LONG-TERM LABORATORY EVOLUTION OF A GENETIC LIFE-HISTORY TRADE-OFF IN DROSOPHILA MELANOGASTER. 2. STABILITY OF GENETIC CORRELATIONS

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Abstract.—Experiments in laboratory populations of Drosophila melanogaster have shown a negative genetic correlation between early-life fecundity on the one hand and starvation resistance and longevity on the other. Selection for late-life reproductive success resulted in long-lived populations that had increased starvation resistance but diminished early-life fecundity relative to short-lived controls. This pattern of differentiation proved, however, to be unstable. When assayed in a standard high-fecundity environment, the relative early fecundity of the long- and short-lived stocks reversed over a decade. That is, the long-lived populations came to have greater relative early-life fecundity, late-life fecundity, longevity and starvation resistance. Nevertheless, when these populations were assayed in other assay environments, the original trade-off was still present. We investigated the genetic structure of the short- and long-lived populations, to ask whether the inconstancy of the trade-off, as inferred from among population comparisons, is reflected in the pattern of genetic correlations within populations. For this purpose, lines from each of the short- and long-lived populations that had been selected for starvation resistance were compared with unselected controls. The direct and correlated responses of these starvation selected populations suggest that (1) the original genetic trade-off was still present in the ancestral short- and long-lived populations, even when it was no longer apparent from their comparison; (2) the trade-off was present in both assay environments; and (3) selectable genotype × environment variation exists for early fecundity. We suggest that a failure of the pattern of differentiation among populations to reflect the pattern of genetic correlations, if common in natural populations, will prevent the reliable inference of genetic trade-offs from comparisons of most natural populations.

Key words.—Antagonistic pleiotropy, Drosophila, genotype × environment interactions, life-history, trade-offs.

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It is frequently suggested that antagonistic pleiotropy between survival and reproduction, manifest as negative genetic correlations, constrains the evolution of life-history traits (Williams 1957; Rose 1985; Partridge and Harvey 1988; Møller et al. 1989; Scheiner et al. 1989; Stearns 1989, 1992; Parker and Maynard Smith 1990). Such antagonisms are presumably caused by physiological (and other) costs for survival exacted by reproduction (Williams 1966a,b; Bell and Koufopanou 1986). But the ease with which such costs can be overcome in the course of evolution is unclear (Partridge and Sibly 1991; Stearns 1992), as is the importance of negative genetic correlations that arise from such costs to the long-term evolution of populations.

A classic example of a trade-off believed to be caused at least partially by costs of reproduction comes from the study of outbred, laboratory-adapted populations of Drosophila. In such populations, early fecundity is often negatively genetically correlated with longevity (Rose and Charlesworth 1981a,b; Rose 1984; Tucic et al. 1988; Luckinbill et al. 1984; Luckinbill and Clare 1985; but see Partridge and Fowler 1992). This particular trade-off has been suggested to be of great importance in shaping the evolution of Drosophila life history (Parker and Maynard Smith 1990).

In this paper, we investigate the ostensible disappearance of antagonistic pleiotropy between reproduction and survival in an assemblage of D. melanogaster populations. The loss of this trade-off was first documented in a companion paper (Leroi et al. 1994a); here we examine the genetical basis of this loss in greater detail. In the next section, we set the stage for this study by briefly outlining the history of these populations and pose the major questions addressed.

EXPERIMENTAL OVERVIEW

We originally detected a trade-off between early fecundity and longevity in a population founded by P. T. Ives in 1975 from flies collected in
South Amherst, Massachusetts. Rose (1984) derived an assemblage of 10 populations from this stock (IV) in 1980, which he then selected for different life-history attributes. Five of these populations, called B₄₋B₉, were maintained on a 2-wk generation cycle; five other populations, called O₄₋O₉, were selected for late-life reproductive success by maintenance on a longer generation cycle. It was later found that the mean longevity of the long-generation O's had increased substantially and that mean O early fecundity had declined—an apparent consequence of the negative genetic correlation between longevity and early fecundity detected by Rose and Charlesworth (1981a). Another trait, starvation resistance, was also found to play a role in this trade-off, it being strongly positively correlated with longevity (Rose et al. 1992), and like longevity, negatively genetically correlated with early fecundity (Service and Rose 1985; Service et al. 1985, 1988).

Given this pattern of genetic variation and covariation, as selection for late-life reproductive success proceeded, the five replicate O and B populations should have become increasingly divergent for mean longevity, starvation resistance, and early fecundity. Indeed, between 1982 and 1992, the difference between B and O mean longevity and starvation resistance increased substantially; the difference in mean early fecundity, however, did not. Initially, O mean early fecundity declined relative to that of the B’s (Rose 1984). But by the mid 1980s, B and O mean early fecundities were indistinguishable, and by 1990, O mean early fecundity was greater than B. The trade-off between early fecundity on the one hand, and starvation resistance and longevity on the other, as manifest in among-population comparisons, had disappeared (Leroi et al. 1994a).

All the life-history trait assays on the B’s and O’s had been conducted in a particular assay environment, and it was in this environment that the between-population life-history trade-off had disappeared. Experiments begun in 1990, however, revealed a more complicated story: although no longer present in some assay environments, this trade-off was still present in others. In 1990, relative B and O early fecundity depended strongly on assay environment, the B’s having greater early fecundity than the O’s in some environments, the O’s being superior in others. Because the O’s had superior starvation resistance regardless of environment, the apparent trade-off between fecundity and starvation resistance also depended on test environment (Leroi et al. 1994a).

The reversals in relative B and O early fecundity now observed across environments is considered a consequence of adaptation of either or both of these stocks to unique aspects of their respective culture regimes. Each generation, after 14 d, the O’s are placed into Plexiglas cages and are given fresh food continuously for the 8-wk of their remaining adult existence. At the end of this period, they are given a substantial feeding of yeast (to stimulate oviposition), and 24 h in which to lay eggs for the following generation. The B’s, however, are housed only in the culture vials in which they were raised, and which contain old, spent culture medium; after this they are allowed to lay eggs for 1 h, rather than 24.

The environment in which we had originally observed the trade-off and its subsequent loss was the “standard” assay environment. This consists of fresh medium and abundant levels of dietary yeast; it is thought to be an optimal environment for egg laying, and it closely approximates the actual culture regime of the O’s described above. The assay environment in which the trade-off is still apparent, that is, in which B’s have superior early fecundity, is called the “B-type” environment—which is designed to approximate the culture environment of the B’s (Leroi et al. 1994a).

This inconsistency of the trade-off, as inferred from comparisons between populations, raises several questions that we address in this paper.

1. Does a trade-off between early fecundity and starvation resistance still exist within the B and O populations? In other words, is there still a negative genetic correlation between early fecundity and starvation resistance within the B and O populations as in their ancestor population? This question is most pressing for the “standard” assay environment in which the interpopulation trade-off originally existed but later disappeared.

2. Does the genetic correlation between early fecundity and starvation resistance depend on environment? The dependence of the trade-off among populations on assay environment may reflect a similar dependence of the sign of genetic correlation within the B’s and O’s on assay environment.

3. Is there a negative genetic correlation between early fecundity in different environments? The reversal of relative B and O early fecundity between the “standard” and “B-type” environ-
ments suggests a cross-environmental trade-off for this trait. Is this reflected in the signs of cross-environmental genetic correlations?

In this paper, we investigate these questions concerning the genetic structures of the B and O populations—as they are after 10 yr of laboratory selection—by examining the direct and correlated responses of selection lines derived from them in 1989 (described in Rose et al. 1992). These lines, which also are replicated fivefold, were mass selected for starvation resistance. We report here the selection responses of these lines for early fecundity and starvation resistance in the "standard" and "B-type" environments.

MATERIALS AND METHODS

Starvation-Selected Stocks: Origin and Culture Regimes

In 1989, two populations were derived from each of the five B and each of the five O populations. Ten of the new populations—one from each of the ancestral B and O populations—served as controls, and were designated CB, or CO, according to its ancestry (see fig. 1). The remaining 10 new populations were selected for starvation resistance and designated SB, or SO, according to their ancestry. For the first 14 d of their life cycles, the control and starvation selected pop-ulations are handled in an identical manner. Each generation, flies are raised at controlled densities of 60–80 per vial in 8-dram vials filled with approximately 5 mL of food, and kept at 25°C in an incubator, as in B and O culture (Rose 1984). At day 14 after oviposition, the eclosed flies from all populations are placed into plexiglass chambers. Whereas the CO and CB flies are given an excess of food in the form of petri dishes of banana-molasses medium replaced every 2 d, the SO and SB flies are not given food but instead receive petri dishes containing nonnutritive agar. After approximately 80%–90% mortality caused by starvation, each S population and its paired control are given yeasted banana-molasses medium on which to recover and lay eggs for the following generation. Census populations sizes prior to selection are approximately 10,000 for each replicate selection line. For a full discussion of the course of selection of these lines see Rose et al. (1992). Since the derivation of the starvation-selected populations and their controls in 1989, the B's and O's have been maintained in their usual fashion (cf. Rose 1984).

Fecundity and Starvation Resistance Assays

Conditioning Environments.—Starvation resistance and fecundity were always assayed in either "standard" or "B-type" conditioning environments. In both treatments, flies were assayed at day 14 after oviposition, and the larval environments were identical; it is after eclosion that the treatments diverge.

In the "standard" assay, flies that have eclosed within the same 24–36-h period are transferred in pairs to assay vials. These vials contained sucrose-yeast medium, and charcoal powder added for coloring. The surface of the food is covered with a thin yeast paste to which dilute acetic acid has been added. Flies are transferred to fresh vials daily for 4 d, at which point they are assayed for either fecundity or starvation resistance (Rose 1984; Rose and Charlesworth 1981a).

In the "B-type" assay environment, the flies are maintained in their culture vials until day 14 after oviposition then assayed for either fecundity or starvation resistance. These "B-type" and "standard" conditioning treatments differ, then, in numerous environmental variables including the freshness of the banana-molasses medium, the presence of excess live yeast, and adult density (60–80 versus 2).

Fecundity Assay.—In the "standard" fecun-
dity assay, the pairs of flies were transferred from their conditioning vials to assay vials supplemented with a dietary yeast and acetic-acid mixture, and permitted to lay eggs for 24 h. In the “B-type” fecundity assay, 60–80 flies were transferred to a single assay vial supplemented with a dietary yeast and acetic-acid mixture and permitted to lay eggs for only 1 h. Female fecundity was estimated by dividing the number of eggs in each vial by the number of females in that vial. In addition, then, to the differences in the conditioning phases of the “B-type” and “standard” assays listed above, these assays differ in the length of time permitted for oviposition, as well as the density of flies.

Starvation Resistance.—In both the “standard” and “B-type” starvation resistance assays, single pairs of flies were transferred from conditioning vials to starvation-resistance assay vials that contained no food but that had a humid atmosphere (Service et al. 1985).

Experimental Design

In 1991, we carried out two experiments to address the questions posed above.

Experiment 1. B, O, and CB Early Fecundity.—Léroï et al. (1994a) suggested that the reversal in relative B and O early fecundity among environments was caused by historical differences in the way that the B’s and the O’s had been cultured. Specifically, each generation the O’s live in cages as imagos, whereas the B’s do not. It was proposed that adaptation of each stock to its own environment, combined with a negative genetic correlation in fecundity among environments, gave rise to an interpopulation trade-off for early fecundity among the “standard” and “B-type” assay environments. This interpretation assumed that the “standard” fecundity assay mimics at least some of the crucial aspects of the O’s cage environment immediately prior to oviposition, as the “B-type” assay does that of the B’s. If such a negative genetic correlation across environments exists for fecundity, then other instances of adaptation to a cage culture regime should also cause an increase in “standard” assay fecundity, and concomitant loss of fecundity in the “B-type” environment.

To investigate this, we compared early fecundity in the CB’s with their ancestors, the B’s. Like the O’s, the CB’s are propagated in cages and hence differ from the B’s in the environment that they experience immediately prior to oviposition. We also assayed the O’s as an additional control. At the time of assay, the B’s and O’s had been evolving independently for about 250 and 55 generations, respectively. The CB’s had been evolving independently from the B’s for approximately 43 generations. In this experiment, approximately 40 females were assayed per population in the “standard” assay for a total of 599 over 15 populations. For the “B-type” assay, 20 replicate vials were assayed per population. Note that the “B-type” assay involves the estimation of female fecundity in a vial containing 60–80 flies; the unit of replication within populations, then, is the vial, and not individual females.

Experiment 2. SB, CB, SO, and CO Early Fecundity and Starvation Resistance.—To gain insight into the genetic structure of the B’s and the O’s, we assayed the 10 starvation-selected populations derived from B’s and O’s (SB’s and SO’s) relative to their 10 paired control (CB’s and CO’s) populations. After 45 generations of starvation selection, all 20 populations were assayed for early fecundity and starvation resistance in the “standard” and “B-type” environments. In the starvation resistance assays, approximately 20 females were assayed per population per treatment to give a total of 782 females (20 females × 20 populations × 2 environments). In the fecundity assays, 20 replicate “B-type” replicate vials, each consisting of 60–80 females, were assayed per population, over 20 populations. For the “standard” treatment, approximately 40 replicate vials, each containing a single male and female, were assayed per treatment to give a total of 776 females for this treatment alone (40 females × 20 populations).

In this experiment, we also assayed B and O early fecundity in the “standard” and “B-type” environments again, to compare them to CB early fecundity as we did in experiment 1. At this point the B’s and O’s had been evolving independently for about 255 and 56 generations respectively.

Statistical Analysis and Experimental Design

All hypothesis testing is based on replicate population means as observed variates. Unless specified otherwise, all means and standard errors are also based on replicate population means as observed variates. To make claims about the genetic structures of the B and O stocks as groups, we based the replication structure of the starvation-selected stocks and their controls on the replication structure of their ancestors. For this
reason, paired t-tests were used to compare means in which the pairs are selected and control populations derived from a common ancestor, for example, SB1 and CB1, both derived from B1. In ANOVA, ancestral lineage was treated as a random block, as was generation when the results from two assays were considered simultaneously. Selection treatment (e.g., SB versus CB) and conditioning treatment (“standard” versus “B-type”) were treated as fixed effects. Because we have explicit predictions of the sign of the direct and correlated responses to starvation resistance in the “standard” environment (Leroi et al. 1994a), one-tailed probabilities were used when appropriate in hypothesis tests. Because we do not have an equivalent expectation for signs of the selection responses in the “B-type” environment (allowing for the possibility of genotype × environment interaction), two-tailed probabilities were used for traits measured in this environment.

RESULTS

Early Fecundity in the “Standard” and “B-Type” Environments: O Versus B and CB Versus B.—First we confirm our earlier observation (Leroi et al. 1994a) that the O's have a higher fecundity in the “standard environment,” but that the reverse is true in the “B-type” environment (table 1, fig. 2). In the “standard” environment, experiment 1 shows a significant difference between B and O; experiment 2 does not, although the relative means of B and O early fecundity are in the expected direction (table 1, fig. 2). Considering both experiments simultaneously; ANOVA shows that the O’s are significantly greater in fecundity than the B’s ($P < 0.005$). In the “B-type” environment, both experiments 1 and 2 confirm that B early fecundity is greater than O early fecundity (table 1, fig. 2); both experiments considered simultaneously by ANOVA show the same result ($P < 0.0005$). The existence of genotype-by-environment interaction for early fecundity as reflected in the differentiation of the B and O stocks for this trait is thus confirmed.

The pattern of B and CB differentiation for early fecundity parallels that of the B and O stocks (fig. 2). Both experiments show CB’s have a higher early fecundity than the B’s in the “standard” environment (table 1); a combined ANOVA shows the same result ($P < 0.005$). In the “B-type” environment, in experiment 1, CB early fecundity is lower than B early fecundity but non-significantly so. Experiment 2 confirmed this re-
result, and here the CB fecundity is significantly lower than that of the B's (table 1); combined ANOVA shows a significant difference \( P < 0.05 \). The failure to detect a difference in this comparison in experiment 1 was probably caused by the loss of one of the replicate populations and hence lack of statistical power.

In being kept in a cage environment, then, the CB populations have apparently evolved an environment-dependent pattern of early fecundity relative to their ancestors, the B's. Furthermore, this pattern of environmental dependence in early fecundity is the same that the O's exhibit with respect to the B's. Because the CB's and O's have quite different demographic regimes (the CB's have short generations, the O's have long generations), but both are kept in cages, we conclude that the CB's have adapted to their cage environment in a manner parallel to the O's. In each case, maintenance of populations in the cage environment was associated with an increase of early fecundity in the “standard” assay environment and a decrease of early fecundity in the “B-type” assay environment. These results strongly suggest the existence of considerable amounts of selectable genotype-by-environment variation for early fecundity.

**Starvation Resistance in the “Standard” and “B-Type” Environments.**—The starvation-selection stocks (SB's and SO's) have far greater starvation resistance in the “standard” environment than do their unselected controls (CB's and CO's) (table 2). Separate ANOVA on the populations derived from the B's and those derived from the O’s show a significant effect of selection treatment \( P < 0.0005 \); a significant effect of conditioning environment \( P < 0.0005 \); and a significant selection-by-conditioning interaction \( P < 0.005 \). After 45 generations, then, the direct response to starvation selection was considerable in both the “standard” and “B-type” environments, although the superiority of both the SO's and SB's over their controls was even greater in the “B-type” environment than in the “standard” environment.

**Early Fecundity in the “Standard” and “B-Type” Environment: SB Versus CB and SO Versus CO.**—Early fecundity in both the starvation-selected stocks is reduced relative to that of their controls when females are conditioned in either the “standard” or “B-type” environment (figs. 3, 4; table 1); three of these four comparisons are significant, the exception being SB versus CB in the “standard” environment \( P = 0.076 \), fig. 3a, table 1).

Considering both environments simultaneously, ANOVA on the fecundities from the populations derived from the B's shows a significant effect of selection treatment \( P < 0.05 \); a significant effect of conditioning environment \( P < 0.0005 \); and no selection-by-conditioning interaction \( P > 0.1 \). ANOVA on the populations derived from the O’s shows a significant effect of selection treatment \( P < 0.005 \); a sig-

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**Table 2.** Starvation resistance (in hours) when females are conditioned in the standard and B-type environments. Means and standard errors based upon \( N - 1 = 4 \) df.

<table>
<thead>
<tr>
<th>Ancestor</th>
<th>Control lines</th>
<th>Starvation selected lines</th>
<th>( P^* )</th>
<th>Control lines</th>
<th>Starvation selected lines</th>
<th>( P^\dagger )</th>
</tr>
</thead>
<tbody>
<tr>
<td>B1</td>
<td>29.33</td>
<td>135.18</td>
<td></td>
<td>49.85</td>
<td>167.50</td>
<td></td>
</tr>
<tr>
<td>B2</td>
<td>34.23</td>
<td>83.85</td>
<td></td>
<td>41.25</td>
<td>182.35</td>
<td></td>
</tr>
<tr>
<td>B3</td>
<td>33.35</td>
<td>117.36</td>
<td></td>
<td>62.25</td>
<td>199.80</td>
<td></td>
</tr>
<tr>
<td>B4</td>
<td>27.55</td>
<td>66.93</td>
<td></td>
<td>44.00</td>
<td>192.80</td>
<td></td>
</tr>
<tr>
<td>B5</td>
<td>28.73</td>
<td>86.33</td>
<td></td>
<td>33.10</td>
<td>163.60</td>
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</tr>
<tr>
<td>Mean</td>
<td>30.64</td>
<td>97.93</td>
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<td>46.09</td>
<td>181.21</td>
<td>&lt; 0.0005</td>
</tr>
<tr>
<td>SE</td>
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<td></td>
<td>4.86</td>
<td>7.00</td>
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</tr>
<tr>
<td>O1</td>
<td>48.95</td>
<td>135.13</td>
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<td>50.75</td>
<td>193.50</td>
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</tr>
<tr>
<td>O2</td>
<td>36.63</td>
<td>112.71</td>
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<td>58.65</td>
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<tr>
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</tr>
<tr>
<td>O4</td>
<td>27.60</td>
<td>85.08</td>
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<td></td>
</tr>
<tr>
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<td>97.18</td>
<td></td>
<td>47.80</td>
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<td></td>
</tr>
<tr>
<td>Mean</td>
<td>36.15</td>
<td>104.35</td>
<td>&lt; 0.0005</td>
<td>62.15</td>
<td>175.50</td>
<td>&lt; 0.0005</td>
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<td>8.95</td>
<td></td>
<td>6.44</td>
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</tr>
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</table>

* One-tailed probabilities estimated using the \( t \)-distribution with \( N - 1 = 4 \) df.

† Two-tailed probabilities estimated using the \( t \)-distribution with \( N - 1 = 4 \) df.
significant effect of conditioning environment \( (P < 0.0005) \); and a marginally nonsignificant selection \( \times \) conditioning interaction effect \( (0.1 > P > 0.05) \). After 45 generations of starvation-selection, then, fecundity has clearly declined in response to starvation selection in three of the four combinations of assay environment and ancestral population with the same qualitative result in the fourth. This result is like that of Hutchinson et al. (1991), who, using other starvation-selected lines derived from the O's, also found a decline in "standard" environment fecundity as starvation resistance increased. In the "B-type" environment, the reduction of SO and SB fecundity relative to their controls strongly suggests that the negative genetic correlation between early fecundity and starvation resistance, first detected in the early 1980s (cf. Service and Rose 1985), was still present in both the B's and O's in 1989. In the "standard" environment, there is similarly strong evidence for a negative genetic correlation in the O's, with the same trend evident in the B's. The "standard" environment results also confirm those of an earlier experiment performed at approximately generation 40, in which the SO's also were found to have a lower early fecundity than the CO's, and the SB's were marginally nonsignificantly lower than their controls, CB; a combined analysis yields the same result (data not shown).

**DISCUSSION**

*The Genetic Structure of the Ancestral Population, IV.*—Several lines of evidence indicate that in the population ancestral to the B's and O's—IV—starvation resistance is strongly positively correlated with longevity, and, like lon-
gevity, negatively genetically correlated with early fecundity. First, when the O’s were initially selected for late-life reproductive success, starvation resistance increased with longevity as early fecundity declined (Rose 1984; Service et al. 1985). Second, when relaxed selected lines were derived from the O’s and cultured on a 2-wk generation cycle identical to that of the B’s, starvation resistance declined with longevity, and early fecundity increased again (Service et al. 1988). Third, sib analysis directly revealed a negative genetic correlation between starvation resistance and early fecundity between −0.453 (± 0.178) and −0.913 (± 0.027), depending on environment (Service and Rose 1985). This accumulation of evidence for a trade-off in IV leaves us, then, with a puzzle: Why, if the difference in B and O early fecundities has reversed over the past 10 yr (in the “standard” environment), have not relative starvation resistance and longevity done so as well? In other words, why has the long-term divergence of the B’s and O’s failed to reflect the influence of the trade-off between early fecundity on the one hand and starvation resistance and longevity on the other?

Genetical Explanations for the Evolution of Trade-Offs. — The trade-off discussed here could be caused by a conflict in allocating materials between two resource sinks: fecundity and starvation resistance pictured as a Y-shaped metabolic pathway (vide Sheridan and Barker 1974; van Noordwijk and de Jong 1986). Variation at loci responsible for allocation will result in a negative genetic correlation between these traits; variation at loci responsible for acquisition will result in a positive genetic correlation (cf. Houle 1991). Under this scenario, the negative genetic correlation between early fecundity and starvation resistance in the ancestral population, IV, was caused by alleles segregating at loci largely responsible for the allocation of resources among these traits, acquisition loci presumably contributing little genetic variance to these traits. This negative genetic correlation would then have given rise to the initial decline in O early fecundity as selection proceeded (Rose 1984).

The subsequent disappearance of this interpopulation trade-off may have occurred in one of two ways: (1) The trade-off may have dissipated within one (or both) of the sets of populations and hence ceased to constrain their divergence. The negative genetic correlation could perhaps have disappeared with the evolution of novel epistatic alleles. Such modifiers have been found for resistance to phage in Escherichia coli populations (Lenski 1988a,b) and pesticide resistance in blowfly populations (McKenzie et al. 1982; Clarke and McKenzie 1987). Alternatively, the genetic correlation might have collapsed because of the early fixation of segregating alleles at allocative loci. (2) The trade-off may still exist within each population yet have become obscured between populations. For instance, novel alleles may have become fixed at acquisition loci in one (or both) of the sets of populations without the negative genetic correlations between early fecundity and starvation resistance having been substantially altered.

Of these two classes of explanation for the disappearance of the trade-off among populations in the “standard” environment, we favor the latter. That is, the direct and correlated responses of the starvation-selected stocks relative to their controls strongly suggest that the negative genetic correlation between early fecundity and starvation resistance still existed in the B and O populations in 1989—long after the trade-off could no longer be detected by comparing their means. Leroi et al. (1994a) argue that the disappearance of the among-population trade-off is caused primarily by adaptation of the O’s to their novel cage environment (and hence to the “standard” assay). In this light, it is of particular significance that the negative genetic correlation—as reflected by the divergence of the SO’s and CO’s—still appears to be present within the O’s when conditioned in this environment (tables 1, 2; fig. 1b). If alleles that confer increased acquisitive ability in the cage environment have indeed increased in frequency in the O populations, then they have done so without perturbing the sign of the genetic correlation between early fecundity and starvation resistance. The negative genetic correlation also probably is preserved in the B’s: our data suggest a small (though marginally nonsignificant—P < 0.10) decline in early fecundity of the SB’s relative to their controls in the “standard” environment.

Do Patterns of Genetic Correlations Constrain Life-History Evolution? — It is often claimed that the life histories of organisms are constrained by trade-offs manifest as negative genetic correlation (e.g., Partridge and Sibly 1991; Rose 1991; Stearns 1992), and therefore the evolutionary trajectories of populations should be predictable from knowledge of their genetic correlation structure. However, the present study illustrates vividly the difficulties that may arise when pre-
predicting the long-term evolution of a set of populations from prior knowledge of genetic correlations.

We have argued that genetic correlations between early fecundity on the one hand, and starvation resistance and longevity on the other, were present in the ancestral IV population, and indeed, are still present in the B’s and O’s after more than 10 yr of laboratory evolution. Nevertheless, in the “standard” assay environment, the O’s now have superior early and late fecundity as well as superior starvation resistance and longevity (Leroi et al. 1994a). We conclude that the negative genetic correlations between these traits concealed the presence of genetic variance that was not associated with longevity or starvation resistance via an antagonistic pleiotropy. The existence of such variance, which possibly affects resource acquisition, was fortuitously revealed by selection in the O’s for the ability to lay eggs in a particular environment. Whether the alleles involved were initially at low frequency in the B’s and O’s and thus had little influence over the original differentiation of these populations, or whether they arose later in the course of their evolution, we cannot say. Our results do not contradict the many selection studies that have successfully predicted short-term selection responses from genetic correlations (e.g., Falconer 1989), but they do suggest that over somewhat longer periods of time such prediction may be problematical. This point has, of course, been made frequently before (Falconer 1989; Turelli 1988). However, failures in the long-term predictability of selection responses are usually attributed to the evolution of genetic correlations because of inbreeding, drift, or selection (Sheridan and Barker 1974; Wilkinson et al. 1990). The novelty of our results lies in the finding that selection responses of the B’s and O’s in the “standard” environment were unpredictable even though the sign of the genetic correlation remains apparently unperturbed in that environment.

It is clear that our inability to predict the long-term evolution of even so simple a system as ours stems from our lack of knowledge of the detailed population genetics of the loci affecting the two characters involved as well as the selection forces that impinge on them. The possibility of obtaining such knowledge must, for most life-history trade-offs in most species, remain in the realm of fantasy; in its absence the prospects for accurately predicting the long-term evolution of natural populations seem bleak.

Constancy of the Sign of the Genetic Correlation between Early Fecundity and Starvation Resistance Across Environments.—It is of interest to note that, at least in the O’s, the negative genetic correlation is found in both the “B-type” and “standard” environments. This is consistent with the idea that this trade-off is caused by a structured pleiotropy, that is, a pleiotropy that is caused by a physiological coupling (cf. Stearns et al. 1991). Given such coupling (perhaps because of the use of common metabolic resources as envisioned above), the average effect of an allele influencing both traits is expected to change sign for both traits at the same points across an environmental gradient (de Jong 1990). This, in turn, implies constancy of the sign of the genetic correlation among these traits (de Jong 1990). Service and Rose (1985), assaying the IV population, showed that in some environments the genetic correlation between these traits was less negative than in others, but in no case did they find that the genetic correlation became positive. Other evidence, from environmental, surgical, and mutational manipulations, suggests that early fecundity and starvation resistance probably draw on common reserves of triglyceride lipids among other resources (see Chippindale et al. 1993).

Trade-Offs in Early Fecundity among Environments.—The existence of strong genotype × environment interactions for early fecundity was first suggested by the observation that in 1990 relative B and O early fecundity reversed among the “B-type” and “standard” assay environments (Leroi et al. 1994a; table 1). Some patterns of genotype × environment interaction can give rise to negative genetic correlations between the expression of a trait in one environment and its expression in another (cf. Via 1987). In other words, the expression of a trait may trade-off among environments (Fry 1990).

Leroi et al. (1994a) argued that these genotype-by-environment interactions for early fecundity had in fact obscured the early fecundity—starvation resistance trade-off among the B and O populations. They argued that these genotype-by-environment interactions took the form of a negative genetic correlation between early fecundity in the B and O culture regimes.

The evolution of CB early fecundity in the two assay environments relative to the B’s provides additional evidence for the existence of such a negative genetic correlation. Here the CB’s, in being kept in cages similar to those that the O’s
are kept in, have gained fecundity in the “standard” environment, and lost it in the “B-type” environment relative to the B’s. The documentation of this negative genetic correlation adds to a small list of cases in which fitness components are thought to trade-off across environments (e.g., Robertson 1965; Scheiner et al. 1989; Fry 1990). Of these, Fry’s 1990 study of vegetable-dwelling mites most unambiguously demonstrates the existence of such a trade-off, and he argues that among-environment trade-offs in fitness components may be far more common in herbivore populations than previously thought, biometrical techniques being biased against their detection. Such trade-offs are interesting for the role that they are thought to play in the evolution of ecological specialization (Futuyma and Moreno 1988). This is because a negative genetic correlation in fitness across environments indicates that the most fit genotype in a population changes with environment (Via 1984a,b). Adaptation to any one environment, then, will cause a population to have high fitness in that environment but not necessarily in others. Nevertheless, it must be added that the caveats listed above concerning the difficulties of viewing negative genetic correlations as evolutionary constraints apply to the evolution of ecological specialization as much as any other form of adaptation.

**Inferring Genetic Correlations from Comparative Data.**—The phylogenetic distribution of life-history traits is often assumed to be the consequence of historical patterns of genetic variation and covariation (Sterns 1992). Indeed, the current fascination with comparative methodology (e.g., Harvey and Keymer 1991; Harvey and Pagel 1991) rests, in part, on the hope such patterns can be recovered from the analysis of phylogeny. When the B’s and O’s are compared, the trade-off between early fecundity and starvation resistance appears in the “B-type” environment but not the “standard” environment. However, analysis of the selection responses of the starvation-selected stocks shows that the negative genetic correlation probably still exists in both environments. Considered overall, no correspondence exists between inter and intrapopulation patterns of covariation among these traits. We argued above that the evolution of the B’s and O’s illustrate the difficulty of predicting evolutionary trends from patterns of genetic correlations. So, too, our results suggest that comparative studies may reveal little about the genetic structure of populations (cf. Reznick 1985; Leroi 1994b).

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**Literature Cited**


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