Review

Avatars of information: towards an inclusive evolutionary synthesis

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Following the discovery that inheritance entails the interaction between genetic and nongenetic processes, biology is undergoing a profound mutation. This paradigm shift implies that the model of heredity that is emerging incorporates genetic and nongenetic processes. A way to integrate all forms of inheritance harmoniously is to consider what unifies genetic and nongenetic heredity. Here, I unify all sources of phenotypic variation within the concept of information and its avatars, discuss a major overlooked methodological problem leading to confounding sources of variation (namely the case of the missing heritability), propose new research avenues, and illustrate how putting concepts of information at the heart of evolutionary approaches will affect the emerging Inclusive Evolutionary Synthesis.

The current call for an 'Inclusive Evolutionary Synthesis'

Biology is undergoing a profound mutation stimulated by discoveries in various fields, including behavioral [1–5] and developmental biology [6–8], as well as epigenetics [9–11] and evolutionary ecology [12–14]. New evidence from these scientific domains led several authors to converge in calling for modernizing the Modern Synthesis of evolution [1,6,8,14–16]. Evolutionary biologists have underlined the importance of formalizing current discoveries in terms of heredity [2,17] to enable the quantitative study of the various sources of phenotypic variation and their consequences in terms of natural selection and evolution [2,5,13,14,17,18]. Today, this weight of evidence implies that the idea that the inheritance of phenotypic variation only rests on genetic variation is no longer tenable [5,14]. Instead, the model of heredity that is emerging incorporates not only genetic, but also nongenetic inheritance into an 'inclusive' [13] evolutionary synthesis [1,5] (equivalent terms used by other authors are 'generalized' [17], 'extended' [8,19], or 'pluralistic' [20] theory of evolution).

In a recent Opinion in *TREE*, Russell Bonduriansky [5] placed this major scientific movement into its historical context, highlighting the controversy between hard and soft inheritance (see Glossary) that was at the heart of the building of the Modern Synthesis of evolution during the first half of the 20th century. Bonduriansky discussed how the evolution of ideas about heredity has been narrowed by the major discoveries of the laws of genetics and the DNA molecule as the material basis of genes. Understandably, we have been so fascinated by the fantastic capacity of genes to encode and transfer information across generations that we became oblivious to evidence of other mechanisms of inheritance. Furthermore, even once it has been recognized that inheritance can encompass the effect of nongenetic mechanisms, the risk of viewing them as parallel and largely independent processes that concur in producing heredity is high. For instance, Günter P. Wagner's claim that 'we know that language, though highly heritable, is entirely nongenetic in its mode of transmission' (http://news.cell.com/discussions/trends-in-ecology-and-evolution/rethinking-inheritance) seems to deny the possibility that language inheritance results from interactions between the genetic capacity to learn language and the social environment.

A way to integrate all forms of inheritance harmoniously can be to consider what unifies genetic and nongenetic

Glossary

Culture: part of variation in a trait that is socially transmitted to offspring [21]. Culture thus incorporates all the information that is inherited through social learning, such as song dialects in birds and whales, language in humans, sexual preferences as revealed by mate copying, and so on.
Epistasis: phenomenon where the effects of one gene are modified by one or several other genes; also called 'epistatic interactions'.
Genome-wide association studies (GWAS): analyze the statistical association between the genetic variation observed at very high numbers of genetic markers distributed across the entire genome and phenotypic variation; only account for additive effects.
Hard inheritance: model of heredity based on the transmission from parents to offspring, at conception, of a set of factors whose nature is unaffected by the environment or phenotype of the parents [5].
Heritability: part of variation in a trait that is genetically transmitted to offspring
Inclusive heritability: heredity of differences, whatever the mechanism of transmission.
Information: any factor that can affect the phenotype in ways that may (or may not) influence fitness [21]. Consequently, phenotypic variation results from variation in the information possessed by individual organisms.
Modern Synthesis of evolution: merging of Darwinism with genetics that occurred from the 1930s to the 1950s.
Nongenetic inheritance: part of variation in a trait that is transmitted to offspring through mechanisms other than genetic variation.
Soft inheritance: 'the belief in a gradual change of the genetic material itself, either by use or disuse, or by some internal progressive tendencies, or through the direct effect of the environment' [61]. This original definition implies direct changes to DNA sequences. This term is sometimes used unduly to describe nongenetic inheritance (e.g., [62]).
Transgenerational epigenetic inheritance: part of variation in a trait that is transmitted to offspring through variation in epigenetic marks (DNA methylation and acetylation, histone modifications, genetic imprinting, miRNAs, and prions) [25].

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Keywords: evolution; ecology; biological information; nongenetic inheritance; missing heritability.pedigree.

0169-5347/$ – see front matter
 http://dx.doi.org/10.1016/j.tree.2013.02.010

Trends in Ecology & Evolution June 2013, Vol. 28, No. 6

heredity. In this article, I (i) unify all sources of phenotypic variations within the concept of information and define an information-driven approach to evolution; (ii) discuss a major overlooked methodological problem leading to confounding sources of variation; and (iii) illustrate how putting concepts of information at the heart of evolutionary approaches will affect the emerging inclusive evolutionary synthesis.

An information-driven approach to ecology and evolution

Information and phenotypic variation

To understand the roots of the current paradigm shift, it is necessary to return to the essence of life, namely the capacity of organisms to reproduce. Reproduction entails the transmission of some information from one generation to the next. Information is a concept that is particularly difficult to grasp in biology. One definition is any 'factor that can affect the phenotype in ways that may [or may not] influence fitness' [21]. According to this view, phenotypic variation arises from the fact that different organisms do not have the same information, including variation in not only their genes, but also all aspects of their environment. Thus, decomposing phenotypic variation into its various components is equivalent to studying the various sources of information that organisms have (Figure 1).

Genes, information, and avatars

Genes are often described as sequences of DNA. However, this does not describe their true nature [22]. An equivalent would be to say that the last film of a given director 'is this CD'. The CD is not the film, but just one of its avatars (i.e., a material form taken by an abstract entity, here the story conveyed by the film). Films can have various avatars, such as a series of still images on a celluloid film, a magnetic tape, a DVD, or an electronic file that can be downloaded on the web. A film is not one of its avatars, but rather a story with various characters, images, and music. Similarly, the DNA sequence is an avatar of genetic information [23,24] and, accordingly, recent definitions of genes stress their functional aspects [22]. It is the genetic information, not the DNA molecule *per se*, that is the target of natural selection [23].

Distinguishing biological information from its avatars is important because the properties of the avatars determine laws of inheritance. For instance, the properties of genetic inheritance emerge from those of the DNA and the molecular and behavioral machinery that duplicate and transfer genetic information across generations. Similarly, it is the properties of avatars of transgenerational epigenetic information, which include DNA methylation and acetylation, histone modifications, genomic imprinting, miRNAs, and prions [25], that determine laws of epigenetic inheritance. Together, these various patterns can be viewed as an epigenetic code that is transferred across generations.

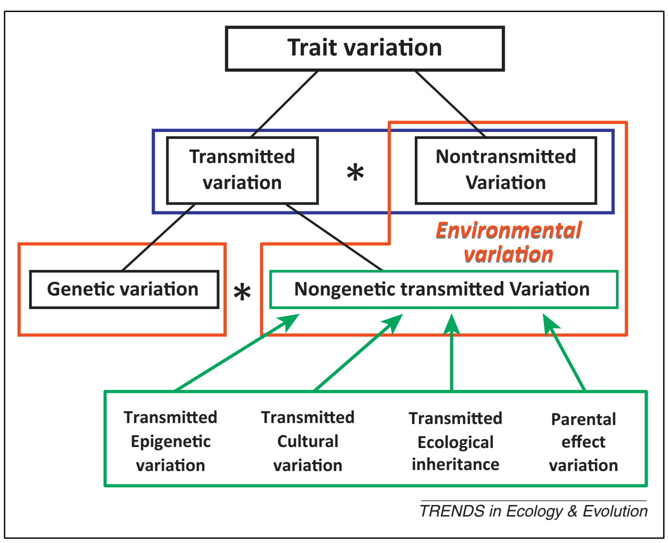

Figure 1. A comprehensive diagram of phenotypic variation accounting for all forms of information inheritance. Evolutionary biologists are particularly interested in estimating the part of phenotypic variation that is transmitted to the next generation because evolution can only affect those traits that are heritable (i.e., whose variation is transmitted to the next generation) [63]. Although genetic information fulfills this important characteristic, it has become clear that this is not the only type of information that is transferred across generations in an inclusively heritable fashion [14]. The bottom green box lists the domains of the biological literature that provide evidence for nongenetic transmitted variation. In red, the current classical partitioning of phenotypic variation, which unavoidably leads to the discarding of some nongenetically transmitted information despite the fact that it is part of evolutionary processes. In blue, the proposed partitioning of phenotypic variance. See [13,14] for definitions of the various nongenetic terms. Stars represent potential interactions among the various components. Adapted from [13,14].

Interactions between the mechanistic and evolutionary approaches

The laws of genetics were discovered during the first decades of the 20th century, long before the discovery of the genetic avatar (i.e., DNA) in the middle of that same century. This multidecade lag shows that it is possible to study the general laws of an inheritance system in the absence of knowledge about its avatar, which is currently the case for most nongenetic inheritance systems. However, it is only after the discovery of the avatar of genetic information that molecular biology and its amazing implications emerged as a new field of biology. Similarly, the study of epigenetics and epigenetic inheritance really accelerated during the past decade, when new technologies enabled the high-throughput study of one of its avatars, in the form of DNA methylation patterns.

Today, many molecular genetic approaches focus on the mechanisms resulting from the detailed properties of the avatar of genetic information. Contrastingly, in the absence of knowledge about the avatars of most nongenetic information, current nongenetic studies focus on informational dynamics to establish general laws about these systems to understand their impact on evolutionary dynamics.

Potential information becomes realized information during development

Genetic information constitutes potential information (see [21]) that is only realized when confronted by environmental information. More generally, development necessarily entails interactions between the various sources of information possessed by individuals, be they inclusively heritable [13] or not, genetic or nongenetic [14].

Moreover, adopting an information-driven approach to ecology and evolution can foster the long called for reconciliation between developmental and evolutionary sciences [15]. Selection acts on phenotypes that result from the