic selection, and show the problems that this approach creates. I shall then argue that a perspective that focuses on multiple inheritance systems and heritably varying phenotypic traits allows a better understanding of evolutionary processes, including aspects relating to the extended phenotype, and provides a more general evolutionary perspective than a replicator-centered view.

It is important to clarify at the outset what will not be the issue: genetic determinism does not follow from gene selectionism, nor does a point of view focused on the single gene as a unit of replication, selection and evolution

imply any simplistic and naïve adaptationism. These misunderstandings have been cleared up, and most biologists realize that gene selectionism is a way of studying evolution, and has no bearing on whether or not a particular gene effect is reversible or otherwise changeable during ontogeny. However, I shall argue that single gene selectionism does affect our view of development. And it has far-reaching effects on our view of evolution.

One more issue has to be clarified before I start examining the genic replicator. I have no argument with the claim that usually what biologists mean when talking about "a gene for trait X" is the "genetic basis of X". I am also fully aware that when geneticists talk about "genes for" they are talking about genetic differences that make a difference to the phenotype. No geneticist thinks about a gene for eyes, nose or intelligence. However, a lot is hidden under the phrase "a genetic difference that makes a phenotypic difference". Is it a single gene difference we are focusing on? Or is it a difference in the functional effects of a genetic network, with many concurrent genetic differences making a difference to the phenotype, and with a difference in a single gene having, on the average, a neutral effect? As I argue below, the answers to these questions are very important for our view of evolution and our approach to replicators.

What is the selectable unit of genetic function?

Chapters 5 and 6 of *The Extended Phenotype* (hereafter, EP) are devoted to the justification of the replicator concept and explain what it entails. The first argument, which is developed in chapter 5, is that in the genetic realm it is the single gene that is the unit for the benefit of which adaptive evolution (which is Dawkins' primary concern) occurs, rather than smaller or larger units. Dawkins adopts Williams' (1966) definition of the gene: "in evolutionary theory, a gene could be defined as any hereditary information for which there is a favorable or unfavorable selection bias equal to several or many times its rate of endogenous change". It is important to stress that it is the role of the gene in evolutionary theory and heredity rather than in development that Dawkins is concerned with. The gene is the unit of choice because it has the required stability over time and because it is assumed that structural (DNA sequence) differences in the gene, make, on the average, consistent functional differences to the phenotype.

What is wrong with this argument? The gene can be thought of as the smallest unit of (genetic) function, and Dawkins' decision to talk of a cistron (the unit responsible for the production of a polypeptide chain) highlights the functional aspect of the gene. However, does it also follow that structural variations in this unit have a variant functional significance? The variations

usually considered are the results of accidental mistakes in replication or in post-replication maintenance of DNA: single nucleotide substitutions or small deletions or insertions. The assumption that, because a gene has a function, a variation in a single gene must have functional consequences does not necessarily follow, and in most cases it seems that this inference is not valid. The majority of single gene variations are selectively neutral. Again, this does not mean that the gene is functionally unimportant: it means only that the vast majority of structural variations in single genes do not make a functional difference. There are of course the well known exceptions – Mendelian genes for yellow or green colored peas, or monogenic diseases (less than 2% of genetically influenced diseases) where single gene substitutions do make a phenotypic-functional difference – but these are the exceptions rather than the rule. Most phenotypic differences are due to the concerted effect of several variations in an interacting genetic/developmental network. The argument that I am advancing here is not simply that the effect of the gene is context-dependent (which it obviously is) – it is also that *the average effect of most single gene variants is selectively neutral*.

It is only because most single gene mutations are assumed to be neutral that we can use mutations to date evolutionary changes and to construct molecular evolutionary trees. The reasons for neutrality at the molecular level are complex. The first and the central reason for selective neutrality is that there is an extremely strong canalization of developmental pathways: a typical (standard, "wild type") phenotypic effect is brought about despite variations in the genetic and the external environment. Network dynamics and various buffering mechanisms compensate for the effects of mutations and environmental variations, leading to the production of a normal, standard, phenotype. Canalization is overcome only in unusual environmental or genetic conditions. This point was realized long ago by developmental geneticists like Waddington and Schmalhausen, and is now widely accepted and intensely studied at the molecular level (for a recent illustration of canalization and its unmasking see Rutherford and Lindquist 1998, and for a more general review of some aspects of canalization see Rutherford 2003). Even knocking out both copies of a gene that is known to have an important role in a major metabolic pathway has, amazingly, been found to have no phenotypic effects in most cases (Morange 2001). Since the role of genetic variation in a canalized developmental path is very often misunderstood, an analogy may help. Imagine that genes are like long words (or short phrases) that are joined together into a message, which has to travel from a source (where the words/phrases are produced) to a receiver. The source makes occasional heritable mistakes in word/phrase production (so words/phrases may have extra, fewer, or modified letters), and the transmission channel is

noisy. It is, however, very important that the correct meaning of the message does reach the receiver – its survival and reproductive success depend on that. The lexicon and grammar used at the source are so designed (by natural selection, if we refer to the biological analogue) that most mistakes made by the source, and most channel noise, will nevertheless result in a correctly interpreted message – the message preserves its meaning for the receiver despite the various "corruptions". Only when the internal and/or the external noise exceed a certain threshold is the meaning of the message changed. The selective value of each word/phrase-variation when looked at in isolation is usually neutral – most small variations in a single word make no difference to the interpretation of the message. A difference is made only when several variations are combined. Canalization thus renders most genetic variations selectively equivalent through its effect on the macroscopic outcome of development, making the outcome typical, or "wild type".

In addition to canalization, there are two more reasons for selective neutrality. The second reason, which was stressed by neutralists 20 years ago, is that because past selection has shaped the DNA sequence in the critical regions of each coding gene into an optimal state, it is genetic drift rather than selection that accounts for most changes in allele frequencies (Kimura 1983). The third reason is that in those relatively rare cases where a difference in a single gene does make a selective difference, the dependence of the allele on the genetic and environmental context often makes the different effects of the allele ("positive" and "negative" effects) cancel out. In this case the selective neutrality occurs not because a change in a gene has no effect on the macroscopic characteristics of the phenotype, but because on the average the effects it has in different individuals leaves fitness unchanged. If, for all three reasons, allelic differences are usually selectively neutral, the basic unit of heritable and selectable function cannot, in the majority of cases, be the single gene variant. It is important to make it absolutely clear that the assertion that single gene variations are usually selectively neutral does not detract from the central importance of genes in development, heredity and evolution. Just as the understanding of a message depends on the understanding of the words, so the understanding of how traits develop and function depends on knowing which genes take part in the underlying network and how their products interact (although often losing just a single word – like losing the two copies of a gene in a knockout experiment – can make no difference to the message's meaning). However, it does not follow that variations in a single allele can make a selective difference to a biological function. Before I look at what this means for the replicator concept I would like to outline the way Dawkins replies to the neutrality argument.

The main reply is that neutral variations in genes are irrelevant to evolution – we are interested only in those single gene effects that do make a selective difference and that do have consistent enough effects for a long enough time (EP p. 32, quoting Maynard Smith). This is, however, a very problematic answer: if most of the time what matters in evolution are variations at several loci simultaneously, with the average effect of single alleles being neutral, it is surely unwise to base a theory of evolutionary change on the relatively rare cases when an allele has a consistent positive selective effect, and completely ignore the other cases (the majority), in which selection among gene networks is going on. In addition, Dawkins argues that on the average, given a long enough time, a genetic variation in a single gene does have a negative or a positive effect. Eventually, even if the path of evolution is long and tortuous, a variation with functional effects will either disappear or become prevalent. However, given the joint effects of canalization and effects on fitness that cancel out, this may take a very long time indeed – long enough for the allele (and its partners in the genetic network) to accumulate several new variations.

If most single gene variations are selectively neutral because of canalization, evolved optimality, and canceling-out effects, what is the relevant unit of genetic function in adaptive evolution? Is it the genetic network? In sexually reproducing organisms genes are re-shuffled each generation, so except for cases of strong genetic disequilibrium the genetic composition of a network changes rapidly. Certainly the rate of endogenous change of genetic networks is much higher than the selective bias for a given network, so genetic networks also do not fit the unit of evolution in Williams'/Dawkins' sense. Nor are organisms, or their equivalents, units of evolutionary change, since, by definition, they do not last more than one generation (a generation is defined in terms of a single lifecycle of an organism). Dawkins rightly stresses this point. He called organisms and other integrated and coherent entities that house replicators, and act, as they interact with the environment, for the preservation of their replicators, vehicles. The same type of entity was called interactor by David Hull, who emphasized its active and causal role in affecting differential replication (Hull 1988). Vehicles/interactors are targets of selection (they survive, die out, reproduce or fail to reproduce), but they are not the units to be followed during evolution.

Since according to the above discussion, neither genes nor vehicles are the functionally relevant units that should be followed during adaptive evolution, what should the selectively significant units be? Obviously, such units must show hereditary variations that affect biological functions, so before I propose an alternative to the replicator, it is necessary to examine what types of hereditary variations there are. In particular, I want to look at the inheritance and functional significance of variations that do not depend on variations in DNA

sequence, discuss their inheritance and their functional significance, and see what they may mean for interpreting evolution.

The body to body arrow

By definition replicators are equivalent to genotypes, not to phenotypes. They are, in Dawkins' version of the term, neither bodies nor parts of bodies. In a response to Patrick Bateson, who noted that since the developmental cause-effect relationship between genes and phenotypes is circular, because the gene can be thought of as a bird's nest's way of making another nest just as the nest is a gene's way of making another gene, Dawkins explains that a bird's nest is not a replicator and "similarly, protein molecules are not replicators, nor is messenger RNA" (EP p. 98). This is because while there is a causal arrow from genotype to phenotype (from genes to mRNA to protein, to nest), there is no causal arrow from phenotypes to genotypes. It seems that the classical distinction between phenotype and genotype, which was made by Johannsen at the beginning of the 20th century and until recently has been the basis of most genetic thinking, is guiding Dawkins' conceptualization of replicator and vehicle. This distinction identifies the genotype not only with potential (versus actualization – the phenotype), but also claims that only the potential is inherited in a biological sense. In other words, only variations in genotypes are heritable, while variations in phenotypes that are independent of variations in genotypes are not, and cannot be, heritable. As we shall see, there are problems with this assumption. Causal arrows from phenotype to phenotype are not considered by the advocates of a replicator-centered view, yet some phenotypic variations that do not depend on variations in DNA are heritable, including variations in some animal artifacts, variations in some proteins, and variations in some ensembles of RNA molecules.

The realization that in addition to variation in DNA sequences other types of variations that do not depend on variations in DNA can also be transmitted between generations has become widely accepted during the last 20 years. These other variations occur at different levels of biological organization, involve different types of entities and traits, and a variety of modes of transmission and change. They call into question the heredity-aspect of the dichotomy between replicator and vehicle, and the sharp distinction between development and evolution. What these heritable variations have in common is that in all cases their transmission involves a body to body arrow. In most cases (there are interesting exceptions) DNA sequence is not altered. What I have in mind are four categories of heritable phenotypic variations: cellular epigenetic variations, whole-organism heritable epigenetic variations, variations in non-symbolic patterns of behavior, and variations in symboli-

cally expressed behaviors. Since the last two categories (and especially the symbolic type) have been considered by Dawkins, and a new replicator, the meme, has been assigned to them, I shall first discuss the first two classes, and then turn to the meme concept and the general problems that a replicator perspective raises.

Cell heredity, or cellular epigenetic inheritance, has become a very hot topic in biology, because it is realized that this type of heredity is crucial for understanding development and differentiation, and opens up new ways of thinking about health and disease. In a single mammalian body there are over 100 different cell types, such as liver cells, skin cells, kidney cells and nerve cells, which all look different, behave differently, and function differently, yet all contain the same DNA. With very few exceptions, the differences between specialized cells in the same body are not genetic. The differences between the cell types are the result of the developmental history of each type of cell, which culminated in a cell-type-specific pattern of gene expression and morphology. However, cells do not just become specialized – they usually maintain their particular cell phenotype for long periods and transmit it to daughter cells through cell division. When liver cells divide their daughters are liver cells, and the daughters of kidney cells are kidney cells. Although their DNA sequences remain unchanged during development, cells within the same multicellular organism acquire and transmit information that they can pass to their progeny cells. This information is transmitted through what are known as 'epigenetic inheritance systems' (or 'EISs'). What is inherited between cell generations through EISs are the structural and functional aspects of the cells that are independent of variations in DNA sequence. In other words, certain variations in the cell's phenotype, are inherited. Since, historically, epigenetic inheritance was studied in the somatic cells of multicellular organisms, it was at first assumed that cellular epigenetic variations are not transmitted through the germline. Subsequent studies of multicellular organisms and research with unicellular organisms led to the realization that the transmission of the epigenetic variations can sometimes occur from one organism generation to the next, and in sexually reproducing organisms epigenetic variations can be transmitted through the germline (see Jablonka and Lamb 1995; for recent examples in different taxa see: Cubas, Vincent and Coen 1999 for plants; Sollars et al. 2003 for flies; Rakyan et al. 2003 for mice).

The heritable epigenetic variations characteristic of cell heredity fall into four general types. The first, very common type, is based on simple or complex self-sustaining metabolic loops, where the activity-state of a network is maintained through positive feedback by one of the gene products in the network. The simplest case is when a gene positively regulates its own

transcription. As a result, two genetically identical lineages of cells in an identical environment can have different heritable metabolic states (just "on" or "off" in this simple case) if their inductive histories have been different. A second type of EIS is based on 3D templating: pre-existing cellular structures act as templates for the production of new daughter-structures. Such architectural templating is thought to underlie the growth, multiplication and transmission of some membrane structures (called "genetic membranes" by Cavalier Smith 2000). 3D templating is also thought to underlie the reproduction of prions, the infectious protein particles that are associated with degenerative diseases of the nervous system such as BSE (the mad cow disease), and CJD (Creutzfeldt-Jakob disease) in humans (Prusiner 1998), and a similar principle was suggested to explain the re-production of variations in cortical structures in paramecia (Grimes and Aufderheide 1991). The third type of EIS, chromatin marking, is based on the inheritance of patterns of DNA-bound molecules such as proteins, RNAs, or small chemical groups, which are referred to as "chromatin marks". The chromatin marks on a gene's DNA sequence are established during development as a result of induction (sometimes also of developmental noise), and the chromatin marks on a gene's DNA sequence affect the regulation of its transcription, and hence how a character is expressed. Crucially, chromatin marks are reproduced when DNA replicates. A relatively well-understood example is the inheritance of patterns of cytosine methylation at CG sites in DNA. Patterns of DNA methylation are reconstructed following semi-conservative DNA replication: when regions of DNA with methylated cytosine sites (CmG sites) replicate, the old strands retain their methylated state (CmG), so immediately after replication the DNA duplex is half-methylated. An enzyme that has a special affinity for these non-symmetrical, half-methylated sites preferentially methylates the new strand, thus reconstructing the original pattern. Other types of chromatin marks, for example patterns of DNA-bound histone and non-histone proteins, are also re-produced following DNA replication. Cells with identical DNA sequences therefore have non-identical marks, which can be inherited for many cell generations (Holliday 1990). The fourth EIS involves a recently discovered epigenetic mechanism known as RNA-mediated gene silencing (McManus and Sharp 2002; Matzke, Matzke and Kooter 2001). The system is based on the silencing effect of small RNA molecules (siRNAs) that originate from much larger RNA transcripts. RNA molecules that have certain topological peculiarities are recognized by an enzyme that chops them up into small siRNAs. Then, with the help of special RNA-replicating enzymes, these siRNAs are replicated many times. Copies are transmitted to daughter cells when the cell divides, and other copies can move from cell to cell (including germ cells), behaving like infectious

agents or chemical signals. The siRNAs seem to associate with and destroy copies of the large transcript from which they were derived (and any similar-enough RNA), and sometimes also to associate with the gene that mothered their transcription. This latter association leads to the formation of a stable chromatin mark (often a methylation pattern), which suppresses the activity of the gene and can be transmitted to the next cell generation. Genetically identical organisms in the same environment can have different patterns of silent genes, depending on their history of RNA-mediated silencing. It is important to stress again that some of these epigenetic variations are transmitted not only between cells within the body, but also between organisms, passing through the cells of the germ-line lineage.

It is worth highlighting the fact that the number of heritable phenotypic heritable states that a single somatic or germ-line cell can assume via these different EISs is enormous. Although at the level of the single heritable cellular trait (a self-maintaining loop, a 3D structure, a chromatin mark, an RNA-mediated state of gene silence), the number of variant heritable states is usually small (sometimes only two), the number of combinations of different active/inactive loops, of cellular architectures, of proteins marks and RNA-mediated silencing patterns in a cell is vast. The evolutionary potential of such systems is therefore considerable (Jablonka and Lamb 1998).

Heritable epigenetic variations can occur at different levels of biological organization. For example, environmentally induced maternal effects in plants can be transmitted for several generations (for an example see Miao, Bazzaz and Primack 1991); multigenerational interactions between symbionts and their hosts that involve direct transmission of the symbionts, or that occur through the re-construction of parental developmental effects can be reproduced (Paracer and Ahmadjian 2000; Sterelny 2001); food preferences and host preferences may be reproduced within lineages of insects (Thompson and Pellmyr 1991); the effects of starvation and of drugs can be inherited across generations (Campbell and Perkins 1988), and gender behavior and sex-ratio can be inherited in lineages of Mongolian gerbils (Clark, Karpiuk and Galef 1993). In all these cases as well as many others, developmental legacies and variations in such legacies are re-produced in the offspring via cells and organ systems. In all cases the re-produced variations are in phenotypic traits.

The transmission between generations of patterns of behavior and of ideas is a fact of which we are all well aware. In *The Selfish Gene* Dawkins suggested that another replicator – the meme, the unit of cultural information – should be added to the genetic replicator. In the EP he discussed this idea in more depth, and pointed out the profound differences between the meme and the gene. In the last 10 years the meme has acquired great popularity,

and although there still is no consensus as to what it actually stands for, it is generally accepted that it is a replicator. According to Dawkins and to most other scholars who embrace the concept, the meme is a unit of information, residing in the brain, embodied as a localized or distributed neural circuit. It has phenotypic effects in the form of behavior patterns, or cultural products. Through these phenotypic effects the meme spreads, by imitation, from brain to brain (see EP p. 109). Some scholars also add to the brain circuits the imitated behavioral acts themselves, i.e. the behavioral phenotypes, and see them too as memes (Dennett 1995; Blackmore 1999). Imitation is usually used in a general sense, and is not restricted to forms of social learning that involve just "doing a thing from seeing how it is done" (which is what imitation usually means), but includes other social learning mechanisms as well.

The problem with the meme concept is twofold. The first problem is that it is not clear why the meme, according to most notions of it, is not regarded as a transmissible phenotypic trait. Why is a circuit in the brain, which is re-constructed during behavioral development and learning, not a phenotypic trait, whereas the concentration of a hormone, or a motor pattern, are non-problematic traits? The second problem with the meme concept is that if we do accept that a meme is a transmissible trait, then this phenotypic trait, like all other traits, is generated during a process of development – in this case, behavioral development and learning. Development is a process which, depending on the plasticity of the developmental system, is sensitive to environmental influences. Phenotypic traits, which are the products of development/learning processes, reflect these influences. Through learning, individuals construct their behavior and acquire new behaviors. Acquired learned changes – reflected in changed neural circuits, hormone concentrations, motor patterns, acts, and products of behavior – can be transmitted through the various mechanisms of social learning. However, since according to Dawkins phenotypes cannot transmit acquired variations, the meme is not a phenotype. The conceptual ambiguity surrounding the status of the meme is the reason why Dawkins was reluctant to push the analogy between genes and memes too far in the EP, although he seems to be more well-disposed to the idea now.

The situation with the meme concept does not become much better if the term is applied only to entities or processes related to symbolic representation and communication. Superficially it may seem that symbolic "memes" share some common properties with the prototypic replicator, the gene. In both cases latent states (unexpressed genes or un-displayed acts) can be transmitted and duplicated, and consequently in both cases the "copying" can be relatively insensitive to the function of the copied element. DNA

polymerase copies with the same fidelity both nonsense and sense sequences, and nonsense and sense symbolic messages can be copied through some forms of blind imitation (through devices like a photocopying machine, for example). However, most human non-machine imitation, especially of complex acts, involves active search and inquiry by the information receiver (Sperber 1996). Moreover, this active search is not blind, but is governed by understanding and by perceived goals. In fact, perceived goals play a particularly large role in human, symbol-based, acquisition and transmission of new and old information. In addition to the complexity of the developmental/learning process already present in non-symbolic forms of learning, new variations are not only targeted and constructed during developmental and human learning processes, but they are also often *planned* – deliberately constructed according to past or future strictures. The instructive aspect of the generation of new memes is central to the symbolic system.

In addition to the direct re-production and multiplication of phenotypes through the various inheritance systems, re-production of phenotypes can also be indirect and extended in space and time, mediated by ecological niche construction (Lewontin 1983; Odling-Smee 1988; Odling-Smee, Laland and Feldman 1996). Organisms often construct an environment in which they and their descendants live. Through their activities, they modify the environment (worms change the properties of the soil, green plants have changed the composition of the atmosphere, beavers alter their landscape, parasites alter their hosts' physiology and behavior, humans alter the world in familiar and varied ways). Since many of the changes that organisms introduce via niche construction alter the niche in a way that is self-perpetuating (the initial conditions for development are re-constructed and re-generated every generation), niches, and some variations in niches, are transmitted between generations. Niche construction does not always involve the multiplication of the trait and its information – the transmission of an artifact such as a beaver's dam does not involve dam duplication – but it always leads to the re-construction of the dam and the information inherent in it. When multiplication and reconstruction are coupled, the relationship between them can be more or less direct: the relationship is relatively direct with DNA replication and other re-production processes that involve material overlap between mother and daughter entities, and it is very much more circuitous and indirect with learning a new complex skill.

The diverse cellular and organismal EISs, as well as the behavioral and symbolic transmission systems and the continuity generated through niche construction, have two major things in common. First, through them, direct or extended phenotypic traits are transmitted (through re-construction) from one generation to the next. Second, the variations generated during the devel-

opment and transmission of these traits are affected by the environmental conditions in which individuals develop and with which they interact. In addition to the Darwinian question: "what is selected and why?", questions such as: "how, when and where does a new heritable variation arise?" and: "what are the system-rules generating and shaping new variations?" need to be asked if we are to understand evolution.

Yet, from Dawkins' replicator-oriented point of view, the inheritance of developmentally modifiable phenotypes is unacceptable, and evolved systems generating targeted, developmentally modifiable variations, are not considered. In the EP Dawkins devoted some space to discussing the impossibility of such "Lamarckism", by examining what he called the "Lamarckian Scare" of the early 1980s – the hypothesis that adaptive variations in antibody genes that are generated during development are incorporated into the germ line. Ted Steele suggested that the genome could change adaptively through the somatic selection of those lymphocyte cells that produce the best fitting antibodies, followed by the movement of these cells' mRNAs into the germ line, reverse transcription into DNA, and the incorporation of this DNA into the cells of the germ line (Steele 1981; Steele, Lindley and Blanden 1998). Dawkins began by considering this mechanism as a candidate Lamarckian system, but then rejected this possibility, and hailed the system as another proof of his replicator view. This mechanism was not seen by Dawkins as a problem for neo-Darwinism, because the environment does not *induce* the precise adaptive variation, it only selects it (Dawkins, EP pp. 165–171).

There are two related problematic aspects of Dawkins' argument which are of general interest. First, Dawkins took for granted the remarkable targeted nature of the generated variations: the (evolved) locus-specificity in the variation that is generated through recombination; the evolved increase in mutation frequency in the very regions of the antibody genes that code for the polypeptide sequence that binds to the antigen, which is triggered when the antigen binds to the lymphocyte; and the evolved somatic selection mechanism. He therefore took for granted just what Lamarckians focus on – the evolved and highly specific system for generating targeted (locus-specific) variations, and the evolved, adaptive, somatic-selection developmental mechanism. Second, it is not clear why Dawkins thought that the fact that Steele's hypothesis involves selection is an argument against Lamarckism. It is only an argument against Lamarckism if it is through selection *alone* that heritable information enters organisms. Somatic variation and selection are indeed very important in producing the particular adaptation in the immune system, but this is related to the special function of the immune system, which has to respond to an unpredictable variety of antigens,

for which a high degree of initial randomness is necessary. Somatic selection could be more or less extensive, depending on the extent of variability introduced by the evolved variation-generating system. A system could, for example, generate a very small range of targeted, fairly adaptive genetic variations, and selection can fine-tune the fit of these already-adaptive variations to the particular local conditions. If so, surely it is at least as important to understand the targeting of variation as it is to understand the selection of a subset of the targeted variations. Although the particular case suggested by Steele and discussed by Dawkins involves variations in nucleic acids, the same arguments apply when we consider other types of heritable variations that do not depend on variations in DNA sequence. Being scared of Lamarckism leads to the neglect of the evolutionary effects of evolved systems that allow the inheritance of targeted and acquired variations. When the fact that variation is highly constrained and is shaped (or, rather, drafted) by the rules of the generating system is ignored, evolution cannot be properly understood.

If acquired variations in phenotypic traits can be, and commonly are, transmitted between generations, the distinction between replicator and vehicle as articulated by Dawkins is in trouble, unless one assumes that a replicator has a dual nature and can also be a phenotypic trait. This, however, is impossible according to Dawkins. Phenotypic traits are by definition not replicators, nor are they individuals. It is impossible to think of traits like methylation patterns, cortical architectures or hormonal levels as individuals.

One way of overcoming these difficulties and retaining the replicator concept is to adhere to an all-inclusive sense of the replicator. The logical status of the replicator concept seems to be unaffected if we take Dawkins' definition of it as "anything in the world of which copies are made" at face value, and interpret "copying" generously, to include not only dedicated systems of copying, like those involving DNA polymerase or methyl transferase enzyme systems, but also local mechanisms of reconstruction such as those involved in 3D templating, the growth and multiplication of self-sustaining sets of metabolic feedback loops, and various non-imitative forms of social learning. Sterelny et al (1996) have suggested such an extension of the replicator concept, and this extension is logically consistent and includes many different entities, from genes to symbionts that are transmitted between generations of hosts.

An alternative, although related approach, which avoids the term replicator and the problems in the replicator/vehicle distinction, is to focus on different types of inheritance systems and study the modes of heredity they introduce and their evolutionary effects (Jablonka and Lamb 1989, 1995, in press; Jablonka, Lamb and Avital 1998; Avital and Jablonka 2000). I prefer this alternative, because I think that the adherence to the replicator concept has

problems. First, the replicator concept implies a misleading replicator/vehicle heredity-based dichotomy. Second, being a replicator may not be a stable property of a trait or an entity – for example, a pattern of learnt behavior may be transmissible to the next generation under some conditions, and not under others. Finally, a focus on replicators may lead us to neglect the multiple reasons for the intergenerational stability and changeability of phenotypic traits. A single type of developmental resource that contributes to the inheritance of a variant phenotypic trait may often be insufficient to account for its functional intergenerational stability.

Both the extended replicator and the multiple inheritance system approaches overlap with the view offered by developmental system theorists like Oyama, Griffiths and Gray, who focus on heritably varying developmental resources (Oyama 1985/2000; Griffiths and Gray 1994, 2001). Their heritable developmental resources include Sterelny's extended replicators and our multiple inheritance system effects, as well as all the self-reproducing interactions of organisms with their external environment.

Heritably varying phenotypic traits as an alternative to replicators, and reproducers as alternative to vehicles

It is not sufficient to point out problems with a concept. It is as important to find an alternative that will be free of these problems and that will offer at least as fruitful a research program as the old perspective. What then is the alternative, and what extra bonus does it offer?

As the discussion in the previous section has implied, the alternative is to abandon the notion of replicator and vehicle, and concentrate on heritable phenotypic traits and variations in heritable phenotypic traits. A phenotypic trait is a characteristic of an organism resulting from the interactions between internal initial conditions (genetic and epigenetic) and the external environment. Varying phenotypic traits are called *trait-variables* by biologists and are the basis of comparisons. For example in: Fred's *eye color* is black, *eye color* is the trait-variable (Fristrup 1992). Since our focus is heredity and evolution, I refer specifically to *heritable* types of such phenotypic trait-variables. Linking trait-variables by heredity means that there is information transmission between "parent" and "offspring" entities at one or more levels of biological organization (genetic, epigenetic, behavioural, and so on).

Following the fortunes of heritably variable phenotypic traits in populations is common practice in evolutionary biology. We measure the genetic component of the variance in a trait in a population; models of phenotypic evolution are regularly constructed (e.g. most game theoretical models); and paleontological data, which is mostly based on morphological traits, is an

accepted source of insights about evolution. Since for an entity to count as a "fitness bearer" – a unit of adaptive evolution – it has to show heritable variation in fitness, variant phenotypic traits are much better candidates than genes for this role. Of course, some variant traits may be selectively neutral, and in such cases drift, transmissibility bias, and additional factors other than selection, will determine the fate of the trait-variable over time. However, the chances that variations in a phenotypic trait that is a functional product of development are selectively significant are much greater than the chances than an allele, which is one of the many contributors to the trait's development, will make a selective difference.

Heritably varying phenotypic traits are products of development and can be more or less complex, in the sense that they can be delimited at different levels of biological organization (cell, tissue, organ, motor behavior, and so on). Moreover, one or several types of heritable resources (generated by the different inheritance systems and their interactions) can be involved in a trait's development. The choice of the level of organization at which we study a heritably varying phenotypic trait is dictated by the evolutionary question that we ask. In the relatively rare cases where a variation in a phenotypic trait is a reflection of a change in a single gene, following the variant gene may be equivalent to following the variant heritable trait. However, since this may not be the only source of inter-generational stability of the phenotypic variation, following variations in phenotypic traits is generally preferred.

Local and extended variant heritable phenotypic traits (and the multiple genetic, epigenetic, behavioral and symbolic networks underlying them) are the relevant entities to be traced and followed in populations during adaptive evolution. Genes are very important developmental resources, and usually concerted variations in several genes contribute to traits' heritable differences, so genetic networks, their regulatory architecture and their constituent alleles have to be studied if we are to understand evolution. However, genes are usually not the only heritable developmental resource, and sometimes variations in genes are irrelevant for trait variations, as with most culturally transmitted traits.

One of the basic properties that a replicator is supposed to have is copying fidelity (EP p. 84). Williams' definition of a gene reflects this requirement, and it makes sense when we are thinking about genetic replication. Since in the genetic system most of the variation is random with respect to the selecting environment, any variation which has a phenotypic effect is likely to be either neutral or, when extensive, deleterious. Therefore, a high degree of fidelity is important. On the other hand, when there are systems with sophisticated variation-generating systems that make "educated guesses" about which variation should be produced (i.e. variation is targeted), and

when there are developmental filters that try out and edit the produced variations before they are re-produced, fidelity is not important in the same sense. For example, there can be evolution of ideas and artefacts, in which, in every generation, the trait is different in obvious and significant ways, but the difference is still adaptive, sometimes even progressively more sophisticated. Technological evolution in the last 150 years illustrates the complex nature of the interactions between targeted and constructed variation and selection that lead to rapid cumulative evolution of technologies (Ziman 2000). Of course, the development of the trait in descendants is causally related to the trait exhibited by ancestors, and the trait's functional adequacy is important, so there is continuity between traits over generations in this respect. However, this is a very different notion of fidelity from that inspired by the gene.

The replicator-based research program was useful in encouraging interest in and clarifying several evolutionary problems, so it is important to see how taking the heritably varying phenotypic trait as a unit of evolution fares when we look at the phenomena and processes that the replicator concept has elucidated. In the EP Dawkins discusses some examples that lend themselves readily to replicator-based interpretations, and more examples have been added since. Notably, the replicator-centred view has made thinking about the evolution of traits that detract from the reproductive success of the individual manifesting them, such as altruistic behavior on the one hand and meiotic drive on the other hand, much easier and more fruitful. It has also highlighted the importance of co-evolution, and especially co-evolution that involves conflicts of interests (for example, conflict between parasites and hosts, between mates, between parents and offspring) and their resolution. Finally, it has made thinking of extended phenotypic effects very natural, since the individual is no longer the focus of the evolutionary process.

Thinking in terms of individual and of group benefits is often a problem, especially when the selected trait detracts from the reproductive success of the individual harboring it. However, as I have already stressed, the choice is not between using individuals or groups as units of evolution and using genes. The alternative is between using genes and using heritably varying traits. What then happens to Dawkins' examples when we choose heritable traits as our units of evolution rather than genes? The answer is that no harm and some good, is done. Evolutionary conflict (and conflict resolution) is very naturally accommodated if we discuss traits rather than genes. In fact, most of the models used to describe such evolutionary conflicts are game theory models, which are models of phenotypic evolution. The language of single gene difference that is sometimes used in the papers describing these models is no more than a comfortable convention, and has usually no empirical basis.

The extended phenotype idea is also readily accommodated when phenotypic traits are the units of evolution. For example, niche construction is a different way of thinking about extended phenotypes. The constructed abiotic and biotic niche can be thought of as an extended phenotype constructed by organisms and groups of organisms as they interact with their environment. What the niche construction perspective adds to the extended phenotype view is a temporal dimension: phenotypes can be extended over generations through non-genetic inheritance and ecological feedback interactions, because constructed niches and the products of an organism's activity can be stable (through dynamic re-generation activity) for long periods of time (Odling-Smee 1988). The ways in which biotic and abiotic niches are constructed, the way in which the development of individuals leads to complex phenotypic effects that extend beyond the organism, and understanding how and why these traits are acquired and selected, do not require a selfish gene/replicator point of view. In fact, such a view disregards explanatory options for the niche's stability that are not based on genetic differences.

The EP makes thinking about the evolution of traits like altruism, which detract from the reproductive success of the organism harboring it, much easier than an organism- or group-oriented view. How should we think of such cases from the heritable-trait perspective? Are we not undermining one of the most beautiful evolutionary theories, Hamilton's kin selection theory, which is based on the way in which genetic relatedness affects the evolution of altruism in social animals? The answer is not at all. Genes are crucial for development and heredity, so genetic relatedness always has to be an important factor when thinking about evolution. When variations in an altruistic behavioral trait are influenced by variations in genetic networks, genetic relatedness will affect the transmissibility and evolution of the altruistic trait in kin groups just as Hamilton suggested. Similarly, altruistic behavior will spread if the behavior benefits the individual in the long run because of reciprocal altruism, or because of trait-selection in groups (see Sober and Wilson 1998). The advantage of focusing on heritable traits rather than genes in this case is that we are not limited to considering genetic inheritance alone as an explanation for the spread of altruism. For example, individuals may obey a "rule" which says: help those individuals that help others in the group, and withdraw help and punish those who receive help but do not reciprocate it. Such behavior can spread through social learning, (i) if individuals recognize those who obey the helping rule, (ii) if naive individuals learn how to behave from experienced ones, and (iii) if altruists tend to stay together. The differences between individuals who show this discriminating behavior and those who don't could be totally unrelated to genetic differences among

individuals: it could be entirely "cultural". The behavior will spread if the gain to the sub-group of altruists practicing it exceeds the individual cost of recognition and punishment (or withdrawal of help), even though the cost can be very high for some particular individuals and detract from their individual reproductive success.

The same is true of the other prototypical example used to illustrate the benefit of thinking in terms of replicators – that of outlaws. In these cases too, the allele benefits/spreads while the individual carrying it may be harmed. Consider for example, a jumping gene in a plant that is duplicated as it moves from one location of the genome to another. In some cases it is known that heavy methylation suppresses jumping, while reduced methylation in the regulatory regions of the chromosome enhances the chances of jumping and of duplication. The patterns of methylation are heritable, so heavy methylation and light methylation are inherited and are a heritable cause of the "out-lawish" or "law-abiding" behavior of the element. Even with a driver allele which leads to meiotic drive in heterozygotes (commonly by leading to the destruction of the gamete carrying its homologue), it may be the case that whether or not an allele will act as a driving allele depends on the epigenetic state of the region in which it is located and this epigenetic state may be heritable. We should consider both genetic and epigenetic variations if we are to understand the evolution of such traits. This broader view of heredity is also shared by the multiple replicators perspective offered by Sterelny et al (1996), and by the heritable developmental resources perspective offered by the developmental system theorists.

There is a further benefit to thinking about evolution in terms of heritable traits and the inheritance systems underlying them. The EP has very little to say about the evolution of development. Although the replicator view lends itself to thinking about developmental processes occurring outside the body, it is not clear why replicators should construct such very cohesive and complex vehicles that go through the bizarre and exotic contortions of ontogeny. Dawkins recognized this problem, and presented very good arguments as to why development should (usually) start from a single cell and why such a start allows the evolution of development (EP chapter 14). But no further insight about the evolution of development is offered in the EP beyond the single cell start, and Dawkins' discussion of the single cell start is compatible with rather than being dependent on the replicator view of evolution. I believe that part of the reason why there is so little discussion of the evolution of development is that the selfish gene view makes it difficult to incorporate the various factors that stabilize and disrupt developmental pathways. Thinking in terms of heritable traits, rather than genes or replicators, directs attention to the evolution of ontogeny, especially developmental

canalization and plasticity. The role of the different inheritance systems and the various buffering systems and their properties become natural foci of study, and the role of genetic assimilation in adaptive evolution acquires a new significance (Jablonka and Lamb 1995, 2002, in press).

Many aspects of development about which the selfish gene advocates have very little to say are rendered more comprehensible if we think about non-genetic inheritance. The most obvious is that EISs allowed the evolution of complex multicellular organisms with several different cell types that retain their characteristics through cell division. But EISs were probably also very important in shaping several other fundamental aspects of development. In fact, some basic features of development can be seen as mechanisms that evolved in response to the existence of cellular memory. The stability of the differentiated state, selection and cell death among somatic cells, the early segregation between somatic and germ line cells in some animal groups, and the massive restructuring of the chromatin of germ cells, all prevent the carry-over of most (though not all) epigenetic variation that could destabilize the development of the next generation. Thus, once EISs were present (as they must have been from the early stages of the evolution of life, since they exist in unicellular organisms), not only did they have some obvious benefits they also created some serious problems for (non-modular) multicellular organisms. Since the benefits of EISs could not be given up, the problems led to the selection of mechanisms that circumvented them or overcome their effects, such as the features of development just mentioned. EISs were thus the architects of multicellular development in both the positive and the negative sense: they allowed the evolution of organisms with stably differentiated cells, and they constructed the selective regimes that led to developmental mechanisms that circumvent and avoid the hazards that cellular memory created (Jablonka and Lamb 1995, in press). The evolution of learning is also made much more comprehensible if we consider the transmission of socially learnt behaviors between generations (Avital and Jablonka 2000).

In addition to opening up more ways of interpreting observations and accounting for evolution, thinking of heritable traits as units of evolution avoids a sore terminological and conceptual problem. Although some traits may spread even though they are harmful, talking of "selfish traits" does not make sense, for a trait is always part of an individual and is always the result of its development. A trait can be beneficial or harmful to an individual's survival or reproduction, but it is not selfish or non-selfish, and it is natural to avoid such metaphors. What Dawkins meant when referring to the "selfish" gene was that an allele may spread even if its "vehicle's" reproductive success is decreased. The metaphor carried no intentional moral meaning, but the rhetoric led to many misunderstandings, as did the vehicle concept, which

implies passivity. Hull's term, the interactor, is from this point of view much better, but the interactor's role in evolution is very similar to that of Dawkins' vehicle.

Nevertheless the vehicle/interactor concept does capture an important property of life – its organization into more or less cohesive units that live, die, and reproduce as units. Is there a viable alternative that will retain the crucial role of a target of selection in evolutionary theory and will avoid the misleading assumptions associated with the vehicle/interactor concept? James Griesemer has suggested such a new concept – the reproducer. The reproducer is a unit of multiplication, heredity and development – of reproduction. For Griesemer, reproduction involves material overlap between parents and offspring, and implies a developmental process, minimally the developmental process required for further multiplication (Griesemer 2000). The reproducer unites development and heredity, heredity being seen as a special aspect of development. The reproducer is an alternative to the vehicle/interactor concept: like it, it is the target of selection, yet it avoids the dichotomies that the replicator/vehicle couplet has created – the dichotomy between heredity and development, and that between development and evolution. It allows one to consider hereditary variations in different types of traits, at different levels of organization, and allows for any mix of selective and instructive processes in both ontogeny and phylogeny. Thinking about developing and heritable traits and about reproducers gives the individual organisms a greater role in development and evolution. The reproducer can (to varying extents) control its own development (for example, by moving to a different habitat, or changing its habits), and when these controllable traits are heritable, it affects the evolution of its own lineage. It is reproducers that according to Griesemer are the units of evolutionary transitions (in the sense developed by Maynard Smith and Szathmáry 1995).

Summary

The replicator-based extended-phenotype perspective was important in overcoming the tendency to think about evolution in terms of benefits accrued to individuals or groups. Since individuals and groups are targets of selection, not units of evolution, thinking in terms of individual benefits has sometimes led to absurdities. Dawkins did a great service in pointing to these absurdities, and popularizing and developing the gene's-eye view which avoided a lot of the problems. However, he insisted that the basic Darwinian question with respect to adaptation has to remain "who benefits?", and in order to give a coherent answer to this question he transferred the benefit from the organism to the gene. The question, however, makes it very unclear whether its subject

is supposed to be the target of selection or the unit of evolution, and creates the illusion that a single beneficiary can be found. Asking instead, "what is selected and why?" avoids this problem, and remains within the basic Darwinian paradigm, although additional questions such as: "what type of new variations are generated, how, when and where?" have to be added if we are to gain deeper understanding of the evolution of reproducers that have evolved sophisticated variation-generating systems.

The replicator view made apparent the many problems inherent in a previous view of evolution, and provided a powerful alternative, which stimulated research. However, this view, including its memetic extension, has many theoretical problems which have become apparent during the last 21 years. The approach suggested here, which is inspired by developmental system theory, focuses on heritably varying traits and reproducers, and proposes alternative units of evolution and alternative targets of selection to those suggested by Dawkins. I have argued that a trait/reproducer-oriented view (i) is more consistent with what we know about the relationship between genes and phenotypic traits, (ii) illuminates the evolution of the traits' development and the diverse sources of a traits' stability and changeability over generations, (iii) gives the organism a more active role in evolution, and (iv) goes some way towards solving the complex problems that arise when we study the relationship between development, heredity and evolution. Nevertheless, it is doubtful that this approach would have been developed without the challenges presented by Dawkins in the EP.

Acknowledgement

I apologize and am very grateful to the biologists and philosophers, who, in many papers written over the last 21 years, suggested ideas that overlap with those presented in this paper, but who were not explicitly mentioned here. The influence of the EP and the replicator/vehicle concepts on the biological community are simply too extensive to do justice to the many critics and reformers of these concepts in one small paper. I am also grateful to my friends and colleagues Marion Lamb, Simona Ginsburg, Susan Ptak and Michael Lachmann, who read the paper and made very useful suggestions, and to Kim Sterelny for his incisive comments.

References

Avital, E. and Jablonka, E.: 2000, *Animal Traditions: Behavioural Inheritance in Evolution*, Cambridge University Press, Cambridge.

Blackmore, S.: 1999, *The Meme Machine*, Oxford University Press, Oxford.
Campbell, J.H. and Perkins, P.: 1988, 'Transgenerational Effects of Drug and Hormonal Treatments in Mammals: A Review of Observations and Ideas', *Progress in Brain Research* **73**, 535–553.
Cavalier-Smith, T.: 2000, 'Membrane Heredity and Early Chloroplast Evolution', *Trends in Plant Science* **5**, 174–182.
Clark, M.M., Karpiuk, P. and Galef, B.G. Jr.: 1993, 'Hormonally Mediated Inheritance of Acquired Characteristics in Mongolian Gerbils', *Nature* **364**, 712.
Cubas, P., Vincent, C. and Coen, E.: 1999, 'An Epigenetic Mutation Responsible for Natural Variation in Floral Symmetry', *Nature* **401**, 157–161.
Dawkins, R.: 1976, *The Selfish Gene*, Oxford University Press, Oxford.
Dawkins, R.: 1982, *The Extended Phenotype*, W. H. Freeman, Oxford.
Dennett, D.C.: 1995, *Darwin's Dangerous Idea: Evolution and the Meaning of Life*, Allen Lane, London.
Fristrup, K.: 1992, 'Character: Current Usages', in E. Fox Keller and E.A. Lloyd (eds), *Keywords in Evolutionary Biology*, Harvard University Press, Cambridge, MA, pp. 45–51.
Griesemer, J.: 2000, 'The Units of Evolutionary Transition', *Selection* **1**, 67–80.
Grimes, G.W. and Aufderheide, K.J.: 1991, *Cellular Aspects of Pattern Formation: The Problem of Assembly*, Monographs in Developmental Biology Vol. 22, Karger, Basel.
Griffiths, P.E. and Gray, R.: 1994, 'Developmental Systems and Evolutionary Explanations', *Journal of Philosophy* **91**, 277–304.
Griffiths, P.E. and Gray, R.D.: 2001, 'Darwinism and Developmental Systems', in S. Oyama, P.E. Griffith and R.D. Gray (eds), *Cycles of Contingency*, MIT Press, Cambridge, MA, pp. 195–218.
Holliday, R.: 1990, 'Mechanisms for the Control of Gene Activity During Development', *Biological Reviews* **65**, 431–471.
Hull, D.L.: 1988, *Science as a Process*, University of Chicago Press, Chicago.
Jablonka, E. and Lamb, M.J.: 1989, 'The Inheritance of Acquired Epigenetic Variations', *Journal of Theoretical Biology* **139**, 69–83.
Jablonka, E. and Lamb, M.J.: 1995, *Epigenetic Inheritance and Evolution: The Lamarckian Dimension*, Oxford University Press, Oxford.
Jablonka, E. and Lamb, M.J.: 1998, 'Epigenetic Inheritance in Evolution', *Journal of Evolutionary Biology* **11**, 159–183.
Jablonka, E. and Lamb, M.J.: 2002, 'The Changing Concept of Epigenetics', *Annals of the New York Academy of Sciences* **981**, 82–96.
Jablonka, E. and Lamb, M.J.: (in press), *Evolution in Four Dimensions*, MIT Press, Cambridge, MA.
Jablonka, E., Lamb, M.J. and Avital, E.: 1998, 'Lamarckian Mechanisms in Darwinian Evolution', *Trends in Ecology and Evolution* **13**, 206–210.
Kimura, M.: 1983, *The Neutral Theory of Molecular Evolution*, Cambridge University Press, Cambridge.
Lewontin, R.C.: 1983, 'Gene, Organism, and Environment', in D.S. Bendall (ed.), *Evolution: From Molecules to Men*, Cambridge University Press, Cambridge, pp. 273–285.
McManus, M.T. and Sharp, P.A.: 2002, 'Gene Silencing in Mammals by Small Interfering RNAs', *Nature Reviews Genetics* **3**, 737–758.
Matzke, M., Matzke, A.J.M. and Kooter, J.M.: 2001, 'RNA: Guiding Gene Silencing', *Science* **293**, 1080–1083.
Maynard Smith, J. and Szathmáry, E.: 1995, *The Major Transitions in Evolution*, Freeman, Oxford.

Miao, S.L., Bazzaz, F.A. and Primack, R.B.: 1991, 'Persistence of Maternal Nutrient Effects in *Plantago major*: The Third Generation', *Ecology* **72**, 1634–1642.

Morange, M.: 2001, *The Misunderstood Gene*, Harvard University Press, Cambridge, MA.

Odling-Smee, J.F.: 1988, 'Niche Constructing Phenotypes', in H.C. Plotkin (ed.), *The Role of Behavior in Evolution*, MIT Press, Cambridge, MA, pp. 73–132.

Odling-Smee, J.F., Laland, K.N. and Feldman, M.W.: 1996, 'Niche Construction', *American Naturalist* **147**, 641–648.

Oyama, S.: 1985/2000, *The Ontogeny of Information: Developmental Systems and Evolution*, Cambridge University Press, Cambridge. 2nd revised edn.: 2000, Duke University Press, Durham, NC.

Paracer, S. and Ahmadjian, V.: 2000, *Symbiosis: An Introduction to Biological Associations*, Oxford University Press, Oxford.

Prusiner, S.B.: 1998, 'Prions', *Proceedings of the National Academy Sciences USA* **95**, 13363–13383.

Rakyan, V.K., Chong, S., Camp, M.E., Cuthbert, P.C., Morgan, H.D., Luu, K.V.K. and Whitelaw, E.: 2003, 'Transgenerational Inheritance of Epigenetic States at the Murine *Axin Fu* Allele Occurs After Maternal and Paternal Transmission', *Proceedings of the National Academy Sciences USA* **100**, 2538–2543.

Rutherford, S.L. and Lindquist, S.: 1998, 'Hsp90 as a Capacitator for Morphological Evolution', *Nature* **396**, 336–342.

Rutherford, S.L.: 2003, 'Between Genotype and Phenotype: Protein Chaperones and Evolvability', *Nature Reviews Genetics* **4**, 263–274.

Sober, E. and Wilson, D.S.: 1998, *Unto Others*, Harvard University Press, Cambridge, MA.

Sollars, V., Lu, X., Xiao, L., Wang, X., Garfinkel, M.D. and Ruden, D.M.: 2003, 'Evidence for an Epigenetic Mechanism by Which Hsp90 Acts as a Capacitator for Morphological Evolution', *Nature Genetics* **33**, 70–74.

Sperber, D.: 1996, *Explaining Culture: A Naturalistic Approach*, Blackwell, Oxford.

Steele, E.J.: 1981, *Somatic Selection and Adaptive Evolution: On the Inheritance of Acquired Characters* (2nd edn.), Chicago University Press, Chicago.

Steele, E.J., Lindley, R.A. and Blanden R.V.: 1998, *Lamarck's Signature*, Allen and Unwin, London.

Sterelny, K.: 2001, 'Niche Construction and the Extended Replicator', in S. Oyama, P.E. Griffiths and R.D. Gray (eds), *Cycles of Contingency*, MIT Press, Cambridge, MA, pp. 333–349.

Sterelny, K., Smith, K.C and Dickison, M.: 1996, 'The Extended Replicator', *Biology and Philosophy* **11**, 377–403.

Thompson, J.N. and Pellmyr, O.: 1991, 'Evolution of Oviposition Behavior and Host Preference in Lepidoptera', *Annual Review of Entomology* **36**, 65–89.

Williams, G.C.: 1966, *Adaptation and Natural Selection*, Princeton University Press, Princeton, NJ.

Ziman, J. (ed.): 2000, *Technological Innovation as an Evolutionary Process*, Cambridge University Press, Cambridge.