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QTL mapping of genotype–environment interaction for fitness in *Drosophila melanogaster*

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Summary

A fundamental assumption of models for the maintenance of genetic variation by environmental heterogeneity is that selection favours alternative alleles in different environments. It is not clear, however, whether such antagonistic pleiotropy is common. We mapped quantitative trait loci (QTLs) causing variation for reproductive performance in each of three environmental treatments among a set of 98 recombinant inbred (RI) lines derived from a cross between two *D. melanogaster* laboratory strains. The three treatments were standard medium at 25 °C, ethanol-supplemented medium at 25 °C, and standard medium at 18 °C. The RI lines showed highly significant genotype–environment interaction for the fitness measure. Of six QTLs with significant effects on fitness in at least one of the environments, five had significantly different effects at the different temperatures. In each case, the QTL by temperature interaction arose because the QTL had stronger effects at one temperature than at the other. No evidence for QTLs with opposite fitness effects in different environments was found. These results, together with those of recent studies of crop plants, suggest that antagonistic pleiotropy is a relatively uncommon form of genotype–environment interaction for fitness, but additional studies of natural populations are needed to confirm this conclusion.

1. Introduction

The maintenance of heritable variation in fitness traits is a fundamental problem in evolutionary quantitative genetics. The naive expectation is that selection should erode genetic variation for traits closely related to fitness, so that little heritable variation for such traits should be present in populations at equilibrium. Genetic variation in basic fitness traits, such as fecundity and juvenile survival, appears to be common in natural populations (Mousseau & Roff, 1987; Simms & Rausher, 1989; Via, 1991), however, and by some measures exceeds that observed for morphometric traits (Houle, 1992).

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Environmental heterogeneity is an oft-cited hypothesis for the maintenance of genetic variation in fitness traits. Models of both single loci (Levene, 1953; Haldane & Jayakar, 1963; Felsenstein, 1976) and polygenic characters (Slatkin, 1978; Gillespie & Turelli, 1989) show that when selection varies across environments, genetic polymorphism can be maintained. The models imply that much additive variation for fitness in any given environment can be present in equilibrium populations, even though genetic variation for overall fitness may be absent. If correct, this view would have a number of important evolutionary implications. For example, if the environmental variation is spatial and predictable, as might occur among different habitats or host types, specialization on a single habitat or host should increase a population's mean fitness, by allowing it to adapt to the habitat or host free of countervailing selection in others (Gould, 1984). Thus, the environmental het-

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erogeneity hypothesis implies the existence of a population-level benefit deriving from ecological specialization. Furthermore, disruptive selection among stable habitats or hosts, if strong, could lead to sympatric speciation (Maynard Smith, 1966; Dickinson & Antonovics, 1973; Diehl & Bush, 1989). The environmental heterogeneity hypothesis also has implications for the evolution of mate choice. Certain types of temporally varying selection could maintain a sufficiently high parent–offspring correlation for fitness to provide a genetic benefit to females that choose high fitness mates (Maynard Smith, 1991). In contrast, in extreme cases of random temporal variation, or in the case of spatial variation with complete mixing each generation, there is no correlation between the environments of parents and offspring; therefore 'good genes' sexual selection would not work, despite the existence of genetic differences in fitness in any one environment.

A fundamental assumption of most models for the maintenance of genetic variation by environmental heterogeneity is that selection favours alternative alleles in different environments (Hedrick, 1986; Gillespie & Turelli, 1989). It is not clear, however, whether such 'antagonistic pleiotropy' across environments is common. Although families or clones typically show different fitness rankings when tested in different environments (for references see Fry *et al.*, 1996), the existence of such crossing of reaction norms for fitness does not necessarily mean that there are loci at which selection favours different alleles in the different environments (de Jong, 1990; Fry, 1993). For example, crossing of reaction norms for fitness could reflect the presence of loci showing conditionally neutral variation, i.e. variation that affects fitness in some environments but not others.

To evaluate the environmental heterogeneity hypothesis, information is needed on whether antagonistic pleiotropy is a common source of crossing of reaction norms for fitness. A promising approach to this problem is mapping the quantitative trait loci (QTLs) causing fitness variation in each of a set of environments. If antagonistic pleiotropy across environments is common, then QTLs associated with high fitness in one environment should sometimes be associated with low fitness in others. Alternatively, crossing of reaction norms for fitness could arise from differences in the magnitude of QTL effects in different environments, without changes in the direction of the effects.

Genotypes of *Drosophila melanogaster* show crossing of reaction norms for fitness traits when grown at different temperatures (Barnes *et al.*, 1989; Partridge *et al.*, 1995) or on different concentrations of ethanol (Oakeshott *et al.*, 1985). Both temperature and ethanol concentration are important environmental variables for natural *D. melanogaster* populations (Gibson *et al.*, 1981; Jones *et al.*, 1987), and variation in either factor could in theory maintain genetic variation in natural populations of the flies. We have mapped QTLs causing variation and crossing of reaction norms for reproductive performance among a set of recombinant inbred (RI) lines reared at two temperatures and in the presence and absence of ethanol. Our goal was to determine whether some of the crossing of reaction norms observed among the RI lines was caused by loci exhibiting antagonistic pleiotropy across environments.

Inbred lines are likely to show different patterns of variation for fitness-related characters compared with the natural populations from which they were derived (Rose, 1984). In particular, rare, wholly or partly recessive alleles make a disproportionate contribution to the variance among inbred lines compared with their contribution to the additive genetic variance of an outbred population (Charlesworth & Hughes, 1998). This is not a critical limitation to our study, because our goal is simply to determine whether loci exhibiting antagonistic pleiotropy are present. If alleles at many such loci segregate at intermediate frequencies in natural populations, then there is a good chance that any two inbred lines will be fixed for different alleles at some of the loci. In this case, the effects of the loci should be detectable in a set of RI lines, provided the effects are not too small. (It is conceivable that a pattern of epistasis exists such that different homozygotes at a locus that reverse fitness ranks across environments in an outbred background do not do so in an inbred background, but we know of no evidence for such a phenomenon.) By using RI lines, we expect to detect the effects of additional loci with recessive alleles that are deleterious in all environments, but this would not alter the conclusions about the presence or absence of antagonistic pleiotropy at other loci.

2. Materials and methods

(i) *RI lines*

The RI lines were derived from two unrelated homozygous parental lines: Oregon-R (Lindsley & Zimm, 1992) and 2b3 (Pasyukova & Nuzhdin, 1993). The F_1 progeny of the parental lines were backcrossed to 2b3, and the backcross progeny were randomly mated for four generations. At generation five, 200 individual pairs were selected, and their progeny were inbred by full-sib mating for 25 generations. Ninety-eight lines that survived inbreeding were maintained by mass matings of *c.* 20 pairs for *c.* 15 generations before the fitness assays reported below were conducted. The lines were maintained in shell vials with approximately 10 ml of standard cornmeal–molasses–agar medium at 25 °C.

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(ii) *Molecular markers*

Insertion sites of the retrotransposable element *roo* were determined by *in situ* hybridization of a biotin-labelled plasmid containing the *roo* element to polytene salivary gland chromosomes of third instar larvae, as described elsewhere (Long *et al*., 1995; Nuzhdin *et al*., 1997). The presence or absence of an element at a particular chromosomal location serves as a genetic marker. Five slides were scored per line; markers showing within-line heterozygosity were rechecked to eliminate the possibility of mis-scoring. There were 16, 22 and 37 informative *roo* markers on the X, second and third chromosomes, respectively, giving an average spacing of about 4 centimorgans (cM). Cytological positions of the markers are given by Nuzhdin *et al*. (1997). The small fourth chromosome of the Oregon-R parent was marked by the eye morphology marker spa^{pol}.

(iii) *Fitness assays*

Reproductive performance of the RI lines was measured in each of three environmental treatments: standard medium at 25 °C ('standard'), standard medium at 18 °C ('low temperature'), and ethanol-supplemented medium at 25 °C ('ethanol'). Ethanol was added to a final concentration of 12% after the medium had cooled to 45–50 °C. A competitive fitness assay was used, similar to the 'female' test of Latter & Robertson (1962). For each replicate, nine mated females from an RI line were placed in a vial along with seven mated females from an unrelated stock bearing the *yellow* body colour mutation. The females were allowed to lay eggs for 5 d and then discarded. Emerged wild-type and *yellow* adults were counted on days 12, 14 and 19 after the vials were set up in the ethanol and standard treatments, and after 21, 28 and 35 d in the low temperature treatment. The mean number of flies emerging per vial was 94 in the low temperature treatment, 110 in the ethanol treatment and 131 in the standard treatment. The assays were conducted in six blocks over a 2-month period, each consisting of one replicate vial for each of the 98 RI lines in each of the three treatments. Within a block, the three treatments were set up on consecutive days, with the treatment order varying randomly from block to block.

The fitness assays reflect variation in egg production and egg-to-adult survival, but are not influenced by competitive male mating success, which is an important component of fitness in *Drosophila* populations (Anderson *et al*., 1979; Miller *et al*., 1993). Elsewhere, however, we report evidence that variation in male fertility (as distinguished from mating success) made an important contribution to fitness variation assayed by the same methods in a set of mutation-accumulation lines (Fry *et al*., 1998).

The females used for the assays were reared by allowing seven pairs to lay eggs in a vial of standard medium at 25 °C for 5 days. On the fourteenth day after initiation of the vials, all emerged adults were transferred to a holding vial, where the females were allowed to mate and mature for 2 more days before being used to set up one replicate vial of the assays. Because a few rearing vials failed to produce enough flies for the assays, 51 assay vials could not be set up, out of 1764 called for by the design. Females from the *yellow* stock were reared in the same manner as those of the RI lines except that adults were transferred on the thirteenth day.

(iv) *Statistical analysis*

The proportion of wild-type flies (out of wild-type plus *yellow*) emerging per vial was used as the analysis variable. Two-way unreplicated analysis of variance (ANOVA), with lines and blocks as random factors, was used to estimate the variance among lines within each environment. Three-way unreplicated ANOVA on data from all three environments, with environments as a fixed factor, was used to test for a line main effect and line by environment interaction. The line main effect was tested over the synthetic denominator mean square: MS(line∗env) + MS(line∗block) − MS(error). These analyses were performed using the VARCOMP (type I option) and GLM procedures (test option of Random statements) in SAS (SAS Institute, 1989).

Composite interval mapping (Jansen & Stam, 1994; Zeng, 1994), as implemented by the QTL cartographer program (Basten *et al*., 1994, 1996), was used to map QTLs affecting the fitness measure in each environment. Composite interval mapping tests the hypothesis that a QTL is located at a given position between two flanking markers, while attempting to control for the effects of QTLs in other intervals. QTL analysis was performed on the least-square means (SAS Institute, 1989) of each line, using the Ri2 design of cartographer, the Kosambi map function, a step size of 1 cm, five background markers, and a window size of 20 cm (effects of varying the last two parameters are discussed below). Critical values of the likelihood ratio test statistic, taking multiple tests into account, were calculated from the cumulative distribution function of the χ^2 distribution for 1 d.f. and a probability of $1-\alpha/76$, where 76 is the number of markers and α is the desired significance level (Zeng, 1994). Map distances between markers were estimated from the observed proportion of recombinants in the RI lines, as described by Nuzhdin *et al*. (1997). No linkage disequilibrium was observed between adjacent second chromosome markers at polytene bands 50F

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and 57C; therefore the second chromosome was split into two linkage groups.

The cartographer program provided estimates of QTL effects in each environment, but did not provide standard errors of effect estimates or tests for QTL by environment interaction. To estimate standard errors of effects, the markers closest to likelihood peaks that were significant in at least one environment were used as independent variables in multiple regressions, with the least-square line means in each environment as the dependent variables. Marker genotypes were coded as zero for lines homozygous for the 2b3 parental allele, and 1 for lines homozygous for the Ore-R allele. Multivariate significance tests (SAS Institute, 1989; Proc REG, Mtest option) were used to test the hypothesis that the regression parameters were the same in the different environments. This method takes into account the non-independence of residuals from the same RI line in the different environments. The first hypothesis tested was that the entire set of regression parameters (except the intercept) was the same between each pair of environments. If this hypothesis could be rejected, then the equivalence of individual regression parameters across environments was tested. Multivariate tests were also used to test the hypothesis that each regression parameter differed from zero when averaged across environments. The proportions of genetic variance in each environment explained by the regressions were calculated as the coefficient of multiple determination, R^2, times $V_{\bar{x}}/V_L$, where $V_{\bar{x}}$ is the variance among line means, and V_L is the variance component among lines from the ANOVA. The $V_{\bar{x}}/V_L$ term corrects for the fraction of variance among the line means that is of purely environmental origin.

In spite of 25 generations of full-sib mating, the RI lines were still segregating for an average of 5% of the autosomal *roo* markers (but for only 0·6% of the X chromosome markers). Segregating sites were treated as missing data for composite interval mapping, and lines still segregating for any of the markers chosen for the regression analysis were not used in that analysis. To test the hypothesis that there was a positive association between heterozygosity and fitness, the rank of the number of segregating sites per line was used as an additional independent variable in the regressions. Ranks were used because the untransformed values were highly skewed to the right, with most lines having zero or one segregating sites, but the remainder having up to 27.

3. Results

(i) *Variation among the RI lines*

The RI lines showed significant variation in the competitive index in each of the three environmental treatments (Table 1), with a wide range of values in each environment (Fig. 1). Line means were positively correlated across environments (Fig. 1), giving rise to a significant main effect of line ($P < 0·0001$) in an ANOVA on data from all three environments. Nonetheless, there were changes in ranking of performance of lines across the environments (Fig. 1), giving rise to significant line by environment interaction ($P < 0·0001$).

Table 1. *Means and variance components in each environmental treatment for the competitive index (proportion of wild-type flies)*

Treatment	Mean	Variance components: Lines	Blocks	Error
Ethanol	0·54	3·08	0·33	3·14
Standard	0·33	1·82	0·14	1·77
Low temperature	0·38	1·83	0·94	2·01

All line and block variance components differ significantly from zero at the 0·0001 level based on the approximate *F*-tests from SAS. Variance components have been multiplied by 100.

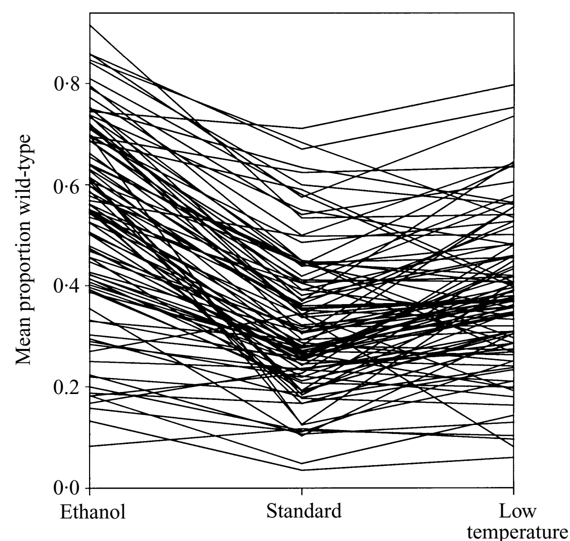

Fig. 1. Mean values of the competitive index for each of the 98 recombinant inbred lines in each of the three environmental treatments.

(ii) *QTL mapping results*

Plots of the likelihood-ratio test statistic for the null hypothesis that there is no QTL affecting the competitive index at a given genomic location are shown in Fig. 2. In the standard environment, there are two significant likelihood peaks ($P < 0·05$ genome-wide), both on the X (first) chromosome. In the low temperature environment, there are two significant

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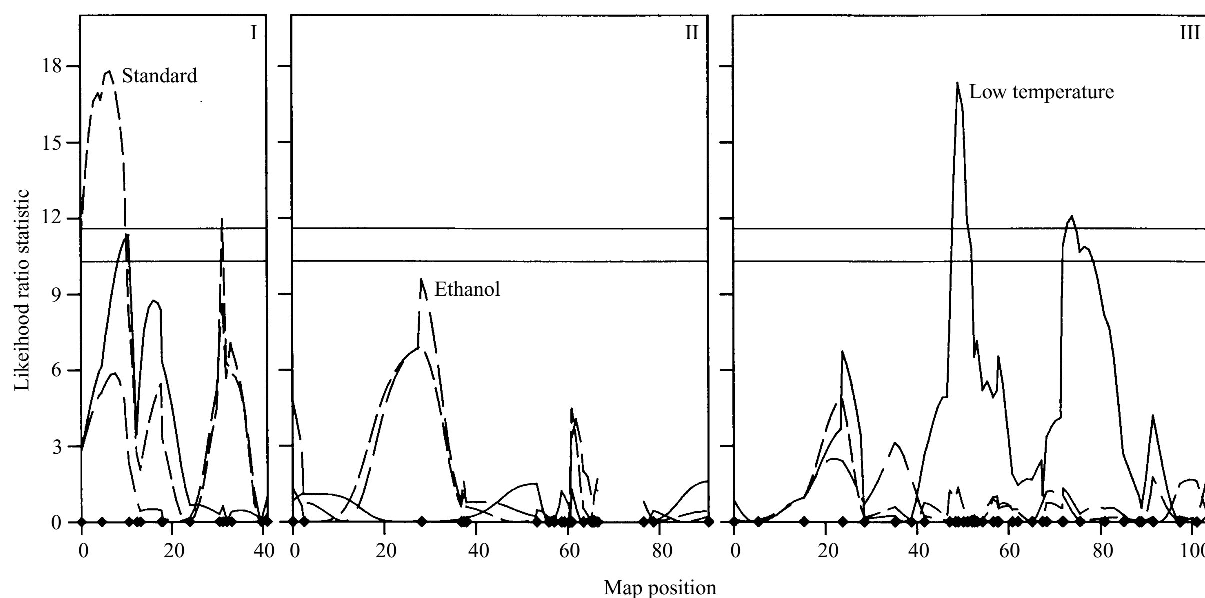

Fig. 2. Plot of likelihood-ratio test statistics from composite interval mapping for the three major chromosomes. Results for the ethanol, standard and low temperature environments are represented by long-dashed lines, short-dashed lines and continuous lines, respectively. Marker positions are indicated by the diamonds. The upper and lower horizontal lines give the genome-wide critical values for $P < 0{\cdot}05$ (11·6) and $P < 0{\cdot}10$ (10·3), respectively.

peaks on the third chromosome. There is also a nearly-significant peak on the X ($0{\cdot}10 < P < 0{\cdot}05$), in the same interval as the first peak in the standard environment. In the ethanol environment, no likelihood peaks are formally significant, although two approach the $P < 0{\cdot}10$ threshold: one on the X, at the same position as the second peak in the standard environment, and one on the second chromosome (Fig. 2).

We examined the effects of varying the window size and number of background markers in the QTL cartographer program, as the choice of these parameters is somewhat arbitrary. Reducing the window size from 20 to 5 cM had no effect on the conclusions; all the significant peaks in Fig. 2 remained significant, and no new peaks appeared. Increasing the number of background markers from five to ten caused the peaks near the third marker on chromosome II in the ethanol and standard environments, and the peak near the fourth marker on chromosome III in the low temperature environment, to become significant (LR statistic > 11·6). In contrast, the peak at *c.* 31 cM on the X chromosome in the standard environment was no longer significant on a genome-wide basis (LR statistic = 5·3). With no background markers, this latter peak in the standard environment was the only peak that was significant at $P < 0{\cdot}05$ genome-wide in any of the three environments (LR statistic = 16·2). The results with five conditioning markers are likely to be more accurate than those with zero or ten, however, for the following reasons. Using no conditioning markers is likely to result in a considerable loss of power, as variation in genetic backgrounds is not accounted for at all. In contrast, background markers beyond the fifth individually explained a small and non-significant or only marginally significant ($P > 0{\cdot}03$) proportion of the variation in each environment. While adding such markers to the model may somewhat increase power to detect unlinked QTLs, such markers may also falsely absorb true QTL effects. Given that the marker at 31 cM on the X by itself explains 18 % of genetic variation in the standard environment, more than any other single marker in any of the environments, this appears to be the most parsimonious explanation for the reduction in significance of the likelihood peak at this marker as more conditioning markers are added.

Effect estimates of the five apparent QTLs corresponding to the significant and near-significant peaks in Fig. 2 are given in Table 2. The QTL between markers 3E and 4F on the X chromosome is associated with strong positive effects on fitness of the Ore-R allele in each environment. The QTL close to marker 11C on the X is associated with strong negative effects of the Ore-Ra allele in the ethanol and standard environments, but a much smaller effect in the low temperature environment. The QTL close to marker 27B on the second chromosome is associated with positive effects of the Ore-R allele in the ethanol and standard environments, but no effect in the low temperature environment. The QTL close to marker 72A on the third chromosome is associated with strong positive effects of the Ore-R allele in the low temperature environment but much weaker effects in

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Table 2. *QTL effects estimated by composite interval mapping*

		Estimated effect by environment		
Marker(s)	Map position	Ethanol	Standard	Low temperature
3E–4F	I 4·6–10·6	0·07, 0·11	0·11, 0·14	0·07, 0·12
11C	I 31·3	−0·13	−0·12	−0·03
27B	II 28·1	0·11	0·07	0·00
72A	III 48·9	0·01	0·03	0·11
93B–94D	III 71·9–75·6	0·02, 0·04	0·00, 0·03	0·09, 0·11

Effects are the estimated difference between the two homozygous classes (*Ore-R–2b3*) in units of the competitive index (proportion of wild-type flies). If the likelihood peak (Fig. 2) occurred between two markers, then the highest and lowest effect estimates for the entire interval are given; if the likelihood peak coincided with a marker, only the effect estimate at the marker position is given.

Table 3. *Results of regression of the competitive index in each of the three environmental treatments on genotype at six marker loci and the rank of the number of segregating sites per line*

	Estimated effect by environment (SE)			Multivariate hypothesis test results			
				$E+S+L=0$		$L=(E+S)/2$	
Marker	Ethanol (E)	Standard (S)	Low temperature (L)	F	P value	F	P value
3E	0·10 (0·04)	0·12 (0·02)	0·09 (0·03)	13·39	0·0005	0·54	0·46
11C	−0·13 (0·05)	−0·11 (0·03)	−0·02 (0·04)	6·39	0·014	13·53	0·0004
27B	0·11 (0·04)	0·08 (0·03)	0·03 (0·03)	6·92	0·010	7·91	0·0062
72A	0·00 (0·04)	−0·01 (0·03)	0·08 (0·03)	0·66	0·42	15·85	0·0002
93B	0·02 (0·04)	0·01 (0·03)	0·08 (0·03)	1·26	0·26	7·68	0·0069
spa	−0·33 (0·10)	−0·14 (0·07)	−0·09 (0·08)	6·18	0·015	6·26	0·014
Rank number seg. sites[a]*	1·2 (0·7)	1·0 (0·5)	1·3 (0·5)	5·28	0·024	0·30	0·59
(%) V_G explained[b]*	39%	45%	37%				

Estimates have the same meaning as in Table 2. The first multivariate test examines whether the effects associated with a given marker differ from zero when averaged over environments; the second examines whether the effects differ between temperatures. The F-statistics have 1 and 80 numerator and denominator degrees of freedom, respectively.
[a] Estimates and standard errors have been multiplied by 1000.
[b] Percentage genetic variance explained by the regression.

the ethanol and standard environments. The final QTL, between markers 93B and 94D on the third chromosome, shows a similar pattern.

Estimates of QTL effects obtained by multiple regression of the competitive index in each environment on marker genotype are similar to those obtained from composite interval mapping (Table 3). The fourth chromosome visible marker *spa* was also included in the regressions; *spa* apparently reduced fitness, especially in the ethanol and standard environments. The rank of the number of segregating sites was positively associated with fitness in each environment. The regressions explained between 37% and 45% of the genetic variance, depending on environment.

Multivariate significance tests were used to test the null hypothesis that the seven regression parameters were the same between each pair of environments. Comparing the ethanol and standard environments, the null hypothesis could not be rejected ($F_{7,80} = 1·45$, $P = 0·20$). In contrast, there was highly significant dependence of the regression parameters on environment in the comparisons between the low temperature environment and each of the ethanol ($F_{7,80} = 5·86$, $P < 0·0001$) and standard ($F_{7,80} = 7·65$, $P < 0·0001$) environments. Thus, there was significant QTL by environment interaction across temperatures, but not between the two treatments at the same temperature.

Because there was no evidence that the regression parameters as a group differed between the ethanol and standard environments, individual regression parameters in the low temperature environment were compared with the mean of the corresponding parameters over the ethanol and standard environ-

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ments (Table 3). Four of the five markers identified by composite interval mapping showed significant differences in estimated effects across temperatures, as did *spa*. The effects of the number of segregating sites per line, and of the QTL near 3E, were homogeneous across temperatures.

4. Discussion

We detected six QTLs that affected reproductive performance in at least one of three environmental treatments in a set of RI lines. Of the six QTLS, five had significantly different effects at the two temperatures used. In each case, the QTL by temperature interaction arose because a QTL that had strong effects at one temperature had little or no effect at the other. Thus, we found the predominant pattern of QTL by temperature interaction to be conditional neutrality, rather than antagonistic pleiotropy. In contrast to the differences in QTL effects at different temperatures, we found no significant differences in QTL effects depending on whether ethanol was present or absent in the medium.

The significant QTLs accounted for only 37–45% of the genetic variance among the lines. Two factors may have contributed to our inability to account for the majority of the genetic variation in terms of QTL effects. First, as in most QTL mapping experiments, our experiment probably lacked power to detect QTLs with relatively small effects. A second factor that probably contributed to the relatively large amount of unexplained variance is spontaneous mutation. Mutations affecting fitness that occurred during the 25 generations of full-sib mating used to form the RI lines would produce variation in the competitive index completely uncorrelated with any of the genetic markers. Studies of the rates of spontaneous mutations affecting fitness in *D. melanogaster* indicate that this source of variation could be substantial in 25 generations (Crow & Simmons, 1983; Fernández & López-Fanjul, 1996; Fry *et al.*, 1996; Houle *et al.*, 1996).

We also detected a significant, positive association between the number of segregating sites per line and the competitive fitness index. Such an association is not surprising, because selection for heterozygosity is the only way to account for the failure of an average of 5% of the autosomal markers per line to become fixed in 25 generations of full-sib mating. A much lower proportion of the X chromosome markers remained segregating (> 1%), as expected due to the hemizygosity of males.

In several recent studies of cultivated plants, significant QTL by environment interaction for fitness-related traits has been detected (Hayes *et al.*, 1993; Berke & Rocheford, 1995; Jansen *et al.*, 1995; Cockerham & Zeng, 1996; Tinker *et al.*, 1996; Sari-Gorla *et al.*, 1997), although interaction was sometimes weak or absent for some traits (e.g. Cockerham & Zeng, 1996). Several additional studies have reported estimates of QTL effects in different environments, without formally testing for QTL by environment interaction (e.g. Stuber *et al.*, 1992; Bubeck *et al.*, 1993; Schön *et al.*, 1993; Redoña & Mackill, 1996; Brummer *et al.*, 1977; other references and summary in Walsh & Lynch, 1997); these studies have often, though not always, given suggestive evidence for interaction in the form of effect estimates or significance test results differing greatly between environments. When QTL by environment interaction has been detected in any of these studies, the pattern has usually been similar to that observed here: variation in the magnitude of QTL effects across environments, without changes in the direction of the effects. Current evidence, therefore, indicates that antagonistic pleiotropy is a relatively uncommon form of genotype–environment interaction. Nonetheless, two studies have found evidence for QTLs with opposite effects in different environments. In maize, Sari-Gorla *et al.* (1997) found significant reversals of estimated QTL effects on two measures of pollen competitive ability in different years. In soybean, Brummer *et al.* (1997) found a marker showing associations with seed protein content that switched direction in different years, although no formal test of QTL by year interaction was reported.

One drawback shared by this study and the QTL studies of crop plants is that the populations studied are not natural. For example, it is not clear whether the QTL alleles detected in this study are segregating in natural populations, and even if they are, it is possible that they would have different effects in non-inbred genetic backgrounds. Studies of QTLs giving rise to genotype–environment interaction for fitness in natural populations are needed to resolve whether antagonistic pleiotropy is a common source of crossing of reaction norms for fitness in nature. Populations that commonly experience selection in each of two environments would be good candidates for such studies, because such populations would be more likely to be segregating for QTL alleles with opposite fitness effects in the two environments than populations that only rarely encounter one of the environments (Maynard Smith & Hoekstra, 1980). Even if two environments are frequently encountered by a population, however, antagonistic pleiotropy does not guarantee the maintenance of polymorphism. With hard selection and random mating, polymorphism due to spatial variation in selection coefficients requires arithmetic mean overdominance (Dempster, 1955). The conditions are somewhat relaxed under soft selection (Levene, 1953), or with restricted gene flow between environments (Christiansen, 1975). QTL mapping studies of natural popu-

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lations hold the prospect of determining whether the conditions for the maintenance of polymorphism by environmental heterogeneity are often met.

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