MINI REVIEW

# The experimental evolution of specialists, generalists, and the maintenance of diversity

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## Abstract

Environmental heterogeneity may be a general explanation for both the quantity of genetic variation in populations and the ecological niche width of individuals. To evaluate this hypothesis, I review the literature on selection experiments in heterogeneous environments. The niche width usually – but not invariably – evolves to match the amount of environmental variation, specialists evolving in homogeneous environments and generalists evolving in heterogeneous environments. The genetics of niche width are more complex than has previously been recognized, particularly with respect to the magnitude of costs of adaptation and the putative constraints on the evolution of generalists. Genetic variation in fitness is more readily maintained in heterogeneous environments than in homogeneous environments and this diversity is often stably maintained through negative frequency-dependent selection. Moreover environmental heterogeneity appears to be a plausible mechanism for at least two well-known patterns of species diversity at the landscape scale. I conclude that environmental heterogeneity is a plausible and possibly very general explanation for diversity across the range of scales from individuals to landscapes.

## Introduction

Environmental heterogeneity has often been proposed as a general explanation for the evolution of genotypic niche breadth, the quantity of genetic variance within populations, and patterns of species diversity across landscapes (Lewontin, 1974; Whittaker & Levin, 1975; Nevo, 1978; Tilman, 1982; Futuyma & Moreno, 1988; Rosenzweig, 1995). At least three lines of evidence lend support to this view. First, niche width is commonly observed to vary among species and among genotypes within species (Pennak, 1951; Cook & Johnson, 1967; Hulburt, 1985). Secondly, reciprocal transplant and implant experiments often reveal abundant genotype-by-environment interaction for fitness in both natural and domesticated populations irrespective of whether the types being tested are sibs, varieties within species or

species themselves (Davies & Snaydon, 1976; Simmonds, 1981; Schoen *et al.*, 1994; Bell, 1997a). Thirdly, correlational studies typically identify environmental heterogeneity as an important contributor to the total variance in species diversity at large spatial scales (MacArthur, 1964; Anderson, 1978; Rosenzweig, 1995).

Conspicuous by their absence, however, are direct, experimental tests of the role of environmental heterogeneity in governing the fate of diversity. No doubt a large part of the reason for the absence of such experiments is that the theory is explicitly concerned with how fitness varies across conditions of growth and through time yet fitness itself, let alone its variation in response to environmental conditions, is notoriously difficult to measure in the field. Additionally, evolutionary ecology appears to have been biased in favour of studying large, complex and long-lived metazoans, making it difficult to perform the relevant *evolutionary* experiments. These difficulties can be largely circumvented by turning to small, short-lived organisms such as microbes and fruit flies where the environmental conditions can be

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controlled by the experimenter and fitness measured directly either by estimating the relevant population growth parameters in pure culture or through competition among marked strains or chromosomes. It is thus possible to construct experiments to test directly the evolutionary fate of diversity in the face of different kinds of environmental heterogeneity.

My goal in this review is to assemble evidence from the literature on experimental evolution in heterogeneous environments in an effort to assess the idea that environmental heterogeneity is a plausible, and possibly quite general, explanation for patterns of diversity in nature. More specifically, I evaluate three hypotheses: (1) the ecological niche of a genotype evolves to match the amount of environmental variation; (2) diversity, by which I specifically mean the genetic variance in fitness, is maintained by environmental heterogeneity; (3) environmental heterogeneity plays a crucial role in governing patterns of species diversity across landscapes.

The theory of selection in heterogeneous environments has been reviewed elsewhere (Felsenstein, 1976; Hedrick, 1986; Futuyma & Moreno, 1988; Chesson, 2000a) so I outline only the broad principles and predictions below. The environment is taken to be composed of a series of patches or habitats that differ in the conditions of growth offered. The niche of any genotype can be described by its mean fitness and its environmental variance in fitness across a range of environments. Given the same mean fitness, ecological specialists, having a narrower niche width (breadth of adaptation) than ecological generalists, will have a higher environmental variance in fitness across the range of patches considered. We are seeking explanations for the evolution of variance in niche width (i.e. – specialists vs. generalists) and for the maintenance of genetic variance in fitness across patches, or genotype-by-environment interaction variance for fitness, among ecologically similar types.

Environmental heterogeneity generates diversifying selection, either in space or time. If there are no constraints on the evolution of the ecological niche, the breadth of adaptation evolves to match the amount of environmental variation (Via & Lande, 1985; Scheiner, 1993). Thus ecological specialists evolve in environments that are relatively homogeneous in space and time whereas ecological generalists evolve in environments that are heterogeneous in either dimension. The scale of environmental variation, relative to the lifetime of an individual, is thought to be important in determining the kinds of generalist that evolve; coarse-grained variation (*sensu* Levins, 1968) favours the evolution of plasticity in the conventional sense of a type being able to respond phenotypically early in development but remaining fixed for that phenotype for the remainder of its life. Fine-grained variation, on the other hand (*sensu* Levins, 1968) favours the evolution of versatile types capable of reversible phenotypic response to the prevailing

environmental conditions. Environmental variation can thus be usefully decomposed according to the pattern and the scale of variation (Fig. 1).

Selection for specialization is expected to lead to the evolution of negative genetic correlations in fitness across environments, different types being favoured in different patches of the environment. This is a necessary, although not sufficient, condition for the stable maintenance of diversity in a heterogeneous environment (Levene, 1953; Dempster, 1955). The manner of population regulation (Dempster, 1955), the frequency of different kinds of sites (Maynard Smith & Hoekstra, 1980), and the amount of gene flow between patches (Endler, 1973; Holt, 1996; Kawecki, 2000) are also important in determining whether or not diversity is stably maintained. Briefly, diversity is most readily maintained when dispersal among patches is low relative to the strength of selection, population regulation is density dependent at the level of the patch, and the number of individuals contributed by each patch to the total population is not too unbalanced. If all these conditions hold, diversity will be stably maintained by negative frequency-dependent selection
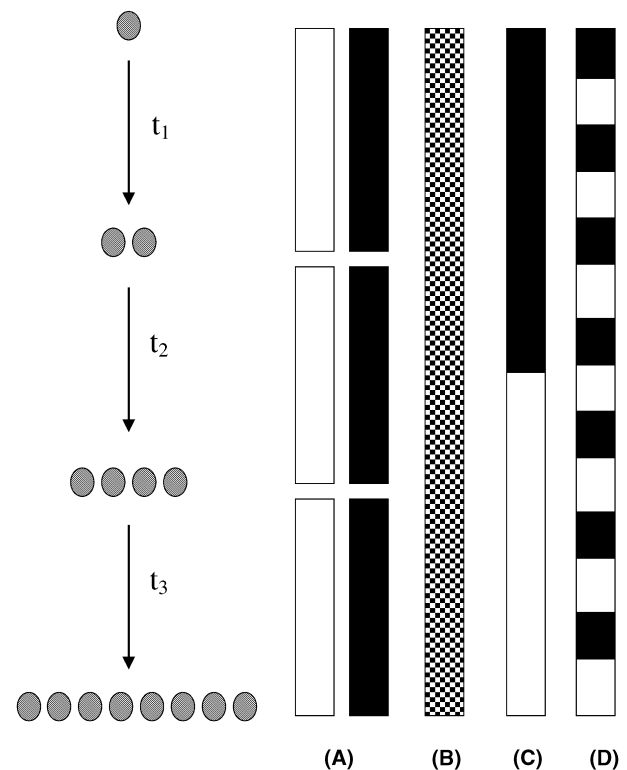


**Fig. 1** Four kinds of environmental variation in relation to the generation time ($t_i$) of a vegetatively dividing unicell. The colour of the bars represents patches of different quality experienced as (A) spatially coarse-grained variation, (B) spatially fine-grained variation, (C) temporally coarse-grained variation and (D) temporally fine-grained variation.

(Levene, 1953; Maynard Smith & Hoekstra, 1980). This is a very general argument, applying with equal force to both asexual and sexual populations as well as the coexistence of species within communities. Ecologists have framed a similar argument in terms of the relative strength of intra vs. interspecific competition for resources or habitats: each species must limit itself more than it limits other species for diversity to be stably maintained (Levins, 1968; Tilman, 1982; Chesson, 2000b). Note that the relative strength of competition within and among types is, in fact, an implicit form of density-dependent population regulation.

Two further points must be made. First, there is at least one alternative mechanism for the stable maintenance of diversity in heterogeneous environments, overdominance of heterozygote fitness across patches (Haldane & Jayakar, 1962; Lewontin, 1974). This cannot be a general explanation, however, because it applies only to sexual diploids. Secondly, it seems reasonable to suggest that environmental heterogeneity should play an important role in governing patterns of species diversity across the larger spatial scales of communities within regions or landscapes, however, the precise mechanism by which this occurs remains controversial (Ricklefs & Schluter, 1993; Rosenzweig, 1995).

### The design and interpretation of selection experiments in heterogeneous environments

The selection experiment has been known as a method for testing fundamental theories of evolution since the late nineteenth century (Dallinger, 1887) and has been employed, in various capacities, ever since (discussed in Bell, 1997a). To understand the fate of diversity in heterogeneous environments, the appropriate experiment is as follows. A base population, which may be genetically uniform or diverse and either sexual or asexual, is inoculated into an environment, which may be heterogeneous or homogeneous, and natural selection is allowed to proceed for as many generations as one's patience allows. Samples are then extracted from each of the selected lines and their fitness assayed across a range of environments, preferably the same environments used during selection. The results are then cast in a genotype-by-environment matrix, where each of the selected lines are the different levels of genotype.

Two sorts of adaptation can be detected in this way. The first is a general adaptation to the conditions of culture, as commonly occurs when a natural population is transferred to the laboratory. This is detected by comparing the performance of the selected lines across all environments against their founders or an unselected control line. The second is specific adaptation to the particular selection regime, such that each line is the fittest in its own environment when compared with lines evolved elsewhere. Specific adaptation is evidenced by the occurrence of genotype-by-environment interaction

among the selected lines, analysed separately from the founder. Within selection line genetic and environmental variances may be estimated by isolating individual genotypes from each selection line and proceeding as before.

The experimental health sciences such as virology and microbiology have also made use of natural selection experiments to study the mechanistic basis of adaptation in specific genotypes, usually termed 'mutants'. A similar procedure is followed, except that instead of assaying genotypes across a range of environments, novel or unusual genotypes are extracted and then characterized genetically and physiologically. Conventional statistical tests are often not employed. I have named these 'mutant-selection' experiments to distinguish them from the more conventional natural selection experiments outlined above.

A second variant of the conventional natural selection experiment starts with well-characterized types, which may be different genotypes or species, and allows them to compete in a heterogeneous environment. If the types coexist, and either can invade a population of the other when rare, then diversity is stably maintained. I term these 'coexistence' experiments. The original methodology dates back to the work of Gause (1934) and was popularized in ecology by Tilman (1977). Bio-engineers also employ coexistence experiments with microbes for use in biochemical engineering (Davison & Stephanopoulos, 1986). In effect, coexistence experiments represent a special instance of conventional natural selection sorting among two, or sometimes three, predefined types.

### Literature search

I searched the major biology databases such as BIOSIS, AGRICOLA, and BIOLOGICAL AND AGRICULTURAL ABSTRACTS using keywords such as 'diversity', 'niche', 'selection', 'adaptation', 'environment' and different combinations thereof. I also searched health science databases such as MEDLINE and CANCERLIT for examples of selection experiments documenting the evolution of human pathogens. I retained only those experiments that report the results of natural, rather than artificial, selection in heterogeneous environments. The search is probably close to being exhaustive within evolutionary ecology, as the field is still quite small. The same cannot be said of the health science literature, which is large and uses a wholly different lexicon from evolutionary ecology to describe natural selection and adaptation in the laboratory. No doubt I have missed some important papers in this area and I would appreciate readers bringing these to my attention.

There is also a vast literature on selection experiments in agronomy and animal breeding, which I have largely ignored because the majority concern artificial, rather than natural, selection and so are difficult to interpret in

the context of the fate of genetic variation in natural environments. Where these sorts of experiments bear directly on the topics under discussion, as for example in the section on selection in environments of different quality, I provide key references for entrance into the literature. Note that because of space constraints, I have not considered experiments on the evolution of habitat choice or character displacement.

## Experimental evolution of the ecological niche

A genotype's niche is often described by a function mapping fitness to a continuously distributed environmental variable. This function is typically envisaged as a humped curve with maximum fitness at some intermediate environmental value and a breadth of adaptation described by the variance in fitness along the environmental axis (e.g. Lynch & Gabriel, 1987). In the absence of genetic constraints, the position of the niche should evolve to match the average state of the environment and the breadth of adaptation should evolve to match the amount of environmental variation (Futuyma & Moreno, 1988) leading to the evolution of ecological generalists in heterogeneous environments and ecological specialists in homogeneous environments. Moreover the pattern of environmental variation is thought to play an important role in the evolution of the niche. Generalists are expected to evolve more readily in temporally varying environments, regardless of scale, than in spatially varying environments, because each type is compelled to grow first in one patch and then another, the fittest type being the one that grows best across all patches. In a spatially varying environment, by contrast, a refuge for more specialized types always exists, so the strength of selection on the breadth of adaptation should be weaker.

A number of experiments have examined the evolution of the breadth of adaptation in heterogeneous and homogeneous environments. As expected, selection in constant environments tends to lead to the evolution of specialists, whereas selection in temporally varying environments leads to the evolution of generalists (bacteria – Bennett et al., 1992; algae – Reboud & Bell, 1997; Kassen & Bell, 1998; viruses – Weaver et al., 1999).

Reboud & Bell (1997) examined the breadth of adaptation after selection in both spatially or temporally varying environments. Lines of Chlamydomonas reinhardtii were first selected for approximately 1000 generations as phototrophs in the light or as heterotrophs in the dark (Bell & Reboud, 1997). This led to the evolution of light-specialists and dark-specialists, as expected. The lines were then further selected for approximately 200 generations under spatial or temporal variation in light and dark conditions. Temporal variation led to the evolution of generalists capable of growing well in both the light and the dark whereas spatial variation prevented the emergence of a single, superior generalist, both light- and dark-specialists being retained in the population. A

similar experiment by Riddle et al. (1986), with Tribolium selected on different flours, found no evidence for adaptation to any of the environments, either uniform or variable. This suggests a lack of genetic variation from which to select in the founding population.

Selection in a spatially varying environment need not lead inevitably to the evolution of specialization, of course. The rate of migration must be sufficiently low, relative to the strength of selection, in order to generate local adaptation to each patch of the environment (Brown & Pavlovic, 1992; Holt, 1996; Kawecki, 2000). Moreover, if one patch is much more frequent or much more productive, adaptation to rare or unproductive patches will be difficult to achieve (Van Tienderen, 1991). I am unaware of any selection experiments that have explicitly explored the role of migration, patch frequency, or patch productivity on the outcome of selection. Bell & Reboud (1997) observed the evolution of both specialists and generalists in originally isogenic lines of C. reinhardtii by selecting them in a spatially coarse-grained environment constructed by mixing and redistributing, after each growth cycle, lines grown in both the light and the dark. A number of experiments have reported adaptation to the different patches in a spatially varying environment (Silver & Mateles, 1969; Dykhuizen & Davies, 1980; Wasserman & Futuyma, 1981; Verdonck, 1987; Garcia-Dorado et al., 1991; Joshi & Thompson, 1997; Taplitz & Coffin, 1997), although their experimental designs preclude a full analysis of the responses to selection. Further experiments designed to test the limits to local adaptation in the face of migration, patch frequency, and patch productivity are sorely needed.

Other experiments that have followed the evolution of the niche in constant and variable environments either show no response to selection in either treatment (Choo et al., 1980; Ehiobou & Goddard, 1989 for egg-to-adult viability, fecundity and oviposition preference in Drosophila melanogaster; Joshi & Thompson, 1997 for development time and survival in D. melanogaster and development time in D. simulans; Scheiner & Yampolsky, 1998) or observe a response to selection in constant environments but not in varying ones (Gao et al., 1992; Hodges et al., 1992; Gao et al., 1994; Bell, 1997b). These latter experiments are particularly interesting because they highlight two important constraints on the evolution of the niche. The first applies only to situations where the population under selection is genetically diverse (as in Bell, 1997b). In this case, a lack of response to selection in a variable environment suggests the existence of strong negative genetic correlations: adaptation to one patch can only come at a cost of adaptation to other patches. Dickerson (1955) has suggested that as the number of environments increases, the value of the genetic correlation, $r_G$, required to prevent a response to selection is $-1/(N - 1)$, where $N$ is the number of patches in the environment. This suggests that diversity should

be more readily maintained as the number of patches increase.

The second constraint pertains to situations where the population under selection is isogenic, all the variation on which selection acts arising *de novo* during the course of the experiment. A lack of response in a variable environment suggests that the appropriate genotype may be inaccessible because multiple beneficial mutations must occur in the same genome for a type to be viable. Indeed, this appears to be exactly that which is happening in the work of Gao and colleagues with drug-resistant strains of HIV multiply-resistant strains can be readily generated through sequential adaptation to different drugs but not through exposure to a mixture of drugs simultaneously. Note the parallel here with the response to selection in genetically diverse populations: the more complex the environment, in terms of the number of patches to which a population must adapt simultaneously, the more difficult it is to achieve a response to selection.

## The population genetics of specialization

Selection in a uniform environment favours types whose fitness is highest in that environment. The genetic correlation across environments should therefore evolve to become negative, either because adaptation to one set of conditions is underlain by a cost of adaptation to alternative conditions or because direct responses to selection simply tend to be larger than correlated responses. Which of these two factors is more often responsible for negative genetic correlations across environments remains an empirical issue.

Nevertheless, the accepted wisdom has been that trade-offs in fitness across environments are underlain by costs of adaptation. Costs of adaptation may arise from two sources (see for example Kawecki *et al.*, 1997). The first is antagonistic pleiotropy, genes favourable in one environment being deleterious in other environments. The second is the accumulation of mutations that are neutral in the environment of selection and deleterious elsewhere. This leads to the simple prediction that specialization is more readily maintained in the short term by strong diversifying selection in strongly contrasted environments, where antagonistic pleiotropy is the largest contributor to the cost of adaptation, and in the long term by prolonged selection under uniform conditions, where mutation accumulation contributes most to the cost of adaptation.

## The evolution of the genetic correlation

The cross-environment genetic correlation in fitness is expected to evolve to become negative after selection of a single founding population for specialization to different environments or for specialization to different patches of a heterogeneous environment. To test this prediction, I collected data from the literature on the sign of the genetic correlation following selection for specialization in different environments and then assayed in both environments (Table 1). This amounts to assuming that the two specialists inhabit a heterogeneous environment with no migration between the component patches. The genetic correlation was negative in 32 of 37 cases, which is significantly different from what one would expect by chance ($\chi^2_1 = 19.7$, $P < 0.0001$). Ebert (1998) has also found that selection of parasites in different hosts tends to generate a negative genetic correlation in fitness. The only experiment to have documented the evolution of a negative genetic correlation following selection in a spatially heterogeneous environment is by Bell & Reboud (1997).

The classic interpretation of a negative genetic correlation across environments sees it as being due to a cost of adaptation; advance over the base population in one environment causes regress in others. A negative genetic correlation may also arise in the absence of costs of adaptation, however, so long as the direct response in the environment of selection exceeds the correlated response in other environments (and both are in the same direction; Bell & Reboud, 1997). Of the pairs of lines exhibiting a negative genetic correlation across environments in Table 1, there was evidence for a cost of adaptation in 11 of 33 experiments reported. In 12 cases, the cost of adaptation was asymmetric: one line showed evidence of a cost of adaptation whereas the other did not. In the 10 remaining cases, the correlated responses were both positive. Thus a cost of adaptation need not always underlie a negative genetic correlation across environments.

## Costs of adaptation

Probably the earliest known demonstration of the existence of a cost of adaptation was an experiment by the Rev. Dallinger (1887), who constructed an incubator for selecting bacteria at different temperatures. Dallinger grew his bacteria at steadily increasing temperatures for 7 years. The optimum temperature for his founding population was between 15.5 and 18.3 °C. By the end of his experiment, which was prematurely terminated by the accidental destruction of the incubator, the bacteria were growing and reproducing normally at 70 °C, well-beyond their normal thermal limit of 60 °C. Dallinger did the appropriate reciprocal transplants, growing the high-temperature adapted lines at 15.5 °C and *vice versa*. Neither of the lines survived in the environments they had not been selected in, thus demonstrating the existence of costs of adaptation.

More recent experiments have focused on identifying the source of costs of adaptation. Reboud & Bell (1997) observed a cost of adaptation when lines of *Chlamydomonas* that had been selected in either the light or the dark for roughly 1000 generations were transferred to

**Table 1** The consequences of selection in single environments on the genetic correlation and the cost of adaptation.

| Species | Selection environments | Generations selected | Selection lines | Genetic correlation | Cost of adaptation | Asymmetry of correlated responses | Citation |
|---|---|---|---|---|---|---|---|
| *Algae* | | | | | | | |
| *Chlamydomonas reinhardtii* | Light | 750 | A+ | – | –,– | N | Bell & Reboud (1997) |
| | Dark | 275 | A– | – | –,– | N | |
| | | | B+ | – | –,– | N | |
| | | | B– | – | –,– | N | |
| | | | C+ | – | –,– | N | |
| | | | C– | – | +,– | Y | |
| | | | D+ | – | –,– | N | |
| | | | D– | – | +,– | Y | |
| *C. reinhardtii* | Light | 200 | 1 | + | –,+ | Y | Reboud & Bell (1997) |
| | Dark | 90 | 2 | + | –,+ | Y | |
| *C. reinhardtii* | Light | 400 | | – | +,+ | N | Kassen & Bell (1998) |
| | Dark | 90 | | | | | |
| *Bacteria* | | | | | | | |
| *Escherichia coli* | 32 °C | 2000 | | | | | Bennett *et al*. (1992) |
| | vs. 37 °C | | | – | +,+ | N | |
| | vs. 42 °C | | | – | –,+ | Y | |
| | 37 °C | | | | | | |
| | vs. 42 °C | | | – | –,+ | Y | |
| *Insects* | | | | | | | |
| *Tetranychus urticae* | Lima bean | ~10 | | 0 | | | Fry (1990) |
| | Tomato | | | | | | |
| *Drosophila melanogaster* | Urea absent | 35 | | – | | | Shiotsugu *et al*. (1997) |
| | Urea present | | | | | | |
| *D. melanogaster* | Unpolluted | | | | | | Shirley & Sibly (1999) |
| | Polluted | | | – (Fecundity) | | | |
| | | | | 0 (Survival) | | | |
| *Viruses* | | | | | | | |
| HIV-1 | Protease inhibitors A7703 | ? at least 6 | | | | | Tisdale *et al*. (1995) |
| | vs. XM323 | | | – | –,– | N | |
| | vs. Ro 31–8959 | | | – | +,+ | N | |
| | vs. L-735,524 | | | – | –,+ | Y | |
| | vs. VX-478 XM323 | | | – | –,– | N | |
| | vs. Ro 31-8959 | | | – | +,– | Y | |
| | vs. L-735,524 | | | – | +,+ | N | |
| | vs. VX-478 Ro 31-8959 | | | – | +,+ | N | |
| | vs. L-735,524 | | | + | +,– | Y | |
| | vs. VX-478 L-735,524 | | | – | –,– | N | |
| | vs. VX-478 | | | – | –,– | N | |
| HIV-1 | AZT | ? | HIV-III$_B$ | _ | 0,– | Y | Gao *et al*. (1992) |
| | ddI | at least 7 | # 187 | | +,+ | N | |
| HIV-1 | AZT | ? at least 7 | HIV-III$_B$ | | | | Gao *et al*. (1994) |
| | vs. ddI | | | – | +,+ | N | |
| | vs. ddC | | | – | +,+ | N | |
| | ddI | | | | | | |
| | vs. ddC | | | | | | |
| | AZT | | #187 | | | | |
| | vs. ddI | | | – | –,+ | Y | |
| | vs. dd | | | – | 0,+ | Y | |
| | ddI | | | | | | |
| | vs. ddC | | | – | –,– | N | |
| Arbovirus | BHK cells | | | – | –,– | N | Weaver *et al*. (1999) |
| | C6/36 cells | ? at least 100 | | | | | |

For the genetic correlation, a– sign indicates a negative genetic correlation in fitness between a pair of lines after selection in different environments whereas a+ sign indicates a positive genetic correlation between a pair of selection lines. Costs of adaptation are noted as – (presence of a cost) and + (absence of a cost), relative to a common founder. Asymmetry of correlated responses occur when, for a pair of selection lines, a cost of adaptation is detected in one line but not the other.

the alternative environment. They ascribed the bulk of this cost to mutation accumulation, based on the fact that generalist lines, selected for approximately 150 generations under temporally varying conditions of light and dark, grew as well in the light and in the dark as both the light- and dark-specialist lines.

Travisano & Lenski (1996), on the other hand, have noted that lines of glucose-adapted *Escherichia coli* show substantial variation in fitness when tested against the ancestor in novel, single-nutrient environments. Moreover, there was pattern to this variation: the more different the substrate was from glucose in terms of its uptake physiology, the more often a cost of adaptation was observed. This result points to antagonistic pleiotropy being the largest contributor to the cost of adaptation. Further support comes from estimates of the number of neutral substitutions occurring during the course of the experiment, which was too small to have contributed substantially to the variation in fitness observed among the selected lines. Similar results had been obtained previously when the performance of the same lines were compared on glucose and maltose only (Travisano *et al.*, 1995).

Recently, Cooper & Lenski (2000) provided a critical test of the role of mutation accumulation and antagonistic pleiotropy in generating costs of adaptation. They compared the fitness of the glucose-selected lines, which included three populations with elevated genome-wide mutation rates, with their common ancestor on 64 novel carbon substrates. The breadth of catabolic function declined in all lines over the 20 000 generations of selection, supporting the prediction that prolonged selection for specialization leads to increasingly narrow niche widths. However, the high-mutation lines did not have substantially narrower niche widths than any of the other lines, as would be expected if mutation accumulation had made a substantial contribution to the cost of adaptation. Thus antagonistic pleiotropy appears to make the largest contribution to the cost of adaptation in these experimental populations.

## Constraints on the evolution of the niche

Bennett *et al.* (1992) and Bennett & Lenski (1993) studied the thermal tolerance of their temperature-adapted lines of *E. coli* in an effort to determine the consequences of long-term selection on the position and width of the thermal niche. Thermal tolerance was defined as the ability to sustain a viable population in serial transfer at a given temperature. Each selection line had maximum fitness at the temperature (or temperatures, in the case of the thermal generalist selected at both high and low temperatures) at which they had been selected, although niche width in all lines was identical to the ancestor's. These results suggest that the upper and lower limits of the niche represent fairly stringent boundaries that are difficult to transcend. Similar

responses of the environmental optimum have been obtained through artificial selection at different temperatures in the fungus *Schizophyllum commune* by Jinks & Connolly (1975).

In *E. coli*, it is possible to obtain mutants capable of growing outside the ancestral thermal niche. These were occasionally observed in the experiment described above, and have also been found through deliberate selection at extreme temperatures (Mongold *et al.*, 1996, 1999). Growth at extreme temperatures beyond the ancestral boundaries apparently involves both a shift in the environmental optimum and a cost of adaptation at different temperatures, as in Dallinger's (1887) experiment. The actual magnitude of the cost, however, varied among clones although on average the costs of adaptation increased as one moved further away from the temperature of selection.

## The population genetics of generalization

The conditions for the coexistence of specialists in a heterogeneous environment are, in fact, fairly stringent: if the selective differences among patches are not large, the balance of production from each patch must be roughly equal for diversity to be maintained (Maynard Smith & Hoekstra, 1980; Van Tienderen, 1997; Kassen *et al.*, 2000). The implication is that there should be plenty of opportunity for ecological generalists to evolve in heterogeneous environments, even if selection favours specialization to the most productive patch in the short term. Indeed, the extreme position is that generalists will *always* evolve if selection is given enough time to do its work. This is obviously not the case, therefore, it is important to ask about the constraints governing the evolution of generalization.

The classic view on the evolution of generalization is that it is constrained by two sources: either there is an intrinsic functional interference involved in performing two qualitatively different tasks equally well leading to a negative genetic correlation across environments (Futuyma & Moreno, 1988) or there is a substantial cost for the maintenance of characters specifically designed to reduce the environmental variance of fitness (Van Tienderen, 1991). Regardless, the existence of these costs to generalization implies that a generalist should be a jack-of-all-trades and a master-of-none.

A more formal way of understanding the evolution of generalization is as follows: The long-term fitness of a genotype in a heterogeneous environment is best described by its geometrical mean fitness across environments (Gillespie, 1973) which is approximately $\bar{\omega} - 1/2\sigma_E^2$ (Bulmer, 1994), where $\bar{\omega}$ refers to the arithmetic mean fitness and $\sigma_E^2$ is the environmental variance of fitness across a given range of conditions of growth. At equilibrium all types have equal geometric mean fitness, which implies a trade-off between the arithmetic mean fitness, $\bar{\omega}$, and the environmental

variance of fitness, $\sigma_E^2$, across the entire range of patches. Note that adaptation to a heterogeneous environment may proceed through two routes, either by increasing fitness within patches or by decreasing the environmental variance of fitness across patches. The environmental variance, therefore, should be a character that responds to selection, much like any other. This in turn implies that the kinds of adaptations that evolve should be specific to the scale of environmental variation (Bradshaw, 1965).

## Selection on the mean vs. the environmental variance

There has been disagreement over whether selection is capable of altering the environmental variance (Via *et al.*, 1995). Artificial selection experiments, dating as far back as the work of Kamshilov (1939), provide ample evidence that it can. The environmental variance has been shown to respond to direct (Waddington, 1960; Kindred, 1965; Hillesheim & Stearns, 1991; Scheiner & Lyman, 1991) and indirect (Waddington & Robertson, 1966; Scharloo *et al.*, 1972; Jinks & Connolly, 1973; Hoard & Crosbie, 1986; Brakefield *et al.*, 1996) artificial selection. Brumpton *et al.* (1977) and Jinks *et al.* (1977) have further demonstrated that the arithmetic mean and the environmental variance of both flowering time and plant height in tobacco can be selected independently.

There is comparatively little data on the response of the environmental variance to natural selection. Leroi *et al.* (1994) have shown that the evolution of broadly thermo- tolerant *E. coli* occurred through changes to mean performance in each temperature regime, rather than through changes in the environmental variance. In contrast, Dykhuizen & Davies (1980) and Silver & Mateles (1969) have documented the selection of constitutive mutants in the *lac* operon of *E. coli* when grown in resource-limited chemostats on a mixture of lactose and either glucose or maltose. The operon is inducible in wild-type cells, so the evolution of constitutive expression is an example of selection acting on the environmental variance of this trait.

## Detecting costs to being a generalist

A number of authors have questioned whether or not substantial costs to generalization exist and, if they do, how important they are in the evolution of broad adaptation (Joshi & Thompson, 1995; Via *et al.*, 1995; Fry, 1996; Whitlock, 1996; DeWitt *et al.*, 1998). One way to resolve this question is to assay the fitness of lines selected for specialization and generalization across the same set of environments in which they had been selected. If generalists trade-off mean performance for breadth of adaptation, then we would expect their joint performance in both environments to fall on or below the line connecting the performance of the specialists in those environments. On the other hand, if there is little cost of generalization, a generalist's performance will fall

above the line, and may even exceed that of either specialist. There is evidence for a trade-off between the arithmetic mean fitness and the environmental variance of fitness in one of four cases (Fig. 2).

These results may be interpreted in two ways. First, one could argue that the appropriate trade-off exists but cannot be detected because the populations are far from equilibrium. This appears to be the case in the experiment of Kassen & Bell (1998) where none of the selection lines exhibited a cost of adaptation, the response to selection being synclinal (*sensu* Bell & Reboud, 1997). Alternatively, there may be little functional interference between fitness in either environment if, for example, the negative genetic correlation between the two specialists is largely because of mutation accumulation, as appears to have been the case in Reboud & Bell's (1997) experiment. Regardless of which of these two interpretations is more often correct, there is little evidence to suggest that substantial costs inevitably constrain the evolution of generalists, at least in the short term. Whitlock (1996) has suggested that a more common trade-off might be between the rate at which specialists and generalists evolve: specialists adapt faster than generalists to a given set of conditions because the fixation and loss of alleles with environment-specific effects proceeds more rapidly when the environment remains constant through time. There are as yet no direct tests of this idea, although Bennett *et al.* (1992) and Kassen & Bell (1998) have reported rates of adaptation that are consistent with the prediction that specialists evolve faster than generalists.

## Adaptation to the scale of environmental variation

Kassen & Bell (1998) selected genetically diverse populations of *C. reinhardtii* in temporally fine-grained and coarse-grained environments that alternated between light and dark growth conditions, which requires that *C. reinhardtii* switch between phototrophy and heterotrophy in the light and dark, respectively. At the end of approximately 250 generations, the lines selected in each of the temporally varying environments were more broadly adapted than lines selected only in the light or dark. However, there was no evidence for specific adaptation to the scale of variation. Other studies of adaptation to different scales of variation have either shown no response to selection (Scheiner & Yampolsky, 1998) or have not looked for evidence of specific adaptation to the scale of variation (Long, 1970; Mackay, 1980; Mackay, 1981).

Environmental variation occurring on very long temporal scales, relative to the lifetime of an individual, may not lead to the evolution of generalists at all but rather the repeated evolution of specialists adapted to each successive set of growth conditions. This has been observed by Crill *et al.* (2000) who documented adaptation of bacteriophage to alternate hosts. Adaptation was quite rapid, occurring
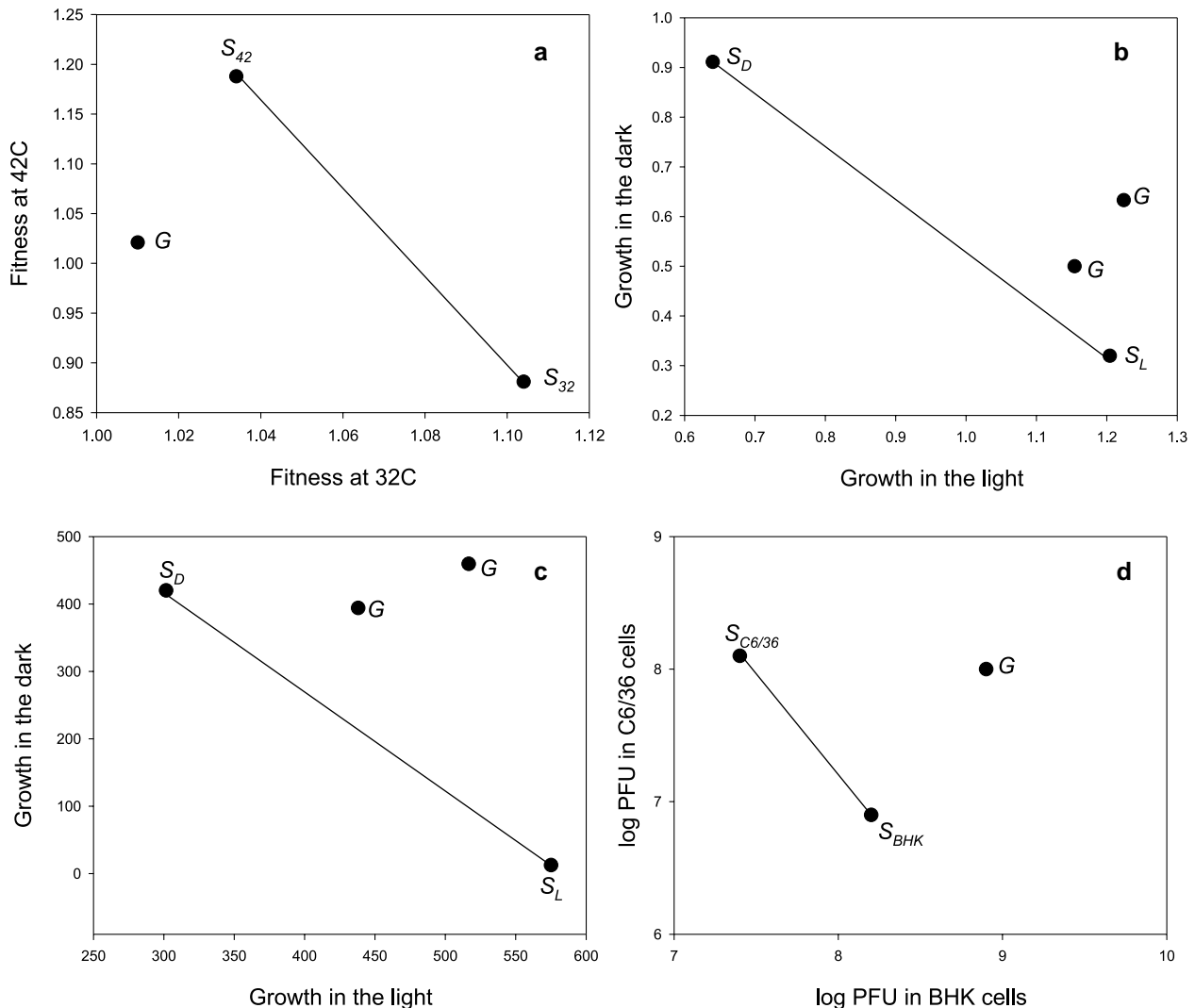
**Fig. 2** Putative trade-offs between mean fitness within an environment and the breadth of adaptation. Generalists (G) trade-off fitness within environments for breadth of adaptation when their joint performance in the two environments falls below the line connecting the performance of the two specialists [S; (a) data from Bennett *et al.*, 1992]. The remaining panels show no evidence for trade-offs [(b), Kassen & Bell, 1998; (c), Reboud & Bell, 1997; (d), Weaver *et al.*, 1999].

within just 11 generations on each host. Because the founding population was isogenic, such rapid rates of evolution must require similarly high rates of mutation, at least on the order of one beneficial mutation per environmental cycle. Generalism might be expected to evolve, therefore, when the rate of supply of beneficial mutations is low relative to the cycle period of the environment, as would be the case in small populations.

## Generalists may sometimes evolve through selection in a single environment

Selection in a heterogeneous environment may not be the only way to obtain broadly adapted generalists.

Agronomists and animal breeders have noted for some time that artificial selection for increased yield in different environments often changes the environmental variance of yield in a predictable manner (Jinks & Connolly, 1973; Falconer, 1990). Consider the consequences of natural selection in two environments differing in quality relative to the overall mean, as shown in the schematic in Fig. 3. Selection within each environment increases the trait's value, which may be fitness, and there is a positive genetic correlation between the value of the trait in both environments. Selection in the 'good' environment leads to types with larger environmental variance than the ancestor (Fig. 3A), whereas selection in the 'poor' environment generates types with smaller environmental

variance (Fig. 3B). Note that the same argument holds for small, negative genetic correlations.

This model was first proposed by Jinks & Connolly (1973) and has been generalized by Falconer (1990), who also reviewed the animal breeding literature on the topic. Falconer found that selection upward in the good environment increased the environmental variance relative to unselected controls but the same selection applied in the poor environment did not always lead to a smaller environmental variance, as expected. These poor-environment lines did, however, have smaller environmental variances after selection than those selected in the good environment. I have found similar results for artificial selection in two *Drosophila* experiments (Scheiner & Lyman, 1991; Noach *et al.*, 1997) but not a third (Hillesheim & Stearns, 1991). The only comparable data from natural selection experiments comes from work with *Chlamydomonas* selected in light



**Fig. 3** Direct and correlated responses to natural selection in 'good' and 'poor' environments. (A) Selection upwards in the good environment. (B) Selection upwards in the bad environment. Solid and dashed lines represent the environmental variance of fitness in the selected and founding populations, respectively. Direct responses to selection are indicated by solid arrows; correlated responses are given by dotted arrows. Note that direct and correlated responses are in the same direction and that direct responses always exceed correlated responses.

(good) and dark (poor) environments. Lines selected in the dark tend to have lower environmental variances than lines selected in the light (Bell & Reboud, 1997; Kassen & Bell, 1998).

## Experimental evolution and the maintenance of diversity

Environmental heterogeneity may support diversity, either because different types are the fittest in different patches of the environment or, for the special case of sexual diploids, heterozygotes are the fittest across all patches. This implies that heterogeneous environments will support more diversity than homogeneous environments independently, so long as the rate of gene flow is low and each patch contributes roughly equal numbers of individuals to the total population. Moreover, because a spatially varying environment provides refuges for specialized types but a temporally varying environment does not, diversity should be maintained more readily under spatial variation when compared with temporal variation. In the absence of heterozygote advantage, diversity may be stably maintained only if density-dependent population regulation occurs within each patch (soft selection) rather than at the level of the global population (hard selection) because the former generates negative frequency-dependent selection, rare types having higher fitness than common types.

## Genetic variation in heterogeneous vs. homogeneous environments

Table 2 summarizes the results of experiments that have tested the prediction that diversity is maintained more readily in heterogeneous rather than homogeneous environments for traits obviously related to fitness. I have noted the form of environmental variation considered (spatial vs. temporal), the form of population regulation practised (where this has been noted by the authors) and the characteristics of the base population on which selection was carried out (sexual or asexual and if sexual, whether haploid or diploid; genetically diverse or uniform). Note also that I have counted nutrient mixtures as a form of spatial heterogeneity. One might criticize such a classification on the grounds that this does not represent a true test of the classic model of spatial variation, which treats the environment as composed of discrete patches (Levene, 1953; Dempster, 1955). Nevertheless, both models characterize the environment as essentially uniform in time, and this is the more important distinction in the present context. Selection in mixtures has been addressed by Strobeck (1975) and Tilman (1977), and reviewed by Gottschal (1986).

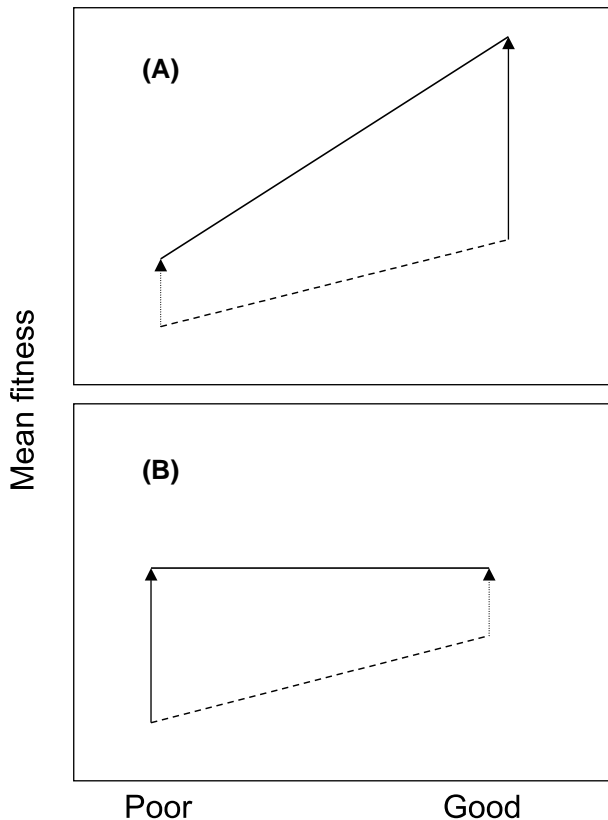Consider spatial heterogeneity first. Genetic variance in fitness was greater in spatially heterogeneous

**Table 2** Genetic variance in fitness in heterogeneous environments. Explanation in text.

| Citation | Form of environmental variation | Genetic variance greatest in heterogeneous environment? | Notes |
|---|---|---|---|
| *Quasi-natural selection* | | | |
| Bell (1997a; b) | Spatial | | Asexual diverse b.p. sorted in eight macronutrient |
| | Soft selection | Y | environments |
| | Hard selection | Y | |
| Bell & Reboud (1997) | Spatial | Y | Asexual isogenic b.p. propogated in light and dark environments |
| Garcia-Dorado *et al.* (1991) | Spatial | Y, N | Habitat preference measured; sexual diploid; diverse b.p. sorted in environments with and without ethanol |
| Korona *et al.* (1994) | Spatial | Y | Asexual isogenic b.p. propogated in liquid (homogeneous) and solid (heterogeneous) medium. |
| Litchman (1998) | Temporal | Y, N | Asexual diverse b.p. sorted under fluctuating light at two average light intensities |
| Rainey & Travisano (1998) | Spatial | Y | Asexual isogenic b.p. propogated in unshaken (heterogeneous) and shaken (homogeneous) microcosms |
| Riddle *et al.* (1986) | Spatial | N | Sexual diploid; diverse b.p. sorted on different flour |
| | Temporal | N | media |
| Scheiner & Yampolsky (1998) | Temporal | N | Asexual & sexual diploid; diverse b.p. propogated in alternating temperatures |
| Sommer (1983) | Spatial | Y | Asexual diverse b.p. sorted in media containing one (homogeneous) or two (heterogeneous) nutrients |
| Sommer (1984) | Temporal | Y | Asexual diverse b.p. sorted in two-nutrient environments where one nutrient is delivered intermittently |
| Sommer (1985) | Temporal | Y | See Sommer (1983, 1984); pulses of two nutrients also included |
| Wallace (1982) | Spatial | Y | Sexual diploid; diverse b.p. selected on two salts. |
| *Competitive coexistence* | | | |
| Brzezinski & Nelson (1988) | Temporal | Y | Two species in fluctuating light on single nutrient |
| Dykhuizen & Davies (1980) | Spatial | Y | Asexual; one specialist, one generalist on two nutrients |
| Gottschal *et al.* (1979) | Spatial | Y | Asexual; two specialists, one generalist on two nutrients |
| Gottschal *et al.* (1981) | Temporal | Y, N | Asexual; two specialists coexist, generalist eliminated on two nutrients |
| Grover (1988) | Temporal | N | Sorting of species through nutrient pulses |
| Laanbroek *et al.* (1979) | Spatial | Y | Asexual; two specialists on two nutrients |
| Legan *et al.* (1987) | Temporal | Y | Asexual; one specialist, one generalist on two nutrients, depending on dilution rate |
| Tilman (1977) | Spatial | Y | two specialist species on two nutrients |

environments compared with spatially uniform environments in 11 of 12 cases. The one exception, an experiment with *Tribolium* by Riddle *et al.* (1986), failed to observe a response to selection in any treatment, suggesting a lack of genetic variation from which to select in the base population. When the environment varies in time the outcome is more variable. Genetic variation in temporally heterogeneous environments exceeded that in unvarying environments in 6 of 11 cases. In two experiments there was probably insufficient genetic variation in the base population to provide an adequate test (Riddle *et al.*, 1986; Scheiner & Yampolsky, 1998); removing these gives a ratio of 6 of 9 in favour of temporal variation maintaining diversity.

Two sets of experiments have contrasted the effects of spatial and temporal variation on the maintenance of diversity. Gottschal *et al.* (1979) showed that a mixture of two essential nutrients could support three species of bacteria grown in continuous culture. Two of the species were specialists for different nutrients and the third, a generalist, was capable of using both nutrients. When the same two nutrients were delivered alternately through time the two specialists coexisted but the generalist was eliminated (Gottschal *et al.*, 1981). Reboud & Bell (1997) showed that specialization for light and dark growth in selection lines of *C. reinhardtii* was maintained under spatial variation whereas temporal variation favoured the evolution of generalists.

Taken together, these experiments provide strong evidence in support of the idea that spatial variation, and to a lesser extent temporal variation, in the environment facilitates the maintenance of diversity. I am unaware of any experiments following the fate of diversity under variable migration rates in a heterogeneous environment, although Warren (1996) has investigated the effect of migration on the diversity of protists in replicate patches of the same growth medium. Furthermore, it is unclear how different scales of environmental variation affect the maintenance of diversity. The bulk of the experiments considered here concern coarse-grained variation in space or in time. The exceptions are the experiments in mixtures, which can be considered a form of spatially fine-grained variation. I know of no experiments that have contrasted the fate of diversity under temporally coarse- and fine-grained variation for traits directly related to fitness, although a number of experiments have considered nonfitness traits (Oakeshott, 1979; Mackay, 1980; Mackay, 1981).

### Mechanisms maintaining genetic variation

The mechanisms through which environmental heterogeneity maintains diversity have only recently received experimental attention. In an elegant experiment, Rainey & Travisano (1998) showed that negative frequency-dependent selection underlies the diversity of colony morphologies in cultures of *Pseudomonas fluorescens* occupying a physically structured microcosm. Bell (1997b), however, did not observe higher diversity when genetically diverse cultures of *C. reinhardtii* were selected in a spatially variable environment under soft selection when compared with hard selection, as might be expected if negative frequency-dependent selection were responsible. Bell was able to rule out heterozygote advantage as a possible explanation, however, as *C. reinhardtii* is a vegetative haploid under the conditions of the experiment. Moreover, there was no indication from the experiments with sexual diploids reported in Table 2 that heterozygote advantage had any general tendency to maintain diversity.

It is interesting to note that negative frequency-dependent selection has been shown to be effective in maintaining substantial variation in fitness among microbial populations even in apparently homogenous environments (reviewed in Rainey *et al.*, 2000). Typically, the maintenance of diversity occurs through cross-feeding, where one genotype feeds on a metabolite excreted by another genotype, although other mechanisms are also possible (Stewart & Levin, 1973; Chao & Levin, 1981). The important point, however, is that the environment is, in effect, heterogeneous from the perspective of the organisms that occupy it, and this heterogeneity supports diversity through negative frequency-dependent selection.

Lastly, Elena & Lenski (1997) provided a direct test of three factors – transient beneficial mutations, mutation-selection balance, and negative frequency dependent selection – in maintaining variance in fitness among clones in the long term selection experiments with *E. coli*. After approximately 10 000 generations in a glucose-limited environment, clones differed from each other in fitness by roughly 4% which, although small relative the overall change in mean fitness throughout the entire experiment, was statistically significant. Again, even within the relatively homogeneous environment of a microcosm, negative frequency-dependent selection emerged as the most likely explanation for the maintenance of diversity.

### Patterns of diversity at regional scales

If environmental heterogeneity is essential to the maintenance of diversity within populations, as evidenced by the experiments reviewed here, then it might also be important in governing patterns of species diversity at the larger spatial scale of a collection of populations or communities within a region. Recent work with the *P. fluorescens* system lends support to this idea. The diversity of colony morphs has been shown to be unimodally related to both productivity (Kassen *et al.*, 2000) and disturbance (Buckling *et al.*, 2000) in heterogeneous but not homogeneous environments. Moreover, these results are consistent with a Levene-style model for selection in heterogeneous environments when fitness is a function of either resource supply rate, in the case of productivity, or time, in the case of disturbance (Levene, 1953). In both cases, the critical feature of the model that generates the unimodal relationship is the relative production of patches: if one patch contributes many more individuals to the community than the other, the type that is better adapted to this patch will come to dominate the community (see also Chesson & Huntly, 1997).

### Discussion

There are three leading results from the experiments I have reviewed here. First, the niche does, in fact, evolve in response to natural selection in heterogeneous environments. In general, the position and breadth of the niche evolve to match the amount of environmental variation experienced during selection, specialists evolving in environments that remain constant in space and time and generalists evolving in environments that vary in either dimension. Secondly, environmental heterogeneity can maintain higher quantities of diversity than homogeneous environments, and in some cases at least, this diversity is stably maintained through frequency-dependent selection. Thirdly, selection in heterogeneous environments has been shown, in the controlled conditions of the laboratory, to be a plausible mechanism underlying two well-known patterns of diversity at the landscape level. This lends strong support to the argument

that environmental heterogeneity does indeed represent a general explanation for diversity in natural systems.

## The evolution of the ecological niche

As a general rule, the position and breadth of the niche evolves to match the amount of environmental variation. This rule does not hold in the absence of appropriate genetic variation or when selection acts to improve short-term fitness in a poor-quality environment. There is also some limited support for the idea that generalists evolve more readily under temporal variation than spatial variation. Further tests of this prediction would be welcome.

The genetics underlying the evolution of niche width are more complicated. The traditional view has been that adaptation to one environment comes at a cost of adaptation to other environments, either because selection fixes genes that are beneficial in one environment and deleterious in others or because of the accumulation of mutations neutral in the environment of selection and deleterious elsewhere. Although there is evidence that both antagonistic pleiotropy and mutation accumulation do contribute to a cost of adaptation, costs do not appear to be as widespread as the traditional view would have them be. Adaptation to one environment may, in the short-term of a few hundred generations at least, incur little cost in alternative environments, or costs may be expressed asymmetrically, being apparent in only one of a pair of lines. Inevitably, as selection proceeds for longer periods of time, conditionally neutral mutations will accumulate and costs of adaptation are expected to become larger. It is also unlikely that the same genes will be beneficial under widely different conditions of growth, implying that costs of adaptation as a result of antagonistic pleiotropy should become more evident as conditions of growth diverge. These predictions are consistent with the observations by Kassen & Bell (2000) and Bell (1992) that the across-environment genetic correlation of fitness in unselected populations of *C. reinhardtii* declines as both the genetic distance among species and the environmental variance increases.

Of course, genetic correlations are not by themselves evidence for a cost of adaptation. A negative genetic correlation of fitness across environments can be generated in the absence of any cost of adaptation. This requires only that the direct response in the environment of selection exceed the correlated response in the other environment, a situation Bell & Reboud (1997) have termed *synclinal selection* in order to distinguish it from the more conventional view of costs of adaptation which they term *anticlinal selection*. Note that the distinction between anticlinal and synclinal selection becomes moot if one is only interested in predicting the conditions under which diversity can be maintained, as it is the sign of the genetic correlation, rather than the presence or

magnitude of a cost of adaptation, that is important for predicting the outcome of selection in the short-term.

Demonstrating the existence of a negative genetic correlation across environments has also been held as evidence that a universally superior generalist could not evolve, as it could not maximize fitness in both environments simultaneously. The data in Fig. 2 illustrate that this assumption may often be incorrect; a fitness trade-off between specialists selected in different environments need not prevent the emergence of a superior generalist if selection is synclinal, as might be expected if the base population is far from equilibrium, or, under anticlinal selection, if the cost of adaptation is predominantly because of mutation accumulation. Only when antagonistic pleiotropy is responsible for a negative genetic correlation will generalists conform to the 'jack-of-all-trades, master-of-none' adage commonly assumed to describe the trade-off in performance within and across environments.

Two further issues pertaining to the genetics of niche width are relevant here. The first concerns selection on the environmental variance. There has been some debate over whether the environmental variance is a character that evolves in the same way as any other character. It has already been pointed out that the environmental variance can evolve through deliberate selection; the evolution of constitutive mutants in bacteria (Silver & Mateles, 1969; Dykhuizen & Davies, 1980) is evidence that it can evolve through natural selection as well.

The second concerns situations where the niche width appears to be much less than the range of environmental variation, as when individuals avoid poor local conditions by maintaining energy-stores, entering resting stages, or migration (e.g. Giesel, 1976; Chesson, 1994). These strategies permit specialization on a subset of the full range of environmental conditions and so may, in some cases, lead to the maintenance of diversity. The maintenance of diversity in chemostats receiving temporal pulses of essential nutrients are consistent with this idea (Sommer, 1984, 1985; Brzezinski & Nelson, 1988; Litchman, 1998).

## Practical considerations

There are at least two important applications of the principles discussed here. First, selection in poor-quality environments has been suggested as a means of broadening the breadth of adaptation in agronomy (Ceccarelli, 1989; Braun *et al.*, 1996) and animal breeding (Falconer, 1990). Falconer (1990) has pointed out that this will only be successful if the genetic correlation across environments is not too negative and the genetic variances in each environment are roughly equal. Note further, that prolonged selection will decrease the efficacy of this strategy for improving the breadth of adaptation due to the accumulation of mutations contributing to the cost of adaptation. Mutation accumulation may not make a

substantial contribution to the cost of adaptation within the time-scale on which most agricultural improvements are made as long as the effective population size is fairly large. In small populations, however, the cost of adaptation due to mutation accumulation may be much greater and realized much sooner.

Secondly, I have noted a number of situations where a population is capable of adapting to the component patches of a variable environment separately but not to the variable environment itself. This is likely either because of the presence of strongly negative genetic correlations between performance in each component patch of a complex environment or to the small probability that multiple beneficial mutations will occur simultaneously in the same genome. In both cases, the evolution of generalists may be dramatically delayed or even prevented altogether. This has important implications for medical practice because it suggests that the treatment of infectious disease with so-called drug cocktails (combinations of drugs with different modes of action) can slow the emergence of multiple-drug resistant types. Moreover, if generalists evolve more readily in temporally varying environments than in spatially varying ones, then multiple drug therapies where combinations of drugs are delivered simultaneously are likely to be more effective than those delivered sequentially, as has been observed in the experiments of Gao and co-workers (Gao *et al.*, 1992, 1994). It is unlikely that the emergence of multiply resistant types could be prevented indefinitely, however, as any mutation that increases fitness in the presence of multiple drugs will be strongly favoured.

### Environmental heterogeneity and the maintenance of diversity

In the majority of experiments, genetic variance in fitness was higher following selection in heterogeneous environments when compared with homogeneous environments. Moreover, there was a tendency for spatial variation to support diversity more readily than temporal variation, although this effect was relatively weak. These results support the interpretation of diversity in natural populations as being supported by environmental heterogeneity.

There are two interpretations of the role of environmental heterogeneity in supporting diversity. The first sees diversity as being stably maintained by environmental heterogeneity through the action of negative frequency-dependent selection. The second holds that diversity is not actively maintained, in the sense that rare types are protected from loss, but rather is supported through equilibrial rates of population genetic processes such as mutation-selection balance or transient beneficial mutations. In effect, these latter mechanisms frustrate the ability of selection to eliminate variation in a heterogenous environment. It should be noted that the

nonequilibrium arguments for the maintenance of diversity advocated by Huston (1979) are a special case of these latter processes. At the moment, there is good evidence from a variety of experimental systems, particularly in bacteria, that support the former interpretation, diversity being actively maintained through negative frequency-dependent selection. Moreover, this interpretation is also a plausible explanation for at least two large-scale patterns of diversity that have been noted for some time by community ecologists: the unimodal relationship of species diversity with both productivity and disturbance. This argues strongly in favour of environmental heterogeneity as an important factor governing the diversity of natural communities.

### When will diversity be lost or maintained?

The experiments reviewed here take us some way to understanding more clearly the conditions under which diversity will be lost or maintained through selection in a heterogeneous environment. First, it is clear that spatial heterogeneity is more likely to support diversity than temporal heterogeneity, as spatial heterogeneity offers refuges to maladapted types and this may thus slow the rate at which diversity is lost, even if diversity is not stably supported through negative frequency-dependent selection. Secondly, the qualitative differences among patches in the environment must be sufficiently great either to generate negative genetic correlations in fitness across pairs of patches or to make the occurrence of multiple beneficial mutations in the same genome highly improbable. This will slow, or may even prevent, the emergence of a single, broadly adapted generalist. Finally, the balance of production from each patch in the environment must be roughly equal, such that no single type comes to dominate the community. This ensures that even if diversity is not stably maintained by negative frequency-dependent selection, it will be lost only very slowly.

### A final caveat

Selection experiments are powerful tools for demonstrating the plausibility of different mechanisms on the outcome of selection. They cannot, however, tell us much about the prevalence or importance of these mechanisms in natural systems. For this, we still need data from the field. The challenge for the future will be to explore how far the mechanisms identified by experimental studies of evolution can go towards explaining the patterns of diversity in nature.

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