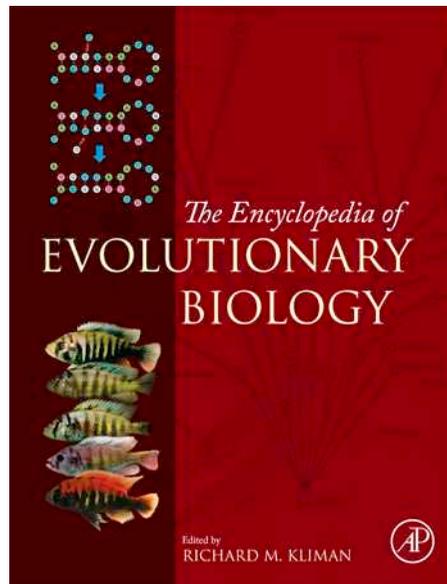


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Artificial Selection

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Glossary

Additive genetic variance The component of the phenotypic variance that causes offspring to resemble their parents.

Covariance A measure of the lack of independence between the values of two traits.

Effective population size (N_e) The size of an idealized population that would experience the same magnitude of genetic drift as the population of interest.

G-matrix The set of additive genetic variances (on the diagonal) and covariances for a group of traits.

Genetic correlation The standardized genetic covariance between a pair of traits.

Genetic covariance The component of covariation between two traits caused by variation at shared gene loci (pleiotropy) or pairs of genes (linkage disequilibrium).

Linkage disequilibrium A nonrandom relationship between the alleles present at two or more loci, which can cause a genetic correlation.

Narrow sense heritability A standardized measure of the degree of resemblance between offspring and their parents, defined as the additive genetic variance divided by the total phenotypic variance.

Pleiotropy It occurs when one locus affects more than one phenotypic trait, contributing to a genetic correlation.

Random genetic drift Fluctuations in allele frequency that occur by chance, particularly in small subpopulations, as a result of random sampling error in the gametes that form the next generation.

Response to selection The change in trait mean across one generation.

Selection differential A measure of the strength of directional selection equal to the mean of the selected group minus the mean of the entire population, or the covariance between relative fitness and trait values.

Introduction

Artificial selection is the process by which humans choose individual organisms with certain phenotypic trait values for breeding. If there is additive genetic variance for the selected trait, it will respond to the selection, that is, the trait will evolve. All of our domesticated species, including crop plants, livestock, and pets, are the products of artificial selection for desirable traits, such as seeds and fruits that do not disperse readily, increased meat and milk production, and docile behavior. The earliest artificial selection may have been unconscious, but it developed into a sophisticated science of plant and animal breeding; indeed, much of the field of quantitative genetics was developed to improve breeding programs.

The importance of artificial selection to the field of evolutionary biology dates back to Darwin, who was likely the first to use the term artificial selection in the 'Origin of Species' (Darwin, 1859). Darwin used the obvious evolutionary results of domesticated species to show the power of selective breeding as an analogy to natural selection. One of the earliest uses of experimental artificial selection to address evolutionary questions was by Holtorp (1944). He selectively bred *Brassica* plants that produced an extra cotyledon and reported an increase in frequency of plants with three and even four cotyledons in subsequent generations. Similarly, Huether (1968) was able to increase and decrease the number of corolla lobes in *Linanthus* through five generations of artificial selection. These early studies established that even traits that are conserved at higher taxonomic levels could evolve.

Artificial selection differs from what has been called laboratory natural selection (Rose *et al.*, 1990) or controlled

natural selection (Conner, 2003). In artificial selection the experimenter chooses specific phenotypic traits to select upon, while in controlled natural selection an environmental factor is manipulated and evolution of the populations in response to this selective agent is monitored. While artificial selection is certainly a form of experimental evolution, often the meaning of the term 'experimental evolution' is confined to controlled natural selection, excluding artificial selection (e.g., Kawecki *et al.*, 2012). Because artificial selection applies a known strength and direction of selection to specific phenotypic traits, it is one of the most powerful methods available for understanding the underlying genetic variation and thus evolvability of those traits; in controlled natural selection the strength and direction of selection cannot be determined by the investigator.

Fundamental Concepts

The rate of adaptive phenotypic evolution depends on the strength of natural selection and the amount of additive genetic variation for the trait in the population. This principle is encapsulated in the breeder's equation:

$$R = h^2 S \quad [1]$$

in which R is the response to selection, defined as the evolutionary change in the trait mean across one generation, h^2 is the heritability, defined as the proportion of the total phenotypic variance due to additive genetic variance, and S is the selection differential, which measures the strength of selection. This form of the equation is useful for evolutionary biologists,

because it allows the prediction of short-term phenotypic evolution (R) from knowledge of the heritability and strength of selection. Additive variance is crucial, particularly in sexual species, because without additive variance a trait will not evolve; if the heritability is zero, so is R in the breeder's equation. The primary utility of artificial selection to evolutionary studies is that it provides the most powerful means of testing for presence of additive genetic variance for a trait. In artificial selection the selection differential is imposed experimentally and the response is measured, yielding an estimate of heritability for the selected trait, as shown by a rearrangement of the breeder's equation:

$$h^2 = R/S \quad [2]$$

This is called the realized heritability (Figure 1).

A serious shortcoming of the breeder's equation for evolutionary studies is that it is univariate, that is, it relates to only a single trait. However, traits commonly covary genetically, which means they share gene loci in common (called pleiotropy) or that allele frequencies at loci that independently affect the two traits are correlated (called linkage disequilibrium; see Conner and Hartl, 2004 Chapter 5 for a fuller explanation). Genetic covariance is commonly standardized as the genetic correlation, just as additive variance is commonly standardized as the heritability. Genetic variances and covariances for a set of traits are expressed in matrix form, called the G-matrix; analogous to the univariate breeder's equation, the rate of evolution of a set of traits is the product of the G-matrix and the strength of direct selection on each of the traits (Conner and Hartl, 2004). If there are traits that covary genetically with a trait under selection, then those traits will also

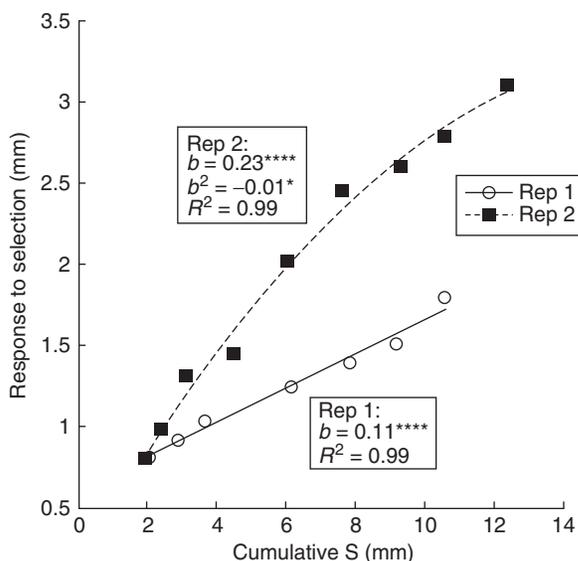


Figure 1 Realized heritability of anther exertion in wild radish, estimated as the slope (b) of the regression of response to selection (R) on the cumulative selection differential (S). Here the two replicates show quite different realized heritabilities, with Replicate 1 less than half that of Replicate 2. Reprinted from Conner, J.K., Karoly, K., Stewart, C., *et al.*, 2011. Rapid independent trait evolution despite a strong pleiotropic genetic correlation. *American Naturalist* 178, 429–441. © 2011 the University of Chicago.

evolve, a phenomenon termed correlated responses to selection. Thus, artificial selection is an excellent way to test for genetic covariance between the selected trait(s) and other traits, in an analogous manner to how additive variance is tested, that is, by measuring phenotypic changes in other traits that were not subjected to artificial selection.

Basic Design Considerations

Careful attention to design is important for producing a convincing outcome of any experiment, and artificial selection is no exception. Only some highlights of experimental design will be addressed here, as excellent detailed discussions are available (e.g., Bohren, 1975; Hill, 1980; Hill and Caballero, 1992). The main issue is to be able to definitively attribute the observed phenotypic response to the selection treatment, as opposed to random genetic drift or differences in the environment across generations. The latter can never be eliminated, even in a growth chamber. First, selection lines need to be replicated; because artificial selection can be time-consuming, often there are only two replicates of each selection treatment, but replication is necessary to separate the effects of selection from random genetic drift.

It is also ideal to include the same number of randomly mated (that is, unselected) control lines, which directly estimate phenotypic change due to drift and environmental differences combined; with replicated controls these two nonselective factors can be distinguished. However, selection can be separated from drift and the environment without control lines in the usual case where a trait is selected in opposite directions in separate replicated selection lines. This is because the response to selection can be tested between the high and low lines; if pairs of high and low lines are grown interspersed randomly in the same environment, the high–low phenotypic difference is due to selection, not the environment, and parallel high–low differences across replicate pairs are most likely due to selection rather than drift. In general, all the lines within one replicate (e.g., high, low, control) should be grown and measured together, so that average phenotypic differences among them are not due to environmental differences.

Besides replication to separate drift from selection, it is important to minimize drift by maximizing the effective population size (N_e) within each selection line, both to increase the precision of estimates of additive variance and also to minimize loss of fitness in multigeneration experiments. Thus, the design of an artificial selection experiment is a trade-off between the number of replicates, control lines, and the effective population size within each line. If the number of organisms that can be maintained is limited, then each set of lines within one replicate (e.g., high, low, and control) can be raised together, but separated in time from other replicates. The trade-off with this procedure is that each generation will take longer.

Another way to increase N_e without increasing the number of organisms is to perform within-family selection rather than mass selection. In mass selection, the most extreme individuals in each line are selected regardless of whether they are related to each other; if the trait is heritable, then families with alleles

for high or low values of the trait will be overrepresented. In within-family selection, a number of offspring of each family are raised and measured, and the same number (often one) of most extreme individuals within each family is selected for the next generation. This maximizes N_e ; in fact, if one individual is chosen per family, and each selected individual has equal numbers of offspring in the next generation, then N_e is double the actual number of individuals selected. The main drawback of within-family selection is that the strength of selection will be weaker than with mass selection.

Weaknesses of Artificial Selection

The more common methods of testing for additive genetic variance and covariance use a breeding design to create known genetic relationships among organisms (parents and offspring, siblings, etc.), or estimating these relationships (i.e., the pedigree) in a natural population using genetic markers, in both cases without selection. Here the disadvantages of artificial selection compared to the more common methods are briefly discussed; the advantages will be made clear under 'Applications in Evolutionary Biology with Examples' section.

Perhaps the biggest disadvantage of artificial selection is that it requires fairly large numbers of individuals to be measured and mated, so this approach is not feasible for many, if not most, species. The traditional quantitative genetic breeding designs also require this, but molecular genetic markers make pedigree analysis possible for some wild populations, and this approach has been used in a few wild mammal and bird populations (e.g., Reale *et al.*, 2003; Kruuk *et al.*, 2000; Charmantier *et al.*, 2008). An advantage of any quantitative genetic study done in the field, pedigree-based or not, is that the G-matrix can be very dependent on the environment due to changes in the expression of additive genetic variances and covariances (e.g., Conner *et al.*, 2003). Artificial selection can in principle be conducted in nature especially in plants or birds in nest-box populations (Postma *et al.*, 2007), but this has rarely been done and for most organisms it will not be feasible.

Another disadvantage of artificial selection is that the number of traits that can be selected is very limited, usually to one or two at a time (but see Hine *et al.*, 2014). In a breeding or pedigree study the full G-matrix for as many traits as can be measured can be estimated. In artificial selection the additive variance for the trait selected upon can be estimated, as well as the genetic covariances between the selected trait and any others that are measured after selection, but the variances of, and covariances between, any traits that were not directly selected upon cannot be estimated. Thus, artificial selection is best reserved for cases where a particular trait is of interest, and to questions other than the full G-matrix (see Applications in Evolutionary Biology with Examples).

Applications in Evolutionary Biology with Examples

Evolutionary Constraints

As noted above, artificial selection is the most powerful test for additive genetic variation and covariation. This is because it is

based on comparisons of means across generations rather than estimating variances and covariances from a breeding design or pedigree; means can be estimated with more precision than variances and covariances. In addition, artificial selection can be conducted over a number of generations, so that very small amounts of genetic variance and covariance can be detected as the response to selection accumulates across generations. This is very important in evaluating whether a lack of evolution, that is, an absolute evolutionary constraint, is caused by a lack of additive variance, because a lack of response to several generations of strong selection is more convincing evidence of constraint than a variance estimate that is not statistically different from zero. The pioneering artificial selection experiments of Holtorp (1944) and Huether (1968) were able to demonstrate additive variance for traits that were highly conserved, showing that this evolutionary conservation is not due to a lack of variance for those traits.

Most artificial selection experiments produce a significant response, suggesting that a lack of additive genetic variance rarely constrains evolutionary change. This is even true in most of a handful of studies that have selected perpendicular to the major axis of a genetic correlation, that is, in the direction of minimum variance in bivariate space (Figure 2; reviewed in Conner *et al.*, 2011). However, some have argued that a fully multivariate approach to constraints is needed, and that for groups of traits there will be directions in multivariate space (typically estimated as eigenvectors) that will lack variance (Blows and Hoffmann, 2005; Walsh and Blows, 2009). To test this hypothesis, Hine *et al.* (2014) applied artificial selection along all eight eigenvectors of eight cuticular hydrocarbons in *Drosophila serrata*; these hydrocarbons have been shown to be involved in mate choice. Significant responses to selection were found for all eight eigenvectors, and for the five eigenvectors that explained the most variance this response was significant for all three replicates. However, for the three eigenvectors that exhibited the least variance, the response was significant for only one or two of the three replicates.

Despite the fact that most artificial selection studies report a statistically significant response to selection, a few studies have not (e.g., Baer and Travis, 2000; Allen *et al.*, 2008; Dorn and Mitchell-Olds, 1991; Hoffmann *et al.*, 2003; Hall *et al.*, 2004). In, perhaps, the most convincing demonstration of a lack of additive variance in a wild species, Hoffmann *et al.* (2003) found no statistically significant response to 28 generations of selection for increased desiccation resistance in a rainforest fly (*Drosophila burchii*; Figure 3), suggesting that adaptation to drier conditions predicted with global warming would be severely constrained. This study is convincing because the large number of generations of selection increases the ability to detect small responses in each generation, and because there was also no response in crosses among the different selected lines, making inbreeding depression caused by drift an unlikely explanation for the lack of response. However, there was an 11% increase in desiccation resistance in two of the three selection lines; while this difference is not statistically significant, the presence of additive genetic variance in the population cannot be ruled out, illustrating the general difficulty in proving that something is absent.

Another important and less common role for artificial selection is investigating the short-term evolutionary effects of

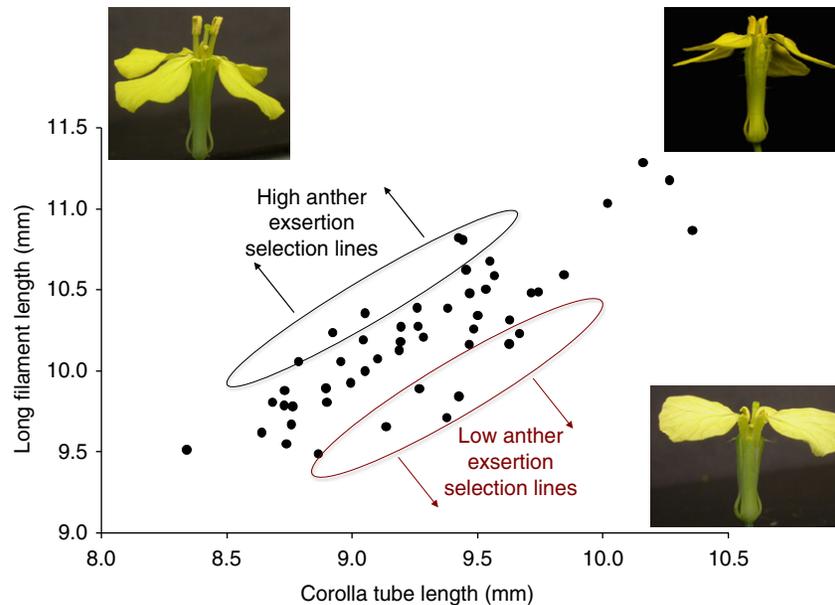


Figure 2 Graphical depiction of selection perpendicular to the major axis of variation for two traits. The genetic correlation of 0.85 between filament and corolla tube in wild radish flowers is depicted by the points in the graph. Anther exertion is a composite trait defined as filament minus corolla tube, which describes how far the anthers protrude from the corolla tube. The picture at upper right shows a plant from the natural population with zero exertion, with the bottom of the anthers at the opening of the corolla tube. Each set of arrows shows the direction of selection for one set of lines; in the high exertion lines the individuals selected have long filaments relative to their corolla tubes (points enclosed by the black ellipse) while in the low lines individuals selected have long tubes relative to their filaments (red ellipse). The two sets of lines are separate, that is, high line individuals are mated to each other, not with low line individuals. Thus, this is directional selection in two directions on the composite trait of anther exertion. Examples of flowers after each direction of artificial selection are shown in the upper left and lower right corners. Redrawn from Conner, J.K., Karoly, K., Stewart, C., *et al.*, 2011. Rapid independent trait evolution despite a strong pleiotropic genetic correlation. *American Naturalist* 178, 429–441.

selection on the genome. A major unresolved issue in evolutionary biology is the stability of the G-matrix across generations (reviewed in Arnold *et al.*, 2008); if the G-matrix is not stable, it is less likely to cause evolutionary constraint. Theory predicts that directional selection on a trait or combination of traits, which is what is almost always conducted in artificial selection studies, will eventually deplete additive genetic variance for that trait, which then constrains further response to that selection. This is one cause of what is called an evolutionary limit or plateau, that is, when a response to artificial selection ceases; however, a plateau can also be caused by natural selection in the opposite direction to the artificial selection, without a depletion of variance (Figure 4). Conner *et al.* (2011) showed that the selection depicted in Figure 2 produced no consistent change in the G-matrix for these two floral traits in wild radish. Delph *et al.* (2011) conducted a different form of selection specifically designed to change the G-matrix. The negative correlational selection imposed significantly reduced the genetic correlation in flower size between male and female plants in two of three replicates. This selection was similar to that depicted in Figure 2, except that the high and low selected plants were mated to each other rather than mated within each group.

Understanding the Genetic Basis of Phenotypic Evolution

The examples discussed above are all of the most common use for artificial selection in evolutionary biology, that is, as a

powerful method for detecting the presence of additive genetic variation for a trait or group of traits. Artificial selection can also be combined with quantitative trait locus (QTL) mapping to help identify gene loci responsible for genetic variation within a natural population, where adaptive evolution occurs. QTL designs generally use crosses between genetically and phenotypically divergent populations, which can be created from a single natural population by artificial selection. Chromosomal regions identified by a QTL analysis of a cross between these lines are those responsible for the response to artificial selection, and must have had allelic variation for loci affecting the trait in the natural base population. This approach was used to discover 26 QTLs for bristle number in *Drosophila melanogaster*, and 20 of these included likely candidate genes for this trait (Long *et al.*, 1995; Gurganus *et al.*, 1999; Nuzhdin *et al.*, 1999).

If there is already a strong candidate gene for a given trait, then allele frequency changes can be tracked across generations of artificial selection on that trait. For example, *FRIGIDA* (*FRI*) and *FLOWERING LOCUS C* (*FLC*) are loci affecting flowering time in the model plant *Arabidopsis thaliana*. Scarcelli and Kover (2009) selected for early flowering under growth chamber conditions simulating fall or spring germination, both of which occur naturally in this species. A large decrease in flowering time occurred in both growth conditions, and a concomitant change in *FRI* allele frequency also occurred, but only under spring germination conditions. *FLC* allele frequencies did not change significantly under either condition.

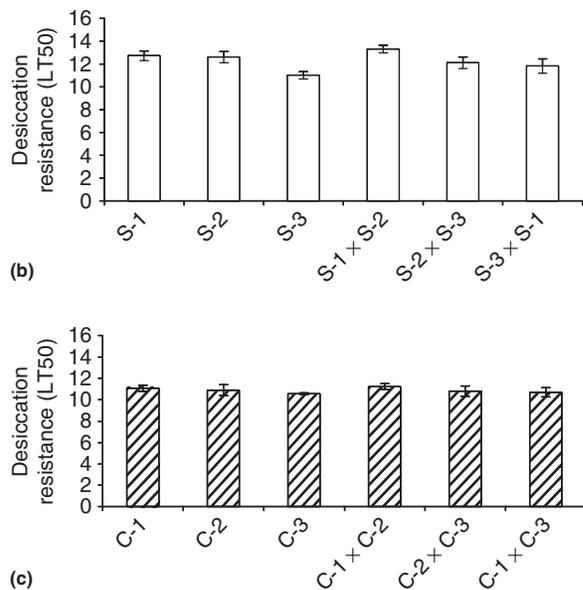


Figure 3 Lack of significant response to 28 generations of artificial selection for increased desiccation tolerance. LT50 is the number of hours it took for 50% of the flies to die in the absence of water. Panel (b) shows the means for the three selection lines and all possible crosses between them, and (c) shows the same results for control lines. S-1 and S-2 show a higher desiccation resistance than controls, but the overall difference between selected and control lines was not statistically significant. Reprinted with permission from Hoffmann, A. A., Hallas, R.J., Dean, J.A., Schiffer, M., 2003. Low potential for climatic stress adaptation in a rainforest *Drosophila* species. *Science* 301, 100–102.

Thus, variation in loci other than *FRI* and *FLC* were responsible for the phenotypic change under fall germination conditions, demonstrating the important point that expression of additive genetic variation for any trait (flowering time in this example) can depend on the environment (e.g., [Conner et al., 2003](#)); this is one type of genotype–environment interaction. Thus, in combination with molecular genetic techniques, artificial selection can be used not only to demonstrate the presence of additive genetic variance, but also to understand what gene loci are responsible for this variance, and how this depends on the environment.

Understanding Natural Selection

The discussion and examples above make clear that artificial selection has most often been used to understand additive genetic variation, which is appropriate based on eqn [2]. By itself, artificial selection does not provide information about natural selection, but it can be used to create experimental populations with altered phenotypic means and variance for additional studies of adaptation and natural selection. If a trait is an adaptation, then we expect that the mean value for that trait will be near the optimum in natural populations due to past selection, assuming that the population is near equilibrium. Thus, artificial selection on an adaptive trait should move it away from this optimum, increasing the strength of natural selection to return the trait to the optimum. Laboratory artificial selection studies have produced many examples of

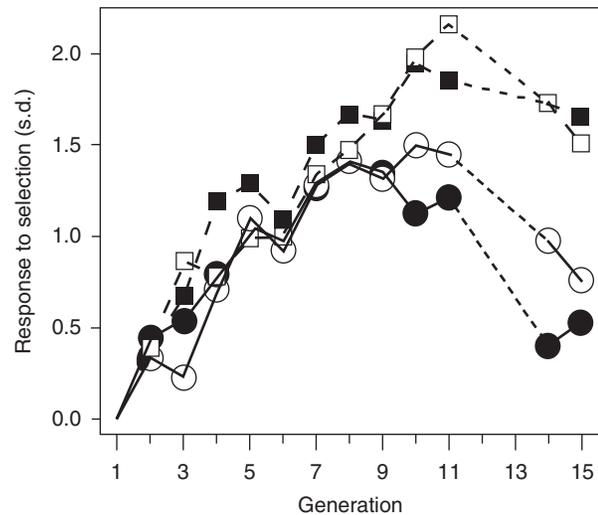


Figure 4 Reversal of response to artificial selection due to natural selection. Cuticular hydrocarbons in *Drosophila serrata* were artificially selected using two different treatments (circles and squares) with two replicates of each. The response to selection reached a plateau at generation 7 in the treatment denoted by circles, and all lines evolved back toward the means in the base population after the artificial selection was stopped ('relaxed'; dashed lines). This indicates that the artificial selection moved the populations away from their laboratory optima, and that the plateau was not caused by a depletion of additive genetic variance for the trait. Reprinted with permission from Hine, E., Mcguigan, K., Blows, M.W., 2011. Natural selection stops the evolution of male attractiveness. *Proceedings of the National Academy of Sciences of the United States of America* 108, 3659–3664.

selected traits that evolve back toward their original mean values when artificial selection is stopped (or 'relaxed'; [Figure 4](#)); this is good evidence that the trait means were moved away from their optimum in the lab environment ([Falconer and Mackay, 1996](#)). This same approach could be applied to study natural selection in the wild, by placing organisms that have been artificially selected for a putatively adaptive trait in the field and following their phenotypic evolution across multiple generations. This approach is most practical in sessile organisms like plants.

The approach above requires observing a response to natural selection over several generations. Another way to use the new phenotypic distributions created by artificial selection to understand natural selection is to combine divergent selection lines into a single experimental population that as a result has increased variance in the selected trait. This population can then be placed in the field and natural selection acting on the trait can be estimated as the slope of the regression of fitness on the trait ([Lande and Arnold, 1983](#)). It has long been recognized that studies of hypothesized adaptive traits are hampered by a lack of variance, because if a trait is adaptive, past directional or stabilizing selection will have removed the unfit variants from the population. Thus, the increased variance in the experimental population can increase the power of measurements of natural selection ([Schluter, 1988](#); [Haller and Hendry, 2014](#)). This approach was used to show that different pollinators selected on different floral traits in wild radish ([Sahli and Conner, 2011](#)).

Summary and Future Directions

As this article has stressed, artificial selection is the most powerful way to test for additive genetic variance for a phenotypic trait, which in turn means that it is an ideal way to determine if a trait can evolve in response to selection. Molecular genetic techniques by themselves will not be able to accomplish this goal until the loci responsible for most of the additive variance in the trait are known, and it is known how each locus contributes to additive variance. However, as discussed above, the combination of artificial selection with molecular genetic techniques can greatly enhance our understanding of the mechanisms underlying genetic variance thus trait evolution, so more studies of this type are clearly needed.

A major challenge for future work is the environmental dependence of additive genetic variance for traits, evidenced by direct measurements of additive variance (e.g., Conner *et al.*, 2003 and references therein) as well as the environmental dependence of QTL (see the discussion of Scarcelli and Kover, 2009 above; Ungerer *et al.*, 2003). Ideally, artificial selection could be conducted in the field (Postma *et al.*, 2007), but this will prove very difficult for most organisms. A more feasible approach is to test the fitness and trait values of populations created by artificial selection in the field (e.g., Sahli and Conner, 2011; Galloway and Burgess, 2012; Kristensen *et al.*, 2007), but this does not test for the presence of additive genetic variance in the field environment.

One exciting future direction for the use of artificial selection in evolutionary biology would be to follow both phenotypic and genetic changes during artificial selection, with the latter done through whole-genome sequencing. This is an extension and combination of some of the approaches described above, enabling an unprecedented understanding of the molecular genetic underpinnings of a phenotypic response to selection. The resulting lines could then be placed in the natural population that the selection lines were derived from and tracked phenotypically and genetically for several generations. The prediction is that both phenotypic means and allele frequencies should evolve back toward those found in the natural population before artificial selection began, but interesting surprises seem likely.

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See also: Evolution and Agriculture II. Evolutionary Applications to Breeding. Evolvability, Quantitative Genetics of. Genotype-by-Environment Interaction. Multivariate Quantitative Genetics. Natural Selection, Measuring. Quantitative Genetics in Natural Populations. Quantitative Genetic Variation. Quantitative Genetic Variation, Comparing Patterns of

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