SYNTHESIS

Evolutionary principles and their practical application

Andrew P. Hendry,[1] Michael T. Kinnison,[2] Mikko Heino,[3,4,20] Troy Day,[5] Thomas B. Smith,[6,7] Gary Fitt,[8] Carl T. Bergstrom,[9] John Oakeshott,[10] Peter S. Jørgensen,[11] Myron P. Zalucki,[12] George Gilchrist,[13] Simon Southerton,[14] Andrew Sih,[15] Sharon Strauss,[16] Robert F. Denison[17] and Scott P. Carroll[18,19]

1 Redpath Museum and Department of Biology, McGill University, Montreal, QC, Canada
2 School of Biology and Ecology, University of Maine, Orono, ME, USA
3 Department of Biology, University of Bergen, Bergen, Norway
4 International Institute for Applied Systems Analysis, Laxenburg, Austria
5 Departments of Mathematics and Statistics and Biology, Queen's University, Kingston, ON, Canada
6 Center for Tropical Research, Institute of the Environment, University of California, Los Angeles, CA, USA
7 Department of Ecology and Evolutionary Biology, University of California, Los Angeles, CA, USA
8 CSIRO Entomology and Cotton Catchment Communities CRC, Long Pocket Laboratories, Indooroopilly, Qld, Australia
9 Department of Biology, University of Washington, Seattle, WA, USA
10 CSIRO Entomology, Black Mountain, Canberra, ACT, Australia
11 Center for Macroecology, Evolution and Climate, Department of Biology, University of Copenhagen, Copenhagen, Denmark
12 School of Biological Sciences, The University of Queensland, Brisbane, Qld, Australia
13 Division of Environmental Biology, National Science Foundation, Arlington, VA, USA
14 CSIRO Plant Industry, Canberra, ACT, Australia
15 Department of Environmental Science and Policy, University of California, Davis, CA, USA
16 Section of Evolution and Ecology, University of California, Davis, CA, USA
17 Ecology Evolution and Behavior, University of Minnesota, Saint Paul, MN, USA
18 Institute for Contemporary Evolution, Davis, CA, USA
19 Department of Entomology, University of California, Davis, CA, USA
20 Institute of Marine Research, Bergen, Norway

Abstract

Evolutionary principles are now routinely incorporated into medicine and agriculture. Examples include the design of treatments that slow the evolution of resistance by weeds, pests, and pathogens, and the design of breeding programs that maximize crop yield or quality. Evolutionary principles are also increasingly incorporated into conservation biology, natural resource management, and environmental science. Examples include the protection of small and isolated populations from inbreeding depression, the identification of key traits involved in adaptation to climate change, the design of harvesting regimes that minimize unwanted life-history evolution, and the setting of conservation priorities based on populations, species, or communities that harbor the greatest evolutionary diversity and potential. The adoption of evolutionary principles has proceeded somewhat independently in these different fields, even though the underlying fundamental concepts are the same. We explore these fundamental concepts under four main themes: variation, selection, connectivity, and eco-evolutionary dynamics. Within each theme, we present several key evolutionary principles and illustrate their use in addressing applied problems. We hope that the resulting primer of evolutionary concepts and their practical utility helps to advance a unified multidisciplinary field of applied evolutionary biology.

Introduction

A basic goal of biology is to understand and predict the diversity and function of life, and to intervene when necessary to achieve desired outcomes. Evolution provides an essential framework for these endeavors because only in its light can we understand fundamental questions about our world and ourselves. Why do we get sick? What determines antibiotic and pesticide effectiveness? How much and in what ways can crops be improved? Why are life histories changing in harvested populations? Can natural populations adapt to environmental change? With this recognition, decision makers are increasingly called on to incorporate evolutionary thinking into environmental science, conservation biology, human health, agriculture, and natural resource exploitation (Futuyma 1995; Nesse and Williams 1998; Palumbi 2001; Ashley et al. 2003; Jørgensen et al. 2007; Smith and Bernatchez 2008; Dunlop et al. 2009; Gluckman et al. 2009a; Neve et al. 2009; Hendry et al. 2010; Omenn 2010).

The incorporation of evolutionary thinking has been largely independent in different areas of applied biology, and yet the relevant principles should be the same. It is important to explore and illustrate this common ground for several reasons. First, evolutionary principles routinely applied in one discipline might not be considered in other disciplines. Through exposure to how these principles play out in different disciplines, investigators might be inspired toward new applications. Second, particular evolutionary principles might not be equally important in all disciplines. The recognition of these differences can help us to understand how evolutionary interventions should be implemented differently in different contexts. Following from these two main reasons, and perhaps most important of all, we need to foster a unified multidisciplinary field of Applied Evolutionary Biology. Such a field would benefit from a primer of evolutionary biology couched in a common framework that can be considered across its various sub-fields. This primer might also facilitate understanding and acceptance by decision makers, who have traditionally been slow to incorporate evolutionary principles into the decision-making process (Smith and Bernatchez 2008; Hendry et al. 2010). Our hope is to provide some steps in this direction.

As an introductory example, one unifying concept that recurs throughout applied biology is the mismatch between the current phenotypes of organisms and the phenotypes that would be best suited for a given environment (Fig. 1). Examples include breeding times under climate warming (Both et al. 2006; Phillimore et al. 2010), antipredator behavior when exposed to exotic predators (Sih et al. 2010), human nutrition under current high-food conditions (Gluckman et al. 2009a), the traits of
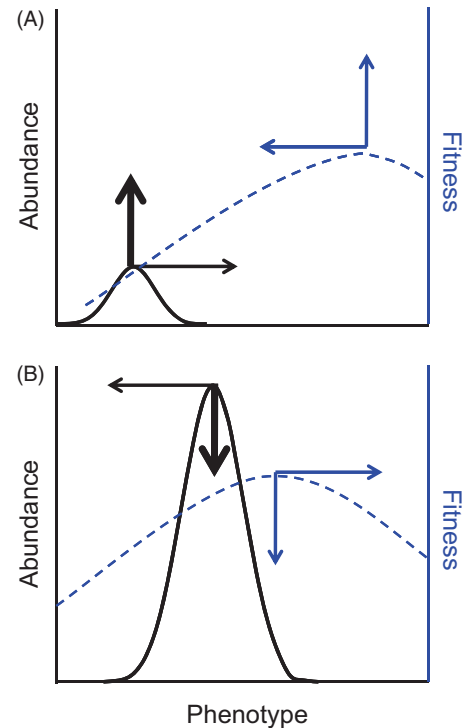

Figure 1 Applied biology often considers mismatches between current phenotypes and those that would be best suited for a given environment. The graph shows the fitness of individuals with a given phenotype (fitness function: blue dashed line) and the distribution of phenotypes in a population under those conditions (numbers of individuals: black curve). The degree of the current mismatch is the distance between the peak of the fitness function and the peak of the frequency distribution. In Panel A, the mismatch is high and so average fitness in the population is low and the population size is small. In Panel B, the mismatch is small and so the average fitness is high and the population size is large. In some cases, we might wish a large mismatch to be smaller (e.g., conservation biology). In Panel A, then, we might manipulate phenotypes or the environment to decrease the mismatch (horizontal arrows). We might also find a way to increase fitness for a given phenotype (thin vertical arrow). The expected outcome is an increase in population size (thick vertical arrow). In other cases, we might wish the mismatch to be larger (e.g., pathogens or pests). In Panel B, then, we might manipulate phenotypes or the environment to increase the mismatch (horizontal arrows). We might also find a way to decrease fitness for a given phenotype (thin vertical arrow). The expected outcome is a decrease in population size (thick vertical arrow).

insects exposed to new pesticides (Carrière and Tabashnik 2001; Beckie and Reboud 2009), and the traits of bacteria exposed to new antibiotics (Bergstrom and Feldgarden 2007). When the mismatches are slight, populations should be well adapted and robust. When the mismatches are large, populations should be poorly adapted and could decline. In applied biology, we sometimes want these mismatches to be small, such as for threatened

species facing environmental change. At other times, we want them to be large, such as when imposing treatments to reduce the impact of unwanted pests, pathogens, or invasive species. Or we may wish to maintain traits that reduce the fitness of individuals because these same traits are useful to us, as in the case of domesticated species (e.g., greater allocation to grain or seed set; Denison et al. 2003) or harvested wild species (e.g., big horns in game animals and large size in fish; Heino 1998; Harris et al. 2002). Evolutionary principles are fundamental to achieving these goals because they help us to understand current mismatches and potential responses, as well as how we might manipulate environments or organisms to achieve the desired mismatch.

Our goal in the present paper is to summarize some basic evolutionary principles and illustrate their practical utility across multiple areas of applied biology. These principles are organized under four main themes: variation, selection, connectivity, and eco-evolutionary dynamics. (A similar categorization appears in Lankau et al. 2011.) Within each theme, we present basic evolutionary principles and describe how they have been used in environmental science, conservation biology, human health, agriculture, and natural resource management. We do not have the space to treat all evolutionary principles, nor all pertinent applications and examples. Moreover, we will often have to provide generalizations that will have exceptions, which we try to highlight and explain. Many more examples are provided in the other papers of this special issue and we show where these ideas fit into the current framework.

Before proceeding, we need to clarify several terms and concepts. First, we follow the standard definition of evolution as changes in allele frequency within a population across generations. Any force causing such changes, including artificial selection, is an evolutionary force. Phenotypic change confirmed to have a genetic basis is also evolution, even if the underlying allele frequencies are not known. Second, when we discuss mismatches (as introduced above), we are usually referring to the average properties of a population, such as mean phenotypic trait values or allele frequencies and the resulting mean absolute fitness of the population (e.g., population size or rate of increase). Adaptation that improves the fitness of individuals within a population (i.e., relative fitness) is also important and might sometimes run counter to population mean fitness, as we will later describe. For individual relative fitness, no particular definition is universally accepted, but lifetime reproductive success is one of the better operational fitness surrogates (Clutton-Brock 1999; Benton and Grant 2000). Even this metric is hard to quantify, however, and so investigators often turn to major fitness components, such as survival or fecundity.

Third, when we say that a particular phenotypic change is *adaptive*, we mean that it improves fitness in a given environment (often reducing a mismatch), but this does not necessarily require genetic change – it instead could be environmentally induced plasticity (see the following paragraphs for details). In contrast, we reserve the term *adaptation* for adaptive *genetic* change. By complement, we use the term 'maladaptive' to refer to phenotypic changes that reduce fitness. Fourth, we will use the term 'contemporary evolution' when referring to evolution occurring on the time frame of less than a few hundred years (Hendry and Kinnison 1999).

Variation

Phenotypic variation determines how organisms interact with their environment and respond to the resulting selection pressures. This variation can come in the form of genetic differences, individual phenotypic plasticity (potential for an organism to produce different phenotypes in different environments), epigenetic changes (gene expression regulated by modification of DNA or histones), maternal effects (phenotype of the mother influences the phenotype of her offspring), and several other forms of nongenetic inheritance (Bonduriansky and Day 2009). Understanding the origins, nature, and maintenance of this variation provides an important foundation for predicting and interpreting responses to changing environmental conditions.

Phenotypes matter

Modern genetic tools have revolutionized the information available to biologists, but this has caused an increasing tendency to forget that phenotypes, rather than just genotypes, matter (Houle 2010). Phenotypes matter because they are the direct interface with the environment, which is critical in two major respects. First, selection acts directly on phenotypes, with genetic change potentially occurring as an indirect consequence. Second, phenotypes have ecological effects, for example, on population dynamics, on community structure, and on ecosystem function (see section on Eco-evolutionary dynamics). An understanding of phenotypes therefore should precede an understanding of genotypes.

Additional compelling reasons exist to study phenotypes. First, adaptation to a given set of environmental conditions will usually involve many genes, as well as interactions among them (more details are given in the following paragraphs), and so examining only a few genes will not be sufficient for understanding adaptive potential or evolutionary responses. Second, phenotypic variation is structured not only by genes, but also by nongenetic
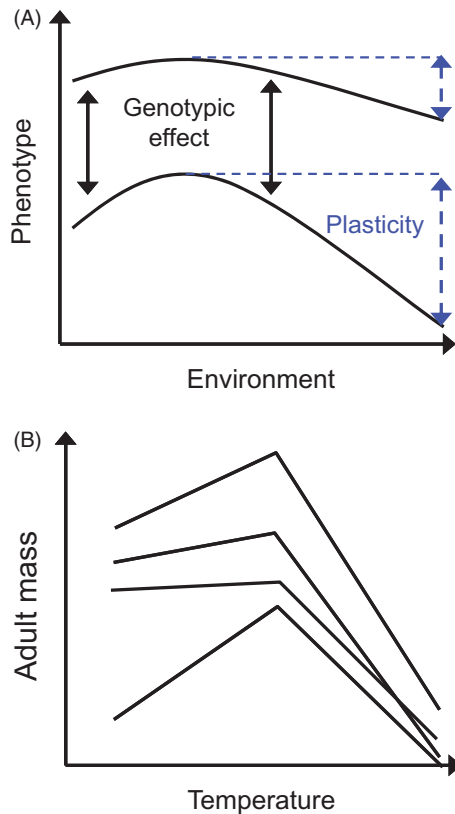
Figure 2 Phenotypic variation can be described by reaction norms. (A) Reaction norms depict the phenotypes a single genotype (or individual or population) expressed in different environments. Differences between reaction norms represent genetic differences. (B) Examples of reaction norms: shown are the adult male body sizes from different populations of male speckled wood butterflies (*Pararge aegeria*) when their larvae are raised at different temperatures (redrawn from Sibly et al. 1997). Temperature has plastic effects on body size in all populations, but the degree of its plasticity differs among populations. Genetic differences among the populations become more evident with decreasing temperature.

effects. As a result, populations that are phenotypically different for a given trait might be genetically similar with respect to that trait, whereas groups that are phenotypically similar for a given trait might be genetically different with respect to that trait (Conover and Schultz 1995). In addition, adaptive responses to changing conditions can be genetic ('adaptation' in the strict sense), nongenetic (e.g., plasticity), or some combination of the two. For instance, the effect of a given genotype can differ between environments, yielding a genotype-by-environment interaction. A recent example at the genomic level is the demonstration that a particular allele can have opposite phenotypic effects in different *Eucalyptus nitens* populations (Southerton et al. 2010). Phenotypic traits should thus be considered as 'reaction norms,' which depict the phenotypes expressed by a given genotype (or population

or species) across a range of different environmental conditions (Stearns 1989; Gluckman et al. 2009b; Fig. 2). Importantly, these reaction norms can evolve in response to selection (Stearns and Koella 1986; Olsen et al. 2004; Lande 2009; Crispo et al. 2010).

Different phenotypic traits will differ in their relevance to both fitness and ecological processes. An important task is therefore to identify 'key' traits or trait complexes – in broad analogy with the search for limiting factors in ecology (Sih and Gleeson 1995). A standard approach is to measure a set of phenotypic traits (e.g., body size and shape) and to relate variation in these traits to (i) some measure of fitness, such as survival, fecundity, or lifetime reproductive success (Lande and Arnold 1983; Brodie et al. 1995); and (ii) some ecological response (e.g., population growth rate, community richness, and nutrient cycling). These methods can identify traits under strong selection and traits that might have large ecological effects.

Notwithstanding the value of the above trait-based approach, 'phenotype' must sometimes be considered as an integrated unit. For example, the ability of a population to persist in the face of environmental change is ultimately determined by the complex multivariate interaction of all traits that contribute to population growth. One way to assess this overall adaptation (i.e., population mean fitness) is to transfer groups of individuals between environments and then measure differences in survival or reproductive success (Kawecki and Ebert 2004; Hereford 2009). Similar methods can be used to estimate how *quickly* individual or population mean fitness can improve through adaptive change following environmental disturbances (e.g., Kinnison et al. 2008; Gordon et al. 2009).

Nongenetic changes can be very important – especially on short time scales

Organisms poorly suited for their local environment can respond adaptively by altering their location to better suit their phenotype (e.g., habitat choice) or by altering their phenotype to better suit their location (e.g., plasticity or evolution). For the former, individuals often avoid newly disturbed areas (e.g., Frid and Dill 2002) and can select areas for which their phenotypes are better suited (review: Edelaar et al. 2008). In many cases, however, such movement is not feasible or sufficient, and so populations must respond *in situ*. In this latter case, the quickest route to adaptive change will often be individual phenotypic plasticity, particularly behavioral plasticity, or maternal effects (Stearns 1989; Price et al. 2003; West-Eberhard 2003; Ghalambor et al. 2007; Räsänen and Kruuk 2007; Sih et al. 2011). Congruent with this
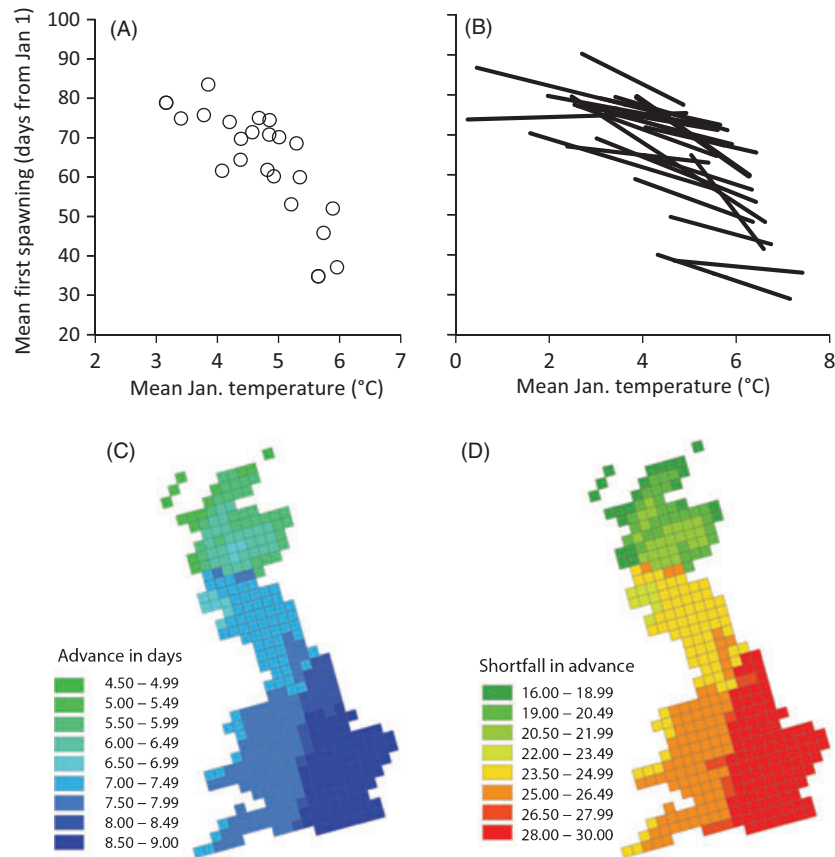
Figure 3 An example of how genetic differences and plasticity are jointly considered when evaluating potential responses to climate change. Panel A shows the mean breeding times of different UK populations of the common frog (*Rana temporaria*) in relation to the mean temperature experienced by those populations. Panel B shows how the mean breeding time within each of those populations varies among years with the mean temperature in those years. The lines thus represent adaptive phenotypic plasticity, and differences between the lines adaptive genetic differences among populations. Panel C shows the breeding time changes that each population is expected to undergo as a result of plasticity in response to projected warming between 2050 and 2070. Panel D shows the difference between these adaptive plastic responses and the changes in breeding time that would be necessary to keep pace with climate change if the trends on Panel A are fully adaptive. These differences thus represent the evolutionary change that will be necessary to maintain full adaptation. Adapted from Phillimore et al. (2010) with data provided by A. Phillimore.

suggestion, a meta-analysis of phenotypic change in natural populations experiencing environmental change concluded that plasticity was probably very important (Hendry et al. 2008). As a specific example, populations of many species experiencing climate warming now reproduce at earlier dates (Parmesan and Yohe 2003), and a large part of this change reflects individuals responding plastically to increased temperature (Gienapp et al. 2008). This does not mean that genetic change does not contribute to these phenological shifts (Bradshaw and Holzapfel 2008) – merely that plasticity certainly does.

Phenotypic plasticity is not, however, a panacea – because it is subject to a number of limits and costs (DeWitt 1998). Hence, most phenotypic responses to environmental change will ultimately involve both plastic and genetic contributions (Dieckmann and Heino 2007;

Visser 2008; Phillimore et al. 2010; Sih et al. 2011; Fig. 3). Variation in humans and domesticated organisms provides nice examples. For instance, lightly pigmented human skin becomes darker under greater exposure to sun, and hemoglobin levels rise at high elevations. At the same time, adaptive genetic differences are present in these same traits: human populations from areas with more sun exposure have genetically darker skin (Jablonski 2004) and human populations living at high elevation have evolved several mechanisms to increase oxygen uptake and transport (Beall 2006). From a reaction-norm perspective, phenotypic variation in these traits reflects both genetic and plastic effects, along with possible genetic variation in this plasticity. These ideas are considered daily in agriculture, where production or quality are maximized by simultaneously seeking the best genetic

strains, creating the best environmental conditions (fertilizer, water, pesticides, and herbicides), and finding the best match between genetic strains and environmental conditions.

Overall, then, applied evolution should evaluate phenotypes and fitness in the context of both genetic and plastic effects, ideally through their integration into reaction norms. The *evolution* of these reaction norms might be especially important under environmental change, as suggested by recent theory (Lande 2009) and meta-analyses (Crispo et al. 2010).

Individual genes rarely capture overall genetic adaptation

Some phenotypic traits, most famously Gregor Mendel's wrinkled versus smooth peas, have a single-gene foundation. Other examples include some human diseases (Roach et al. 2010), the evolution of insecticide resistance by some mosquitoes (Raymond et al. 2001), and many instances of artificial selection by humans for particular traits. In agriculture, wheat yield nearly doubled between 1950 and 1965 (Ortiz-Monasterio et al. 1997) largely because of the introduction of a dwarfing gene (*Rht*) that increased yield by 57% (Miralles and Slafer 1995). In dog domestication, traits that identify particular breeds seem to have a very simple genetic basis (Boyko et al. 2010). Overall, however, most traits are controlled by many genes and their interactions. This is strikingly seen in the so-called 'missing heritability paradox,' where genome-wide association studies (GWAS) can explain very little of the heritable variation in many traits (Manolio et al. 2009; Crespi 2011). For instance, 'highly significant and well-replicated single nucleotide polymorphisms (SNPs) identified to date explain only ∼5% of the phenotypic variance for height … common SNPs in total explain another ∼40% of phenotypic variance. Hence, 88% (40/45) of the variation caused by SNPs has been undetected in published GWASs, because the effects of the SNPs are too small to be statistically significant' (Yang et al. 2010).

Aside from specific traits, we are often concerned with overall adaptation to a given environment, which will be determined by multiple traits and therefore even more genes. To exemplify this point, we turn to the influential work on adaptation to fresh water in threespine stickleback fish (*Gasterosteus aculeatus*). Some large-effect genes have been discovered: *EDA* explains 78% of the variation in the number of bony plates (Colosimo et al. 2004), *PitX1* explains 65% of the variation in pelvic spine length (Shapiro et al. 2004), and *Kit ligand* explains 56% of the variation in gill color (Miller et al. 2007). Overall adaptation to fresh water in stickleback, however, involves dozens of phenotypic traits, and so the above large-effect genes for specific traits might contribute relatively little to

overall adaptation. Indeed, Hohenlohe et al. (2010) used SNPs to find many chromosomal regions in stickleback that contribute to adaptation to fresh water – and even their assay remained biased toward the detection of large-effect genes found in multiple watersheds. In short, it is increasingly apparent that adaptation to a given environment will often involve many genes of small to modest effect.

The limitations of single-gene approaches are also evident in health and agriculture. For instance, the finding of specific genes that influence certain human ailments (e.g., Roach et al. 2010) does not change the fact that such genes often explain relatively little of the variation in that ailment (Weiss 2008; Manolio et al. 2009; Crespi 2011). Likewise, the search for genomic regions of large effect in plants of commercial value (e.g., forest trees) has often been disappointing. Thumma et al. (2010) did not find any quantitative trait loci (QTL) in *E. nitens* that explained more than 16% of the variation in any wood trait – and most QTL explained much less. Low variance explained by individual QTL appears to be a common result across many tree traits and species (Butcher and Southerton 2007). Although individual QTL can be very important to some traits in some species, and thereby of great use in selective breeding, most of the variation in most traits of most species will be influenced by multiple genes (e.g., Laurie et al. 2004; Manolio et al. 2009; Yang et al. 2010).

Although current adaptation is thus usually the product of many genes, adaptation to new conditions might sometimes initially proceed through only a subset of those genes – particularly those of largest effect (Orr 1998; Schoustra et al. 2009). So the search for large-effect genes or QTL can indeed contribute to our understanding of how adaptation might proceed in changed environments – as long as we remember that those genes likely explain only a small part of overall adaptation in the long run. The future would ideally see an integration of quantitative genetic approaches, QTL approaches, and functional genomics.

Standing genetic variation will be the primary fuel for contemporary evolution

Adaptation to changing environments might proceed through standing genetic variation or new mutations. In general, the former is probably more important, at least on short time scales and for organisms that do not have very short generation lengths (Aitken et al. 2008; Barrett and Schluter 2008; Orr and Unckless 2008). Humans provide an exemplar; some alleles that provide advantages under recent conditions clearly arose earlier – probably because they were favored by some other selective force in the past. One putative example is the allele that confers
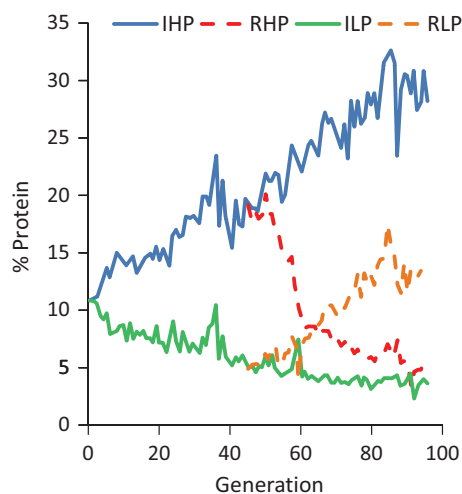
Figure 4 Changes in protein content as a result of artificial selection in the Illinois maize (*Zea mays*) selection experiment. Initially, one line was selected for high protein (solid line trending up: IHP) and another for low protein (solid line trending down: ILP). Half way through the time series, new lines were established taking the high protein line and selecting for low protein (dashed line trending down: RHP) or taking the low protein line and selecting for high protein (dashed line trending up: RLP). Adapted from Moose et al. (2004).

lactose tolerance in adult Europeans (Myles et al. 2005). Another is the 32-bp deletion allele (CCR5Δ32) of the chemokine receptor gene that confers resistance to HIV (Galvani and Novembre 2005).

In agriculture, evolution from standing genetic variation is particularly dramatic. After 100 years of annual selection in the Illinois maize experiment (Fig. 4) '… responses of both protein and oil are >20 standard deviations from the original population mean in the positive direction and four standard deviations in the negative direction' (Moose et al. 2004). The reason why this dramatic change could be driven by standing genetic variation is that these traits were influenced by many alleles and many loci, such that selection on each allele was relatively weak and recombination allowed for new variation (Moose et al. 2004). Of course, the favorable conditions in laboratories or agriculture may free genes formerly constrained by stabilizing selection to evolve in novel directions. Thus, responses to artificial selection for a specific end (e.g., high protein) might not be representative of evolution in general. And yet, adaptation from standing genetic variation is also prevalent in weeds or pests adapting to herbicides or pesticides. For instance, brown rats (*Rattus norvegicus*) have evolved resistance to warfarin at least partly through pre-existing variants of the gene *VKORC1* (Pelz et al. 2005), and the same is true for blowflies (*Lucilia cuprina*) evolving resistance to malathion (Hartley et al. 2006).

Even outside of the human sphere of influence, most recent adaptation is probably driven by standing genetic variation (Barrett and Schluter 2008). In stickleback, for example, the allele at *EDA* that is favored in fresh water is of the same lineage in many independent watersheds, implying that this allele is present in ancestral marine populations (Colosimo et al. 2005). The retention of this allele in the ocean, where it is not selectively favored, is probably possible because it is recessive and therefore partially shielded from selection (see below for more about recessive alleles). Moreover, recent population genomic analyses suggest that standing genetic variation in many gene regions is important to freshwater adaptation by stickleback (Hohenlohe et al. 2010).

Standing genetic variation thus provides the best indication of evolutionary potential and 'resilience' of natural populations facing environmental change (Sgrò et al. 2011). A common proxy for this potential is the proportion of the total genetic variation that has an additive genetic basis (i.e., heritability) (Visscher et al. 2008). Heritability has now been assayed for many traits in many populations of many species, and nearly all estimates indicate substantial evolutionary potential (Mousseau and Roff 1987; Houle 1992), although exceptions are known (Kellermann et al. 2009). Heritability estimates depend on the environment in which they are assayed (Hoffmann and Merilä 1999), and so will be most relevant when they are for the specific population and environmental conditions under consideration (McGuigan and Sgrò 2009). This is much easier said than done and so a quick-and-dirty substitute for evolutionary potential has been sought. Neutral genetic variation was hoped to fulfill this role, but it has proven to be only weakly associated with quantitative genetic variation (Reed and Frankham 2001). More recently, genome scans have been used to search for chromosome regions under selection (e.g., Hohenlohe et al. 2010). Perhaps variation in such regions might be used to infer adaptive potential – but whether they accurately reflect variation at the phenotypic level remains uncertain (Latta 1998; Manolio et al. 2009; Yang et al. 2010).

New mutations provide fuel for longer-term evolution

Standing genetic variation is sometimes absent or can be depleted in the direction of selection. Continuing adaptive evolution will then require new mutations – or intragenic recombination in bacteria. The supply rate of these new mutations is an important determinant of 'sustainable rates of evolution' in theoretical models (e.g., Lynch et al. 1995). The contribution of new mutations to contemporary adaptation is expected to be greatest for large populations with short generation times. For example,

new mutations are so important in HIV evolution that very large genetic changes are evident through time for virus populations within individual patients (Shankarappa et al. 1999). Also, laboratory studies on adaptation in micro-organisms often start with single clones and reveal dramatic evolution by new mutations (review: Bell 2008). A particularly relevant example is the demonstration of 'evolutionary rescue' through new adaptive mutations in laboratory yeast populations exposed to stressful environments (Bell and Gonzalez 2009).

Even for species with longer generation times than micro-organisms, new mutations sometimes contribute to adaptation. For example, resistance to pesticides has sometimes evolved through new mutations, such as diazinon resistance in blowflies (Hartley et al. 2006). In stickleback, alleles at *PitX1* that enable adaptive pelvic reduction in fresh water appear to have arisen independently in different watersheds following the last glaciation (Chan et al. 2010). In humans, several new lactose tolerant alleles apparently arose de novo and then spread in Sub-Saharan Africa following the advent of pastoralism (Myles et al. 2005). But despite these and other examples, mutational supply rates will be too low to provide major contributions to the contemporary evolution of macro-organisms facing environmental change.

Bacteria and archaea blur the lines between standing genetic variation and new mutations. First, they often undergo lateral (horizontal) gene transfer, which effectively gives individual 'species' access to a near limitless supply of variants (Lerat et al. 2005; Dagan and Martin 2007; Russell et al. 2011). These variants are often a part of standing genetic variation in bacteria/archaea as a whole, but their incorporation into a particular species is equivalent to a new mutation. Second, different genes collectively required for a new function are often progressively condensed into operons through a series of transposon-mediated transposition events, and so they end up behaving essentially as a single, coordinated genetic unit (Lal et al. 2010). In this case, both standing genetic variation and new mutations (transpositions) are used to assemble new biochemical pathways.

Small and isolated populations can have genetic problems

In addition to their demographic vulnerability, small and isolated populations can have genetic problems. One problem is that genetic variation can be lost owing to drift, low mutational inputs, and low immigration. These effects might be especially strong in the case of founder events or bottlenecks, i.e., populations founded or perpetuated by only a few individuals will have only a small portion of the initial standing genetic variation. The

result might be a limited potential to respond to future environmental changes. So far, however, the empirical evidence suggests that evolutionary potential is severely compromised in only the very smallest populations (Willi et al. 2006). And this can also be seen in the Illinois maize experiment, where dramatic evolution continued despite effective population sizes of only 4–12 individuals per line (Moose et al. 2004). Part of the reason why genetic variation might only rarely be limiting in small populations is that bottlenecks can alter the genetic background of interacting alleles (epistatic effects) and thus potentially increase genetic variation (e.g., Cheverud and Routman 1996; Carroll et al. 2003). And, even when bottleneck effects are initially strong, they can be transitory owing to ongoing immigration (Keller et al. 2001) or selection against individuals with low genetic variation (Kaeuffer et al. 2007).

A related problem in small, isolated, and bottlenecked populations of eukaryotes is inbreeding; i.e., mating with close relatives (Keller and Waller 2002). As examples, inbreeding appears to increase extinction risk in local populations of butterflies (Saccheri et al. 1998), and appears to cause low fecundity or fertility in Florida panthers (*Puma concolor coryi*; Pimm et al. 2006) and Greater Prairie Chickens (*Tympanuchus cupido pinnatus*; Westemeier et al. 1998). Similar effects can be seen in humans. As just one example, Finland was colonized by relatively few people, who then spread rapidly within the region, forming small and isolated groups. The result has been a high frequency of more than 30 diseases that are typically masked in larger populations (Peltonen et al. 1999). And yet, inbreeding will not always be associated with major problems, with agriculture providing a case in point. Crops and domesticated animals are often very inbred (because humans have attempted to fix desirable genetic variants) and yet can have very large population sizes and high reproductive output. This is possible because (i) humans provide beneficial conditions and aid reproduction, (ii) frequent polyploidy buffers crops from inbreeding problems, and (iii) deleterious mutations were likely purged through past bottlenecks and selection. This purging is also seen in natural populations (Crnokrak and Barrett 2002). Despite these exceptions, the general conclusion is that inbreeding reduces population mean fitness.

Under the right conditions, genetic bottlenecks could be used to our advantage. As just one example, bottlenecked viruses show considerable fitness declines owing to the accumulation of deleterious mutations through 'Muller's ratchet' (Elena et al. 2000). That is, high mutation rates and bottlenecks in small populations lead to the irreversible accumulation of genotypes with more mutations (Muller 1964). This effect varies greatly among

different viruses but fitness decreases can be quite large, such as in experimentally bottlenecked HIV-1 (Yuste et al. 1999). This example serves to remind us that demographic and genetic considerations align quite nicely when it comes to population size. That is, reductions in the population size of bothersome organisms will not only reduce their immediate impact but also could limit their evolutionary potential and therefore their future impacts. And the reverse applies for beneficial organisms. Of course, changes in population density can also change selective pressures in ways that cause unexpected evolutionary change (Lankau and Strauss 2011).

Evolutionary history influences current traits and future responses

The evolutionary history of a lineage influences the phenotypes and genotypes currently present, which then influences the direction and speed of contemporary evolution. Knowledge of evolutionary history thus improves our understanding of the current state of affairs and helps to craft predictions about the future (Denison 2011; Crespi 2011; Gluckman et al. 2011; Thrall et al. 2011). As an example, we can understand our craving for high-energy foods that are rich in fat and sugar as a result of past selection to consume such foods as a buffer against times of food scarcity. Now that these foods are available in abundance, overindulgence has led to many health problems, including diabetes, heart disease, and obesity (Schlaepfer et al. 2002; Gluckman et al. 2009a). Similarly, we can understand why some human traits are prevalent in some geographical areas rather than others, such as lactose tolerance in areas where pastoralism led to milk consumption past childhood (Tishkoff et al. 2007). Evolutionary history can also help us to understand the seemingly greater ease with which generalist insects evolve resistance to pesticides (Krieger et al. 1971) and why relatedness to native species can influence the success of invasive species (Ricciardi and Ward 2006; Strauss et al. 2006).

Evolutionary history also helps us to understand past extinctions and future extinction risk. In isolated habitats, such as islands, local fauna often evolved without serious predators and so lacked appropriate responses when predators later arrived (Cox and Lima 2006; Sih et al. 2010). This evolutionary naiveté led to many extinctions, including flightless rails in the South Pacific after the arrival of Polynesians (Steadman 1995) and bird species on Guam after the introduction of brown treesnakes (*Boiga irregularis*) (Fritts and Rodda 1998). In plants, extinction risk in the face of environmental change might be exacerbated by reliance on specialized pollinators (Pauw 2007) or the use of photoperiod rather than temperature as a cue for flowering

time (Willis et al. 2008). It also seems likely that species evolving low dispersal will be more vulnerable to extinction in the face of local disturbances and climate change (Kotiaho et al. 2005). Conversely, species evolved for high dispersal can be in trouble if the matrix between good patches becomes inhospitable or dangerous (Fahrig 2007).

Knowledge of evolutionary history is increasingly used to set conservation priorities (Lankau et al. 2011; Thomassen et al. 2011). At the organismal level, species or populations that have a longer history of evolutionary independence are more likely to harbor unique genetic variation, including novel adaptive traits (Waples 1991; Smith et al. 1993; Moritz 1994). At the regional level, communities with greater phylogenetic diversity can harbor greater genetic diversity, including novel adaptive traits with important potential services for humanity (Forest et al. 2007; Faith et al. 2010). But current evolutionary processes should also be considered. For instance, Thomassen et al. (2011) show that areas harboring the greatest intra-specific genetic and morphological diversity, presumably reflecting contemporary evolution, are not always those that have the highest inter-specific diversity.

Some evolution is not possible

Although evolution can accomplish remarkable things, it is not omnipotent. Severe limits on adaptation might occur in several ways: (i) genetic variation might be lacking in the direction of selection (Kellermann et al. 2009), (ii) some trait combinations might not be possible given biophysical constraints, and (iii) transitional states between the current phenotype and better phenotypes might have low fitness (i.e., fitness valleys). The human appendix might typify this last situation because, although its absence might be best, further size reductions would reduce blood flow, making infections more life-threatening (Nesse and Williams 1998).

Evolutionary limits have frequently been invoked in agricultural contexts. For instance, rusts can attack many cereals but not rice. Perhaps rice has resistance genes that simply cannot be circumvented by rusts. Evolutionary limits also hamper attempts to improve crop yield, especially for traits, like drought tolerance, that already have been long subject to improvement by natural and artificial selection (Denison et al. 2003). In the case of global warming, temperature tolerance might represent an evolutionary limit. For aquatic organisms, increasing temperature increases oxygen demand but also decreases oxygen supply, until aerobic metabolism eventually becomes impossible. Pörtner and Knust (2007) have argued that the resulting constraint explains inter-annual variation in the population

size of eelpout (*Zoarces viviparus*) in the North and Baltic Seas. An outstanding question is the extent to which this constraint is a true evolutionary limit, given that other fishes are certainly very successful in much warmer waters. At the extreme, Lake Migadi Tilapia (*Oreochromis alcalicus grahami*) live in 42°C water, in part because they can breathe air (Franklin et al. 1995). So temperature tolerance can clearly evolve – but perhaps not always, or not quickly enough. These issues are clearly important for modeling changes in the geographic distribution of organisms under climate change (Skelly et al. 2007), but this is only rarely carried out (Urban et al. 2007).

Evolutionary constraints can be used to our advantage in slowing the unwanted evolution of weeds, pests, and pathogens. For example, pheromone traps used to attract and kill pest insects might long retain their effectiveness because reduced responses to these pheromones could reduce mating success (Witzgall et al. 2010). Evolutionary constraints are also a key premise of biological control programs. The choice of agents for release in these programs generally emphasizes very strong specificity for a chosen target species, and hence a hoped for inability to evolve to nontarget species. Although biocontrol agents have certainly impacted nontarget species (Louda et al. 1997; Henneman and Memmott 2001), it is not clear how often contemporary evolution has been the reason. For instance, van Klinken and Edwards (2002) reviewed 352 intentionally released exotic biocontrol agents of weeds and concluded that none had evolved a novel propensity to use new hosts. However, rare variants might have been missed and native insects at least have evolved an increased ability to use introduced plants (Carroll et al. 2005; Carroll 2011).

The difficulty in correctly identifying evolutionary limits and constraints is well illustrated in medicine. Ribosomally synthesized antimicrobial peptides (RAMPs) are a natural part of the human immune system and act on negatively charged phospholipid head groups on the outer surface of bacterial membranes. Given that this is a fundamental property of prokaryotic but not eukaryotic cells, it was argued that bacteria would have difficulty evolving resistance to RAMPs even if they were synthesized and used as topical antibiotics (Zasloff 2002). However, Perron et al. (2005) showed that resistance to synthesized RAMPs evolved rapidly in many lines of two bacteria species (Fig. 5). It is not clear how the bacteria solved the supposed problem, but their success in doing so raised alarms that widespread application of synthesized RAMPs could lead to bacteria also evolving around an important component of the human immune system (Bell and Gouyon 2003). Incorrectly identified evolutionary limits could also be very dangerous in the case of biocontrol agents evolving to use nontarget species.
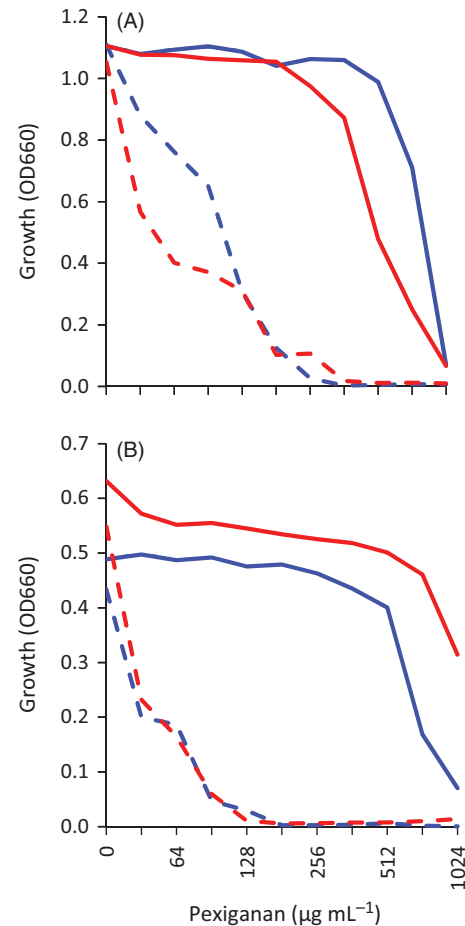

Figure 5 The evolution of resistance to the cationic antimicrobial peptide pexiganan by *Escherichia coli* (Panel A) and *Pseudomonas fluorescens* (Panel B). Shown is growth rate (*y*-axis) in relation to the test concentration of pexiganan at the end of the selection experiment. The different colored lines in each panel represent different strains (each the average of multiple lines) selected for resistance (solid lines) and the same strains not selected for resistance (dashed lines). Adapted from Perron et al. (2005) with data provided by G. Perron.

One way that organisms might circumvent some evolutionary limits is through the big leaps that can attend hybridization or polyploid events. Another way is to acquire new genes from a divergent source, such as lateral gene transfer in prokaryotes. And humans get into the act through the introduction of transgenes (genes taken from one species and inserted into another) that enable evolutionary jumps that by chance or design land organisms on new adaptive peaks. The insertion of insect-resistant genes from the bacterium *Bacillus thuringiensis* (*Bt*) into cotton and corn has certainly revolutionized their agriculture (Tabashnik et al. 2008). However, pests do at least sometimes evolve resistance even to genetically engineered plants (Hilder and Boulter 1999; Tabashnik et al. 2008). In short, the consideration of evolutionary limits and

how they might or might not be circumvented is a major area of evolutionary applications.

Traits are correlated and so do not evolve independently

Different phenotypic traits are often correlated with one another. This can occur if the same genes influence multiple traits, if genes for different traits are closely linked on chromosomes, or if environmental effects (e.g., temperature or diet) simultaneously influence multiple traits. If traits are phenotypically correlated, direct selection on one will lead to indirect selection on the others (Lande and Arnold 1983). If traits are genetically correlated, the evolution of one will lead to the evolution of others (Hansen and Houle 2008). The upshot is that trait correlations will influence evolutionary potential, sometimes called 'evolvability' (Hansen and Houle 2008). In the 'evo-devo' literature, the ties between trait correlations and evolvability are often discussed in the context of 'modularity,' where correlations are strong between traits within a given module but weak between traits in different modules (Wagner and Altenberg 1996; Hansen 2003).

In applied biology, trait correlations have been considered in several contexts. One context occurs when correlations between traits act in opposition to the direction of selection (Hellmann and Pineda-Krch 2007). For example, climate change is expected to favor more and thicker leaves in the annual legume *Chamaecrista fasciculata*, but these two traits are negatively genetically correlated, which will slow their joint adaptive evolution (Etterson and Shaw 2001). Another example is when behaviors expressed in different contexts (e.g., mating versus foraging) are tied together into behavioral 'types,' 'personalities,' or 'syndromes' (e.g., bold versus shy) (Sih et al. 2004). Even if selection favors different behaviors in different contexts (e.g., bold while mating but shy while foraging), the shared systems that determine behavior may limit their independent expression. Another context is trade-offs, where beneficial changes in one trait (e.g., increasing egg size) necessarily cause detrimental changes in another trait (e.g., decreasing egg number). In wild salmon, the balance between egg size and number evolves under conflicting selection pressures for high fecundity versus large juvenile size (Einum and Fleming 2000). In hatcheries, selection still favors high fecundity but no longer strongly favors large eggs. The result can be the evolution of higher fecundity and smaller egg size, which might have maladaptive effects when hatchery fish interbreed with wild populations (Heath et al. 2003). In agriculture, Denison et al. (2003) have emphasized that trade-offs, including constraints from conservation of matter, limit our ability to improve crop genetics through

traditional breeding or biotechnology. For example, molecular biologists suggested that we might increase the photosynthetic efficiency of crops by replacing a key photosynthetic enzyme with its equivalent from red algae (Mann 1999), but it turns out that more efficient versions of this enzyme have slower reaction rates (Tcherkez et al. 2006). And, of course, trade-offs are also an important part of the human condition. A classic example is pelvic width: bipedal locomotion generally favors a narrow pelvis, but large neonate head size generally favors a wide pelvis. The compromise is a pelvis that is narrower than optimal for child birth but wider than optimal for locomotion (Hogervorst et al. 2009).

Trade-offs can be used in a proactive way to manipulate evolutionary trajectories, such as in the design of drug treatments that slow resistance evolution (Levin et al. 2000; Normark and Normark 2002). For example, the periodic cessation of a drug treatment can lead to a decline in the prevalence of resistance when the resistance genes are costly in the absence of the treatment. Unfortunately, this trade-off can be circumvented by the evolution of compensatory mutations that mask resistance costs (Davies et al. 1996; Levin et al. 2000; Normark and Normark 2002). The consideration of trade-offs is a valuable part of applied evolutionary biology but evolutionarily unbreakable trade-offs, if they exist, can be difficult to confirm.

Selection

Natural selection is the engine that converts variation into evolutionary change. Selection occurs when particular phenotypes/genotypes have higher fitness than others. In well-adapted populations, selection may be relatively weak because most individuals will be near a local fitness peak. As environments change, however, maladaptation is expected to increase and the result can be strong selection and contemporary evolution.

Selection and adaptation can occur at multiple levels

Evolution by natural selection can occur at any level of biological organization, so long as the requisite ingredients are in place: heritable variation among entities that differ in fitness (Keller 1999). These entities can be species, populations (groups), families, individuals, genes, or alleles. Sometimes selection acts in different directions at different levels, for example, traits that improve individual fitness can arise at the expense of overall population fitness. The tension between levels of selection can play out in a number of ways depending on selection and variation present at each level. These factors often combine in ways that make individual-level selection the most

influential for evolution, but this does not mean that the other levels should be ignored.

The relevance of higher-level selection is particularly clear in agriculture and natural resource management. In these contexts, humans often strive to maximize yield, but this can run counter to selection for increased individual competitiveness (Donald 1968; Denison et al. 2003). For instance, competition among individual plants favors larger root systems and larger leaves, but productivity at the population level is maximized at intermediate root and leaf sizes (Schieving and Poorter 1999; Zhang et al. 1999). Cognizance of these trade-offs can improve the design of breeding programs and cultivation methods for evolutionary improvements in yield (Donald 1968; Harper 1977; Denison et al. 2003; Denison 2011). In fisheries, the frequent evolution of smaller size or earlier maturation under intensive harvesting leads to the evolution of life histories that can decrease yield (Conover and Munch 2002; Olsen et al. 2004). The challenge is to design harvest programs that slow, avert, or reverse this yield-impairing evolution (Law and Grey 1989).

In the context of virulence (pathogen-induced host mortality), natural selection at the between-host level (different infected individuals) can favor reduced virulence because, all else being equal, killing the host often reduces transmission to new hosts. But if infections are genetically diverse (infection of an individual host by multiple strains), competitive interactions among strains within a host can also be evolutionarily important (Frank 1996; Brown et al. 2002). In some cases, the evolution of increased within-host competitiveness can lead to higher virulence, as in some malaria parasites (de Roode et al. 2005). This trade-off between competitiveness and virulence can generate antagonistic selection at the between-host versus within-host levels. In principle, this could result in a level of virulence that is higher (or lower) than expected solely from between (or within)-host competition (Brown et al. 2002). In the case of malaria, it has been argued that the host's immune response, which also damages host tissue (immunopathology), disrupts the virulence-transmission trade-off, and so medical interventions to deal with immunopathology can influence virulence evolution (Long et al. 2011). Bringing gene-level selection into the picture, it has been argued that meiotic drive, which subverts meiosis in favor of a particular gamete, can be used to artificially increase the frequency of anti-pathogen transgenes in mosquito disease vectors (Cha et al. 2006; Huang et al. 2007).

Theory suggests that individual-level selection can be so detrimental to population growth that it can lead to extinction (Webb 2003; Rankin and López-Sepulcre 2005). The idea here is that benefits to individuals can spread even if they are costly to population size and therefore persistence. Empirical confirmation of this 'evolutionary suicide' or 'Darwinian extinction' is currently lacking, but it is certainly true that intra-specific competition, including resource monopolization (e.g., territoriality), can reduce population size to the point that extinction risk increases. Management practices that enhance phenotypic diversity (e.g., polymorphisms that reduce intra-specific competition) may increase the carrying capacity of a habitat and thus the population densities it can sustain (Carroll and Watters 2008). In short, the consideration of multi-level selection can help us to better attain desired population-level traits.

Selection overwhelms drift

Populations frequently differ from each other in a number of phenotypic traits and genes. If these differences are the result of genetic drift, they indicate restricted gene flow but little else. If the differences are adaptive, however, they are more likely to (i) trigger protection in conservation efforts (Waples 1991; Smith et al. 1993; Moritz 1994), (ii) influence productivity in agricultural settings (Denison et al. 2003), and (iii) suggest ways to combat pathogens or invasive species. At one level are inferences about whether populations are adaptively divergent in general (i.e., local adaptation). At another level are inferences about whether and why particular phenotypic differences or changes are adaptive.

Many, perhaps most, overt phenotypic differences among populations are likely adaptive. For example, human populations clearly show adaptive differences in skin color, body size and shape, oxygen use, lactose tolerance, disease resistance, and many other traits (Jablonski 2004; Balter 2005; Beall 2006; Tishkoff et al. 2007; Gluckman et al. 2009a). And the same is true for natural populations of other organisms. First, different populations or species in similar environments tend to have similar phenotypes: i.e., convergent or parallel evolution (Endler 1986; Schluter 2000). Second, populations introduced to new environments often evolve phenotypes expected for those environments (Reznick and Ghalambor 2005). Third, reciprocal transplants show that individual fitness is usually higher for local individuals than for foreign individuals (Hereford 2009), even when those populations diverged only recently (Kinnison et al. 2008; Gordon et al. 2009). Fourth, selection in wild populations is usually quite weak (Kingsolver et al. 2001; Hersch and Phillips 2004) and variable (Siepielski et al. 2009) – consistent with the idea that most populations are relatively well adapted to local conditions (Estes and Arnold 2007; Hendry and Gonzalez 2008).

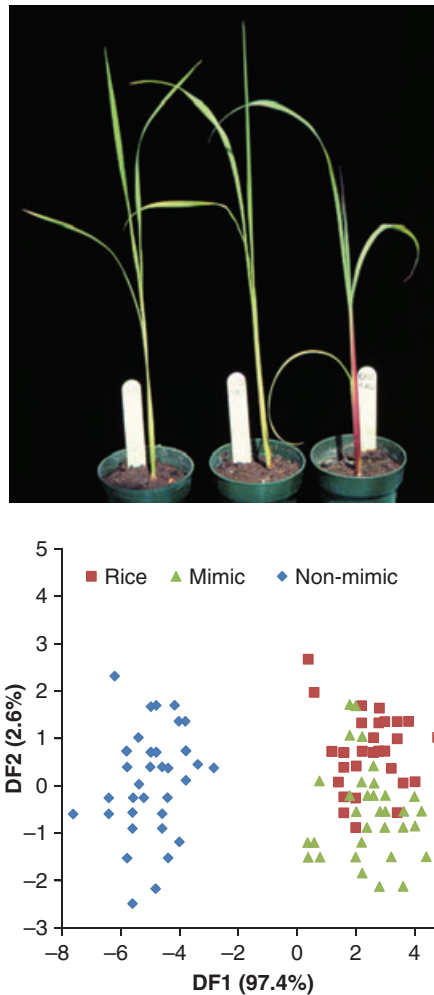Also, phenotypic changes through time will be adaptive in many cases. Perhaps most obvious is the repeated

Figure 6 Crop mimicry in barnyard grass. Panel A shows rice (*Oryza sativa*) on the left, a barnyard grass (*Echinochloa crus-galli* var. *oryzicola*) that mimics rice in the center, and a very closely related barnyard grass (*Echinochloa crus-galli* var. *crus-galli*) that does not mimic rice on the right. Panel B is a discriminant functions plot that shows the morphological similarity of multiple individuals (points) in these three groups. Centuries of hand weeding is thought to have led to the close similarity of rice and its barnyard grass mimic. Adapted from Barrett (1983) with a photograph and data provided by S. Barrett.

evolution of resistance to chemicals by weeds, pests, and pathogens – as discussed in more detail later. And the same is true for mechanical weed control: barnyard grass that grows in hand-weeded rice fields has evolved to be more cryptic by morphologically converging on rice (Barrett 1983; Fig. 6). In fisheries, intensively harvested wild populations have repeatedly evolved smaller body size, younger age at first reproduction, and higher reproductive allocation (Jørgensen et al. 2007; Dunlop et al. 2009; Sharpe and Hendry 2009). These parallel phenotypic changes in response to parallel shifts in selection

strongly implicate selection and adaptation – although the genetic basis for temporal change is hard to confirm.

Not all phenotypic differences and changes will be adaptive, and so it is prudent to also consider alternatives. Nonadaptive or maladaptive differences might sometimes arise through genetic drift, although probably only for very small populations and traits under very weak selection. Maladaptive variation can also be caused by high gene flow (Hendry and Taylor 2004; Bolnick and Nosil 2007) or ongoing environmental change (Grant and Grant 2006), with the latter increasingly important in a human dominated world (see next section). In addition, past selection pressures that led to the evolution of particular traits might no longer be present ('relaxed selection'), but the traits might take a long time to decay if they are now selectively neutral (Lahti et al. 2009). The remnant pelvic bones of whales and some snakes are not adaptive *per se*, but have persisted because they have not been strongly selected against. In addition, nutritional limitation can cause trait change in ways that are not necessarily adaptive (Grether 2005). Regardless, it is safest to start from the premise that phenotypic differences are adaptive (remembering that they might be plastic or genetic), because this will often be true and it is the precautionary approach while awaiting confirmation.

Human activities impose particularly strong selection

Humans cause dramatic environmental changes and should therefore impose particularly strong selection. Especially obvious are the many examples of bacteria evolving resistance to antibiotics (Palumbi 2001). As noted by Bergstrom and Feldgarden (2007): 'The evolution of resistance to a clinical antibiotic occurs with near certainty after several years of widespread use'. Human viruses, such as HIV, also evolve resistance to a variety of treatments (Little et al. 2002), as does cancer in response to chemotherapy (Pepper et al. 2009). Insects that are vectors of human diseases, particularly mosquitoes, frequently evolve resistance to insecticides (Hemingway and Ranson 2000; Raymond et al. 2001). Agriculture is rife with analogous situations. Heap (1997) reports '183 herbicide-resistant weed biotypes (124 different species) in 42 countries'. Whalon et al. (2008) list 7747 cases of resistance evolution to 331 compounds in 553 pest arthropod species.

For wild populations of vertebrates, meta-analyses have revealed that phenotypic changes are greatest when environmental changes are the result of human activities, including pollution, translocations, invasive species, hunting, and harvesting (Hendry et al. 2008). An example described in this special issue is the difference in morphological traits of *Anolis sagrei* lizards in urban areas versus natural habitats (Marnocha et al. 2011). Phenotypic

changes are especially strong when they involve the hunting/harvesting of wild populations (Darimont et al. 2009) – probably because humans here directly select on the population, rather than having an *indirect* effect acting through human-induced environmental change. Some of the observed phenotypic changes are probably the immediate result of phenotypic plasticity, whereas others will represent genetic change (Dieckmann and Heino 2007; Bradshaw and Holzapfel 2008; Gienapp et al. 2008; Hendry et al. 2008; Crispo et al. 2010). In short, humans cause particularly dramatic changes in organisms – and these changes are probably often adaptive.

Selection can be manipulated to help or harm populations

Selection is a demographic process that can alter birth and death rates, and so it can have an immediate influence on population dynamics. Selection also drives adaptation, and so it can have future influences on population dynamics. We discuss these points further in the section on Eco-evolutionary dynamics. For now, we focus on how selection can be manipulated to achieve desired population consequences. On the one hand, selection on pests, weeds, or pathogens might be designed to exceed their adaptive potential, thus decreasing population sizes and potentially causing eradication. On the other hand, selection in conservation situations might be eased in order to give populations a more gradual (and therefore achievable) route to adaptation.

Altering the *intensity* of selection is one possible manipulation. For example, one can apply more, or more powerful, herbicides, pesticides, antibiotics, or antivirals in the hope of causing severe population declines. But if eradication does not occur, this stronger selection can lead to increased rates of adaptation, effectively undoing any progress initially achieved. On the flip side, decreasing the intensity of selection can be problematic if one wishes to speed adaptation in threatened species. Other strategies might therefore be implemented to manipulate selection so as to promote desired demographic consequences while reducing undesired evolutionary consequences. One strategy is to increase the *dimensionality* of selection by altering the environment in multiple ways. Another is to alter the *timing* of selection by changing the life stage when selection acts.

An example of altering the *dimensionality* of selection comes from HIV treatment, where the initial problem was that resistance quickly evolved to single drugs (Little et al. 2002). The advance was to use multiple drugs specifically designed to act in different ways that require independent mutations for the virus to circumvent. These 'highly active anti-retroviral therapy' treatments can include a combination of nucleoside/nucleotide reverse transcriptase inhibitors, non-nucleoside reverse transcriptase inhibitors, and aspartic protease inhibitors, sometimes combined with fusion inhibitors (Barbaro et al. 2005). Resistance to these drug cocktails does evolve more slowly, not only in HIV but also in tuberculosis (Bonhoeffer et al. 1997). Unfortunately, multi-drug resistance does still ultimately evolve in many cases (Coker 2004). Selection dimensionality plays into agriculture through 'toxin stacking' or 'pyramiding' in pest control – essentially layering one selective force on top of another. For instance, rotations or mixtures of herbicides or pesticides with 'discrete modes of action' are a common strategy to slow the evolution of resistance (Beckie and Reboud 2009). Likewise, multiple insecticidal toxin genes from bacterial sources can be incorporated into transgenic crop plants (Roush 1998). Although this method is not yet widely deployed, two-gene transgenic *Bt* cotton is being used in Australia (Fitt 2008).

Altering the *timing* of selection has its motivation in the evolutionary theory of senescence (Medawar 1952; Williams 1957). This theory argues that unavoidable extrinsic mortality (from predators, pathogens, starvation, or accidents) dictates that few individuals reach advanced ages, and so selection against deleterious alleles that act late in life will be relatively weak. Applying this idea to infectious diseases, Read et al. (2009) proposed that insecticides targeting older mosquitoes could reduce malaria transmission without imposing strong selection for resistance in the mosquitoes. The reason is that malaria transmission becomes more likely late in the life of mosquitoes after they have already reproduced at least once (see also Koella et al. 2009). Because relatively few mosquitoes make it to this age, late-life-acting insecticides might be 'evolution proof' (Read et al. 2009), in contrast to the current early-life-acting insecticides to which mosquitoes have so routinely evolved resistance (Raymond et al. 2001). Although experience teaches that 'evolution proof' is a long shot for organisms with short generation times and large population sizes, late-life treatments might be at least 'evolution resistant.'

Selection is influenced by allelic interactions (e.g., recessivity)

Interactions between alleles at a given locus can dramatically alter selection and evolutionary responses. Of particular relevance, some alleles are recessive, having phenotypic effects only (or mainly) in homozygous form. When these alleles are rare, it is hard to change their frequency because they primarily occur in heterozygous form and so are shielded from selection. Recessive alleles have played an important role in management strategies

to slow the evolution of resistance. One strategy has been to promote interbreeding between resistant and nonresistant individuals, the latter often coming from reserves or from controlled releases (see the Connectivity section). If the genes for resistance are recessive, they will be selected against when the resulting heterozygotes are exposed to the control strategy (Carrière and Tabashnik 2001). Recessive alleles are also relevant in the conservation of small populations. Breeding between close relatives in these situations can increase the frequency of homozygotes and thereby increase the expression of recessive deleterious mutations (Lynch et al. 1995), which can decrease fitness (Keller and Waller 2002). These effects are also recognized in human populations, as codified in social norms that discourage marriage between close relatives.

A different type of allelic interaction occurs with 'imprinted genes' in mammals (Wilkins and Haig 2003), where the allele from only one parent is expressed in the offspring, often as a result of methylation of the other allele. This imprinting has several effects. First, it shelters one allele from selection in each generation – and this might, by chance, be the same allele across several successive generations. Second, and in counterpoint, it is unlikely that the same allele will be sheltered for a number of successive generations, and so recessive deleterious mutations are less likely to escape selection for long. Imprinted genes represent only about 1% of autosomal genes – but they nevertheless have important effects and are related to a number of developmental disorders (Wilkins and Haig 2003; Jirtle and Skinner 2007).

Connectivity

Connectivity determines the movement of individuals and gametes across a landscape. Connectivity is influenced by organismal attributes (e.g., behavior and body size), by population densities and distributions, and by natural and man-made structures (e.g., mountains, oceans, roads, dams, canals, corridors, and currents). From an ecological perspective, increased connectivity can have consequences that are either positive (demographic rescue) or negative (spread of diseases or invasive species). From a genetic perspective, increased connectivity increases gene flow, which generally increases genetic variation within populations (by bringing it from elsewhere) and decreases genetic variation among populations (by mixing their gene pools). These genetic effects can either enhance or constrain adaptive evolution, depending on the circumstances (review: Garant et al. 2007). Some potential enhancing effects include reduced inbreeding and increased genetic variation for future adaptation. A potential constraining

effect is the erosion of local adaptation by the influx of locally maladaptive genes. Although connectivity plays into many of the topics and examples discussed elsewhere in this article, we treat it separately here because the manipulation of connectivity has played an important role in applied evolution.

Gene flow can be manipulated to achieve desired outcomes

Increased gene flow is commonly considered in efforts genetically 'rescue' small and isolated populations from inbreeding depression (Keller and Waller 2002). Famous examples include the aforementioned Greater Prairie Chickens (Westemeier et al. 1998) and Florida panthers (Hedrick 1995; Pimm et al. 2006). Less commonly, increased gene flow has been considered in efforts to enhance the adaptive potential of populations facing environmental change. For instance, a population threatened by maladaptation to increasing temperatures might be rescued by gene flow from populations adapted to warmer conditions. As a possible natural analog, the lineage of field mice (Peromyscus leucopus) present in the Chicago area prior to the 1980s has been completely replaced by a different lineage that appears better adapted to the new conditions (Pergams and Lacy 2008).

Increased gene flow has been intentionally used in agriculture to either enhance adaptation or to constrain it. Toward the first purpose, considerable success has been achieved by crossing cultivars with their wild relatives to 'pyramid' independent genomic regions that increase yield (Gur and Zamir 2004). Toward the second purpose, gene flow is often used to slow the evolution of resistance to pesticides. A common approach is to match fields of transgenic Bt crops, where insects are under selection to evolve resistance, with adjacent 'reserves' of non-Bt crops, where insects are not under this selection (Carrière and Tabashnik 2001). Mating between insects from the two areas then hampers the evolution of resistance – to a degree that depends on recessive inheritance, incomplete resistance, fitness costs, and the degree of assortative mating (Carrière and Tabashnik 2001; Tabashnik et al. 2005, 2008). The refuge strategy does hinder resistance evolution in at least some systems, such as pink bollworm (Pectinophora gossypiella) in the USA (Tabashnik et al. 2005) and cotton bollworm (Helicoverpa armigera) in Australia (Downes et al. 2010). An alternative to crop reserves as a source of nonresistant genotypes is their mass culture and release (Alphey et al. 2007). Alternatively, sterile individuals can be released that reduce the reproductive success of wild individuals with which they mate (Benedict and Robinson 2003). Or mosquitoes can be released that have been bred to be less able to transmit

malaria (Ito et al. 2002) or to have heritable life-shortening *Wolbachia* infections (McMeniman et al. 2009).

Decreased gene flow is also a management tool. Theory suggests that high gene flow between populations in different environments can compromise adaptation, leading to population declines and possible extirpation (Boulding and Hay 2001). This concern has become pervasive when considering the effects of cultured organisms on wild populations (Tufto 2010). Hatcheries and fish farms often use nonlocal genotypes or cause the evolution of traits that are maladaptive in the wild (Araki et al. 2008). Frequent releases or escapes from such facilities can cause maladaptive gene flow that compromises adaptation in wild populations (Hindar et al. 2006). Attempts have therefore been made to reduce gene flow from captive to wild populations (Cotter et al. 2000). Related to this, concerns surround the possible spread of transgenes from genetically modified organisms (GMOs) into wild populations (Ellstrand 2001; Andow and Zwahlen 2006). These transgenes could cause problems for wild populations or, alternatively, enhance the fitness of potentially weedy species (Marvier 2008). For example, gene flow among canola (*Brassica napus*) crops with different insecticide resistance genes has resulted in multiple-herbicide resistance in 'volunteer' canola plants growing as weeds in other crops (Beckie et al. 2003).

Gene flow can evolve when organismal traits influencing connectivity or movement experience altered selection. As possible examples, marine reserves that provide refuges from fishermen (Baskett et al. 2007), or roads that kill migrants traveling between habitats, might favor the evolution of reduced dispersal. Reduced dispersal can then decrease gene flow between populations (although not under all circumstances, Heino and Hanski 2001), and thus alter the aforementioned effects.

Eco-evolutionary dynamics

In our consideration of how variation, selection, and connectivity influence the evolution of phenotypic traits, we have sometimes discussed how this evolution can have consequences for population dynamics. These effects fall under the umbrella of interactions between ecology and evolution, wherein ecological change drives evolutionary change and evolutionary change can feed back to influence ecological change, i.e., 'eco-evolutionary dynamics' (Fussmann et al. 2007; Kinnison and Hairston 2007; Palkovacs and Post 2009; Pelletier et al. 2009). We now expand on the second part of this dynamic (evo-to-eco) by more explicitly discussing the effects of phenotypic/ genetic change on population dynamics (e.g., numbers of individuals and population persistence), community structure (e.g., species richness or diversity), and ecosys-

tem function (e.g., nutrient cycling, decomposition, and primary productivity).

Evolution influences population dynamics

Evolution can influence population dynamics in two basic ways (Saccheri and Hanski 2006; Kinnison and Hairston 2007), roughly corresponding to so-called 'hard' versus 'soft' selection (Wallace 1975). In the first instance, evolution can alter the rate of increase of a population in the absence of density dependence: better-adapted populations have higher birth rates or lower death rates. In the second instance, evolution can alter the population size at which density dependence becomes limiting: better-adapted populations sustain more individuals at a given resource level. These population parameters can be depressed when organisms are poorly adapted for their local environments – and extinction can be the result. However, contemporary adaptation to those changed environments can boost these parameters and thereby aid population recovery (Gomulkiewicz and Holt 1995; Bell and Gonzalez 2009; Enberg et al. 2009). As obvious examples, new treatments to which weeds, pests, or pathogens are not well adapted can cause initial population declines, but adaptation can then allow their recovery.

Will similar dynamics be important for wild populations facing environmental change (Lakau et al. 2011)? Some evidence has certainly accumulated that environmental change can generate maladaptation that causes population declines (Both et al. 2006; Pörtner and Knust 2007). Evidence also exists that contemporary adaptive change improves the fitness of individuals or populations facing environmental change. For example, survival and reproductive output increase through time as fish populations adapt following an abrupt environmental change (Kinnison et al. 2008; Gordon et al. 2009). And changes in the population size of ungulates from 1 year to the next are influenced by phenotypic changes on the same time scale (Pelletier et al. 2007; Ezard et al. 2009). In most cases, it is not clear to what extent these improvements are the result of plasticity or genetic change or both. However, genetic effects have been confirmed for improvements in the individual fitness of chinook salmon (*Oncorhynchus tshawytscha*) introduced to new environments (Kinnison et al. 2008) and the growth rate of local populations within a metapopulation of Glanville Fritillary butterflies (*Melitaea cinxia*) (Saccheri and Hanski 2006).

In the case of invasive species, demographic costs of initial maladaptation are implied in the observation that introduced species usually fail to become established (Sax and Brown 2000). And the demographic benefits of contemporary adaptation are implied in the observation that

introduced species that become invasive often do so only after a lag period or repeated introductions, which are often accompanied by phenotypic changes (Facon et al. 2006). Weese et al. (2011) provide an experimental example wherein population recovery following disturbance was mostly driven by locally adapted individuals rather than maladapted immigrants.

Evolution influences communities and ecosystems

Phenotypic variation can have direct or indirect consequences for community structure and ecosystem function. Direct effects can occur if specific phenotypes influence ecological variables, such as different foraging traits influencing consumption patterns that then alter food web structure (Palkovacs and Post 2009). Indirect effects could occur if phenotypes influence population size (as described earlier) and population size then has ecological effects. For example, adaptive evolution that increases the size of a predator population could have cascading effects on other trophic levels. These direct and indirect effects can be considered in the context of standing variation within or between populations, or dynamic changes in the composition of populations through time. These ecological consequences of phenotypic variation/change are expected to be particularly important in species with large per capita ecological roles (e.g., keystone species and foundation species) or that are very abundant or rapidly evolving (e.g., some pathogens or pests).

One approach to eco-evolutionary effects is to examine how genetic variation among individual plants influences their ecological effects, such as on attendant arthropod or plant communities. These effects can be quite strong (Whitham et al. 2006; Bailey et al. 2009; Johnson et al. 2009), implying that dynamic *changes* in the composition of populations should cause dynamic *changes* in ecological variables. These changes are much harder to study than are the effects of standing variation. One approach has been to use mesocosms to compare the ecological effects of fish populations that recently diverged from a common ancestor (Fig. 7). Guppy (*Poecilia reticulata*) and killifish (*Rivulus hartii*) populations that colonized divergent environments thousands to millions of years ago now differentially influence algal biomass, algal accrual, aquatic invertebrates, decomposition rates, and nutrient fluxes (Palkovacs et al. 2009; Bassar et al. 2010). Stickleback populations that colonized divergent environments thousands of years ago now differentially influence zooplankton communities, primary productivity, dissolved organic materials, and light transmission (Harmon et al. 2009). Alewife (*Alosa pseudoharengus*) populations that colonized divergent environments
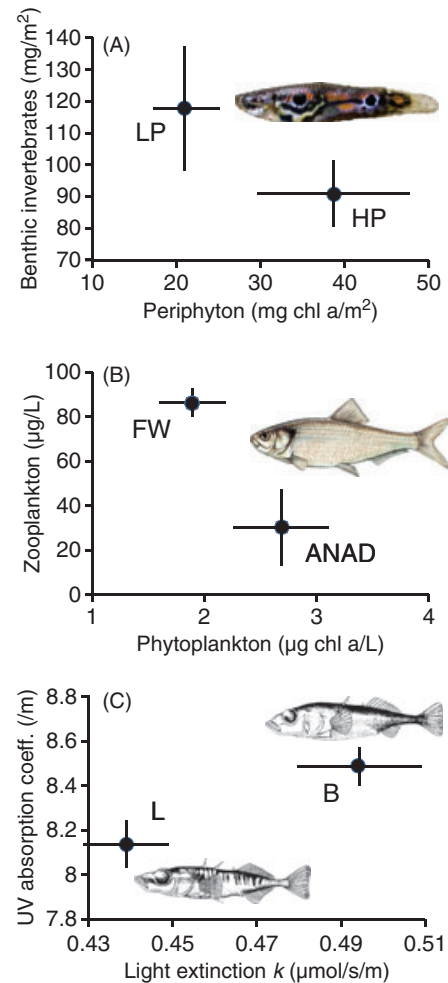

Figure 7 Examples of the community and ecosystem effects of phenotypic differences between fish populations. Panel A shows that mesocosms with guppies (*Poecilia reticulata*) from high-predation (HP) populations have more periphyton and fewer benthic macroinvertebrates than do mesocosms with guppies from low-predation (LP) populations. These data are adapted from Palkovacs and Post (2009) – see also Bassar et al. (2010). Panel B shows that mesocosms with alewife (*Alosa pseudoharengus*) from anadromous (ANAD) populations have fewer zooplankton and more phytoplankton than do mesocosms with alewife from resident freshwater (FW) populations. These data are for the first sampling date after fish were added to the mesocosms and are from Palkovacs et al. (2009) for zooplankton and from E. Palkovacs (unpublished) for phytoplankton. Panel C shows that mesocosms with benthic threespine stickleback (*Gasterosteus aculeatus*) have greater light extinction coefficients and greater UV absorption than do mesocosms with limnetic threespine stickleback. These data are adapted from Harmon et al. (2009) with data provided by L. Harmon. In all panels, the bars are standard errors around the mean value across replicate mesocosms.

hundreds of years ago now differentially influence zooplankton communities, with potential feedbacks to alewife evolution (Palkovacs and Post 2009).

Effects of contemporary evolution on communities and ecosystems are likely common on even shorter time scales – given the ample evidence that adaptive traits can evolve on the time scale of just a few generations (Hendry et al. 2008). Such effects are obvious in medical and agricultural settings, where the evolution of resistance clearly has consequences for human populations and crops. In more natural settings, a putative example is the rabbit–myxoma interaction in Australia: introduced rabbits (*Oryctolagus cuniculus*) had dramatic ecological consequences, which abated when myxomatosis was introduced to kill the rabbits, but increased again when mortality rates declined owing to co-evolution of the rabbits and myxomatosis (Dwyer et al. 1990). In addition, selective herbivory has been shown to alter the chemical composition of tree communities, which has consequences for other ecological processes. For example, beaver (*Castor canadensis*) avoid *Populus* trees with high tannin content, the increasing frequency of which then reduces nitrogen mineralization (Whitham et al. 2006). We suspect that many more ecological effects of contemporary evolution will be revealed as more investigators turn to this problem.

Take home summary

1 Understanding phenotypes (as opposed to just genotypes) is important because phenotypes interact with the environment, come under direct selection, and have ecological effects.

2 Individual and population mean fitness can improve more rapidly through plasticity than through genetic change – at least in the short term. Genetic change, however, will often be necessary to finish any recovery.

3 In the study of adaptation, the examination of specific genes is often insufficient. Adaptation will usually involve many genes, which highlights the importance of a quantitative genetic approach.

4 Standing genetic variation in fitness-related traits is nearly ubiquitous, and so is likely to be the initial fuel for evolutionary change in response to environmental change.

5 New mutations become important when standing genetic variation is absent or depleted. New mutations will be particularly important for organisms with short generation times and large population sizes (e.g., viruses, bacteria, and some insects and plants).

6 Small population sizes, and especially bottlenecks, can lead to genetic problems. These problems will apply more often to current fitness (e.g., inbreeding depression) than to future evolutionary potential.

7 Current trait distributions are a product of past selection. Evolutionary history can therefore help to understand the current state of affairs and to predict responses to future environmental change.

8 Some evolutionary change is not possible because of limited genetic variation, trade-offs, or physiological constraints. Identifying these limits is difficult but can aid attempts to slow unwanted evolution.

9 The phenotypes of organisms are an integrated complex of traits in association with each other. These associations influence the rate and trajectory of evolution.

10 Natural selection generally favors traits that improve individual-level fitness, whereas humans often care about population-level traits, such as productivity or yield. Cognizance of these different levels of selection can be used to tailor evolutionary trajectories as desired.

11 Phenotypic differences among populations or through time are usually adaptive, rather than the product of genetic drift. Exceptions do exist, particularly for very small populations or for traits under relaxed selection.

12 Human activities impose particularly strong selection. Adaptive phenotypic change will be the result, and at least some of this change will be genetically based.

13 Selection can be manipulated to help or harm organisms, but the resulting contemporary evolution can hamper these goals. Manipulating the dimensionality or timing of selection can have desired demographic effects while reducing undesired evolutionary effects.

14 Allelic interactions alter natural selection in important ways. For example, recessive alleles are often sheltered from selection, which can be exploited to slow the evolution of resistance.

15 Manipulations of connectivity that alter gene flow are an important management tool. Gene flow can be increased to reduce inbreeding or increase evolutionary potential. Gene flow can be decreased to reduce impacts of cultured organisms on wild populations.

16 Adaptive evolution influences population dynamics and sometimes allows evolutionary rescue. Such effects are not inevitably large, and so an important topic becomes the conditions under which they will be important.

17 Adaptive evolution will alter how organisms interact with their environment and can therefore influence community structure and ecosystem function. These effects are particularly pronounced for organisms that have large ecological effects (e.g., keystone species, foundation species) or that are very numerous (e.g., pathogens, pests, and weeds).

This listing is only a starting point. As additional knowledge and experience accumulate, some of the above points will need to be deleted or altered – and new ones added. Nevertheless, we are struck by how each of the aforementioned principles has clear existing or envisioned applications in multiple areas of biology, ranging across

health, medicine, agriculture, conservation biology, natural resource management, and environmental science. This cross-disciplinary relevance serves to illustrate the unifying aspect of evolution and its ramifications across the applied biological sciences. Hopefully, this illustration will inspire practitioners within a given applied discipline to consider evolutionary principles currently applied in other disciplines.

Applied evolutionary biology is on the cusp of coming into its own as a discipline, and we hope that it will eventually be so seamlessly integrated into 'applied biology' that this more general term will immediately evoke a strong evolutionary foundation. This integration will not always be smooth sailing. Some ecologists still do not think evolution is relevant on short time scales. Some manipulations of connectivity might be ruled out based on ethical issues. Some theoretically sensible evolutionary interventions might be ruled out owing to their initial cost or environmental effects (Thrall et al. 2011). And, of course, a surprising fraction of humans still 'don't believe in evolution.' However, it seems to us that the benefits of applying evolutionary principles will eventually be so obvious that their widespread application will be insidiously inevitable. Thus, while doctors or farmers might euphemistically talk about acquired resistance, when they really mean the evolution of resistance, they nonetheless think about and apply some evolutionary principles on a daily basis.

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