Evolutionary Applications ISSN 1752-4571

PERSPECTIVE ARTICLE

Evolutionary origins of invasive populations

Carol Eunmi Lee and Gregory William Gelembiuk

Center of Rapid Evolution (*CORE*), Department of Zoology, University of Wisconsin, Madison, WI, USA

Keywords
additive genetic variance, balancing selection, biological invasion, disturbance, evolvability, fluctuating selection, M-matrix, modularity, plasticity.

Correspondence
Carol Eunmi Lee, Center of Rapid Evolution (*CORE*), Department of Zoology, University of Wisconsin, 430 Lincoln Drive, Madison, WI 53706, USA.
Tel.: +1 (608) 262-2675;
e-mail: carollee@wisc.edu

Received: 16 November 2007
Accepted: 16 May 2008
First published online: 28 June 2008

doi:10.1111/j.1752-4571.2008.00039.x

Abstract

What factors shape the evolution of invasive populations? Recent theoretical and empirical studies suggest that an evolutionary history of disturbance might be an important factor. This perspective presents hypotheses regarding the impact of disturbance on the evolution of invasive populations, based on a synthesis of the existing literature. Disturbance might select for life-history traits that are favorable for colonizing novel habitats, such as rapid population growth and persistence. Theoretical results suggest that disturbance in the form of fluctuating environments might select for organismal flexibility, or alternatively, the evolution of evolvability. Rapidly fluctuating environments might favor organismal flexibility, such as broad tolerance or plasticity. Alternatively, longer fluctuations or environmental stress might lead to the evolution of evolvability by acting on features of the mutation matrix. Once genetic variance is generated via mutations, temporally fluctuating selection across generations might promote the accumulation and maintenance of genetic variation. Deeper insights into how disturbance in native habitats affects evolutionary and physiological responses of populations would give us greater capacity to predict the populations that are most likely to tolerate or adapt to novel environments during habitat invasions. Moreover, we would gain fundamental insights into the evolutionary origins of invasive populations.

On the origins of invasive populations

Of the large number of species that are introduced into novel habitats, few are successful as invaders (Williamson and Fitter 1996). What allows some species to invade, when most cannot? In many cases, populations might invade habitats with environmental conditions that resemble those of their native range (Peterson and Vieglais 2001; Peterson 2003). In other cases, populations might survive novel habitats through a plastic response or by having broad physiological tolerance (Sultan 2001; Parker et al. 2003; Yeh and Price 2004; Sol et al. 2005). Increasingly, it is becoming recognized that, in many cases, response to selection and rapid evolution might be important (Huey et al. 2000; Carroll et al. 2001; Lee 2002; Bossdorf et al. 2005; Donohue et al. 2005; Lee et al. 2007; Kane and Rieseberg 2008). Such cases involve niche evolution, which entails the evolution of survival and persistence in novel habitats (Lee 2002).

Striking patterns are beginning to emerge, revealing biases in the geographic origins of invasive populations. These biases suggest that characteristics of particular source habitats within native ranges might shape the evolution of invasive populations. Invasive species are often composed of highly differentiated populations or sibling species distributed across their native ranges (Geller et al. 1997; Lee 2000; Tsutsui and Case 2001; Lee and Frost 2002; Gelembiuk et al. 2006; Caldera et al. 2008; Winkler et al. 2008). Often, only subsets of these populations become invasive (Lee 1999; Tsutsui and Case 2001; Saltonstall 2002; Meusnier et al. 2004; Brown and Idris 2005; Chu et al. 2006; Gelembiuk et al. 2006; May et al. 2006; Caldera et al. 2008; Winkler et al. 2008).

Empirical observations have suggested that invasive populations tend to arise from regions prone to 'disturbance' (Box 1). For example, weedy plants, many of which are invasive, are generally thought to be adapted to disturbance (Baker 1974; Thébaud et al. 1996).

In addition, species from the Old World have been speculated to have higher invasive potential than those from the New World, due to a history of greater natural and anthropogenic disturbance (Di Castri 1989; Lonsdale 1999). In a striking example, the Black and Caspian (Ponto-Caspian) Sea basins have served as major donors of invaders into the Great Lakes (Jazdzewski 1980; Spidle et al. 1994; Lee and Bell 1999; Cristescu et al. 2001, 2004), giving rise to the vast majority of invaders between 1985 and 2000 (Ricciardi and MacIsaac 2000). The Ponto-Caspian basin has a history marked by fluctuations in environmental variables on multiple timescales (Kaplin 1995; Svitoch et al. 2000; Reid and Orlova 2002). This region also has a relatively long history of anthropogenic disturbances, including canal and reservoir construction and large-scale transplantation of Ponto-Caspian species for use in aquaculture (Jazdzewski 1980).

For species with broad distributions, recent molecular population genetic analyses have begun to identify the less-stable habitats within the native ranges as frequent sources of invasive populations. For instance, the native range of the zebra mussel *Dreissena polymorpha* encompasses genetically distinct populations (and sibling species) spanning brackish estuaries of the Black and Caspian Sea region and ancient lakes to the south of the seas. However, invasive populations most likely arose from the northern estuaries of the Black and Caspian Sea rather than from the more stable ancient lakes to the south of the seas (Gelembiuk et al. 2006; May et al. 2006). Within the St Lawrence estuary, two genetically divergent clades of the copepod *Eurytemora affinis* overlap in distribution. However, only the clade residing primarily in the marginal near-shore and salt-marsh habitats has invaded freshwater habitats, whereas the clade restricted primarily to the more stable central portion of the estuary has not (Winkler et al. 2008). The native ranges of many invasive ant species (e.g. *Linepithema humile*, *Solenopsis invicta*, *Solenopsis richteri*, *Wasmannia auropunctata* and *Pheidole obscurithorax*) include unstable flood plains of northern Argentina (Suarez and Tsutsui 2008). In particular, the Argentine ant *L. humile* and the fire ant *S. invicta* exhibit considerable population genetic structure across their native ranges in South America (Tsutsui and Case 2001; Ross et al. 2007), yet the invasive populations of both species arose from regions of northeastern Argentina characterized by large-scale disturbances in the form of regular flooding (Tsutsui and Case 2001; Caldera et al. 2008; Suarez and Tsutsui 2008).

An evolutionary history of disturbance in the native range might select for the propensity to invade. In many cases, biases in geographic sources of invasions could have resulted from biases in transport routes and opportunity. However, the preponderance of invaders from disturbed habitats suggests that disturbance itself might have served as an evolutionary force leading to invasive success. An increasing number of theoretical and empirical studies suggest that disturbance might, through a variety of mechanisms, promote the evolution of invasive populations.

This perspective advances a hypothesis regarding the potential impact of disturbance on the evolution of invasive populations based on a synthesis of the existing literature. The ideas presented here remain to be tested with empirical data. Additional theoretical studies are required to delimit the range of parameter values that are plausible, and further guide the hypotheses to be tested. In addition, mechanisms underlying results obtained from some of the theoretical simulation studies are not transparent, and require further analyses. This perspective aims to promote the study of forces that shape the evolution of invasive populations, and illuminate areas of research that warrant further exploration.

Impacts of disturbance on the evolution of invasive populations

Two distinct types of strategies might evolve to increase fitness in disturbance-prone fluctuating environments (Gillespie 1974; Kawecki 2000; Meyers and Bull 2002; Turelli and Barton 2004). On the one hand, organisms might evolve generalist strategies, which would allow them to prosper across a wide range of conditions. Alternatively, organisms might develop increased evolvability (Boxes 1 and 2), with an increased capacity to adapt rapidly to changing conditions. The strategy that predominates would depend on a variety of factors, including the frequency and amplitude of environmental change. Both strategies reflect selection pressure to maximize time-averaged fitness, and could contribute to increased invasive potential in new habitats.

Disturbance in the form of environmental fluctuations might serve as a general means for promoting either organismal flexibility or evolvability, depending on the rate of fluctuations relative to generation time (Kawecki 2000; Meyers and Bull 2002; Holt et al. 2004; Turelli and Barton 2004; Meyers et al. 2005). Rapid fluctuations occurring within generations could potentially select for organismal flexibility, such as broad tolerance or short-term phenotypic plasticity at the individual level (Turelli and Barton 2004; Meyers et al. 2005). Fluctuations occurring at the timescale of a generation might select for genetic canalization (Box 1) (Kawecki 2000). At this timescale, evolutionary change could also be damped by the buffering effect of developmental plasticity (Meyers and Bull 2002). In contrast, fluctuations spanning across an

Box 1. Definitions of terms and concepts

Disturbance

Ecological disturbance could be thought of as discrete events, either natural or human-induced, that cause temporary changes that deviate from average environmental conditions. Disturbances could occur as discrete episodes or in a cyclical manner. In addition, cyclical disturbances could be random or regular in frequency. Examples of disturbances include fires, flooding, storms, pathogen outbreaks, tidal cycles, climatic cycles and human activity. Some habitats are more prone to disturbance than others, such as pathways of tropical storms, salt marshes, estuaries, agricultural farms and reservoirs.

Evolvability

Usage of this term varies, partly depending on the subdiscipline within evolutionary biology (Pigliucci 2008). For example, Wagner and Altenberg (1996) define evolvability as the ability of genomes within a population to produce adaptive variants, such that the population could respond to selection. In their definition, they focus on the generation of the genetic substrate available for selection through mutational variability and recombination. Alternatively, evolvability is defined in terms of the ability of a population to respond to selection due to its standing genetic variance, as quantified by the genetic coefficient of variation ($CV_A = 100\sqrt{V_A}/\bar{X}$, where V_A is the additive genetic variation and $\bar{X}$ is the trait mean) (Houle 1992). Evolvability is a trait that is under indirect selection, as it does not improve the fitness of a population immediately, but tends to be beneficial in future environments (Reisinger and Miikkulainen 2006; Jones et al. 2007).

Evolutionary landscape

Evolution can be represented as movement on a landscape. This landscape relates one or more underlying factors (e.g. alleles or environmental variables) to the value of the resulting phenotypic trait (phenotypic landscape; Rice 1998) or the fitness of organisms (the adaptive landscape; Wright 1932). The trait value or the fitness value is given by the height of the landscape. On an adaptive landscape, populations will tend to climb fitness peaks, as selection will favor an increase in fitness. In some cases, populations of organisms can become trapped on local (suboptimal) fitness peaks, as moving to the global fitness peak might require traversing a valley of reduced fitness. Multidimensional adaptive landscapes (i.e. which represent fitness as a function of many underlying genetic variables) typically have extensive ridges of high fitness (they are 'holey'), facilitating movement across the landscape (Gavrilets 1999).

Genetic canalization

Canalization refers to stabilization of a phenotype against genetic or environmental perturbation (Schmalhausen 1949; Waddington 1957; Flatt 2005). Variation in the phenotype is thus reduced. In the case of genetic canalization, this involves buffering against mutations. Some have argued that genetic canalization might frequently arise as an incidental byproduct of canalization against environmental perturbation (Gibson and Wagner 2000).

G-matrix

Selection response depends on the standing additive genetic variances (V_A) and covariances for a suite of traits in a population, or the G-matrix. The G-matrix contains additive genetic variances on the diagonal elements and additive genetic covariances on the off-diagonal elements. Genetic variances and covariances can be calculated based on the phenotypic similarity among relatives. The G-matrix relies on the generation of new mutations (the M-matrix).

M-matrix

The mutation matrix (M-matrix) represents the effects of new mutations on trait variances and covariances. Below is a mutation matrix for three traits (t_1, t_2 and t_3). The diagonal elements are the mutational variances for each trait (t_1, t_2 and t_3), while off-diagonal elements are mutational covariances between the traits. The structure of the M-matrix could evolve in three ways:

1. Evolution of global mutation rate: changes in the magnitude of all the elements.
2. Evolution of mutational variances of individual traits: changes in individual diagonal elements (blue). Mutational variances are affected by mutation rates of individual traits and the sensitivity of the traits to mutations (genetic potential).
3. Evolution of mutational covariances between individual traits: changes in the off-diagonal elements (red). These values reflect pairwise pleiotropic effects due to mutations in different traits (t_1, t_2 and t_3).

$$\begin{pmatrix} t_1^2 & t_1t_2 & t_1t_3 \\ t_2t_1 & t_2^2 & t_2t_3 \\ t_3t_1 & t_3t_2 & t_3^2 \end{pmatrix}$$

Modularity

The concept of modularity varies among and within different disciplines of biology (Schlosser and Thieffry 2000). For the purposes of this paper, modularity is the degree of independence among traits in genetic variance structure and evolutionary response. Within the context of quantitative genetics, modularity is maximized when the mutational and genetic covariances between traits are close to zero, such that pleiotropic constraints are minimized. Modules could consist of sets of traits that covary among individuals within a population and that coevolve. Modularity is thought to enhance evolvability by limiting the interference between the adaptation of different functions (Wagner and Altenberg 1996).

Balancing selection

Balancing selection refers to any type of selection that maintains genetic variance in a population, such as frequency-dependent selection, temporally or spatially fluctuating selection, and overdominance.

intermediate number of generations might select for enhanced evolvability at the population level, and might also lead to the maintenance of genetic variation (Turelli and Barton 2004; Meyers et al. 2005). Larger timescale fluctuations would increasingly be experienced as constant conditions, and would allow the population to become fixed for the optimal phenotypes that are insensitive to mutations ('genetic robustness') (Meyers et al. 2005).

Fluctuating selection might act to facilitate the generation of adaptive genetic variation, and enhance evolvability, by selecting on various aspects of the mutation matrix of a population (Box 1, see sections below) (Meyers et al. 2005; Moxon et al. 2006; Reisinger and Miikkulainen 2006; Jones et al. 2007; Kashtan et al. 2007). Once genetic variance is generated through new mutations, mechanisms that enhance the accumulation and maintenance of this genetic variance would also serve to increase evolutionary potential. Under appropriate conditions, temporally fluctuating selection could promote the accumulation and maintenance of genetic variation, through the action of balancing selection across generations (Gillespie and Turelli 1989; Turelli and Barton 2004).

Moreover, disturbance-prone environments might be an important source of major evolutionary innovations (Rice 1990). Disturbance would alter the shape of the adaptive landscape and promote the generation of diverse unique phenotypes, elevating the evolutionary and invasion potential from such habitats. Populations in disturbed environments would spend much of their time far from a local optimum on an adaptive landscape (see Box 1, Evolutionary Landscape), where drastically altered phenotypes would more likely be adaptive, or at least less deleterious (Rice 1990). Thus, populations subjected to severe environmental shifts would more likely possess phenotypes that could only be accessed (i.e. brought about) by mutations of large effect (Collins et al. 2007). Therefore, more mutations, and especially more mutations of large effect, would be adaptive. Environmental fluctuations could also temporarily relax stabilizing selection around local adaptive peaks and alter relative peak heights, thereby facilitating peak shifts (Whitlock 1997). Such effects might explain a trend observed in marine habitats, where speciation events in the disturbance-prone nearshore environment result more frequently in new families and orders, even though speciation rates are higher offshore (Jablonski et al. 1983; Sepkoski and Miller 1985).

The evolution of enhanced evolvability would enable invasive populations to more readily undergo niche evolution. Niche evolution during biological invasions might be fairly common, given the mounting evidence of phenotypic evolution following invasions (Huey et al. 2000; Lee et al. 2003, 2007; Müller-Schärer et al. 2004; Bossdorf et al. 2005; Donohue et al. 2005; Gilchrist and Lee 2007). Such niche evolution could involve both new mutations as well as adaptation from standing genetic variance. Theoretical studies indicate that standing additive genetic variance (V_A) within source populations limits colonization into novel stressful habitats (Gomulkiewicz et al. 1999; Boulding and Hay 2001; Holt et al. 2003). For example, selection on standing genetic variance for osmotic tolerance appears to underlie the evolution of freshwater tolerance in the copepod *E. affinis* (Lee et al. 2007).

Additional theoretical studies, greater integration across theoretical studies, and integration between theoretical and empirical results would deepen our understanding of the effects of fluctuating selection on evolvability. In addition, it appears that theoretical simulations have not examined the simultaneous effects of fluctuating selection on the mutation matrix and on standing genetic variance. The sections below discuss the diverse ways in which disturbance or fluctuating environments might impact the response of populations to novel environments.

Generalists: selection for disturbance-adapted traits, including organismal flexibility

Disturbance occurring on rapid time scales would tend to select for generalist organisms with enhanced invasive potential. Such organisms could arise in several ways, including (i) selection for life history and demographic traits that facilitate escape from harsh conditions or promote rapid population growth, (ii) selection for broad tolerance or phenotypic plasticity, and (iii) selection for genetic architectures that prevent evolutionary decay of functions needed in alternative environments.

Disturbance might select for particular characteristics that are favorable for colonizing novel habitats, such as those that promote rapid population growth and population persistence. Disturbances often cause local extinctions, producing areas with high resource availability and low competition. Under such conditions, organisms with the highest population growth rate would most effectively exploit the high resource levels. Thus, selection would favor life-history strategies that would promote rapid population growth, such as high specific growth rate, early maturation, high fecundity and selfing (Stearns 1992; Dillon 2000; Gelembiuk et al. 2006; Hintz et al. 2006; Pasiecznik et al. 2006; Feng et al. 2007). Environments with frequent local extinctions would select for life-history traits that would promote population persistence, such as diapause (e.g. resting eggs), seed banks and high dispersal (Cohen 1966; Metz *et al.*, 1983; Levin *et al.*, 1984; Mahdjoub and Menu 2008). Resting stages could increase transport opportunities and accelerate spread during invasion of new disturbance-prone environments,

as diapaused eggs would be more resistant to biocide flushing of ballast tanks (Gray et al. 2006) and digestion in bird and fish guts (Conway et al. 1994). Upon introductions, populations with rapid growth and high dispersal would tend to obtain high biomass, spread rapidly and have detrimental ecosystem impacts. For example, the highly invasive zebra mussel *D. polymorpha*, which originates from the unstable Ponto-Caspian basin, has high fecundity (Sprung 1991) and rapid maturation relative to other bivalve species, such as the unionid mussels that they are often driving to local extinctions (Mackie 1991).

Populations of the same taxon, but from habitats of differing levels of disturbance, could differ in levels of disturbance-adaptedness. For example, genomes of the cyanobacteria *Synechococcus* sp. from differing habitat types exhibited marked differences, consistent with differences in adaptation to disturbance (Palenik et al. 2006). The genome of *Synechococcus* sp. from the dynamic coastal environment showed an almost a twofold increase in the number of sensor and response-regulator genes, relative to the genome from more stable open-ocean environments, reflecting a greater need to respond to changing environmental conditions. Such mechanisms for sensing rapidly changing conditions might facilitate colonization into novel habitats.

A diverse set of theoretical models predicts that rapidly fluctuating environments would select for populations with generalist strategies (Gillespie 1974; Kawecki 2000; Meyers and Bull 2002; Travis and Travis 2002; Ketola et al. 2004; Turelli and Barton 2004). Such rapid fluctuations might select for Baker's 'General Purpose Genotypes', which are often successful as invasive weeds (Baker 1965). Under a model where fluctuations were shorter relative to generation time, selection favored greater physiological tolerance or plasticity (Turelli and Barton 2004). In another model where fluctuations were slightly longer, occurring at the timescale of a generation, genetic canalization was favored, because a response to selection at one generation might be maladaptive at the next (Kawecki 2000). A theoretical model examining the effects of mutations on phenotypes predicted that rapid fluctuations (i.e. every few generations or shorter) would select for 'organismal flexibility' (Meyers et al. 2005). Organisms favored under these conditions would have genotypes of intermediate fitness that could tolerate diverse conditions, but none exceptionally well (Meyers et al. 2005). Organismal flexibility would allow populations to colonize a range of environments and might involve concurrent genetic canalization (Box 1).

Based on the studies above, types of generalist strategies used by organisms in rapidly fluctuating environments might include broad physiological tolerance, short-term plasticity or developmental plasticity. These properties would evolve under fluctuations of different timescales. Broad tolerance would evolve under the most rapid fluctuations, while developmental plasticity would evolve under fluctuations at the timescale of a generation.

Broad physiological tolerance might arise from the selection for enzymes that could function over broad conditions (O'Loughlin et al. 2006) or increased expression of heat shock proteins (HSP) and other chaperones that could buffer against physiological stress and developmental decanalization (Feder and Krebs 1998; Rutherford and Lindquist 1998; Bettencourt and Feder 2001; Ketola et al. 2004). For example, lines of the ciliated protist *Tetrahymena thermophila* that were reared under the most rapidly fluctuating temperatures experienced the greatest evolutionary increases in *Hsp90* expression (Ketola et al. 2004).

Under rapid environmental fluctuations, occurring within a generation, short-term plasticity would allow organisms to respond to instantaneous changes in the environment, as the response is generally reversible. Short-term morphological, physiological or behavioral plasticity has been found to facilitate invasions into novel environments (Sexton et al. 2002; Sol et al. 2002, 2005; Yeh and Price 2004). For example, bird species with relatively larger brains and a high frequency of foraging innovations in their native ranges showed higher probability of invasive success into novel environments (Sol et al. 2002, 2005). However, some theoretical studies have found that specialists could still evolve under within-generation fluctuations, given appropriate circumstances (Gilchrist 1995, 2000). Specifically, this would require windows of time where the specialist could excel, and also the ability to persist under unfavorable conditions without severe detrimental consequences.

Theoretical results show that developmental plasticity is favored when rates of fluctuations are at the timescale of a generation (Meyers and Bull 2002). The stability within a generation would allow the environment experienced at the early stages of a developing organism to serve as a good predictor of future environmental conditions that the organism would experience (Meyers and Bull 2002). As developmental plasticity arises from gene expression during development, it is generally not reversible, particularly in animals, and presents an unfavorable strategy under rapid fluctuations within a generation. Developmental plasticity is often a strategy used for plants invading into novel environments (Weinig 2000; Parker et al. 2003; Chun et al. 2007).

In general, as stated above, frequent fluctuations and disturbance would tend to select for generalist organisms that are robust to changing environmental conditions. This type of adaptation has complex implications for the

future evolution of these organisms. Such robust generalists would initially evolve more slowly upon introduction into a new habitat, because they would initially experience reduced selection pressure (Wright 1931; Ancel 2000) and might be canalized to maintain their original phenotype (Kawecki 2000). However, in their native habitat, robust generalists would also have accumulated cryptic genetic variation, i.e. nearly neutral genetic variation masked by the organism's robustness (Gibson and Dworkin 2004). Under novel conditions, selection of increased intensity or duration would tend to lead to an accelerating selection response (Rice 1998; Kawecki 2000), with decanalization of robust phenotypes. Theoretical results suggest that cryptic genetic variation might actually be enriched for adaptive variants (Masel 2006) and could contribute to the ultimate adaptive response (Kim 2007). In addition, upon invasion into a new habitat, robust organisms might be better able to accept new beneficial mutations, as the phenotypic changes upon new mutations would less likely lead to developmental/physiological catastrophe. A similar principal has been illustrated in protein evolution, whereby increased protein stability facilitates the evolution of new functions (Bloom et al. 2006), as new mutations are less likely to denature or produce destructive conformational changes in a stable protein.

In addition, fluctuating environments could lead to the maintenance of generalist phenotypes by selecting for an integrated genetic architecture, preserving functions and genes that are only intermittently advantageous (Li and Wilke 2004). For example, an overlap of genetic instructions required for different functions could prevent the loss of unrewarded functions (Ostrowski et al. 2007). Given such a genetic architecture, a mutation that is deleterious to a function that is currently rewarded would also likely be deleterious to a function that is not currently rewarded. Selection for such an integrated genetic architecture has been observed in simulations using digital organisms in a persistently fluctuating environment (Li and Wilke 2004). By selecting for such an architecture, fluctuations of intermediate frequency maintained intermittently unrewarded functions, preserving the generalist phenotype (Li and Wilke 2004).

As anthropogenic disturbance becomes increasingly widespread, much more territory is now available for invasion by disturbance-adapted species. Possession of disturbance-adapted traits would facilitate invasions into anthropogenically altered environments (agriculture, reservoirs, construction, etc.). Thus, invasive populations that originate from habitats characterized by disturbance will increasingly have greater opportunities to invade correspondingly disturbed habitats (Weinig 2000; Clements et al. 2004; Havel et al. 2005).

Evolvability 1: generation of adaptive variants

The term 'evolvability' has various meanings and definitions, partly depending on the subdiscipline within evolutionary biology (Pigliucci 2008). Wagner and Altenberg (1996) define evolvability as the ability of genomes within a population to produce adaptive variants, such that the population could respond to selection. In their definition, they focus on the generation of genetic substrate available for selection through mutational variability and recombination. Alternatively, evolvability is defined in terms of the ability of a population to respond to selection due to its standing genetic variance, as quantified by the genetic coefficient of variation ($CV_A = 100\sqrt{V_A}/\bar{X}$, where V_A is the additive genetic variation and $\bar{X}$ is the trait mean) (Houle 1992). Evolvability is a trait that is under indirect selection, as it does not improve the fitness of a population immediately, but tends to be beneficial in future environments (Reisinger and Miikkulainen 2006; Jones et al. 2007).

The extent to which selection molds evolvability, and the role of such adaptive changes in driving large-scale patterns, is still poorly understood and controversial. For example, it has been argued that selection for evolvability could occur only through group selection (Lynch 2007). However, numerous theoretical studies have shown that individual-level selection is sufficient to promote evolvability (Leigh 1970; Gillespie 1981; Ishii et al. 1989; Taddei et al. 1997; Rice 1998; Travis and Travis 2002; Hadany and Beker 2003; Pepper 2003; Tanaka et al. 2003; Toussaint 2003; Earl and Deem 2004; Masel 2005; Meyers et al. 2005; Reisinger and Miikkulainen 2006; Jones et al. 2007; Kashtan et al. 2007; Draghi and Wagner 2008). It has also been argued that there is no evidence that differences between organisms in variety-generating properties (e.g. mutation or recombination rate) are due to selection on these properties (Lynch 2007). Indeed, experiments using bacteria clearly show that environmental shifts could successfully select for constitutively elevated mutation rates in bacteria (mutator strains, see sections below) (Sniegowski et al. 1997; Giraud et al. 2001), in accordance with theoretical predictions. Refer to Box 2 for a more expanded discussion on some of the critiques of the capacity of natural selection to promote evolvability.

Evolvability according to Wagner and Altenberg (1996) refers to the ability to produce 'adaptive variants', which could be generated by (i) mutation or (ii) genetic exchange (e.g. recombination). Both of these mechanisms could serve as potential targets of selection (e.g. via fluctuating selection), and could also be altered as a byproduct of stress in disturbance-prone environments. In the next two sections, we discuss how fluctuating conditions or stress could promote evolvability by acting on aspects of genetic exchange and on the mutation matrix.

Journal compilation © 2008 Blackwell Publishing Ltd **1** (2008) 427–448

Box 2. Discussion of critiques of evolvability

It has been argued that the selection for evolvability can only occur through group selection (Lynch 2007). This leads to a common objection that group selection would typically tend to be a much weaker force than individual-level selection. However, it is worth recognizing that (1) theory indicates that group selection can be an important evolutionary force for particular types of traits (e.g. complex characters) across a biologically plausible parameter range (Rice 1995; Pepper 2000; Wilson and Wilson 2007) and (2) numerous theoretical studies have shown that individual-level selection is sufficient to promote evolvability (Leigh 1970; Gillespie 1981; Ishii et al. 1989; Taddei et al. 1997; Rice 1998; Travis and Travis 2002; Hadany and Beker 2003; Pepper 2003; Tanaka et al. 2003; Toussaint 2003; Earl and Deem 2004; Masel 2005; Meyers et al. 2005; Reisinger and Miikkulainen 2006; Jones et al. 2007; Kashtan et al. 2007; Draghi and Wagner 2008). The source of conceptual confusion (in the perceived requirement for group selection) may lie in the fact that evolvability, such as sexual dioecy or bet hedging, is a trait of populations, as individuals do not evolve. But this semantic property does not imply that selection could only promote evolvability by selecting among groups (e.g. demes or clades).

The following example illustrates how individual-level selection could act on evolvability. Consider a trait and an accelerating fitness function, for which the benefit of deviating from the population mean in the beneficial direction exceeds the cost of deviating in the opposite, detrimental direction. Further consider a modifier allele that on average has no main effect, but that increases variance in the trait (e.g. through epistatic interactions or by increasing mutation rate at the trait). Such an allele could increase in frequency, as an individual bearing this allele, and the progeny of such an individual, would on average have higher fitness (Layzer 1980; Rice 1998). Thus, selection for increased individual-level fitness would have the effect of increasing evolvability, without a need for selection among groups.

Although recombination would tend to dissociate such a modifier from the beneficial genotype it helped produce (Leigh 1970; Partridge and Barton 2000; Sniegowski and Murphy 2006), this would reduce the selective force favoring evolvability but not entirely eliminate it (Gillespie 1981; Johnson 1999; Tenaillon et al. 2000; Hadany and Beker 2003; Masel and Bergman 2003; Jones et al. 2007; Draghi and Wagner 2008). Furthermore, certain types of evolvability modifiers could not be readily decoupled by recombination. For example, in bacterial contingency loci, genes that control the trait under selection can readily mutate between discrete states (Zieg et al. 1977; Kearns et al. 2004; Martin et al. 2005; Moxon et al. 2006). Essentially, local mutation modifiers (e.g. sequence repeats prone to slippage) are embedded within such genes. Also, a modifier that increases evolvability through a purely epistatic interaction (e.g. increasing phenotypic variance by increasing sensitivity to allelic substitutions at a second locus) would resist being dissociated by recombination, as selection would favor preservation of a beneficial allelic combination at the loci (Draghi and Wagner 2008).

It has also been argued that there is no evidence that differences between organisms in variety-generating properties (e.g. mutation or recombination rate) are due to selection on these properties (Lynch 2007). Under this line of reasoning, all differences in variety-generating properties might merely be incidental byproducts of other physical properties. However, there is no reason that variety-generating properties should not respond to selection, just as any other trait, and different variety-generating properties would be optimal under different environmental conditions. Indeed, experiments using bacteria clearly show that environmental shifts can successfully select for constitutively elevated mutation rates in bacteria (mutator strains) (Sniegowski et al. 1997; Giraud et al. 2001), in accordance with theoretical predictions.

The arguments delineated in this perspective support specific, circumscribed claims regarding evolvability. They do not imply that the selection for evolvability is responsible for organismal or genomic complexity, or that complex organisms are most adaptable. There are reasons to believe that high organismal complexity can act as a drag on adaptation (Fisher 1930; Orr 2000a), and that selection for evolvability may favor compact genomes (Toussaint 2005). Furthermore, although evolution in a disturbance-prone environment might increase evolvability along all phenotypic dimensions (e.g. by increasing mutation rates across the genome), it should predominantly tend to increase evolvability along specific phenotypic dimensions that align with long-term fluctuations in the environment (Altenberg 2005). For example, salinity tolerance might become more evolvable for Ponto-Caspian species subjected to long-term fluctuations in salinity. In contrast, mechanisms that globally increase evolvability would be more likely to have high associated costs (e.g. a global increase in mutation rates would lead to an increase in deleterious mutations). In addition, it is worth noting that empirical data from experiments (using biological and digital organisms) supports the position that environmental shifts and fluctuation could increase evolvability (Sniegowski et al. 1997; Earl and Deem 2004; Meyers et al. 2005; Reisinger and Miikkulainen 2006; Kashtan et al. 2007; Draghi and Wagner 2008). Therefore, consideration of evolvability might be relevant for studies of invasive species, regardless of whether the increases occur as a product of direct selection for evolvability or as a byproduct of other forces.

Evolution of genetic exchange

Genetic exchange can create new variants by combining genetic material from different individuals within a species (sex) or from different species (horizontal gene transfer). Mechanisms that increase the rate of genetic exchange could be selected for in a changing environment, as genetic exchange could accelerate adaptation to new environmental conditions (Otto and Barton 1997). For example, recombination could increase the rate of adaptation by bringing together beneficial mutations from different lineages and by separating beneficial mutations

from linked deleterious mutations (Fisher 1930; Muller 1932; Crow and Kimura 1965; Cooper 2007). Selecting for the capacity to bring together beneficial mutations, thereby reducing competition between lineages with different beneficial mutations and accelerating adaptation, actually constitutes one of the primary hypothesized mechanisms for the origin and maintenance of sex (the Fisher–Muller hypothesis) (Fisher 1930; Muller 1932).

Evolution could alter rates of genetic exchange by acting on a number of different mechanisms. First of all, recombination rates are under heritable control (Coop and Przeworski 2007), and can also show a plastic increase in response to environmental stress (Belyaev and Borodin 1982; Tracey and Dempsey 1982; Parsons 1988). Domesticated plants show increased rates of recombination relative to their wild progenitors (Ross-Ibarra 2004). Existing data support the hypothesis that recent intense selection pressure associated with domestication indirectly selected for this increase in recombination (Ross-Ibarra 2004). Second, many organisms can reproduce both sexually and asexually, with genetic and environmental inputs determining the choice of reproductive mode (Bell 1982; Bernstein and Johns 1989; West et al. 2001; Eads et al. 2008). Finally, many organisms (especially microbes) can take up and incorporate foreign DNA. In bacteria, the capacity to take up foreign DNA from the environment is referred to as competence. This typically involves dedicated machinery and occurs in response to specific environmental cues. For example, in the waterborne bacteria *Vibrio cholerae* competence is induced by chitin (Meibom et al. 2005; Miller et al. 2007). Thus, integration of foreign DNA would preferentially occur when *V. cholerae* is associated with copepods or other crustacean hosts, a niche environment in which *V. cholerae* would be in close proximity to a high density of other microbes. Interestingly, metagenomic analysis of microbes in the human gut (a prototypical disturbance-prone but resource-rich environment) revealed over-representation of gene families involved in horizontal gene transfer (Kurokawa et al. 2007).

There are potential tradeoffs between increased versus reduced recombination in invasive populations. Asexual reproduction could double the population growth rate, as the fitness cost of males is removed. In addition, asexually reproducing founders would have reproductive assurance, diminishing allee effects and facilitating colonization of new sites. In addition, organisms that reproduce sexually could suffer inbreeding depression during founder events, while asexually reproducing organisms would not (Haag and Ebert 2004). Indeed, many of the most notorious invaders are asexual (Lyman and Ellstrand 1984; Raybould et al. 1991; Poulin et al. 2005). However, as discussed above, sexual reproduction could facilitate adaptation and long-term invasion potential. A possible example of this involves two invasive grass species in the genus *Cortaderia* (Lambrinos 2001). Although morphologically similar, the species *Cortaderia selloana* reproduces sexually while another, *Cortaderia jubata*, reproduces asexually. The invasiveness of the sexually reproducing species appears to have increased over time (and populations have experienced directional morphological change), while the invasiveness of the asexually reproducing species has remained relatively constant. There is also empirical evidence that biological control can be achieved more readily in asexually reproducing than in sexually reproducing weeds, presumably because of reduced genetic diversity and the capacity to adapt in asexual species (Burdon and Marshall 1981).

Evolution of the mutation matrix

Mutations are the ultimate source of all genetic variation. The contribution of spontaneous mutations to the variability of a quantitative trait can be quantified as the mutational variance (V_M), or the new genetic variance arising in one generation for that trait (Clayton and Robertson 1955; Wagner and Altenberg 1996). Such a property is referred to as the 'variability' of the trait, as opposed to its observable standing variation (Houle et al. 1996; Wagner and Altenberg 1996). Studies on model systems suggest that new mutations could make substantial contributions to the long-term selection response of quantitative traits (López and López-Fanjul 1993; Mackay et al. 1994; Keightley 1998; Azevedo et al. 2002). The amount of mutational variance that is generated for particular traits is an inherent property of the organism, and depends on the number of genes involved in the trait, the phenotypic effect of mutations at those genes and the spontaneous genomic mutation rates (Houle 1998). The mutational variances for traits and the covariances between the traits can be depicted as the mutation matrix (M-matrix, Box 1).

Fluctuating environments or environmental stress could act to facilitate the generation of novel genetic variation by acting on various aspects of the mutation matrix. First of all, stressful conditions (Miller 1998; Bjedov et al. 2003; Foster 2005) and fluctuating selection (Taddei et al. 1997; André and Godelle 2006; Denamur and Matic 2006) could increase global mutation rates. Secondly, fluctuating selection could increase mutational variances of particular traits (V_M), either by increasing mutation rates at loci underlying those traits (Jansen and Stumpf 2005) or by increasing sensitivity of the traits to mutations ('genetic potential') (Meyers et al. 2005). Such increases in mutational variance could then contribute to additive genetic variance (V_A), upon which selection

Journal compilation © 2008 Blackwell Publishing Ltd **1** (2008) 427–448

could act. Thirdly, fluctuating selection might alter the mutational covariance structure to increase modularity and the potential speed of evolution (Kashtan and Alon 2005; Reisinger and Miikkulainen 2006).

Two forces, recombination and accumulation of deleterious mutations, would tend to act against the selection for globally elevated mutation rates. Therefore, global constitutive hypermutation might be disfavored relative to local hypermutation or facultative hypermutation. Local hypermutation might in some cases alleviate the problem of recombination, as the locus affecting mutation rate might be tightly linked to its mutational target (preventing dissociation via recombination). Transient facultative hypermutation, which might be induced in response to environmental conditions, might be favored as it would reduce mutational load.

Differences among populations, clades or species in mutational variances or covariances for critical traits might in some cases account for differences in their potential to evolve during range expansions. Differences in mutational variance have been found among strains of *Caenorhabditis elegans* (Baer et al. 2005). However, inter-population comparisons of mutational variances of traits do not exist for most species. The three subsections below outline how selection might act on various aspects of the mutation matrix.

a) Increases in global mutation rate

Both empirical data (Sniegowski et al. 1997; Giraud et al. 2001; Denamur and Matic 2006) and theoretical studies (Leigh 1970; Gillespie 1981; Taddei et al. 1997; Johnson 1999; Tenaillon et al. 2000; Tanaka et al. 2003; André and Godelle 2006; Palmer and Lipsitch 2006) indicate that disturbance could select for elevated global mutation rates. Under conditions where adaptation is limited by mutation rates, such as during environmental change, new beneficial mutations would facilitate adaptation to changing conditions. Stable environments, on the other hand, would select for low rates of mutation, as most mutations are deleterious (Kimura 1967). Three primary forces contribute to selection pressure on mutation rate: (i) negative effects of deleterious mutations, (ii) positive effects of beneficial mutations and (iii) costs associated with high replication fidelity (Dawson 1998; Drake et al. 1998; Johnson 1999; André and Godelle 2006).

In addition, the level of recombination is also critical for mutation rate evolution (see Box 2). The reason is that mutation rate is only selected on indirectly, and recombination affects the capacity of indirect selection to act on mutation rate. Under low levels of recombination, an allele that confers an elevated mutation rate might more readily hitchhike to fixation with a linked beneficial allele (which was brought about by the elevated mutation rate). One implication is that selection could more readily favor high mutation rate in asexual populations (see Box 2).

In bacteria, changing environmental conditions have been found to favor bacterial strains with constitutively elevated mutation rates ('mutators') (Sniegowski et al. 1997; Miller 1998; Giraud et al. 2001; Shaver and Sniegowski 2003; Matic et al. 2004; Maciá et al. 2005; Denamur and Matic 2006). Such strains tend to have deficiencies in genetic fidelity functions, such as mutational inactivation of the mismatch repair system (Miller 1998; Shaver and Sniegowski 2003; Denamur and Matic 2006). Most mutator strains have been isolated from pathogenic bacteria, which are exposed to changing stressful environments due to host defenses and antibiotic treatments (Maciá et al. 2005; Denamur and Matic 2006).

The long-term evolutionary importance of bacterial mutator strains is still under debate. Although the fitness increase conferred by mutator alleles after an environmental shift is often sufficient to drive fixation in populations, this fitness increase is often relatively small (Sniegowski et al. 2000; Shaver et al. 2002). Deleterious alleles would also accumulate, diminishing fitness. Moreover, an increase in the deleterious mutation rate in mutators could cause the loss of functions that are not essential at present, but might be required in future environments (de Visser 2002). Yet, in an ever-changing environment, mutator strains might continue to accrue a fitness advantage. In some cases, back mutation of the mutator allele might allow reversion to wild-type mutation rates, such that deleterious alleles would not continue to accumulate indefinitely. For example, in *Escherichia coli*, global hypermutation is often caused by potentially reversible changes in the number of copies of a six base repeat located within the mismatch repair gene *mutL* (Shaver and Sniegowski 2003). In addition, recombination between mutator and wild-type strains could restore functions lost to deleterious mutations.

Mutator strains can exhibit a dramatic advantage when facing multiple environmental challenges. For example, among *Pseudomonas aeruginosa* strains isolated from chronic lung infections, all strains resistant to multiple antibiotics and most of the strains resistant to at least one antibiotic were hypermutable (Maciá et al. 2005). Construction of *P. aeruginosa* mutator strains *in vitro*, by deletion of the *mutS* gene, resulted in the development of resistance within 24–36 h against all anti-pseudomonal antibiotics tested (Oliver et al. 2004). An elevated but intermediate mutation rate appears to be associated with resistance to the greatest number of antibiotics (Denamur et al. 2005). Intermediate mutation frequencies might be most optimal because highly elevated mutation rates would increase the burden of deleterious mutations. In

general, theoretical studies indicate that intermediate levels of mutation are most favorable for adaptation (Orr 2000b).

Bacterial mutator strains can also show a large advantage when colonizing novel environments. In one experiment, mice, which represent a novel environment, were simultaneously inoculated with two *E. coli* strains that differed only in mutation rate (Giraud et al. 2001). The mutator strain showed a large short-term competitive advantage, although it was ultimately outperformed by the wild-type strain. In the first 9 days postinoculation, the ratio of mutators to nonmutators rose 800-fold. Moreover, mice inoculated only with mutators showed much larger *E. coli* population sizes in the first 2 weeks after inoculation than mice inoculated with the wild-type strain (Giraud et al. 2001). These results might have applications for understanding the role of high mutation rate in promoting the adaptation and rapid population growth of destructive invaders.

Theoretical studies have provided insights into conditions required for increases in global mutation rates (Leigh 1970, 1973; Gillespie 1981; Taddei et al. 1997; Johnson 1999; Tenaillon et al. 2000; Tanaka et al. 2003; André and Godelle 2006; Palmer and Lipsitch 2006). Such studies have found that fixation of alleles for elevated mutation rate might largely be restricted to asexual lineages (Leigh 1970, 1973; Johnson 1999; Tenaillon et al. 2000). In addition, for fluctuating environments, fluctuations of intermediate frequency appear most favorable for elevating mutation rate (Travis and Travis 2002; Palmer and Lipsitch 2006). However, indirect selection for beneficial mutations could still substantially increase the mutation rate in sexual organisms if the replication accuracy cost function has low slope (i.e. the physiological cost of increasing replication accuracy to bring about a unit reduction in mutation rate is low) (Johnson 1999).

Moreover, in asexual species, recent theoretical results suggest that mutation rate could not evolve to a stable optimum, but would be inherently unstable (André and Godelle 2006). Given only alleles with a small effect on mutation rate, the forces that affect mutation rate evolution (i.e. deleterious mutation, beneficial mutation and accuracy cost) would push the mutation rate of a population toward a convergence stable state. However, if alleles could arise that produce large changes in mutation rate, adaptation would destabilize the mutation rate, allowing large-effect mutators to invade during periods requiring adaptation to new environmental conditions. Thus, under individual-level selection, mutation rate would not stably converge to the intermediate frequency of mutations that would maximize adaptive potential. However, one might expect a higher variance of mutation rates and higher incidence of mutator alleles in fluctuating environments, potentially leading to increases in adaptive potential.

Changes in mutation rate could also occur in a transient and plastic manner, rather than being constitutively expressed. Transient increases in mutation rate could occur through a variety of mechanisms (Foster 2005). For example, under conditions of stress-induced DNA damage, the SOS repair response system in bacteria prioritizes rapid DNA repair over accuracy, resulting in elevated rates of mutations (Matic et al. 2004). It is not clear whether such transient increases in mutation rate are the consequence of selection for increased mutation, or simply a by-product of stress. It would be useful to model or experimentally test whether such transient hypermutation facilitates adaptation to the stressful conditions.

In addition to changes in global mutation rate, global genetic variance could also be increased by evolutionary 'capacitance'. Evolutionary capacitance refers to a mechanism whereby organisms could accumulate genetic variation that has no phenotypic effect under one set of circumstances (cryptic genetic variation), but where this genetic variation could be exposed and subjected to natural selection under altered circumstances. Such exposure could either occur in response to environmental stress or stochastically (bet hedging). Evolutionary capacitance is a mechanism that could itself be selected for and would allow for rapid phenotypic change in a population and rapid adaptation to new environmental conditions.

One putative case of stress-responsive capacitance involves *heat shock protein 90* (*Hsp90*) (Rutherford and Lindquist 1998; Queitsch et al. 2002). Under stress, the capacity of *Hsp90* to maintain proper protein folding is overloaded (due to an increase in protein denaturation), and *Hsp90* is shunted from roles in maintenance of developmental stability. Cryptic genetic variation that is exposed could then be selected upon, allowing 'genetic assimilation' (Waddington 1953) of beneficial phenotypes that were initially visible only under stress. After such genetic assimilation, the beneficial phenotype is exhibited even in the absence of stress. Thus, *Hsp90* acts as a capacitor, releasing hidden genetic variation under stress, when it might provide a survival advantage. Meanwhile, a putative case of stochastic capacitance involves the yeast prion *PSI+* (Patino et al. 1996; True et al. 2004). This protein sporadically switches between heritable conformations, with one of the conformations permitting partial readthrough of stop codons, thereby exposing cryptic genetic variation that has accumulated in 3′ untranslated regions. Theoretical modeling has shown that fluctuating selection can permit the evolution and maintenance of capacitance mechanisms, at least in asexual populations (and perhaps even in sexual populations) (Masel 2005; King and Masel 2007).

b) Changes in mutational variance of particular traits (diagonals of the M-matrix)

Environmental stress or fluctuations could enhance evolvability by selecting for increases in the mutational variances of important traits (Box 1, diagonal elements of the M-matrix). Such evolutionary changes might arise by either increasing mutation rates at loci underlying the traits (Zieg et al. 1977; Kearns et al. 2004; Wright 2004; Martin et al. 2005; Moxon et al. 2006) or increasing the sensitivity of the traits to mutations ('genetic potential') (Meyers et al. 2005).

Environmental stress (e.g. starvation, osmotic or temperature stress) could directly affect mutation rates of particular traits by inducing stress-directed mutagenesis (Wright 2004; Heidenreich 2007). Stress induces transcription of particular genes, such that those genes become vulnerable to mutations (Heidenreich 2007). For example, if tryptophan were limiting, transcription rates of the *trpA* gene would increase and therefore elevate mutation rates at that particular gene (Wright et al. 2003). In bacteria, transcription could drive supercoiling of DNA strands, which would create secondary stem-loop structures containing nucleotides that are unpaired and thus vulnerable to mutation (Wright 2004).

There is substantial evidence for the evolution of elevated mutation rates at particular loci or traits in response to fluctuating environments (Jansen and Stumpf 2005). Much empirical data from bacteria indicates that fluctuating selection favors hypermutability of traits and rapid reversible shifts between phenotypic states. These shifts frequently correspond to heritable but reversible mutations at specific 'contingency loci' (i.e. hypermutable loci that allow a contingent response to changing environmental circumstances) (Zieg et al. 1977; Kearns et al. 2004; Martin et al. 2005; Moxon et al. 2006). For a wide variety of bacteria, this hypermutability is induced by slippage of simple sequence repeats, resulting in insertions and deletions (Kearns et al. 2004; Martin et al. 2005; Moxon et al. 2006). In other cases, hypermutability is induced by inversions of specific DNA segments (Zieg et al. 1977). Under fluctuating selection across generations, stochastic switching resulting from hypermutability could be favored over short-term phenotypic response to the environment (plasticity) (Kussell and Leibler 2005).

Theoretical models predict the evolution of elevated mutation rates at particular loci under temporally fluctuating selection (Ishii et al. 1989; Travis and Travis 2002), particularly at intermediate levels of fluctuations (Travis and Travis 2002). This class of theoretical models (Ishii et al. 1989; Travis and Travis 2002) assumes that alleles mutate back and forth between defined states that are most beneficial in either of two different environments (i.e. high reversion rates, with an absence of unconditionally deleterious alleles). Thus, the structure of these models closely matches the mechanisms observed for switch-like contingency loci, and might be less applicable to mutational processes that are less constrained. Alternative mutational processes (e.g. random point mutations, random indels, etc.) would produce a high proportion of unconditionally deleterious alleles and reversion rates would be low. In addition, it is noteworthy that one of these models (Ishii et al. 1989) showed that fluctuating conditions could select for a modifier that increased mutation rate at a target locus even if the mutation rate modifier was unlinked to the target locus. This mechanism would allow for selection on evolvability even in the presence of recombination.

Alternatively, under fluctuating selection across generations, mutational variance might increase for particular phenotypes due to increases in 'genetic potential', or heightened sensitivity of the phenotype to mutations (Meyers et al. 2005). Such increases in mutational variance would occur without increases in mutation rate. Genetic potential increases when selection favors the alleles that would more likely code for altered phenotypes upon mutations, facilitating switching between phenotypes (Meyers et al. 2005). In a theoretical model of codon substitution and amino acid evolution, populations evolved genetic potential when the environment fluctuated at a rate of approximately every 10–10^6 generations, with a mutation rate of 10^{-5} (Meyers et al. 2005). With increasing mutation rate, such as 10^{-2}, genetic potential evolved with more rapid fluctuations, such as approximately every 1–10^3 generations (Meyers et al. 2005). A question remains on the effect that overlapping generations would have on the evolution of genetic potential, and whether switching between genetically robust states would become more common.

There are circumstances under which fluctuating selection could actually select for decreased evolvability (increased canalization) (Kawecki 2000). However, whereas Gaussian selection with a stable optimum (i.e. classical stabilizing selection) would generally select for increased canalization (Schmalhausen 1949; Wagner et al. 1997; Rice 1998; Kawecki 2000) (but see paragraph below), Gaussian selection with a fluctuating optimum would only select for canalization under quite restricted conditions (Kawecki 2000). Specifically, selection for canalization would require shifts in the direction of selection on the order of every one to eight generations and would also require a low amplitude of oscillation (small fluctuations) (Kawecki 2000). Canalization is favored for shifts of this frequency because a selection response in one generation could prove disadvantageous in the next generation. A linear rather than Gaussian fitness function would not impose

the requirement of low oscillatory amplitude (relaxing the conditions for canalizing selection), but such a fitness function also seems less realistic. Slower fluctuations, or greater oscillatory amplitude, would instead select for increased evolvability.

The evolution of evolvability in a trait under fluctuating selection is governed by epistatic interactions between loci. However, the effects of epistasis in this context are poorly understood. Epistasis is important to consider, because evolvability could evolve whenever a phenotype is the product of two or more heritable factors (e.g. gene products) that interact in a nonlinear fashion (Rice 1998, 2002). Such interaction creates curvature in the phenotypic landscape, with areas of steeper slope corresponding to increased evolvability. The effects of epistasis on the evolution of evolvability under simple directional selection have recently been studied using multilinear epistatic models (Carter et al. 2005; Hansen et al. 2006). It was found that with sustained directional selection, evolvability could increase or decrease depending on the direction of epistatic interactions. Negative epistasis, in which genetic substitutions diminish each other's effects in the direction of selection, could be quite constraining. Asymptotically, on long timescales, an accelerating response to selection was found to occur regardless of the initial epistatic architecture (although assumptions underlying multilinear epistatic models are dubious on very long timescales).

Fluctuating conditions might facilitate trait optimization in the presence of epistasis, because changes in the selection gradient could dislodge populations that would otherwise be trapped by local constraints (e.g. local peaks or plateaus) under purely directional selection (Kashtan et al. 2007). However, a great deal of additional theoretical work will be required to fully understand the manner and degree to which different conditions could select for evolvability or canalization in the presence of epistatic interactions. For example, some theoretical studies yield unexpected results. Contrary to expectation, it has recently been revealed that stabilizing selection in the presence of epistatic interaction would frequently not absolutely minimize mutational variance (i.e. would not fully maximize canalization) (Hermisson et al. 2003). This is the case even though these conditions would select for minimized additive genetic variance. This result indicates that the reality of the situation is complex, and much more research is required to determine how epistatic interactions shape the evolution of evolvability (see Hansen 2006).

c) Changes in mutational covariances between traits (off-diagonals of the M-matrix)

Mutational covariances between traits reflect levels of pleiotropic constraints that are imposed on phenotypic effects due to new mutations. Modularity is maximized when mutational covariances between traits are minimal. High modularity between traits is generally thought to increase evolvability, as the traits can evolve independently (Wagner and Altenberg 1996). However, a theoretical study suggests that low but nonzero pleiotropy should maximize evolvability (i.e. nonzero due to a balance between the reduction of mutational variances under low pleiotropy and greater constraint under high pleiotropy) (Hansen 2003).

Moreover, modularity requires a particular form in order to increase evolvability, specifically an alignment between environmental selection gradients and organismal variation in phenotypic space (Altenberg 2005). An appropriate pattern of modularity and integration of traits (e.g. high pleiotropy among head morphology traits, and low pleiotropy between head traits and arm traits) would result in a distribution of new mutants that are better matched to (and better able to exploit) the adaptive landscape. Selection on phenotypic traits indirectly generates such structuring within organisms, as it indirectly selects on genetic and mutational covariances to produce an alignment of the M-matrix, the G-matrix and the adaptive landscape (Reisinger and Miikkulainen 2006; Jones et al. 2007; Toussaint and von Seelen 2007).

Evolutionary simulation studies found that systematically changing fitness functions tend to increase organismal modularity. One theoretical study found that the degree of modularization directly covaries with the frequency of environmental change (Lipson et al. 2002). Likewise, simulations of network evolution (i.e. Alife simulations) resulted in the spontaneous evolution of modularity when the simulations applied fluctuating selection with 'modularly varying goals' (Kashtan and Alon 2005). Modularly varying goals refers to the case of switching between several goals that rely on different combinations of subgoals, with subgoals being analogous to basic biological functions (e.g. a biochemical network motif) (Kashtan and Alon 2005). An empirical study of metabolic network structure in bacteria found that metabolic networks of taxa from more variable environments were significantly more modular than networks of those that evolved under more constant conditions (Parter et al. 2007).

Furthermore, fluctuating selection might greatly accelerate the speed of evolution, mostly as a result of the generation of appropriate modularity or pleiotropic linkages between traits (Reisinger and Miikkulainen 2006; Kashtan et al. 2007). A simulation study using genetic algorithms found that both randomly varying goals and modularly varying goals increased the rate of evolution, with modularly varying goals producing the greatest increases in speed (Kashtan et al. 2007). Moreover, the artificial organisms that evolved under such a selection

Journal compilation © 2008 Blackwell Publishing Ltd **1** (2008) 427–448

regime could quickly adapt between alternate goals (i.e. high genetic potential, with few mutations required to achieve high fitness after each environmental shift) (Kashtan et al. 2007). Similarly, another study using genetic algorithms that allowed indirect selection on pleiotropy found that fluctuating selection could increase evolvability (Reisinger and Miikkulainen 2006). Applying a fitness function that varied over time while retaining certain invariant features in the adaptive landscape (e.g. persistently favoring bilateral symmetry) successfully selected for enhanced evolvability (Reisinger and Miikkulainen 2006). These results suggest that sharply fluctuating natural environments might harbor organisms with disproportionately modular and evolvable structures.

Evolvability 2: maintenance of genetic variation (G-matrix) through balancing selection

Once genetic variation is created through new mutations, mechanisms must exist to maintain the variation within populations, in order for the populations to readily evolve. Temporally fluctuating selection might serve as a means to promote the accumulation and maintenance of genetic variance within source habitats that give rise to invasive populations. Theoretical models indicate that temporally fluctuating selection across generations could promote the maintenance of genetic variance for quantitative traits under appropriate conditions (Gillespie and Turelli 1989; Ellner and Hairston 1994; Ellner and Sasaki 1996; Sasaki and Ellner 1997; Turelli et al. 2001; Bürger and Gimelfarb 2002; Turelli and Barton 2004). In addition, many forms of disturbance (e.g. fires, floods) could also increase spatial heterogeneity, which might further augment the potential for balancing selection (Levene 1953; Hedrick 1998, 2006). This maintenance of variation would affect response to selection and the potential for phenotypic evolution.

Temporally fluctuating selection could maintain genetic variation under particular conditions. Genotype by environment interaction ($G \times E$), and particularly antagonistic pleiotropy between traits across environments, would facilitate the maintenance of genetic variation under fluctuating environments or spatial heterogeneity, by favoring different traits at different times or locations (Gillespie and Turelli 1989; Turelli and Barton 2004). For example, for the copepod *E. affinis*, negative genetic correlations between fresh and saltwater tolerance would mean that seasonal fluctuations in salinity would select for different phenotypes at different seasons (Lee et al. 2003, 2007). Theoretical analyses show that balanced polymorphism could be maintained through fluctuating selection when the geometric mean fitness of the heterozygotes exceeds that of the homozygotes (e.g. marginal overdominance) (Haldane and Jayakar 1963; Turelli 1981). Such conditions protect less-favored alleles against elimination during environmental fluctuations (Levene 1953; Haldane and Jayakar 1963; Wallis 1968; Gillespie and Turelli 1989; Curtsinger et al. 1994; Hedrick 1999; Rand et al. 2002). In addition, in the presence of recurrent mutation, fluctuating selection can increase additive genetic variance under conditions that are much less stringent than those required to maintain protected balanced polymorphisms (Bürger and Gimelfarb 2002).

While the requirement for higher geometric mean fitness of heterozygotes might be viewed as quite restrictive (Hedrick 1974), two considerations argue for the potentially high prevalence of balanced polymorphisms maintained through fluctuating selection. First, beneficial reversal of dominance is plausibly a common phenomenon (Gillespie 1998). Beneficial reversal of dominance (Curtsinger et al. 1994; Hedrick 1999) is a form of marginal overdominance in which, hypothetically, freshwater tolerance in the copepod *E. affinis* might be dominant in freshwater environments, while saltwater tolerance might be dominant in saline environments. Such a pattern of dominance would arise when the favored allele in the heterozygote compensates for the lowered function of the less-favored allele in each environment, so that the heterozygote resembles fitness of the favored homozygote (Wright 1929; Kacser and Burns 1981). The relatively high frequency of the less-favored genotype in both saline and freshwater populations of *E. affinis* suggests that this mechanism might be operating in this species (Lee et al. 2003). Secondly, the presence of overlapping generations greatly expands the conditions under which fluctuating selection could protect polymorphism, by preserving genotypes that had been subjected to different selection regimes across generations (Hedrick 1995; Ellner and Sasaki 1996). Many species exhibit extreme generational overlap in the form of dormant stages, such as seeds, spores, or diapause eggs.

A few empirical studies support the theoretical predictions (Hairston et al. 1996; Schemske and Bierzychudek 2001; Kassen 2002). For example, a population of the copepod *Diaptomus sanguineus* exhibits heritable variation in timing of spring diapause. Mean timing of diapause shifts between years in response to fluctuations in selection, with selection favoring early diapause in years of high predatory fish density (Hairston and Dillon 1990). These populations have overlapping generations in the form of a diapause egg bank, where diapause eggs could remain in the sediment for decades (Hairston 1996; Hairston and Kearns 2002). A mechanistic model that incorporated laboratory and field data confirmed that the injection of diapause eggs from past selection regimes

contributes to standing genetic variation (Ellner and Hairston 1994; Ellner et al. 1999). In another example, flower color in the desert annual *Linanthus parryae* is subject to selection due to temporal and spatial variation in rainfall (Schemske and Bierzychudek 2001, 2007). Blue-flowered plants typically have a fitness advantage in years of low spring precipitation, whereas white-flowered plants have a fitness advantage in years of high spring precipitation (Schemske and Bierzychudek 2001). A model using fitness parameters estimated from Schemske and Bierzychudek's (2001) data suggests that the maintenance of flower color polymorphism might be explained by fluctuating selection (Turelli et al. 2001).

Fluctuating conditions in either the source or sink ranges could increase the probability of invasive success into novel environments (Holt et al. 2004, 2005). Adaptation during fluctuations within potential source habitats would cause the source population to periodically more closely resemble the sink habitat. Thus, these conditions would favor the accumulation and maintenance of alleles in the source habitat that would be beneficial in the sink habitat, and facilitate invasions from the source to the sink.

Maintenance of genetic variation across geographic space could also facilitate invasive success by harboring a vast range of phenotypes, some of which might be better matched to the environment being invaded. Increased genetic polymorphism in invasive populations could be achieved through recurrent invasions (Holt et al. 2005), invasions from multiple sources (Kolbe et al. 2004; Lavergne and Molofsky 2007) and hybridization (Ellstrand and Schierenbeck 2000; Rieseberg et al. 2003). Such mechanisms would effectively bring together, into genomes or populations, alleles that have been selected for in different environments.

Testing hypotheses on the evolutionary origins of invasive populations

The goal that we envision is to develop a synthesis regarding the conditions that lead to the evolution of invasive populations. Much more theoretical work is needed, including on the effects of epistasis and pleiotropy. For instance, a key area that requires greater understanding regards the extent to which selection molds evolvability. In addition, more data are required from the native range of invasive populations regarding: (i) specific geographic origins of invasive populations within the native range, (ii) characteristics of disturbance in the native range and (iii) responses of individuals and populations to disturbance.

How do we proceed with testing hypotheses on the impact of disturbance on the potential to invade? Theoretical results could guide us on hypotheses to test, and also the range of parameter values that are plausible. In order to make better model predictions, we would require more detailed information on the environmental conditions within the native range. Within the native habitats of invasive populations, we would need to determine the nature of selection regimes experienced by populations, and quantify levels of disturbance. We would need to determine the variables, both biotic and abiotic, that might impose selection on the populations. In particular, we would need to determine the period, relative to generation time, and magnitude of fluctuations of those environmental variables.

We can, currently, make a few predictions based on first principals. One important prediction is that, as more data become available, the geographic sources of invasive populations will be found disproportionately in disturbed habitats (after accounting for transport opportunity). Native ranges of invasive species are heterogeneous, and not all populations within the native range necessarily have the potential to invade (Lee 1999; Tsutsui and Case 2001; Saltonstall 2002; Meusnier et al. 2004; Brown and Idris 2005; Chu et al. 2006; Gelembiuk et al. 2006; May et al. 2006; Caldera et al. 2008; Winkler et al. 2008). Thus, it is important to accurately genotype and identify the actual geographic sources of invasive populations.

Furthermore, it is possible to use genomic data to test hypotheses regarding the impact of fluctuating selection. Specifically, sequence data could be used to estimate the intensity of fluctuating selection, as captured by two parameters corresponding to the strength of selection and fluctuation rate (Mustonen and Lassig 2007). A testable prediction is that invasive populations would have higher parameter estimates (i.e. stronger fluctuating selection) relative to noninvasive populations.

In addition, various hypotheses could be tested regarding specific mechanisms that might play a role in the evolution of invasive populations. For example, performing common-garden reaction norm experiments would reveal the degree of broad tolerance or plasticity of individuals within populations (Lee et al. 2007, 2003). In addition, with the increasing ease of genomic analyses, we could compare genomes of sister taxa from disturbed versus nondisturbed habitats, and those that are invasive versus noninvasive (Palenik et al. 2006). For example, we might expect a greater number of genes to be involved in perceiving and responding to unpredictable conditions (e.g. plasticity) in disturbed habitats.

Another prediction that we have outlined above is that organisms from habitats differing in disturbance might differ in variation generating properties, including recombination, mutational variance and modularity (see section on Evolvability 1: generation of adaptive variants). These properties could be measured using populations or sister taxa from disturbance-prone versus stable habitats, and

also populations that successfully invade versus those that do not, despite transport opportunity. Mutational variances of relevant traits could be determined in haploid organisms or inbred lines of diploid organisms (Mackay et al. 1994; Houle et al. 1996; Houle 1998; Keightley 1998; Azevedo et al. 2002). In addition, the prevalence of mutator strains of bacteria could be measured in different habitat types. The degree of modularity of the genotype–phenotype map could be analyzed by estimating M-matrices (Box 1) of populations from habitats of differing degrees of disturbance.

Finally, more research could combine theory and empirical data to examine the prevalence of balanced polymorphisms maintained by environmental heterogeneity. The analysis of color morph polymorphism in the desert flower *L. parryae* is a paradigmatic example (see previous section) (Schemske and Bierzychudek 2001; Turelli et al. 2001). Hypotheses regarding the maintenance of genetic variance could be tested by quantifying additive genetic variance for critical traits of populations that reside in habitats that vary in the degree of environmental fluctuations (Ellner and Sasaki 1996).

Management and policy implications

Our understanding of factors that contribute to the evolution of invasive populations remains poor (Lee 2002). Our ability to make concrete predictions on the invasive potential of populations would be greatly enhanced by more empirical and quantitative analyses of disturbance in the native ranges. Unfortunately, such information is unavailable for most invasive species. Integrating information on environmental conditions in the native habitats, such as the magnitude and duration of environmental fluctuations, along with physiological and other responses of the native populations would allow us to discern the types of environmental conditions that might give rise to invasive populations (see previous section). Such insights would allow us to focus management and mitigation efforts toward those populations that are likely to successfully tolerate or adapt to novel environments during invasions.

The topic of niche expansions is fundamental to understanding how organisms respond to environmental change, and has far-reaching implications for global climate change and responses to other anthropogenically induced alterations in the environment (Bradshaw and Holzapfel 2006; Chown et al. 2007). The gaps in our understanding on niche evolution are becoming apparent as we attempt to grapple with the problem of invasive species. Our understanding of anthropogenically induced evolutionary changes would greatly benefit from promoting invasion biology into a predictive science, where there is greater integration among theoretical studies, between empirical data and theory, and between ecological and evolutionary models and approaches for studying invasive species.

As a final note regarding disturbance, increasing levels of disturbance created by human activities are likely to promote future invasions. Given their preadaptation to disturbance, many invasive species would be favored in environments altered by anthropogenic activity. The initial invasions into disturbed habitats would allow these invaders to subsequently invade nearby pristine habitats, perhaps following a period of adaptation in the new environment (Havel et al. 2005). With increasing alterations to the environment, we are likely to create a world of invaders, adapted to ongoing disturbance.

Acknowledgments

The authors thank Louis Bernatchez for the invitation to contribute to this issue. Funding for this study was provided by National Science Foundation DEB-0448827 to CE Lee. The authors thank Thomas Hansen and George Gilchrist for insightful comments and suggestions.

References

Altenberg, L. 2005. Modularity in evolution: some low-level questions. In W. Callebaut, and D. Rasskin-Gutman, eds. *Modularity: Understanding the Development and Evolution of Complex Natural Systems*, MIT Press.

Ancel, L. W. 2000. Undermining the Baldwin expediting effect: does phenotypic plasticity accelerate evolution? *Theoretical Population Biology* **58**:307–319.

André, J.-B., and B. Godelle. 2006. The evolution of mutation rate in finite asexual populations. *Genetics* **172**:611–626.

Azevedo, R. B. R., P. D. Keightley, C. Laurén-Määttä, L. L. Vassilieva, M. Lynch, and A. M. Leroi. 2002. Spontaneous mutational variation for body size in *Caenorhabditis elegans*. *Genetics* **162**:755–765.

Baer, C. F., F. Shaw, C. Steding, M. Baurngartner, A. Hawkins, A. Houppert, N. Mason *et al.* 2005. Comparative evolutionary genetics of spontaneous mutations affecting fitness in rhabditid nematodes. *Proceedings of the National Academy of Sciences of the United States of America* **102**:5785–5790.

Baker, H. G. 1965. Characteristics and modes of origin of weeds. In H. G. Baker, and G. L. Stebbins, eds. *The Genetics of Colonizing Species*, pp. 147–168. Academic Press, New York.

Baker, H. G. 1974. The evolution of weeds. *Annual Review of Ecology and Systematics* **5**:1–24.

Bell, G. 1982. *The Masterpiece of Nature: The Evolution and Genetics of Sexuality*. University of California Press, Berkeley.

Belyaev, D. K., and P. M. Borodin. 1982. The influence of stress on variation and its role in evolution. *Biologisches Zentralblatt* **100**:705–714.

Bernstein, C., and V. Johns. 1989. Sexual reproduction as a response to H_2O_2 damage in *Schizosaccharomyces pombe*. *Journal of Bacteriology* **171**:1893–1897.

Bettencourt, B. R., and M. E. Feder. 2001. Hsp70 duplication in the *Drosophila melanogaster* species group: how and when did two become five? *Molecular Biology and Evolution* **18**:1272–1282.

Bjedov, I., O. Tenaillon, B. Gérard, V. Souza, E. Denamur, M. Radman, F. Taddei *et al.* 2003. Stress-induced mutagenesis in bacteria. *Science* **300**:1404–1409.

Bloom, J. D., S. T. Labthavikul, C. R. Otey, and F. H. Arnold. 2006. Protein stability promotes evolvability. *Proceedings of the National Academy of Sciences of the United States of America* **103**:5869–5874.

Bossdorf, O., H. Auge, L. Lafuma, W. E. Rogers, E. Siemann, and D. Prati. 2005. Phenotypic and genetic differentiation between native and introduced plant populations. *Oecologia* **144**:1–11.

Boulding, E. G., and T. Hay. 2001. Genetic and demographic parameters determining population persistence after a discrete change in the environment. *Heredity* **86**:313–324.

Bradshaw, W. E., and C. M. Holzapfel. 2006. Evolutionary response to rapid climate change. *Science* **312**:1477–1478.

Brown, J., and A. Idris. 2005. Genetic differentiation of whitefly *Bemisia tabaci* mitochondrial cytochrome oxidase I, and phylogeographic concordance with the coat protein of the plant virus genus *Begomovirus*. *Annals of the Entomological Society of America* **98**:827–837.

Burdon, J. J., and D. R. Marshall. 1981. Biological control and the reproductive mode of weeds. *Journal of Applied Ecology* **18**:649–658.

Bürger, R., and A. Gimelfarb. 2002. Fluctuating environments and the role of mutation in maintaining quantitative genetic variation. *Genetical Research* **80**:31–46.

Caldera, E. J., K. J. Ross, C. J. DeHeer, and D. D. Shoemaker. 2008. Putative native source of the invasive fire ant *Solenopsis invicta* in the U.S.A. *Biological Invasions* (online early).

Carroll, S. P., H. Dingle, T. R. Famula, and C. W. Fox. 2001. Genetic architecture of adaptive differentiation in evolving host races of the soapberry bug, *Jadera haematoloma*. *Genetica* **112**:257–272.

Carter, A. J. R., J. Hermisson, and T. F. Hansen. 2005. The role of epistatic gene interactions in the response to selection and the evolution of evolvability. *Theoretical and Population Biology* **68**:179–196.

Chown, S. L., S. Slabber, M. A. McGeoch, C. Janion, and H. P. Leinaas. 2007. Phenotypic plasticity mediates climate change responses among invasive and indigenous arthropods. *Proceedings of the Royal Society of London, Series B* **274**:2531–2537.

Chu, D., Y.-J. Zhang, J. K. Brown, B. Cong, B.-Y. Xu, Q.-J. Wu, and G.-R. Zhu. 2006. The introduction of the exotic Q biotype of *Bemisia tabaci* from the Mediterranean region into China on ornamental crops. *Florida Entomologist* **89**:168–174.

Chun, Y. J., M. L. Collyer, K. A. Moloney, and J. D. Nason. 2007. Phenotypic plasticity of native vs. invasive purple loosestrife: a two-state multivariate approach. *Ecology* **88**:1499–1512.

Clayton, G. A., and A. Robertson. 1955. Mutation and quantitative variation. *American Naturalist* **89**:151–159.

Clements, D. R., A. DiTommaso, N. Jordan, B. D. Booth, J. Cardina, D. Doohan, C. L. Mohler *et al.* 2004. Adaptability of plants invading North American cropland. *Agriculture Ecosystems and Environment* **104**:379–398.

Cohen, D. 1966. Optimizing reproduction in a randomly varying environment. *Journal of Theoretical Biology* **12**:119–129.

Collins, S., J. de Meaux, and C. Acquisti. 2007. Adaptive walks toward a moving optimum. *Genetics* **176**:1089–1099.

Conway, D. V. P., I. R. B. McFadzen, and P. R. G. Tranter. 1994. Digestion of copepod eggs by larval turbot *Scophthalmus maximus* and egg viability following gut passage. *Marine Ecology Progress Series* **106**:303–309.

Coop, G., and M. Przeworski. 2007. An evolutionary view of human recombination. *Nature Reviews Genetics* **8**:23–34.

Cooper, T. F. 2007. Recombination speeds adaptation by reducing competition between beneficial mutations in populations of *Escherichia coli*. *PLoS Biology* **5**:e225.

Cristescu, M. E. A., P. D. N. Hebert, J. D. S. Witt, H. J. MacIsaac, and I. A. Grigorovich. 2001. An invasion history for *Cercopagis pengoi* based on mitochondrial gene sequences. *Limnology and Oceanography* **46**:224–229.

Cristescu, M. E. A., J. D. S. Witt, I. A. Grigorovich, P. D. N.Hebert, and H. J. MacIsaac. 2004. Dispersal of the Ponto-Caspian amphipod *Echinogammarus ischnus*: invasion waves from the Pleistocene to the present. *Heredity* **92**:197–203.

Crow, J. F., and M. Kimura. 1965. Evolution in sexual and asexual populations. *American Naturalist* **99**:439–450.

Curtsinger, J. W., P. M. Service, and T. Prout. 1994. Antagonistic pleiotropy, reversal of dominance, and genetic-polymorphism. *American Naturalist* **144**:210–228.

Dawson, K. J. 1998. Evolutionarily stable mutation rates. *Journal of Theoretical Biology* **194**:43–157.

Denamur, E., and I. Matic. 2006. Evolution of mutation rates in bacteria. *Molecular Microbiology* **60**:820–827.

Denamur, E., O. Tenaillon, C. Deschamps, D. Skurnik, E. Ronco, J. L. Gaillard, B. Picard *et al.* 2005. Intermediate mutation frequencies favor evolution of multidrug resistance in *Escherichia coli*. *Genetics* **171**:825–827.

Di Castri, F. 1989. History of biological invasions with special emphasis on the Old World. In J. A. Drake, H. A. Mooney, F. di Castri, R. H. Groves, F. J. Kruger, M. Rejmanek, and M. Williamson, eds. *Biological Invasions: A Global Perspective*, pp. 1–30. John Wiley, Chichester, UK.

Dillon, R. T. 2000. *The Ecology of Freshwater Molluscs*. Cambridge University Press, Cambridge.

Donohue, K., L. Dorn, C. Griffith, E. Kim, A. Aguilera, C. R. Polisetty, and J. Schmitt. 2005. The evolutionary ecology of seed germination of *Arabidopsis thaliana*: variable

natural selection on germination timing. *Evolution* **59**:758–770.

Draghi, J., and G. P. Wagner. 2008. Evolution of evolvability in a developmental model. *Evolution* **62**:301–315.

Drake, J. W., B. Charlesworth, D. Charlesworth, and J. F. Crow. 1998. Rates of spontaneous mutation. *Genetics* **148**:1667–1686.

Eads, B. D., J. Andrews, and J. K. Colbourne. 2008. Ecological genomics in *Daphnia*: stress responses and environmental sex determination. *Heredity* **100**:184–190.

Earl, D. J., and M. W. Deem. 2004. Evolvability is a selectable trait. *Proceedings of the National Academy of Sciences of the United States of America* **101**:11531–11536.

Ellner, S., and N. G. Hairston. 1994. Role of overlapping generations in maintaining genetic variation in a fluctuating environment. *American Naturalist* **143**:403–417.

Ellner, S., and A. Sasaki. 1996. Patterns of genetic polymorphism maintained by fluctuating selection with overlapping generations. *Theoretical Population Biology* **50**:31–65.

Ellner, S. P., N. G. Hairston, C. M. Kearns, and D. Babai. 1999. The roles of fluctuating selection and long-term diapause in microevolution of diapause timing in a freshwater copepod. *Evolution* **53**:111–122.

Ellstrand, N. C., and K. A. Schierenbeck. 2000. Hybridization as a stimulus for the evolution of invasiveness in plants? *Proceedings of the National Academy of Sciences of the United States of America* **97**:7043–7050.

Feder, M. E., and R. A. Krebs. 1998. Natural and genetic engineering of the heat-shock protein Hsp70 in *Drosophila melanogaster*: consequences for thermotolerance. *American Zoologist* **38**:503–517.

Feng, Y. L., H. Auge, and S. K. Ebeling. 2007. Invasive *Buddleja davidii* allocates more nitrogen to its photosynthetic machinery than five native woody species. *Oecologia* **153**:501–510.

Fisher, R. A. 1930. *The Genetical Theory of Natural Selection*. Clarendon Press, Oxford.

Flatt, T. 2005. The evolutionary genetics of canalization. *The Quarterly Review of Biology* **80**:287–316.

Foster, P. L. 2005. Stress responses and genetic variation in bacteria. *Mutation Research – Fundamental and Molecular Mechanisms of Mutagenesis* **569**:3–11.

Gavrilets, S. 1999. A dynamical theory of speciation on holey adaptive landscapes. *American Naturalist* **154**:1–22.

Gelembiuk, G. W., G. E. May, and C. E. Lee. 2006. Phylogeography and systematics of zebra mussels and related species. *Molecular Ecology* **15**:1021–1031.

Geller, J. B., E. D. Walton, E. D. Grosholz, and G. M. Ruiz. 1997. Cryptic invasions of the crab *Carcinus* detected by molecular phylogeography. *Molecular Ecology* **6**:901–906.

Gibson, G., and I. Dworkin. 2004. Uncovering cryptic genetic variation. *Nature Reviews Genetics* **5**:681–690.

Gibson, G., and G. Wagner. 2000. Canalization in evolutionary genetics: a stabilizing theory? *BioEssays* **22**:372–380.

Gilchrist, G. W. 1995. Specialists and generalists in changing environments. 1. Fitness landscapes of thermal sensitivity. *American Naturalist* **146**:252–270.

Gilchrist, G. W. 2000. The evolution of thermal sensitivity in changing environment. In K. B. Storey, and J. M. Storey, eds. *Environmental Stressors and Gene Responses*, pp. 55–70. Elsevier Science, Amsterdam.

Gilchrist, G. W., and C. E. Lee. 2007. All stressed out and nowhere to go: does evolvability limit adaptation in invasive species? *Genetica* **129**:127–132.

Gillespie, J. H. 1974. The role of environmental grain in the maintenance of genetic variation. *American Naturalist* **108**:831–836.

Gillespie, J. H. 1981. Mutation modification in a random environment. *Evolution* **35**:468–476.

Gillespie, J. H. 1998. *Population Genetics: A Concise Guide*. Johns Hopkins University Press, Baltimore, MD.

Gillespie, J. H., and M. Turelli. 1989. Genotype-environment interactions and the maintenance of polygenic variation. *Genetics* **121**:129–138.

Giraud, A., I. Matic, O. Tenaillon, A. Clara, M. Radman, M. Fons, and F. Taddei. 2001. Costs and benefits of high mutation rates: adaptive evolution of bacteria in the mouse gut. *Science* **291**:2606–2608.

Gomulkiewicz, R., R. D. Holt, and M. Barfield. 1999. The effects of density dependence and immigration on adaptation and niche evolution in a black-hole sink environment. *Theoretical Population Biology* **55**:283–296.

Gray, D. K., I. C. Duggan, and H. J. MacIsaac. 2006. Can sodium hypochlorite reduce the risk of species introductions from diapausing invertebrate eggs in non-ballasted ships? *Marine Pollution Bulletin* **52**:689–695.

Haag, C. R., and D. Ebert. 2004. A new hypothesis to explain geographic parthenogenesis. *Annales Zoologici Fennici* **41**:539–544.

Hadany, L., and T. Beker. 2003. On the evolutionary advantage of fitness-associated recombination. *Genetics* **165**:2167–2179.

Hairston, N. G. J. 1996. Zooplankton egg banks as biotic reservoirs in changing environments. *Limnology and Oceanography* **41**:1087–1092.

Hairston, N. G., and T. A. Dillon. 1990. Fluctuating selection and response in a population of fresh-water copepods. *Evolution* **44**:1796–1805.

Hairston, N. G., and C. M. Kearns. 2002. Temporal dispersal: ecological and evolutionary aspects of zooplankton egg banks and the role of sediment mixing. *Integrative and Comparative Biology* **42**:481–491.

Hairston, N. G., C. M. Kearns, and S. P. Ellner. 1996. Phenotypic variation in a zooplankton egg bank. *Ecology* **77**:2382–2392.

Haldane, J. B. S., and S. D. Jayakar. 1963. Polymorphism due to selection of varying direction. *Journal of Genetics* **58**: 237–242.

Hansen, T. F. 2003. Is modularity necessary for evolvability? Remarks on the relationship between pleiotropy and evolvability *Biosystems* **69**:83–94.

Hansen, T. F. 2006. The evolution of genetic architecture. *Annual Review of Ecology and Systematics* **37**:123–157.

Hansen, T. F., J. M. Alvarez-Castro, A. J. Carter, J. Hermisson, and G. P. Wagner. 2006. Evolution of genetic architecture under directional selection. *Evolution* **60**:1523–1536.

Havel, J. E., C. E. Lee, and M. J. Vander Zanden. 2005. Do reservoirs facilitate passive invasions into landscapes? *BioScience* **55**:518–525.

Hedrick, P. W. 1974. Genetic variation in a heterogeneous environment. I. Temporal heterogeneity and the absolute dominance model. *Genetics* **78**:757–770.

Hedrick, P. W. 1995. Genetic-polymorphism in a temporally varying environment – effects of delayed germination or diapause. *Heredity* **75**:164–170.

Hedrick, P. W. 1998. Maintenance of genetic variation: spatial selection and self-fertilization. *American Naturalist* **152**: 145–150.

Hedrick, P. W. 1999. Antagonistic pleiotropy and genetic polymorphism: a perspective. *Heredity* **82**:126–133.

Hedrick, P. W. 2006. Genetic polymorphism in heterogeneous environments: the age of genomics. *Annual Review of Ecology and Systematics* **37**:67–93.

Heidenreich, E. 2007. Adaptive mutation in *Saccharomyces cerevisiae*. *Critical Reviews in Biochemistry and Molecular Biology* **42**:285–311.

Hermisson, J., T. F. Hansen, and G. P. Wagner. 2003. Epistasis in polygenic traits and the evolution of genetic architecture under stabilizing selection. *American Naturalist* **161**:708–734.

Hintz, M., C. Bartholmes, P. Nutt, J. Ziermann, S. Hameister, B. Neuffer, and G. Theissen. 2006. Catching a 'hopeful monster': shepherd's purse (*Capsella bursa-pastoris*) as a model system to study the evolution of flower development. *Journal of Experimental Botany* **57**:3531–3542.

Holt, R. D., R. Gomulkiewicz, and M. Barfield. 2003. The phenomenology of niche evolution via quantitative traits in a black-hole sink: a mechanism for punctuated evolution? *Proceedings of the Royal Society of London, Series B* **270**:215–224.

Holt, R. D., M. Barfield, and R. Gomulkiewicz. 2004. Temporal variation can facilitate niche evolution in harsh sink environments. *American Naturalist* **164**:187–200.

Holt, R. D., M. Barfield, and R. Gomulkiewicz. 2005. Theories of niche conservatism and evolution: could exotic species be potential tests?. In D. F. Sax, J. J. Stachowicz, and S. D. Gaines, eds. *Species Invasions: Insights into Ecology, Evolution and Biogeography*, pp. 259–290. Sinauer Associates, Sunderland, MA.

Houle, D. 1992. Comparing evolvability and variability of quantitative traits. *Genetics* **130**:195–204.

Houle, D. 1998. How should we explain variation in the genetic variance of traits? *Genetica* **102/103**:241–253.

Houle, D., B. Morikawa, and M. Lynch. 1996. Comparing mutational variabilities. *Genetics* **43**:1467–1483.

Huey, R. B., G. W. Gilchrist, M. L. Carlson, D. Berrigan, and L. Serra. 2000. Rapid evolution of a geographic cline in size in an introduced fly. *Science* **287**:308–309.

Ishii, K., H. Matsuda, Y. Iwasa, and A. Sasaki. 1989. Evolutionarily stable mutation rate in a periodically changing environment. *Genetics* **121**:163–174.

Jablonski, D., J. J. Jablonski Jr, D. J. Bottjer, and P. M. Sheehan. 1983. Onshore-offshore patterns in the evolution of Phanerozoic shelf communities *Science* **222**:1123–1125.

Jansen, V. A. A., and M. P. H. Stumpf. 2005. Making sense of evolution in an uncertain world. *Science* **309**:2005–2007.

Jazdzewski, K. 1980. Range extensions of some gammaridean species in European inland waters caused by human activity. *Crustaceana (Supplement)* **6**:84–107.

Johnson, T. 1999. Beneficial mutations, hitchhiking and the evolution of mutation rates in sexual populations. *Genetics* **151**:1621–1631.

Jones, A. G., S. J. Arnold, and R. Bürger. 2007. The mutation matrix and the evolution of evolvability. *Evolution* **61**: 727–745.

Kacser, H., and J. A. Burns. 1981. The molecular basis of dominance. *Genetics* **97**:639–666.

Kane, N. C., and L. H. Rieseberg. 2008. Genetics and evolution of weedy *Helianthus annuus* populations: adaptation of an agricultural weed. *Molecular Ecology* **17**:384–394.

Kaplin, P. A. 1995. The Caspian: its past, present, and future. In A. F. Mandych, ed. *In Enclosed Seas and Large Lakes of Eastern Europe and Middle Asia*, pp. 71–118. SPB Academic Publishing, Amsterdam, The Netherlands.

Kashtan, N., and U. Alon. 2005. Spontaneous evolution of modularity and network motifs. *Proceedings of the National Academy of Sciences of the United States of America* **102**:13773–13778.

Kashtan, N., E. Noor, and U. Alon. 2007. Varying environments can speed up evolution. *Proceedings of the National Academy of Sciences of the United States of America* **104**:13711–13716.

Kassen, R. 2002. The experimental evolution of specialists, generalists, and the maintenance of diversity. *Journal of Evolutionary Biology* **15**:173–190.

Kawecki, T. J. 2000. The evolution of genetic canalization under fluctuating selection. *Evolution* **54**:1–12.

Kearns, D. B., F. Chu, R. Rudner, and R. Losick. 2004. Genes governing swarming in *Bacillus subtilis* and evidence for a phase variation mechanism controlling surface motility. *Molecular Microbiology* **52**:357–369.

Keightley, P. D. 1998. Genetic basis of response to 50 generations of selection on body weight in inbred mice. *Genetics* **148**:1931–1939.

Ketola, T., J. Laakso, V. Kaitala, and S. Airaksinen. 2004. Evolution of Hsp90 expression in *Tetrahymena thermophila* (Protozoa, Ciliata) populations exposed to thermally variable environments. *Evolution* **58**:741–748.

Kim, Y. 2007. Rate of adaptive peak shifts with partial genetic robustness. *Evolution* **61**:1847–1856.

Kimura, M. 1967. On the evolutionary adjustment of spontaneous mutation rates. *Genetical Research* **9**:23–34.

King, O. D., and J. Masel. 2007. The evolution of bet-hedging adaptations to rare scenarios. *Theoretical Population Biology* **72**:560–575.

Kolbe, J. J., R. E. Glor, L. R. G. Schettino, A. C. Lara, A. Larson, and J. B. Losos. 2004. Genetic variation increases during biological invasion by a Cuban lizard. *Nature* **431**:177–181.

Kurokawa, K., T. Itoh, T. Kuwahara, K. Oshima, H. Toh, A. Toyoda, H. Takami *et al.* 2007. Comparative metagenomics revealed commonly enriched gene sets in human gut microbiomes. *DNA Research* **14**:169–181.

Kussell, E., and S. Leibler. 2005. Phenotypic diversity, population growth, and information in fluctuating environments. *Science* **309**:2075–2078.

Lambrinos, J. G. 2001. The expansion history of a sexual and asexual species of *Cortaderia* in California, USA. *Journal of Ecology* **89**:88–98.

Lavergne, S., and J. Molofsky. 2007. Increased genetic variation and evolutionary potential drive the success of an invasive grass. *Proceedings of the National Academy of Sciences of the United States of America* **104**:3883–3888.

Layzer, D. 1980. Genetic variation and progressive evolution. *American Naturalist* **115**:809–826.

Lee, C. E. 1999. Rapid and repeated invasions of fresh water by the saltwater copepod *Eurytemora affinis*. *Evolution* **53**:1423–1434.

Lee, C. E. 2000. Global phylogeography of a cryptic copepod species complex and reproductive isolation between genetically proximate "populations". *Evolution* **54**:2014–2027.

Lee, C. E. 2002. Evolutionary genetics of invasive species. *Trends in Ecology and Evolution* **17**:386–391.

Lee, C. E., and M. A. Bell. 1999. Causes and consequences of recent freshwater invasions by saltwater animals. *Trends in Ecology and Evolution* **14**:284–288.

Lee, C. E., and B. W. Frost. 2002. Morphological stasis in the *Eurytemora affinis* species complex (Copepoda: Temoridae). *Hydrobiologia* **480**:111–128.

Lee, C. E., J. L. Remfert, and G. W. Gelembiuk. 2003. Evolution of physiological tolerance and performance during freshwater invasions. *Integrative and Comparative Biology* **43**:439–449.

Lee, C. E., J. L. Remfert, and Y.-M. Chang. 2007. Response to selection and evolvability of invasive populations. *Genetica* **129**:179–192.

Leigh, E. G. Jr. 1970. Natural selection and mutability. *American Naturalist* **104**:301–305.

Leigh, E. G. Jr 1973. The evolution of mutation rates. *Genetics* **73**(Suppl.):1–18.

Levene, H. 1953. Genetic equilibrium when more than one ecological niche is available. *American Naturalist* **87**:331–333.

Levin, S. A., D. Cohen, and A. Hastings. 1984. Dispersal strategies in patchy environments. *Theoretical Population Biology* **26**:165–191.

Li, Y., and C. O. Wilke. 2004. Digital evolution in time-dependent fitness landscapes. *Artificial Life* **10**:123–134.

Lipson, H., J. B. Pollack, and N. P. Suh. 2002. On the origin of modular variation. *Evolution* **56**:1549–1556.

Lonsdale, W. M. 1999. Global patterns of plant invasions and the concept of invasibility. *Ecology* **80**:1522–1536.

López, M. A., and C. López-Fanjul. 1993. Spontaneous mutation for a quantitative trait in *Drosophila melanogaster*. I. Response to artificial selection. *Genetical Research* **61**:107–116.

Lyman, J. C., and N. C. Ellstrand. 1984. Clonal diversity in *Taraxacum officinale* (Compositae), an apomict. *Heredity* **53**:1–10.

Lynch, M. 2007. The frailty of adaptive hypotheses for the origins of organismal complexity. *Proceedings of the National Academy of Sciences of the United States of America* **104**:8597–8604.

Maciá, M. D., D. Blanquer, B. Togores, J. Sauleda, J. L. Pérez, and A. Oliver. 2005. Hypermutation Is a key factor in development of multiple-antimicrobial resistance in *Pseudomonas aeruginosa* strains causing chronic lung infections. *Antimicrobial Agents and Chemotherapy* **49**:3382–3386.

Mackay, T. F. C., J. D. Fry, R. F. Lyman, and S. V. Nuzhdin. 1994. Polygenic mutation in *Drosophila melanogaster*: estimates from response to selection of inbred strains. *Genetics* **136**:937–951.

Mackie, G. L. 1991. Biology of the exotic zebra mussel, *Dreissena polymorpha*, in relation to native bivalves and its potential impact in Lake St. Clair. *Hydrobiologia* **219**:251–268.

Mahdjoub, T., and F. Menu. 2008. Prolonged diapause: a trait increasing invasion speed? *Journal of Theoretical Biology* **251**:317–330.

Martin, P., K. Makepeace, S. A. Hill, D. W. Hood, and E. R. Moxon. 2005. Microsatellite instability regulates transcription factor binding and gene expression. *Proceedings of the National Academy of Sciences of the United States of America* **102**:3800–3804.

Masel, J. 2005. Evolutionary capacitance may be favored by natural selection. *Genetics* **170**:1359–1371.

Masel, J. 2006. Cryptic genetic variation is enriched for potential adaptations. *Genetics* **172**:1985–1991.

Masel, J., and A. Bergman. 2003. The evolution of the evolvability properties of the yeast prion [PSI$^+$]. *Evolution* **57**:1498–1512.

Matic, I., F. Taddei, and M. Radman. 2004. Survival versus maintenance of genetic stability: a conflict of priorities during stress. *Research in Microbiology* **155**:337–341.

May, G. E., G. W. Gelembiuk, V. E. Panov, M. Orlova, and C. E. Lee. 2006. Molecular ecology of zebra mussel invasions. *Molecular Ecology* **15**:1033–1050.

Meibom, K. L., M. Blokesch, N. A. Dolganov, C.-Y. Wu, and G. K. Schoolnik. 2005. Chitin Induces Natural Competence in *Vibrio cholerae*. *Science* **310**:1824–1827.

Metz, J. A. J., T. J. de Jong, and P. G. L. Klinkhamer. 1983. What are the advantages of dispersing; a paper by Kuno explained and extended. *Oecologia* **57**:166–169.

Meusnier, I., M. Valero, J. Olsen, and W. Stam. 2004. Analysis of rDNA ITS1 indels in *Caulerpa taxifolia* (Chlorophyta) supports a derived, incipient species status for the invasive strain. *European Journal of Phycology* **39**:83–92.

Meyers, L. A., and J. J. Bull. 2002. Fighting change with change: adaptive variation in an uncertain world. *Trends in Ecology and Evolution* **17**:551–557.

Meyers, L. A., F. D. Ancel, and M. Lachmann. 2005. Evolution of genetic potential. *PLoS Computational Biology* **1**: 0236–0243.

Miller, J. H. 1998. Mutators in *Escherichia coli*. *Mutation Research* **409**:99–106.

Miller, M. C., D. P. Keymer, A. Avelar, A. B. Boehm, and G. K. Schoolnik. 2007. Detection and transformation of genome segments that differ within a coastal population of *Vibrio cholerae* strains. *Applied and Environmental Microbiology* **73**:3695–3704.

Moxon, R., C. Bayliss, and D. Hood. 2006. Bacterial contingency loci: the role of simple sequence DNA repeats in bacterial adaptation. *Annual Review of Genetics* **40**: 307–333.

Muller, H. J. 1932. Some genetic aspects of sex. *American Naturalist* **66**:118–138.

Müller-Schärer, H., U. Schaffner, and T. Steinger. 2004. Evolution in invasive plants: implications for biological control. *Trends in Ecology and Evolution* **19**:417–422.

Mustonen, V., and M. Lassig. 2007. Adaptations to fluctuating selection in Drosophila *Proceedings of the National Academy of Sciences of the United States of America* **104**:2277–2282.

O'Loughlin, T. L., W. M. Patrick, and I. Matsumura. 2006. Natural history as a predictor of protein evolvability. *Protein Engineering Design and Selection* **19**:439–442.

Oliver, A., B. R. Levin, C. Juan, F. Baquero, and J. Blázquez. 2004. Hypermutation and the preexistence of antibiotic-resistant *Pseudomonas aeruginosa* mutants: implications for susceptibility testing and treatment of chronic infections. *Antimicrobial Agents and Chemotherapy* **48**:4226–4233.

Orr, H. A. 2000a. Adaptation and the cost of complexity. *Evolution* **54**:13–20.

Orr, H. A. 2000b. The rate of adaptation in asexuals. *Genetics* **155**:961–968.

Ostrowski, E. A., C. Ofria, and R. E. Lenski. 2007. Ecological specialization and adaptive decay in digital organisms. *American Naturalist* **169**:E1–E20.

Otto, S. P., and N. H. Barton. 1997. The evolution of recombination: removing the limits to natural selection. *Genetics* **147**:879–906.

Palenik, B., Q. Ren, C. L. Dupont, G. S. Myers, J. F. Heidelberg, J. H. Badger, R. Madupu *et al.* 2006. Genome sequence of *Synechococcus* CC9311: insights into adaptation to a coastal environment. *Proceedings of the National Academy of Sciences of the United States of America* **103**:13555–13559.

Palmer, M. E., and M. Lipsitch. 2006. The influence of hitchhiking and deleterious mutation upon asexual mutation rates. *Genetics* **173**:461–472.

Parker, I. M., J. Rodriguez, and M. E. Loik. 2003. An evolutionary approach to understanding the biology of invasions: local adaptation and general-purpose genotypes in the weed *Verbascum thapsus*. *Conservation Biology* **17**:59–72.

Parsons, P. A. 1988. Evolutionary rates: effects of stress upon recombination. *Biological Journal of the Linnean Society, London* **35**:49–68.

Parter, M., N. Kashtan, and U. Alon. 2007. Environmental variability and modularity of bacterial metabolic networks. *BMC Evolutionary Biology* **7**:169.

Partridge, L., and N. H. Barton. 2000. Natural selection: evolving evolvability. *Nature* **407**:457–458.

Pasiecznik, N. M., A. O. M. Vall, S. Nourissier-Mountou, P. Danthu, J. Murch, M. J. McHugh, and P. J. C. Harris. 2006. Discovery of a life history shift: precocious flowering in an introduced population of *Prosopis*. *Biological Invasions* **8**:1681–1687.

Patino, M. M., J.-J. Liu, J. R. Glover, and S. Lindquist. 1996. Support for the prion hypothesis for inheritance of a phenotypic trait in yeast. *Science* **273**:622–626.

Pepper, J. W. 2000. An agent-based model of group selection. In C. C. Maley, and E. Boudreau, eds. *Artificial Life 7 Workshop Proceedings*. Santa Fe Institute, Santa Fe, NM.

Pepper, J. W. 2003. The evolution of evolvability in genetic linkage patterns. *Biosystems* **69**:115–126.

Peterson, A. T. 2003. Predicting the geography of species' invasions via ecological niche modeling. *Quarterly Review of Biology* **78**:419–433.

Peterson, A. T., and D. A. Vieglais. 2001. Predicting species invasions using ecological niche modeling. *BioScience* **51**:363–371.

Pigliucci, M. 2008. Is evolvability evolvable? *Nature Reviews Genetics* **9**:75–82.

Poulin, J., S. G. Weller, and A. K. Sakai. 2005. Genetic diversity does not affect the invasiveness of fountain grass (*Pennisetum setaceum*) in Arizona, California and Hawaii. *Diversity and Distributions* **11**:241–247.

Queitsch, C., T. A. Sangster, and S. Lindquist. 2002. Hsp90 as a capacitor of phenotypic variation. *Nature* **417**:618–624.

Rand, D. M., P. S. Spaeth, T. B. Sackton, and P. S. Schmidt. 2002. Ecological genetics of Mpi and Gpi polymorphisms in the acorn barnacle and the spatial scale of neutral and non-neutral variation. *Integrative and Comparative Biology* **42**:825–836.

Raybould, A. F., A. J. Gray, M. J. Lawrence, and D. F. Marshall. 1991. The evolution of *Spartina anglica* C. E. Hubbard (Gramineae): origin and genetic variability. *Biological Journal of the Linnean Society* **43**:111–126.

Reid, D., and M. I. Orlova. 2002. Geological and evolutionary underpinnings for the success of Ponto-Caspian species invasions in the Baltic Sea and North American Great Lakes. *Canadian Journal of Fisheries and Aquatic Sciences* **59**:1144–1158.

Reisinger, J., and R. Miikkulainen. 2006. Selecting for evolvable representations. *Proceedings of the Genetic and*

Evolutionary Computation Conference **GECCO-2006**: 1297–1304.

Ricciardi, A., and H. J. MacIsaac. 2000. Recent mass invasion of the North American Great Lakes by Ponto-Caspian species. *Trends in Ecology and Evolution* **15**:62–65.

Rice, S. H. 1990. A geometric model for the evolution of development. *Journal of Theoretical Biology* **143**:319–342.

Rice, S. H. 1995. A genetical theory of species selection. *Journal of Theoretical Biology* **177**:237–245.

Rice, S. H. 1998. The evolution of canalization and the breaking of von Baer's laws: modeling the evolution of development with epistasis. *Evolution* **52**:647–656.

Rice, S. H. 2002. A general population genetic theory for the evolution of developmental interactions. *Proceedings of the National Academy of Sciences of the United States of America* **99**:15518–15523.

Rieseberg, L. H., O. Raymond, D. M. Rosenthal, Z. Lai, K. Livingstone, T. Nakazato, J. L. Durphy *et al.* 2003. Major ecological transitions in wild sunflowers facilitated by hybridization. *Science* **301**:1211–1216.

Ross, K. G., M. J. B. Krieger, L. Keller, and D. D. Shoemaker. 2007. *Genetic Variation and Structure in Native Populations of the Fire Ant Solenopsis invicta*: Evolutionary and Demographic Implications. Biological Journal of the Linnean Society, London Accepted.

Ross-Ibarra, J. 2004. The evolution of recombination under domestication: a test of two hypotheses. *American Naturalist* **163**:105–112.

Rutherford, S. L., and S. Lindquist. 1998. Hsp90 as a capacitor for morphological evolution. *Nature* **396**:336–342.

Saltonstall, K. 2002. Cryptic invasion by a non-native genotype of the common reed, *Phragmites australis*, into North America. *Proceedings of the National Academy of Sciences of the United States of America* **99**:2445–2449.

Sasaki, A., and S. Ellner. 1997. Quantitative genetic variance maintained by fluctuating selection with overlapping generations: variance components and covariances. *Evolution* **51**:682–696.

Schemske, D. W., and P. Bierzychudek. 2001. Perspective: evolution of flower color in the desert annual *Linanthus parryae*: wright revisited. *Evolution* **55**:1269–1282.

Schemske, D. W., and P. Bierzychudek. 2007. Spatial differentiation for flower color in the desert annual *Linanthus parryae*: was Wright right? *Evolution* **61**:2528–2543.

Schlosser, G., and D. Thieffry. 2000. Modularity in development and evolution. *BioEssays* **22**:1043–1045.

Schmalhausen, I. I. 1949. *The Factors of Evolution: The Theory of Stabilizing Selection*. Blakiston, Philadelphia, PA, USA.

Sepkoski Jr, J. J., and A. I. Miller. 1985. Evolutionary faunas and the distribution of Paleozoic benthic communities in space and time. In J. W. Valentine, ed. *Phanerozoic Diversity Patterns: Profiles in Macroevolution*, pp. 153–190. Princeton University Press, Princeton, NJ.

Sexton, J. P., J. K. McKay, and A. Sala. 2002. Plasticity and genetic diversity may allow saltcedar to invade cold climates in North America. *Ecological Applications* **12**:1652–1660.

Shaver, A. C., and P. D. Sniegowski. 2003. Spontaneously arising *mutL* mutators in evolving *Escherichia coli* populations are the result of changes in repeat length. *Journal of Bacteriology* **185**:6076–6082.

Shaver, A. C., P. G. Dombrowski, J. Y. Sweeney, T. Treis, R. M. Zappala, and P. D. Sniegowski. 2002. Fitness evolution and the rise of mutator alleles in experimental *Escherichia coli* populations. *Genetics* **62**:557–566.

Sniegowski, P., and H. Murphy. 2006. Evolvability. *Current Biology* **16**:R831–R834.

Sniegowski, P. D., P. J. Gerrish, and R. E. Lenski. 1997. Evolution of high mutation rates in experimental populations of *E. coli*. *Nature* **387**:703–705.

Sniegowski, P. D., P. J. Gerrish, T. Johnson, and A. Shaver. 2000. The evolution of mutation rates: separating causes from consequences. *BioEssays* **22**:1057–1066.

Sol, D., S. Timmermans, and L. Lefebvre. 2002. Behavioural flexibility and invasion success in birds. *Animal Behaviour* **63**:495–502.

Sol, D., R. P. Duncan, T. M. Blackburn, P. Cassey, and L. Lefebvre. 2005. Big brains, enhanced cognition, and response of birds to novel environments. *Proceedings of the National Academy of Sciences of the United States of America* **102**:5460–5465.

Spidle, A. P., J. E. Marsden, and B. May. 1994. Identification of the Great Lakes quagga mussel as *Dreissena bugensis* from the Dnieper River, Ukraine, on the basis of allozyme variation. *Canadian Journal of Fisheries and Aquatic Sciences* **51**:1485–1489.

Sprung, M. 1991. Costs of reproduction: a study on metabolic requirements of the gonads and fecundity of the bivalve *Dreissena polymorpha*. *Malacologia* **33**:63–70.

Stearns, S. C. 1992. *The Evolution of Life Histories*. Oxford University Press, Oxford.

Suarez, A. V., and N. D. Tsutsui. 2008. The evolutionary consequences of biological invasions. *Molecular Ecology* **17**: 351–360.

Sultan, S. E. 2001. Phenotypic plasticity for fitness components in *Polygonum* species of contrasting ecological breadth. *Ecology* **82**:328–343.

Svitoch, A. A., A. O. Selivanov, and T. A. Yanina. 2000. The Pont-Caspian and Mediterranean basins in the Pleistocene (paleogeography and correlation). *Oceanology* **40**:868–881.

Taddei, F., M. Radman, J. Maynard-Smith, B. Toupance, P. H. Gouyon, and B. Godelle. 1997. Role of mutator alleles in adaptive evolution. *Nature* **387**:700–702.

Tanaka, M. M., C. T. Bergstrom, and B. R. Levin. 2003. The evolution of mutator genes in bacterial populations: the roles of environmental change and timing. *Genetics* **164**: 843–854.

Tenaillon, O., H. Le Nagard, B. Godelle, and F. Taddei. 2000. Mutators and sex in bacteria: conflict between adaptive

strategies. *Proceedings of the National Academy of Sciences of the United States of America* **97**:10465–10470.

Thébaud, C., A. C. Finzi, L. Affre, M. Debussche, and J. Escarre. 1996. Assessing why two introduced *Conyza* differ in their ability to invade Mediterranean old fields. *Ecology* **77**:791–804.

Toussaint, M. 2003. The evolution of genetic representations and modular adaptation. PhD thesis, Ruhr-Universität Bochum, Bochum, Germany.

Toussaint, M. 2005. *Compact Genetic Codes as a Search Strategy of Evolutionary Processes Foundations of Genetic Algorithms*. Springer Berlin, Heidelberg.

Toussaint, M., and W. von Seelen. 2007. Complex adaptation and system structure. *BioSystems* **90**:769–782.

Tracey, M. L., and B. Dempsey. 1982. Recombination rate variability in *D. melanogaster* females subjected to temperature stress. *Journal of Heredity* **72**:427–428.

Travis, J. M. J., and E. R. Travis. 2002. Mutator dynamics in fluctuating environments. *Proceedings of the Royal Society of London, Series B* **269**:591–597.

True, H. L., I. Berlin, and S. L. Lindquist. 2004. Epigenetic regulation of translation reveals hidden genetic variation to produce complex traits. *Nature* **431**:184–187.

Tsutsui, N. D., and T. J. Case. 2001. Population genetics and colony structure of the argentine ant (*Linepithema humile*) in its native and introduced ranges. *Evolution* **55**:976–985.

Turelli, M. 1981. Temporally varying selection on mulltiple alleles – a diffusion analysis. *Journal of Mathematical Biology* **13**:115–129.

Turelli, M., and N. H. Barton. 2004. Polygenic variation maintained by balancing selection: pleiotropy, sex-dependent allelic effects and GxE interactions. *Genetics* **166**:1053–1079.

Turelli, M., D. W. Schemske, and P. Bierzychudek. 2001. Stable two-allele polymorphisms maintained by fluctuating fitnesses and seed banks: protecting the blues in *Linanthus parryae*. *Evolution* **55**:1283–1298.

de Visser, J. A. G. M. 2002. The fate of microbial mutators. *Microbiology* **148**:1247–1252.

Waddington, C. H. 1953. Genetic assimilation of an acquired character. *Evolution* **7**:118–126.

Waddington, C. H. 1957. *The Strategy of the Genes*. Macmillan, New York.

Wagner, G. P., and L. Altenberg. 1996. Complex adaptations and the evolution of evolvability. *Evolution* **50**:967–976.

Wagner, G. P., G. Booth, and H. Bagheri-Chaichain. 1997. A population genetic theory of canalization. *Evolution* **51**: 329–347.

Wallis, B. 1968. *Topics in Population Genetics*. W. W. Norton and Co., New York.

Weinig, C. 2000. Plasticity versus canalization: population differences in the timing of shade-avoidance responses. *Evolution* **54**:441–451.

West, S. A., A. W. Gemmill, A. Graham, M. E. Viney, and A. F. Read. 2001. Immune stress and facultative sex in a parasitic nematode. *Journal of Evolutionary Biology*, **14**:333–337.

Whitlock, M. C. 1997. Founder effects and peak shifts without genetic drift: adaptive peak shifts occur easily when environments fluctuate slightly. *Evolution* **51**:1044–1048.

Williamson, M., and A. Fitter. 1996. The varying success of invaders. *Ecology* **77**:1661–1666.

Wilson, D. S., and E. O. Wilson. 2007. Rethinking the theoretical foundations of sociobiology. *The Quarterly Review of Biology* **82**:327–348.

Winkler, G., J. J. Dodson, and C. E. Lee. 2008. Heterogeneity within the native range: population genetic analyses of sympatric invasive and noninvasive clades of the freshwater invading copepod *Eurytemora affinis*. *Molecular Ecology* **17**:415–430.

Wright, S. 1929. Fisher's theory of dominance. *American Naturalist* **63**:274–279.

Wright, S. 1931. Evolution in mendelian populations. *Genetics* **16**:97–159.

Wright, S. 1932. The roles of mutation, inbreeding, crossbreeding and selection in evolution. *Proceedings of the VI International Congress of Genetics* **1**:356–366.

Wright, B. E. 2004. Stress-directed adaptive mutations and evolution. *Molecular Microbiology* **52**:643–650.

Wright, B. E., D. K. Reschke, K. H. Schmidt, J. M. Reimers, and W. Knight. 2003. Predicting mutation frequencies in stem-loop structures of derepressed genes: implications for evolution. *Molecular Microbiology* **48**:429–441.

Yeh, P. J., and T. D. Price. 2004. Adaptive phenotypic plasticity and the successful colonization of a novel environment. *American Naturalist* **164**:531–542.

Zieg, J., M. Silverman, M. Hilmen, and M. Simon. 1977. Recombinational switch for gene expression. *Science* **196**:170–172.