

## SYNTHESIS

**Adaptation, extinction and global change**Graham Bell<sup>1,2</sup> and Sinéad Collins<sup>3</sup>

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**Abstract**

We discuss three interlinked issues: the natural pace of environmental change and adaptation, the likelihood that a population will adapt to a potentially lethal change, and adaptation to elevated CO<sub>2</sub>, the prime mover of global change.

1. Environmental variability is governed by power laws showing that ln difference in conditions increases with ln elapsed time at a rate of 0.3–0.4. This leads to strong but fluctuating selection in many natural populations.
2. The effect of repeated adverse change on mean fitness depends on its frequency rather than its severity. If the depression of mean fitness leads to population decline, however, severe stress may cause extinction. Evolutionary rescue from extinction requires abundant genetic variation or a high mutation supply rate, and thus a large population size. Although natural populations can sustain quite intense selection, they often fail to adapt to anthropogenic stresses such as pollution and acidification and instead become extinct.
3. Experimental selection lines of algae show no specific adaptation to elevated CO<sub>2</sub>, but instead lose their carbon-concentrating mechanism through mutational degradation. This is likely to reduce the effectiveness of the oceanic carbon pump. Elevated CO<sub>2</sub> is also likely to lead to changes in phytoplankton community composition, although it is not yet clear what these will be.

We emphasize the importance of experimental evolution in understanding and predicting the biological response to global change. This will be one of the main tasks of evolutionary biologists in the coming decade.

Global change presents a clear, immediate and urgent challenge for evolutionary biology. The transformation of environments by agriculture and industry has created, and continues to create, a wide range of unintentional experiments in which populations are exposed to severe and novel perturbations, and either adapt to them or cease to exist. The greatest of these experiments is now under way: the alteration of the atmosphere and climate of the Earth, with consequences for every living thing. In this opening article of a new journal, we shall not attempt to offer a review of the whole field, which would be too intricate and extensive to fit within the confines of a short paper. We shall instead try to sketch the main tasks that we think that evolutionary biologists should undertake to

contribute to our understanding of the future. Our account is organized into three sections. The first deals with the variability that is commonly experienced by natural populations, and how they respond to it. The second is concerned with whether or not populations can adapt to a novel and severe stress before being extinguished by it. The final section describes how phytoplankton populations may adapt to the prime mover of change, the increase in atmospheric concentration of carbon dioxide. The emphasis throughout is quantitative and experimental. We hope, and we believe, that evolutionary biology is the key to predicting how the world will change, and we see this as the principal task of evolutionary biologists in the next few decades.

## Selection in variable environments

### Change is generally for the worse

It is widely believed that most populations, most of the time, should have become well adapted to their conditions of life through the past operation of natural selection. Mutation is generally deleterious, at least in natural conditions (Keightley and Lynch 2003). Environmental change tends to move the average phenotype of well-adapted populations further from its optimal value and thereby to reduce mean fitness. Moreover, enemies such as pathogens and predators are likely to be selected to exploit the most frequent types in their target populations, driving a continuous reduction in mean fitness (Van Valen 1973). Consequently, either genetic or environmental change will be perceived by most individuals as harmful.

### The natural pace of environmental change

A physical factor changes on all time scales, and at any given time scale varies by some characteristic amount. The rate of increase in environmental variance over time provides a quantitative measure of variability. This is often adequately described by a power law,  $V_E = at^z$ , where the exponent  $z$  expresses the rate of increase of variance over time. This means that the log difference in physical conditions at a site increases with log elapsed time at a rate  $z/2$ . For example, Koscielny-Bunde et al. (1998) analysed deviations of daily maximum temperature from their seasonal average values, estimated with very voluminous and exact data taken at weather stations around the world over a period of more than a century. They found that plots of  $\log V_E$  on log elapsed time are almost perfectly linear with slope  $z = 0.65$ . Pelletier (1997) obtained  $z = 0.75$  for ice-core samples for periods between 1 month and 2000 years. This environmental variability may drive changes in the growth and abundance of populations. Pimm and Redfearn (1988) showed that  $\ln$  abundance  $N$  of animals also follows a power law, and since the  $\ln$  variance of  $\ln N$  is equivalent to  $\ln [N(t+1)/N(t)]$  this implies that the variance of realized growth rate increases indefinitely over time, apparently with exponent 0.36 (Inchausti and Halley 2002). Spatial variation also increases with distance according to a power law, typically with smaller exponents of  $z = 0.1-0.2$  (Bell et al. 1993). Hence, as a lineage is extended through time the conditions that its members experience will grow steadily more variable.

### Variable and fluctuating selection

Environmental variability will cause the strength and direction of selection to change over time. Studies of

natural populations have shown that selection is often strong (Hereford et al. 2004) and that heritability is often high (Mousseau and Roff 1987). One explanation of these apparently contradictory generalizations is that selection often changes direction, because offspring grow up in a different place and at a different time from their parents. The variability of selection among isozyme genotypes in *Daphnia* populations was documented by Lynch (1987), who found that the standard deviation of the selection coefficient over time was at least 0.1. There are many detailed case studies of selection that varies widely in time (Grant and Grant 2002) or space (Snaydon and Davies 1982), even in within a few square metres of natural environment (Stewart and Schoen 1987). Hence, populations might often be rather imprecisely adapted to local conditions of growth. This can be evaluated by measuring the selection gradient (partial regression of fitness on character state) and calculating the distance between the optimal phenotype and the population mean, in units of phenotypic standard deviations. For the studies of stabilizing selection collated by Kingsolver et al. (2001) this distance is exponentially distributed with mean 3.9; that is, the population was further than one phenotypic standard deviation from the optimum in about one-half of all cases, and further than 2 SD in one-third. It can also be evaluated by reciprocal transplant experiments. Where these involve clearly distinct ecotypes or species they usually show that residents are markedly superior to incomers (Schluter 2000; Table 5.1). When morphologically undifferentiated populations are transplanted, however, there is little tendency for residents to be superior except at very large distances or between clearly distinct habitats (Bell 2008, Table 5). These facts are consistent with the view that conditions often vary widely in time and space, generating strong but fluctuating selection.

### Rescue from extinction by adaptation

Most individuals are sufficiently versatile to accommodate the mundane level of variability experienced within a lifetime. Offspring will encounter conditions different from their parents but will adjust to them through phenotypic plasticity. The perpetual increase of environmental variance, however, may eventually lead to a change in conditions too great for individuals to survive or reproduce successfully, so that the population begins to decline. Lineages can still persist by migrating or dispersing to new sites. If neither plasticity nor dispersal will serve, however, they must either adapt or die out. Natural selection may succeed in restoring adaptedness if types capable of growing in the new conditions exist in the population or arise before it becomes extinct. It is most likely to do so when the change is modest and the

amount of genetic variance (or the mutation supply rate) is high. Although this notion dates back at least to the 'lag load' of Stenseth and Maynard Smith (1984) it seems not to have been explored very thoroughly (but see Martin and Lenormand 2006, whose parameter  $s_0$  is a lag load), with the exceptions that we discuss below. Although selection lines in the laboratory sometimes die out through excessive stress or high levels of inbreeding, this is normally regarded as a nuisance, and we are unaware of any experimental literature demonstrating the conditions in which evolutionary rescue does and does not occur. The closest approach to experimental evidence was described by Bradshaw (1991), who pointed out that some species of plant consistently adapt to heavy metal pollution whereas others do not, and attributed the failures to 'genostasis', the chronic and insuperable lack of appropriate genetic variation.

### The pace of current global change

There has been very marked environmental change during the Cenozoic, including (for example) extensive glaciations within the last million years alone. Many organisms have become extinct during this time, in many cases, no doubt, because of these changes. Overall diversity has not altered much in most groups, however, showing that selection and speciation are effective in buffering the global biota against extinction or impoverishment. We have emphasized that strong, fluctuating selection is probably commonplace in contemporary populations. The optimistic view is therefore that selection will continue to be equally effective in rescuing populations that experience high levels of stress, so that extinction rates will not exceed long-term averages except, perhaps, when extinction is willfully pursued, for example through pest eradication or overfishing. A more pessimistic view is that some important environmental factors are currently changing at unprecedented rates as the result of human activities. The most prominent is atmospheric CO<sub>2</sub>, which has risen from preindustrial levels of 280–380 ppm at present and is forecast to attain 700–1000 ppm in the next 100 years (Watson et al. 2001). This is likely to entrain secondary effects such as substantially higher temperatures, acidification and a greater frequency of extreme events. Human activities are also responsible for high levels of pollution by synthetic chemicals, extensive changes in landscape structure and the release of many species from dispersal limitation. In many cases these changes manifestly exceed the capacity of individuals to accommodate to them, or of populations to avoid them by migration or dispersal. It is of great interest, therefore, to ask whether adaptation can be expected to rescue populations threatened with extinction, and, more broadly, how

natural populations and communities will evolve in response to global change.

## Adapt or die

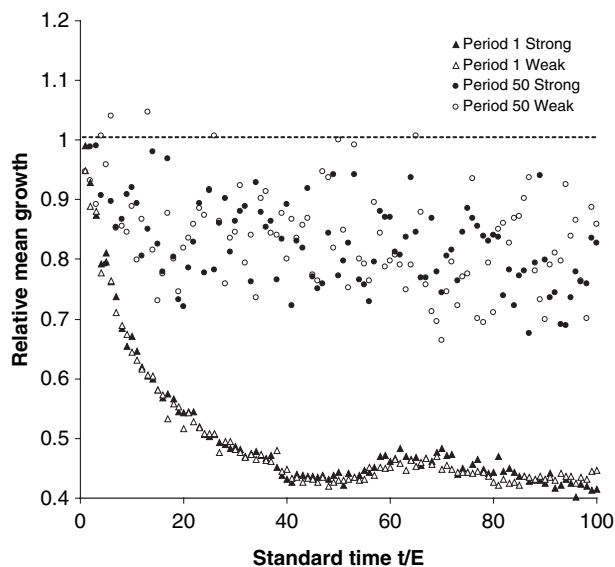
### Adaptive walks

Selection in a constant environment will result in an adaptive walk, the substitution of a series of beneficial mutations of successively higher fitness. At any particular point in time, all alleles at a locus affecting fitness can be ranked from the most to the least fit. The fitnesses of the very small fraction of alleles whose fitness exceeds that of the wild type will follow an extreme-value distribution, almost regardless of the overall distribution of fitness (Gillespie 1984). Supposing the difference in fitness between the best and second-best alleles to be  $\Delta_1$ , the difference between alleles with adjacent ranks  $i$  and  $j$  is a random variable with expected value  $\Delta_i = \Delta_1/i$ . This does not apply to the great majority of low-fitness alleles, but these can be neglected because they will never contribute to adaptation. Most beneficial alleles have only slightly greater fitness than the wild type, but rare alleles with very high fitness are less likely to be lost stochastically soon after they arise; hence, the first step of the adaptive walk will often involve a mutation with a large effect on fitness (Orr 2002). To model the walk as a whole, we could treat the extreme-value distribution based on the current wild type as a fixed allelic series, and follow the successive substitution of mutations of greater effect until the most fit allele has been fixed. A more realistic procedure is to regenerate a random series of allelic values whenever a substitution occurs, until the walk ends because no allele is superior to the current wild type; this is the 'mutational landscape' model of Gillespie (1984).

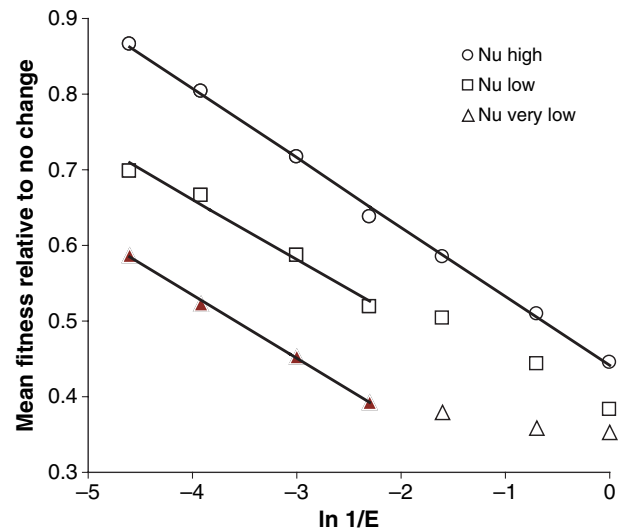
In practice, no population becomes permanently adapted, because conditions will change sooner or later. If the environment changes only rarely, each successive adaptive walk will be completed, and the population will be well adapted most of the time. If it changes more rapidly, few adaptive walks will be completed, and the population will be poorly adapted most of the time. If it changes very rapidly selection may be inadequate to restore adaptation quickly enough, and the population will dwindle and eventually become extinct. Recurrent change can be modeled by shifting the distribution of fitness to the left at intervals, reducing the fitness and increasing the rank of the current wild type. In a mutational landscape model, this can be accomplished by drawing new random values for each fitness rank while increasing the rank of each allele by a specified amount and thereby creating a new series of alleles whose fitness in the changed conditions exceeds that of any pre-existing type.

### Effects of frequency and severity of change

Suppose that conditions are unchanged for a period  $E$ , after which fitness is abruptly reduced by an amount proportional to  $\Delta_1$ . The overall rate of deterioration then has two components, the rate and the severity of deterioration. These combine to lower the fitness of alleles, but at the same time expose a longer series of potentially beneficial alleles and thereby increase the mutation supply rate. At some point the supply of mutations is sufficient to allow selection to restore adaptation, and the population comes into a dynamic equilibrium with its continually worsening environment. Long-term mean fitness depends on the frequency of change but not on its severity (Fig. 1). Although a more severe change will produce a steeper decline in mean fitness, adaptation will be restored more effectively because selection will be more intense. The depression of mean fitness can be expressed relative to a comparable population whose environment does not change. Numerical simulation of a mutational landscape model suggests that mean fitness  $w_s = w_0 - b \ln(1/E)$ , where  $b \approx 0.1$  and  $w_0$  depends on the mutation supply rate (Fig. 2). This result does not seem to depend on the details of the model: a fixed allelic series, or even a model with fitness increments of equal size, yields similar results. It suggests that populations may be able to adapt to quite rapid deterioration, provided that the mutation supply rate is fairly large.



**Figure 1** The effect of the frequency and severity of environmental change on adaptedness. Mutational landscape model with series of 100 alleles; environmental change simulated by shifting back the wild type one rank after a specified period  $E$  (1 or 50 time units) with weak or strong selection ( $\Delta_1 = 0.01$  or  $0.1$ ). From Bell (2008).

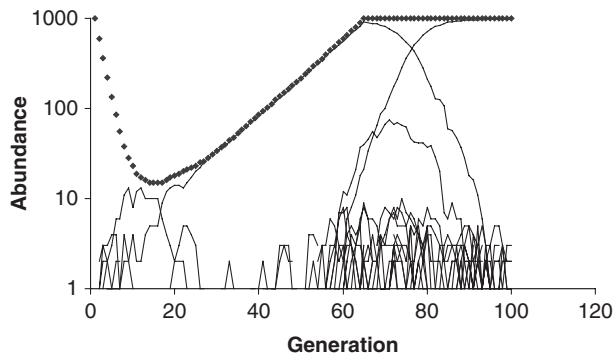


**Figure 2** Effect of environmental change on mean fitness in relation to mutation supply rate. Based on a mutational landscape model as in Fig. 1. From Bell (2008).

### Evolutionary rescue

The outlook is much less benign, however, if lower mean fitness leads to a reduction in population size and thereby in the mutation supply rate. This will happen if environmental deterioration causes the growth rate of the current wild type to become negative,  $r_0 < 0$ , so that population size begins to decline from its initial carrying capacity of  $N_0$  individuals. This tendency is opposed by rescue mutations, all with growth rate  $r_1 > 0$ , which comprise a fraction  $\phi$  of the overall genomic mutation rate  $U$ . The number of new rescue mutations appearing before the population becomes extinct depends on the total number of individuals that live during its period of decline, which will be  $-N_0/r_0$ . The probability that a new rescue mutation will spread is about  $2(r_1 - r_0)$ . Hence, the expected number of fixed rescue mutations is  $B = 2N_0U\phi(r_0 - r_1)/r_0$ , and the Poisson probability that at least one will spread is  $P = 1 - \exp(-B)$ . Evolutionary rescue therefore requires that the frequency of rescue mutations is sufficiently high,  $\phi > -[r_0/(r_0 - r_1)][\ln(1-P)]/(2N_0U)$ . For example, to attain  $P = 1/2$  in a small population ( $N_0 = 1000$ ) with genomic mutation rate  $U = 1$ , moderately rapid decline ( $r_0 = -0.1$ ) and moderately strong selection ( $r_1 = 0.1$ ) requires  $\phi > 0.0002$  approximately.

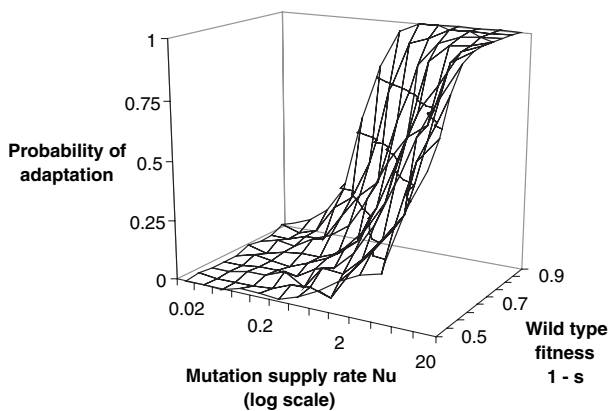
Evolutionary rescue in an extreme-value model is illustrated in Fig. 3. A single severe depression of fitness ( $r_0 = -0.5$ ) is countered by an extreme-value series of beneficial mutations of which the top three are rescue alleles with  $r > 0$ . The initial decline of the population is buffered by the increase in frequency of alleles with



**Figure 3** Dynamics of evolutionary rescue. The population has  $N_0 = 1000$ ,  $U = 1$ ,  $\Delta_1 = 0.25$  and  $r_0 = -0.5$ . The lines show the flux in frequency of a fixed series of 20 alleles, of which the top three have  $r > 0$ . The diamonds are overall population size.

growth  $r_0 < r < 0$ , but this effect is slight. The third-ranking allele appears at about generation 10 and rapidly spreads, rescuing the population. When it has nearly reached fixation the population is invaded first by the second-ranking and shortly afterwards by the top allele, which contribute to adaptation but were not responsible for rescue. Once the population has become abundant, a shifting spectrum of low-frequency mutations appears as mutation-selection balance is restored. The diagram shows a successful rescue; in most replicate simulations the population swiftly collapses.

The probability that a population will adapt to an abrupt stress depends on the severity of the stress and on the supply of beneficial mutations (Fig. 4). The two are linked, because for a given value of  $\Delta_1$  rescue mutations will be more frequent when the stress is less severe. These simulations suggest that there will be a substantial proba-



**Figure 4** The probability of evolutionary rescue in relation to the severity of environmental deterioration and the mutation supply rate. Output of extreme-value model with 20 alleles,  $\Delta_1 = 0.25$ ,  $N_0 = 1000$ ; plotted points each based on 100 simulations.

bility of adaptation ( $P > 0.2$  or so) only if the number of rescue mutants appearing exceeds one per generation. This condition might be difficult to meet, especially for small populations.

### Quantitative variation in sexual populations

These ideas stem from thinking about microbial populations, which are typically large, asexual and highly resistant to extinction. Small sexual populations where the response to selection depends on standing genetic variance are more directly related to conservation issues. Suppose that viability in such a population with  $\lambda = e^r > 1$  is governed by some quantitative character with phenotypic variance  $\sigma_p^2$  subject to stabilizing selection under a Gaussian fitness function with width  $\omega^2$ . The population mean phenotype is close to its current optimum, but this optimal value now begins to change over time at a rate  $k$  per generation. This induces a response to selection  $R$  that shifts the population mean closer to the new optimum. Consequently, the population shadows the moving optimum, changing at a corresponding rate  $k$  per generation but lagging behind the current optimum by a quantity  $k/R$  (Charlesworth 1993; Lynch and Lande 1993). The disparity between the population mean and the optimum reduces  $\lambda$ , however, and if the rate of environmental change exceeds some critical value  $k_{crit}$  then  $\lambda < 1$  and the population will decline in abundance and eventually become extinct. Provided that the environment changes rather smoothly, with little stochastic variation around its expected value, this critical value is given approximately by  $k_{crit} \approx R (2 V_\lambda \ln \lambda^*)^{0.5}$ , where  $V_\lambda = \sigma_p^2 + \omega^2$  and  $\lambda^*$  is the maximal rate of increase attained when the population mean phenotype matches the optimal value (cf equation 10 of Burger and Lynch 1995). Hence, the population is most likely to escape extinction through adaptation if genetic variance is large ( $R$  and  $\sigma_p^2$  large), selection is weak ( $\omega^2$  and  $V_\lambda$  large), and fecundity is high ( $\lambda^*$  large). Gomulkiewicz and Holt (1995) present a similar analysis in which environmental change reduces the population rate of increase below replacement level. This will eventually be restored by selection, but the population is likely to become extinct through demographic stochasticity if it remains rare for too long. The analytical theory does not yet handle the evolution of the genetic variance over time, but simulations show that large population size, high fecundity and an abundant supply of genetic variation through mutation facilitate escape from extinction by adaptation (Holt and Gomulkiewicz 2004). Although the microbial and quantitative-genetic models are constructed in very different ways they give broadly concordant results, and hold out the hope that a general theory of adaptation in relation to extinction can be

constructed. This would also imply that microbial models can be used to calibrate and test theories of evolutionary rescue. No such experiments have yet been reported, although we expect that they will become an important item on the agenda of evolutionary biology in the first decade of *Evolutionary Applications*. All we can do is to put forward some guesses to be tested by experience.

### Rate of beneficial mutation

The rate of mutation to beneficial alleles depends both on the fundamental mutation rate and on the degree of adaptation of the population, and so cannot be estimated without knowing both the state of the environment and the state of the population. The actual frequency of beneficial mutations is poorly known, although it is usually thought to be very low (Eyre-Walker and Keightley 2007). This is not necessarily the case: Shaw et al. (2000) claimed that roughly half of all mutations in *Arabidopsis* are beneficial. This claim was vigorously rebutted by Keightley and Lynch (2003), but at least 40% of all viable loss-of-function mutations in yeast are neutral or mildly beneficial under laboratory conditions (Bell 2008). This may explain why the decline of isolate lines where mutations are periodically trapped in bottlenecked populations is often very slow (e.g. Vassilieva et al. 1999), as beneficial as well as deleterious mutations are liable to be trapped. For example, Joseph and Hall (2004) found that about 5% of mutations in yeast mutation-accumulation lines were beneficial. The most precise estimate of the beneficial mutation rate at a nucleotide level is the study of an RNA virus by Sanjuan et al. (2004), who found 2/29 viable single-nucleotide mutations were beneficial. They used a chimaeric ancestral sequence that had not been cultured long under laboratory conditions and may well have been poorly adapted. Other virus experiments yield much lower estimates: the initial probability that a random mutation will increase fitness is about 0.0034 for phage  $\phi$ X174 adapting to high temperature and about 0.0009 for RNA VSV adapting to a new host cell type. Kassen and Bataillon (2006) trapped beneficial mutations in laboratory population of *Pseudomonas* and estimated that they arose at a frequency of  $7.6 \times 10^{-11}$  per gene per replication, equivalent in their system to  $\phi = 0.031$ . It is quite possible that mutations are more strongly deleterious in natural conditions than in the laboratory, but in that case laboratory estimates of the effect of mutation are difficult to interpret.

The rate of mutation to rescue alleles is even less well known. It could be estimated by adapt-or-die experiments in which a dilution series of a test organism is exposed to a stress severe enough to cause population decline, but we do not know of any published estimates except those

involving resistance to a lethal stress, usually a toxin such as an antibiotic. Moreover, even the rate of mutation to antibiotic resistance is far from being a simple parameter with a single value, but rather depends on the underlying physiology and genetics of the organism, its previous conditions of growth and the physical structure of the environment (Martinez and Baquero 2000). Resistance to quinolones, for example, may involve mutations in seven or eight genes, in each of which several nucleotide substitutions may be responsible (Hooper 1999), so that estimates of the rescue mutation rate can vary over four orders of magnitude, from  $1 \times 10^{-6}$  to  $4 \times 10^{-10}$  per genome per replication (Kohler et al. 1997).

### Variation and selection

The immediate response to selection in most animals and plants will depend on the level of standing genetic variation in the population. Inbred lines of *Drosophila* respond only slowly to artificial selection, at about 10% of the rate of outbred lines. Outbred lines successfully adapted to much higher concentrations of salt than lines in which variation was restricted by inbreeding or bottlenecks (Frankham et al. 1999). The average heritability of characters measured in outbred natural populations is about 0.5 (Mousseau and Roff 1987). Detailed analyses of exceptionally well-studied populations give a lower but still substantial average of 0.28 (Kruuk 2004). As most characters have substantial phenotypic variation, this implies that additive genetic variance may often be sufficient to support adaptation to rapid environmental change. Hendry et al. (2007) showed that phenotypic changes induced by human activities often exceed those associated with natural environmental variation, but concluded that this was attributable in large part to phenotypic plasticity. Réale et al. (2003) found that the parturition date of red squirrels in northern Canada advanced by 3.7 days per generation between 1989 and 1998, with adaptation contributing 0.8 days and plasticity the remainder. In short, natural populations often have the potential to adapt to global change, and have been documented to do so.

The recuperation of fitness by selection is equal to the standardized additive variance of fitness,  $SV_A = \sigma_G^2/w^2$  by the fundamental theorem (Fisher 1930), and on a few occasions this has been measured in natural populations. In the annual plant *Impatiens pallida* the corresponding phenotypic variance  $SV_P$  was 15.8 in natural conditions of growth, a very high value largely attributable to the majority of individuals that fail to reproduce at all; when these are neglected  $SV_P$  falls to 1.1 (Bell et al. 1991). Only a very small fraction of this was genetic, however, with  $SV_A = 0.03$  (Schoen et al. 1994). In the great tit *Parus*

major long-term observations of marked individuals yielded estimates of  $SV_P = 1.9$  and  $SV_A = 0.014$  (averaged over males and females) (McCleery et al. 2004). Similar work with another small bird, the collared flycatcher *Ficedula albicollis*, gave  $SV_P = 0.4$  and sex-averaged  $SV_A = 0.057$  (Merilä and Sheldon 2000). Although detailed field studies are scarce, the similarity of estimates from birds and plants suggests that  $SV_A$  might often lie between 0.01 and 0.05. Although not directly equivalent to the selective response to environmental change, this indicates that natural populations routinely cope with fitness degradation of a few per cent per generation.

### Adaptation to stressful conditions

The abundant genetic variation of many natural populations explains why they can often respond rapidly to changed conditions of growth. Field studies collated by Endler (1986) reported average selection coefficients of 0.33 for undisturbed environments and 0.30 for situations involving recent anthropogenic disturbance. The modal selection coefficient calculated from more recent selection gradient studies collated by Hoekstra et al. (2001) and Kingsolver et al. (2001) is between 0.15 and 0.35. These values may be inflated by reporting bias, but Hendry and Kinnison (1999) and Reznick and Ghalambor (2001) have emphasized that populations can often adapt successfully to abrupt environmental degradation. In the laboratory, artificial selection of a quantitative character over 30–50 generations can readily shift the population mean by 10  $\sigma_P$  or more (Hill and Bünger 2004), and the response increases with population size (Weber 2004). Moreover, many instances of evolutionary rescue have been reported, especially the evolution of antibiotic resistance in microbes, pesticide resistance in insects, and herbicide resistance in plants (see Palumbi 2001). This gives some reason to hope that many organisms will be able to adapt successfully to the relatively mild stresses imposed by global change (see Frankham and Kingsolver 2004).

Most of these example, however, involve rather mild stresses, very large populations of individuals or meristems, or experimental situations in which the propagation of the line is assured. When severe stress is encountered, one route to evolutionary rescue is the high mutation supply rate provided by a large population. As a crude rule of thumb, intended to be no more than a stimulus for more exact analyses, a substantial probability of adaptation may require at least one rescue mutation per generation, independently of the severity of the stress. Although we do not yet have good estimates of this rate, some unintentional natural experiments suggest that it may often be very low. Elm and chestnut trees have failed to evolve substantial resistance to introduced fungal

pathogens, despite populations of billions of trees. Vultures in India have failed to adapt to diclofenac, and will surely become extinct unless conservation efforts are successful, despite an initial population size of  $2\text{--}3 \times 10^7$  individuals (Green et al. 2004). In the first systematic discussion of adaptation to global change, Bradshaw and McNeilly (1991) were skeptical that selection will often succeed in rescuing stressed populations from extinction. They drew on their extensive experience with heavy-metal tolerance in plants to point out that tolerance readily evolves in a minority of species, but seldom, if ever, in most. Hundreds of species grow next to stressful environments such as salt marshes or serpentine soils without ever becoming adapted to them. Changing climates often cause shifts in plant distribution, such that species remain within the same range of conditions, with little evidence for adaptation *in situ*. The sporadic occurrence of adaptation to particular kinds of stressful conditions suggests that it may often depend on idiosyncratic properties of particular species, which either preadapt them to survive or make it more likely that adaptation will often occur. Any given stress would then sort the existing community and lead to the emergence of a less diverse group of the luckiest species.

Even very large population size is not necessarily an effective prophylactic against extinction. For example, Kwiatkowski and Roff (1976) reported high rates of extinction among the phytoplankton of a group of acidified oligotrophic lakes on the northern shore of Lake Huron. A nonacidified lake with low concentrations of heavy metals supported 55 species of eukaryotic algae. Only 34 species remained in Carlyle Lake, which had a mean pH of about 5 and elevated levels of heavy metals. It had a chlorophyll a concentration of about  $1 \mu\text{g L}^{-1}$ , equivalent to  $50 \mu\text{g L}^{-1}$  of algae, or about  $5 \times 10^4$  cells  $\text{L}^{-1}$  of algae the size of *Chlamydomonas*. This amounts to a whole-lake population of  $2.5 \times 10^{11}$  cells, or roughly  $10^{10}$  cells per species on average. The time period of acidification is not known, but is unlikely to have been <20 years, so the total number of cells exposed to mutation is likely to have been at least  $10^{12}$  on average per species. Nevertheless, about one-third of species became extinct. A more severely affected lake nearby, with pH 4–4.6 had only 12 species remaining. Baby Lake, close to a big nickel smelter at Sudbury, was almost devoid of eukaryotic life in 1972 except for a sparse population of *Chlorella*. This was attributable to its pH of 4 and very high heavy metal concentrations (Ni 3.2 ppm, Cu 0.7 ppm), and when isolates of *Chlorella* from the lake were tested in laboratory media they were found to have evolved tolerance to high levels of Ni and Cu (Stokes et al. 1973). *Scenedesmus* from a nearby lake was likewise tolerant of high levels of Cu. Hence, microbes can

become adapted even to very stressful conditions, but even microbes are likely to become extinct as stress becomes more severe, until only the most abundant (or the luckiest) survive.

### Life in the new atmosphere

The environmental factor that is driving potentially stressful change is not in itself stressful at all: elevated CO<sub>2</sub> is unlikely to represent a lethal stress to any organism, and will actually increase the growth of green plants and algae. It is likely to alter the species composition of communities, however, and some species may become extinct as a consequence. Moreover, shifts in composition, together with the evolution of individual species, may alter whole-community properties such as primary productivity. There is an urgent need to understand how populations and communities will respond to elevated CO<sub>2</sub>, because the atmosphere is changing so rapidly: there has been an increase in atmospheric CO<sub>2</sub> of approximately 90 ppm since the beginning of the industrial revolution, with the largest increase occurring during the past century (see for example Watson et al. 2001). Phytoplankton organisms can evolve in response to global change because they reproduce quickly relative to the timescale of global change and have large populations, so that future populations may be genetically different from contemporary ones. Here, we review selected examples of how experimental evolution can be used to advance understanding of how phytoplankton communities may respond to increases in atmospheric CO<sub>2</sub> over the next few decades.

### The oceanic carbon sink

Although the potential for adaptation to atmospheric change is an interesting issue, and one that will surely be used as a model system to make advances in general theory, the main reason for our interest in phytoplankton responses to elevated CO<sub>2</sub> is pragmatic: there is a potential carbon sink in the ocean, and we would like to be able to make predictions about it. About one-half of all photosynthetic carbon fixation on the planet occurs in oceans (Falkowski 1994; Beardall and Raven 2004). Phytoplankton have the potential to absorb a portion of anthropogenic CO<sub>2</sub> as fixed organic carbon and trap it in deep ocean sediments (Sarmiento and Toggweiler 1984; Raven and Falkowski 1999; Schippers et al. 2004), although debate exists over the size of such a sink. The biological carbon sink has generated interest in terms of its possible role in slowing global CO<sub>2</sub> enrichment, and has given rise to large-scale experiments designed to increase phytoplankton blooms and subsequent C sinking by adding iron dust to sections of ocean (Boyd et al.

2000; Buesseler et al. 2004; Coale et al. 2004). Although some increase in phytoplankton biomass has been observed, it has been difficult to assess how much carbon was exported to deeper waters, and in the two cases where carbon export was reported, it was modest compared with expected levels (de Baar et al. 2005). Experiments like this show continued interest in the idea that phytoplankton may have the potential to help manage global CO<sub>2</sub> enrichment.

Experimental evolution will enable us to make predictions about the carbon cycle that have clear ecological and economic value. To study a simple version of this in terms of the biological carbon pump, we need two pieces of information: which species will be present, and how much carbon will they sink? In other words, what will be the future composition of phytoplankton communities, and will descendants of individual species (or functional groups) continue to take up carbon at the same rate as contemporary taxa?

### The evolved high-CO<sub>2</sub> syndrome

Carbon uptake in model phytoplankton species is relatively well understood (see Raven 1991; Beardall et al. 1998; Riebesell 2004 for reviews). Progress continues to be made in documenting carbon uptake and growth in other species that are thought to play an important role in marine carbon fixation (for example Fu et al. 2007; Hutchins et al. 2007; de Castro Araújo and Garcia 2005; Bidigare 2002). Most recent studies, including those just cited, tend to report responses to changes in carbon availability coupled with other environmental change (see for example Schippers et al. 2004). While detailed physiological work can tell us a great deal about how phytoplankton respond to short-term increases in carbon availability, either alone or as part of a more complex environmental change, there is ample evidence that these responses are not reliably maintained over longer timescales (Polle et al. 2001; Collins and Bell 2004).

Most ecological and evolutionary theory is framed in terms of adapting to scarcity or stress. In contrast, contemporary global change is characterized by nutrient enrichment. Marine phytoplankton are not typically CO<sub>2</sub> limited for growth, in part because most actively transport carbon into the cell using an inducible carbon-concentrating mechanism (CCM) (Badger et al. 1998; Sültemeyer 1998; Badger and Spalding 2000; Coleman et al. 2002). The CCM tends to be tightly regulated such that it is downregulated when CO<sub>2</sub> is abundant (Bozzo and Coleman 2000). Information about the presence and affinities of CCMs is vital to determining how much carbon algal populations take up under a given CO<sub>2</sub> regime. Here, experimental evolution can help to understand

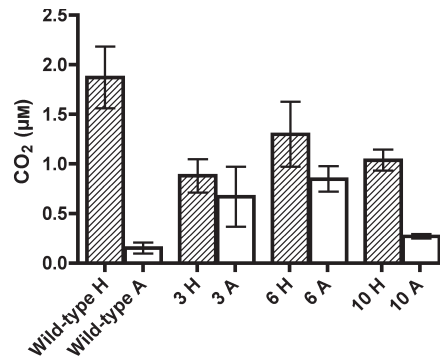


whether CCMs will continue to be maintained in their current state, and from this, how stable we expect the CO<sub>2</sub> affinity and rate of carbon uptake of phytoplankton to be over long timescales. This directly addresses the question of how closely we expect future phytoplankton populations to resemble contemporary ones.

To identify the long-term response to elevated CO<sub>2</sub>, Collins and Bell (2004) cultured the unicellular alga *Chlamydomonas reinhardtii* for 1000 generations at concentrations of CO<sub>2</sub> that gradually increased from ambient values to 1000 ppm.

We found that the lines evolved a syndrome characterized by increased photosynthesis without increased growth or insensitivity of both growth and photosynthesis to elevated CO<sub>2</sub> (Collins and Bell 2004). Microalgae isolated from the soil around naturally occurring CO<sub>2</sub> springs expressed a similar phenotype (Collins and Bell 2006), strengthening the case that the laboratory selection experiment could be used to predict the response of natural populations. The evolved syndrome is contrary to the short-term response of *C. reinhardtii* to elevated CO<sub>2</sub>, which involves an increase in both photosynthesis and growth. Hence, the evolutionary responses differed in both direction and magnitude from physiological responses. It follows that the predicted net CO<sub>2</sub> uptake of future phytoplankton communities is 38% less than the value expected from contemporary populations held under the same elevated CO<sub>2</sub> conditions, when the evolutionary response is taken into account (Collins et al. 2006) (Fig. 5). Moreover, there was significant divergence between initially similar replicates, showing that physiological responses are unlikely to remain constant or to scale up predictably over hundreds of generations. The statement that short-term responses may not scale up predictably to longer timescales is hardly surprising or novel, and studies such as these highlight the need for experimental tests of evolutionary responses to elevated CO<sub>2</sub> in marine phytoplankton. Long-term selection experiments with diatoms, coccolithophores and cyanobacteria are feasible, although more cumbersome than those with *Chlamydomonas*, which grows faster and reaches greater densities.

The main outcome of selection at elevated CO<sub>2</sub> in our experimental lines of *Chlamydomonas* was the degeneration of a regulated CCM (Collins et al. 2006). There was neither a fitness cost nor a benefit to the degeneration of the CCM, nor to the loss of its regulation at high CO<sub>2</sub>, suggesting that the pathway simply deteriorated through the accumulation of conditionally neutral mutations. Studies of pathway degeneration in yeast (Sliwa and Korona 2005; Maclean 2007) are consistent with unused or unnecessary pathways being lost by mutation accumulation, although there is also ample evidence that unused pathways are often maintained, perhaps because they are



Relative rates of net CO<sub>2</sub> uptake per population in wild-type and high selected lines at current and high levels (1050 ppm) of CO<sub>2</sub>

	Ambient (current) CO <sub>2</sub>	High (projected) CO <sub>2</sub>
Wild type	250	607
High selected lines	57.6 ± 16	375 ± 26

Rates are in arbitrary units, and are only intended to show relative values. Rates for high selected lines represent the average of three selected lines studied ± standard error. Rate for wild type is estimated from a single wild type line of *C.reinhardtii* (11–32b)

**Figure 5** Affinity of net total carbon uptake, shown as  $K_{0.5}$  in wild-type and high selection (numbered) lines acclimated to 1050 ppm CO<sub>2</sub> (filled bars, H) and air (white bars, A). Net total carbon uptake was calculated as bicarbonate uptake + net CO<sub>2</sub> uptake). Each bar represents averages ± standard error of the mean from independent duplicate or triplicate measurements. Accompanying table shows effect of changes in carbon uptake rates and population size on carbon sink calculations. From Collins et al. (2006).

tightly regulated and do not incur a metabolic cost when they are not in use (Maclean 2007).

Understanding how CCMs might change in response to elevated CO<sub>2</sub> is further complicated by the biology of marine phytoplankton growth. As marine phytoplankton form blooms that may locally deplete CO<sub>2</sub> supplies, the loss of a regulated CCM may be deleterious in natural populations even if global levels of CO<sub>2</sub> rise. In this case, the CCM might be maintained by periodic strong selection, even though experiments done at constant high CO<sub>2</sub> predict its degradation. To make an educated guess on whether carbon uptake will be maintained in its current form by purifying selection, more realistic experiments incorporating nutrient fluctuations seen in bloom-bust growth cycles are needed.

#### The effect of elevated CO<sub>2</sub> on community composition

There have been several attempts to investigate how high CO<sub>2</sub> levels may affect community composition. Some

studies have tested the hypothesis that an important response to CO<sub>2</sub> enrichment will be species succession, based on competition between two or more species with different resource requirements (Burkhardt et al. 2001; Rost et al. 2003). The findings from short-term enrichment studies on natural phytoplankton assemblages have been equivocal, depending on the initial assemblage used and the duration of the study (Tortell et al. 2000, 2002). While there is still debate about whether phytoplankton will respond to CO<sub>2</sub> enrichment by increasing growth or photosynthesis rates, phytoplankton usually have some other response to elevated CO<sub>2</sub>, such as changes in calcification, nitrogen use, or the productions of extracellular polymers (Beardall et al. 1998; Clark and Flynn 2000). Here, microcosm studies can be used to ask how increasing CO<sub>2</sub> may change more complex community dynamics. Shikano and Kawabata (2000) investigated the effect of elevated CO<sub>2</sub> and nutrient levels on a model community made up of *Escherichia coli* (bacteria), *Tetrahymena thermophila* (ciliate) and *Euglena gracilis* (green flagellate). This work showed differences in community composition that were both directly and indirectly attributable to elevated CO<sub>2</sub>. The main effect of CO<sub>2</sub> enrichment in this system was an increase in algal biomass. This was correlated with several indirect effects, most notably a reduction in bacterial biomass, which is the opposite effect from CO<sub>2</sub> enrichment in pure cultures of *E. coli*. Interestingly, the indirect effects of CO<sub>2</sub> enrichment were not observed to the same extent, or even in the same direction, if concentrations of other nutrients were not also increased. This shows how elevated CO<sub>2</sub> and nutrient levels may affect dynamics in a specific community.

Recent studies in experimental evolution have begun to address the effects of ecological processes on evolutionary outcomes. For example, natural enemies retarded the diversification of microbial systems whose diversity was high in the absence of the enemy by reducing population size (Morgan and Buckling 2004; Meyer and Kassen 2007). However, the opposite effect occurred in cases where diversity was low in the absence of an enemy (Gallet et al. 2007). These sorts of studies can help to establish general principles that will help to reconcile the apparent contradictions between studies documenting community-level responses to environmental change, including elevated CO<sub>2</sub>.

### Adaptation and the rate of global change

In the studies we have described, experimental evolution overlaps with shorter-term studies involving phytoplankton responses to global change. There are, however, some noteworthy issues that experimental evolution is uniquely equipped to study. One of the most obvious

features of contemporary global change is that the increase in CO<sub>2</sub> is much more rapid than in the geological past. While it seems clear that rates of environmental change should have a systematic effect on evolutionary outcomes, there is little explicit discussion of how this may occur. Both short-term (physiology) and long-term (evolution) experiments typically begin by suddenly placing a population in a stressful environment. The population is then allowed to either acclimate (reach some sort of steady-state physiological response) or adapt (reach some sort of steady-state evolutionary response). By contrast, global change is occurring gradually, so that populations will experience a continuous range of intermediate environments. A few simulation studies have made testable predictions about the effect of constantly changing environments on adaptive outcomes, in particular that lower rates of environmental change affect the dynamics of adaptive walks by reducing the fitness effect of fixed beneficial mutations, and increasing the range of time where the substitutions of largest effect are likely to occur. In addition, adaptation to slower rates of environmental change results in fewer possible outcomes relative to lineages that adapt to a sudden change (Collins et al. 2007; Kopp and Hermisson 2007). These simulations are in good agreement with mathematical models quantifying the lag with which a population is able to track a changing environment (Waxman and Peck 1999; Broom et al. 2003). At present, there are no published experimental tests of these hypotheses. Understanding how rates of environmental change affect evolutionary outcomes will help interpret laboratory experiments, where environments must be changed much faster than natural environments, and to use historical data more effectively, where rates of global change were many orders of magnitude slower than contemporary climate change.

From the above studies, how can experimental evolution help us to make predictions, or at least educated guesses, about future populations of phytoplankton and how much carbon they may sink? Based on the sparse experimental data, it is likely that phytoplankton will evolve in response to elevated CO<sub>2</sub>. The direct evolutionary response may not be adaptive, however, and may instead result in populations that are less productive than their ancestors. It is likely that rising CO<sub>2</sub> will also cause changes in phytoplankton community composition. Although there are predictions as to what these changes might be (Rost et al. 2003), they have yet to be tested using assemblages that have had the opportunity to undergo both ecological interactions and evolutionary change. At present, we are not in a position to make an informed guess about the composition of future phytoplankton communities, nor do we know how competitive

interactions may alter the evolutionary response to elevated CO<sub>2</sub>.

The main practical limitation to understand microalgal evolutionary responses to global change is simply the lack of published studies. There is no basis for determining how much variation in evolutionary responses is likely to exist within or between taxa. Work in terrestrial systems near CO<sub>2</sub> springs suggests that long-term responses vary idiosyncratically within or between taxa (Bettarini *et al.* 1999), whereas in microalgal communities at the same springs different genera responded in much the same way (Collins and Bell 2006).

Although detailed natural history information is needed to understand how the biology of particular taxa may change, there are also aspects of general evolutionary theory relevant to understanding the likely effects of global change on phytoplankton populations. As one of the important effects is likely to be a shift in the taxonomic composition of phytoplankton communities, it will be necessary to understand how ecological processes such as competition and predation affect evolutionary outcomes. This research program is well-advanced, and general patterns are already beginning to emerge (Brockhurst 2007). A second area where advances in general theory will help is in expanding our understanding of adaptation to accommodate more complex environmental change, such as constantly changing environments or scenarios where several aspects of the environment change simultaneously. Our current basis for understanding adaptation is most useful when a large, well-adapted population is subjected to a sudden change, and then allowed to adapt to a stable environment. While this is often a useful and sufficient simplification, it does not allow us to learn as much as possible from historical data or laboratory experiments that investigate responses to global change.

## Conclusions

We draw two main conclusions from this brief overview of the likely consequences of global change. The first is that evolutionary rescue is an onerous concept. Theory leads us to expect that it might be quite common, but the crucial parameter, the rate of rescue mutations, is almost completely unknown, and the fact that large populations can succumb to severe stress suggests that it may often be very low. The second is that evolutionary response to the coming increase in CO<sub>2</sub> seems to involve primarily a degradation of existing regulatory mechanisms rather than specific adaptation that increases productivity. This implies that future populations will be less efficient rather than more productive. We regret that the tone of our essay is therefore somewhat sombre, but we emphasize that the experimental program to investigate the

long-term effects of global change on populations and communities is still in its infancy. As more and more effort is drawn into this program, the outlines of the future will become sharper. We hope that they will also become more realistic, and more benevolent.

## Literature cited

- de Baar, H. J. W., P. W. Boyd, K. H. Coale *et al.* 2005. Synthesis of iron fertilization experiments: from the iron age in the age of enlightenment. *Journal of Geophysical Research* **110**:C09S16.
- Badger, M. R., and M. H. Spalding. 2000. CO<sub>2</sub> acquisition, concentration and fixation in cyanobacteria and algae. In R. C. Leegood, T. D. Sharkey, and S. von Caemmerer, eds. *Photosynthesis; Physiology and Metabolism*, pp. 369–397. Kluwer Academic Publishers, New York.
- Badger, M. R., T. J. Andrews, S. M. Whitney, M. Ludwig, D. C. Yellowlees, W. Leggat, and G. D. Price. 1998. The diversity and coevolution of Rubisco, plastids, pyrenoids, and chloroplast-based CO<sub>2</sub> concentrating mechanisms in algae. *Canadian Journal of Botany* **76**:1052–1071.
- Beardall, J., and J. A. Raven. 2004. The potential effects of global climate change on microalgal photosynthesis, growth and ecology. *Phycologia* **43**:26–41.
- Beardall, J., A. Johnston, and J. Raven. 1998. Environmental regulation of CO<sub>2</sub>-concentrating mechanisms in microalgae. *Canadian Journal of Botany* **76**:1010–1017.
- Bell, G. 2008. *Selection. The Mechanism of Evolution*, 2nd edn. Oxford Univ Press, Oxford.
- Bell, G., M. J. Lechowicz, and D. J. Schoen. 1991. The ecology and genetics of fitness in forest plants. III. Environmental variance in natural populations of *Impatiens pallida*. *The Journal of Ecology* **79**:697–713.
- Bell, G., M. J. Lechowicz, A. Appenzeller, M. Chandler, E. Deblois, L. Jackson, B. Mackenzie *et al.* 1993. The spatial structure of the physical environment. *Oecologia*, **96**:114–121.
- Bettarini, I., F. P. Vaccari, F. Miglietta, and A. Raschi. 1999. Stomatal physiology and morphology of calcareous grasslands in a future CO<sub>2</sub>-enriched world. In A. Raschi, F. P. Vaccari, and F. Miglietta, eds. *Ecosystem Response to CO<sub>2</sub>: The MAPLE Project Results*, pp. 39–52. European Commission Directorate-General for Research Unit D.1.1.- Preserving the ecosystem, Brussels.
- Bidigare, R. R.. 2002. Sources of inorganic carbon for photosynthesis in a strain of *Phaedactylum tricornutum*. *Limnology and Oceanography* **47**:1192–1197.
- Boyd, P. W., A. J. Watson, C. S. Law, E. R. Abraham, T. Trull, R. Murdoch, D. C. E. Bakker *et al.* 2000. A mesoscale phytoplankton bloom in the polar Southern Ocean stimulated by iron fertilization. *Nature* **407**:695–702.
- Bozzo, G. G., and B. Coleman. 2000. The induction of inorganic carbon transport and external carbonic anhydrase in

- Chlamydomonas reinhardtii* is regulated by external CO<sub>2</sub> concentration. *Plant Cell & Environment* **23**:1137–1144.
- Bradshaw, A. D. 1991. Genostasis and the limits to evolution. *Philosophical Transactions of the Royal Society of London. Series B* **333**:289–305.
- Bradshaw, A. D., and T. McNeilly. 1991. Evolutionary response to global climate change. *Annals of Botany* **67**(Suppl. 1):5–14.
- Brockhurst, M. A. 2007. Ecology: death and destruction determine diversity. *Current Biology* **17**:512–514.
- Broom, M., O. Tang, and D. Waxman. 2003. Mathematical analysis of a model describing evolution of an asexual population in a changing environment. *Mathematical Biosciences* **186**:93–108.
- Buesseler, K. O., J. E. Andrews, S. M. Pike, and M. A. Charette. 2004. The effects of iron fertilization on carbon sequestration in the Southern Ocean. *Science* **304**:414–417.
- Burger, R., and M. Lynch. 1995. Evolution and extinction in a changing environment: a quantitative-genetic analysis. *Evolution* **49**:151–163.
- Burkhardt, S., G. Amoroso, U. Riebesell, and D. Stütemeyer. 2001. CO<sub>2</sub> and HCO<sub>3</sub><sup>-</sup> uptake in marine diatoms acclimated to different CO<sub>2</sub> concentrations. *Limnology and Oceanography* **46**:1378–1391.
- de Castro Araújo, S., and V. M. T. Garcia. 2005. Growth and biochemical composition of the diatom *Chaetoceros* cf. *Wighamii* brightwell under different temperature, salinity and carbon dioxide levels. I. Protein, carbohydrates and lipids. *Aquaculture* **246**:405–412.
- Charlesworth, B. 1993. Directional selection and the evolution of sex and recombination. *Genetical Research* **61**:205–224.
- Clark, D. R., and K. J. Flynn. 2000. The relationship between the dissolved inorganic carbon concentration and growth rate in marine phytoplankton. *Proceedings of the Royal Society. London B* **267**:953–959.
- Coale, K. H. *et al.* 2004. Southern Ocean iron enrichment experiment: carbon cycling in high- and low-Si waters. *Science* **304**:408–414.
- Coleman, B., I. E. Huertas, S. Bhatti, and J. S. Dason. 2002. The diversity of inorganic carbon acquisition mechanisms in eukaryotic microalgae. *Functional Plant Biology* **29**:261–270.
- Collins, S., and G. Bell. 2004. Phenotypic consequences of 1,000 generations of selection at elevated CO<sub>2</sub> in a green alga. *Nature* **431**:566–569.
- Collins, S., and G. Bell. 2006. Evolution of natural algal populations at elevated CO<sub>2</sub>. *Ecological Letters* **9**:129–135.
- Collins, S., D. Stütemeyer, and G. Bell. 2006. Changes in carbon uptake in populations of *Chlamydomonas reinhardtii* selected at high CO<sub>2</sub>. *Plant, Cell & Environment* **29**:1812–1819.
- Collins, S., J. de Meaux, and C. Acquisti. 2007. Adaptive walks towards a moving optimum. *Genetics* **176**:1089–1099.
- Endler, J. A. 1986. *Natural Selection in the Wild*. Princeton University Press, Princeton, NJ.
- Eyre-Walker, A., and P. D. Keightley. 2007. The distribution of fitness effects of new mutations. *Nature Reviews Genetics* **8**:610–618.
- Falkowski, P. G. 1994. The role of phytoplankton photosynthesis in global biogeochemical cycles. *Photosynthesis Research* **39**:235–258.
- Fisher, R. A. 1930. *The Genetical Theory of Natural Selection*. Oxford University Press, Oxford.
- Frankham, R., and J. Kingsolver. 2004. *Responses to Environmental Change: Adaptation or Extinction*. In *Evolutionary Conservation Biology*, (R. Ferrière, U. Dieckmann, and D. Couvet, eds.) pp. 85–100. Cambridge Univ Press, Cambridge.
- Frankham, R., K. Lees, M. E. Montgomery, P. R. England, E. H. Lowe, and D. A. Briscoe. 1999. Do population size bottlenecks reduce evolutionary potential? *Animal Conservation* **2**:255–260.
- Fu, F.-X., M. E. Warner, Y. Zhang, Y. Feng, and D. A. Hutchins. 2007. Effects of increased temperature and CO<sub>2</sub> on photosynthesis, growth, and elemental ratios in marine *Synechococcus* and *Prochlorococcus* (cyanobacteria). *Journal of Phycology* **43**:485–496.
- Gallet, R., S. Alizon, P.-A. Comte, A. Gutierrez, F. Depaulis, M. van Baalen, E. Michel, and C. D. M. Müller-Graf. 2007. Predation and disturbance interact to shape prey species diversity. *The American Naturalist* **170**:143–154.
- Gillespie, J. H. 1984. Molecular evolution over the mutational landscape. *Evolution* **38**:1116–1129.
- Gomulkiewicz, R., and R. D. Holt. 1995. When does evolution by natural selection prevent extinction? *Evolution* **49**:201–207.
- Grant, P. R., and B. R. Grant. 2002. Unpredictable evolution in a 30-year study of Darwin's finches. *Science* **296**:707–711.
- Green, R., I. Newton, S. Schultz, A. A. Cunningham, M. Gilbert, D. J. Pain, and V. Prakash. 2004. Diclofenac poisoning as a cause of vulture population declines across the Indian subcontinent. *The Journal of Applied Ecology* **41**:793–800.
- Hendry, A. P., and M. T. Kinnison. 1999. The pace of modern life: measuring rates of contemporary microevolution. *Evolution* **53**:1637–1653.
- Hendry, A. P., T. J. Farrugia, and M. T. Kinnison. 2007. Human influences on rates of phenotypic change in wild animal populations. *Molecular Ecology* **17**:20–29.
- Hereford, J., T. F. Hansen, and D. Houle. 2004. Comparing strengths of directional selection: how strong is strong? *Evolution* **58**:2133–2143.
- Hill, W. G., and L. Bünger. 2004. Inferences on the genetics of quantitative traits from long-term selection in laboratory and domestic animals. *Plant Breeding Reviews* **24**, Part 2:169–210.
- Hoekstra, H. E. *et al.* 2001. Strength and tempo of natural selection in the wild. *Proceedings of the National Academy of Sciences of the United States of America* **98**:9157–9160.

- Holt, R. D., and R. Gomulkiewicz. 2004. Conservation implications of niche conservatism and evolution in heterogeneous environments. In *Evolutionary Conservation Biology*, (R. Ferrière, U. Dieckmann, and D. Couvet, eds.) pp. 244–264. Cambridge Univ Press, Cambridge.
- Hooper, D. C. 1999. Mechanisms of fluoroquinolone resistance. *Drug Updates* 2:38–55.
- Hutchins, D. A., F.-X. Fu, Y. Zhang, M. E. Warner, Y. Feng, K. Portune, P. W. Bernhardt, and M. R. Mulholland. 2007. CO<sub>2</sub> control of *Trichodesmium* N<sub>2</sub> fixation, photosynthesis, growth rates, and elemental ratios: implications for past, present, and future ocean biogeochemistry. *Limnology and Oceanography* 52:1293–1304.
- Inchausti, P., and J. Halley. 2002. The long-term temporal variability and spectral colour of animal populations. *Evolutionary Ecology Research* 4:1033–1048.
- Joseph, S. B., and D. W. Hall. 2004. Spontaneous mutations in diploid *Saccharomyces cerevisiae*: more beneficial than expected. *Genetics* 168:1817–1825.
- Kassen, R., and T. Bataillon. 2006. Distribution of fitness effects among beneficial mutations before selection in experimental populations of bacteria. *Nature Genetics* 38:484–488.
- Keightley, P. D., and M. Lynch. 2003. Toward a realistic model of mutations affecting fitness. *Evolution* 57:683–685.
- Kingsolver, J. G. *et al.* 2001. The strength of phenotypic selection in natural populations. *The American Naturalist* 157:245–261.
- Kohler, T., M. Michea-Hamzepour, P. Plesiat, A. L. Kahr, and J. C. Pechere. 1997. Differential selection of multidrug efflux systems by quinolones in *Pseudomonas aeruginosa*. *Antimicrobial Agents and Chemotherapy* 41:2540–2543.
- Kopp, M., and J. Hermisson. 2007. Adaptation of a quantitative trait to a moving optimum. *Genetics* 176:715–719.
- Koscielny-Bunde, E., A. Bunde, S. Havlin, H. E. Roman, Y. Goldreich, and H.-J. Schellnhuber. 1998. Indication of a universal persistence law governing atmospheric variability. *Physical Review Letters* 81:729–732.
- Kruuk, L. E. B. 2004. Estimating genetic parameters in natural populations using the ‘animal model’. *Philosophical Transactions of the Royal Society of London. Series B* 359:873–890.
- Kwiatkowski, R. E., and J. C. Roff. 1976. Effects of acidity on the phytoplankton and primary productivity of selected northern Ontario lakes. *Canadian J Botany* 54:2546–2561.
- Lynch, M. 1987. The consequences of fluctuating selection for isozyme polymorphisms in *Daphnia*. *Genetics* 115:657–669.
- Lynch, M., and R. Lande. 1993. Evolution and extinction in response to environmental change. In P. M. Kareiva, J. G. Kingsolver, and R. B. Huey, eds. *Biotic Interactions and Global Climate Change*, pp. 234–250. Sinauer, Sunderland, MA.
- Macleán, R. C. 2007. Pleiotropy and GAL pathway degeneration in yeast. *Journal of Evolutionary Biology* 20:1333–1338.
- Martin, G., and T. Lenormand. 2006. A general multivariate extension of Fisher’s geometrical model and the distribution of mutation fitness effects across species. *Evolution* 60:893–907.
- Martinez, J. L., and F. Baquero. 2000. Mutation frequencies and antibiotic resistance. *Antimicrobial Agents and Chemotherapy* 44:1771–1777.
- McCleery, R. H., R. A. Pettifor, P. Armbruster, K. Meyer, B. C. Sheldon, and C. M. Perrins. 2004. Components of variance underlying fitness in a natural population of the great tit *Parus major*. *The American Naturalist* 164:E62–E72.
- Merilä, J., and B. C. Sheldon. 2000. Lifetime reproductive success and heritability in nature. *The American Naturalist* 155:301–310.
- Meyer, J. R., and R. Kassen. 2007. The effects of competition and predation on diversification in a model adaptive radiation. *Nature* 446:432–435.
- Morgan, A. D., and A. Buckling. 2004. Parasites mediate the relationship between host diversity and disturbance. *Ecological Letters* 7:1029–1034.
- Mousseau, T. A., and D. A. Roff. 1987. Natural selection and the heritability of fitness components. *Heredity* 59:181–197.
- Orr, H. A. 2002. The population genetics of adaptation: the adaptation of DNA sequences. *Evolution* 56:1317–1330.
- Palumbi, S. R. 2001. *The Evolution Explosion*. Norton & Co, New York & London.
- Pimm, S. L., and A. Redfearn. 1988. The variability of population densities. *Nature* 334:613–614.
- Polle, A., I. McKee, and L. Blaschke. 2001. Altered physiological and growth responses to elevated [CO<sub>2</sub>] in offspring from hold oak (*Quercus ilex* L.) mother trees with lifetime exposure to naturally elevated [CO<sub>2</sub>]. *Plant Cell & Environment* 24:1075–1083.
- Raven, J. A. 1991. Physiology of inorganic carbon acquisition and implications for resource use efficiency by marine phytoplankton: relation to increased CO<sub>2</sub> and temperature. *Plant Cell & Environment* 14:779–794.
- Raven, J. A., and P. G. Falkowski. 1999. Oceanic sinks for atmospheric CO<sub>2</sub>. *Plant Cell & Environment* 22:741–755.
- Réale, D., A. G. McAdam, S. Boutin, and D. Bertaux. 2003. Genetic and plastic responses of a northern mammal to climate change. *Proceedings of the Royal Society of London* 270:591–596.
- Reznick, D. N., and C. K. Ghalambor. 2001. The population ecology of rapid evolution. *Genetica* 112/113:183–198.
- Riebesell, U. 2004. Effects of CO<sub>2</sub> enrichment on marine phytoplankton. *Journal of Oceanography* 60:719–729.
- Rost, B., U. Riebesell, and S. Burkhardt. 2003. Carbon acquisition of bloom-forming marine phytoplankton. *Limnology and Oceanography* 48:55–67.
- Sanjuan, R., A. Moya, and S. F. Elena. 2004. The distribution of fitness effects caused by single-nucleotide substitutions in an RNA virus. *Proceedings of the National Academy of Sciences of the United States of America* 101:8396–8401.
- Sarmiento, J. L., and J. R. Toggweiler. 1984. A new model for the oceans in determining atmospheric pCO<sub>2</sub>. *Nature* 308:621–624.

- Schippers, P., M. Lüring, and M. Scheffer. 2004. Increase of atmospheric CO<sub>2</sub> promotes phytoplankton productivity. *Ecological Letters* 7:446–451.
- Schluter, D. 2000. *The Ecology of Adaptive Radiation*. Oxford University Press, Oxford.
- Schoen, D. J., G. Bell, and M. J. Lechowicz. 1994. The ecology and genetics of fitness in forest plants. IV. Quantitative genetics of fitness components in *Impatiens pallida*. *American Journal of Botany* 81:232–239.
- Shaw, R. G., D. L. Byers, and E. Darms. 2000. Spontaneous mutational effects on reproductive traits of *Arabidopsis thaliana*. *Genetics* 155:369–378.
- Shikano, S., and Z. Kawabata. 2000. Effect at the ecosystem level of elevated atmospheric CO<sub>2</sub> in an aquatic microcosm. *Hydrobiologia* 436:209–216.
- Sliwa, P., and R. Korona. 2005. Loss of dispensable genes is not adaptive in yeast. *Proceedings of the National Academy of Sciences of the United States of America* 102:17670–17674.
- Snaydon, R. W., and M. S. Davies. 1982. Rapid divergence of plant populations in response to recent changes in soil conditions. *Evolution* 36:289–297.
- Stenseth, N.-C., and J. Maynard Smith. 1984. Coevolution in ecosystems: Red Queen evolution or stasis? *Evolution* 38:870–880.
- Stewart, S. C., and D. J. Schoen. 1987. Pattern of phenotypic viability and fecundity selection in a natural population of *Impatiens pallida*. *Evolution* 41:1290–1301.
- Stokes, P. M., T. C. Hutchinson, and K. Krauter. 1973. Heavy-metal tolerance in algae isolated from contaminated lakes near Sudbury, Ontario. *Canadian Journal of Botany* 51:2155–2168.
- Sültemeyer, D. 1998. Carbonic anhydrase in eukaryotic algae: characterization, regulation, and possible function during photosynthesis. *Canadian Journal of Botany* 76:962–972.
- Tortell, P. D., G. H. Rau, and F. M. M. Morel. 2000. Inorganic carbon acquisition in coastal Pacific phytoplankton communities. *Limnology and Oceanography* 47:1485–1500.
- Tortell, P. D., G. R. DiTullio, D. M. Sigman, and F. M. M. Morel. 2002. CO<sub>2</sub> effects on taxonomic composition and nutrient utilization in an Equatorial Pacific phytoplankton assemblage. *Marine Ecology Progress Series* 236:37–43.
- Van Valen, L. 1973. A new evolutionary law. *Evolutionary Theory* 1:1–30.
- Vassilieva, L. L., A. M. Hook, and M. Lynch. 1999. The fitness effects of spontaneous mutations in *Caenorhabditis elegans*. *Evolution* 54:1234–1246.
- Watson, R., J. Houghton, and D. Yihui. (Editors) 2001. *Climate Change 2001: The Scientific Basis*. Intergovernmental Panel on Climate Change, Cambridge Univ Press, Cambridge.
- Waxman, D., and J. R. Peck. 1999. Sex and adaptation in a changing environment. *Genetics* 153:1041–1053.
- Weber, K. 2004. Population size and long-term selection. *Plant Breeding Reviews* 24, Part 1:249–268.