

The Evolution of Genetic Architectures and the Divergence of Natural Populations

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In this chapter, we are concerned with the evolution of genetic architectures in natural populations and the role that genic interactions play in this evolution. The genetic architecture of a population refers to the number of loci and the number and frequency of alleles at those loci that affect a particular trait, their allelic (dominance) and genic (epistatic) interactions, and their relationship to other traits (pleiotropy). Since most traits that affect fitness result from the expression of multiple loci, each of varying effect, our understanding of the genetics of fitness-related traits and the evolution of life histories has required the application of quantitative genetics. Much of the attention of quantitative genetic studies of life-history evolution has focused on genetic tradeoffs, or antagonistic pleiotropy, both as a constraint to the independent evolution of genetically correlated traits, and as an explanation for standing additive genetic variation for fitness traits within populations.

Studies of tradeoffs have dealt primarily with additive genetic variation and correlation within and among fitness traits of laboratory populations (Roff 1992; Stearns 1992). Two problems arise as a result of these biases. First, interactions among loci (epistasis) "greatly complicate quantitative genetic theory and, hence, they are generally assumed to be absent" (Roff 1997, p. 31), despite the fact that the extent and consequences of epistasis constitute a major source of the differences between Fisher and Wright in their fundamental view of evolution in natural populations (Wade and Goodnight 1998; Brodie, chap. 1, this volume). Second, the genetic variance-covariance structure of a population depends to a great extent upon the environment that the population experiences. When populations encounter a novel environment, such as an unnatural laboratory setting,

non-tradeoffs or reinforcing genetic correlations are likely to emerge (Stearns 1976; Gupta and Lewontin 1982; Bell 1984; Service and Rose 1985; Clark 1987b; Hoffmann and Parsons 1991). One approach to this problem has been to rear populations of *Drosophila melanogaster* for hundreds of generations in the laboratory before probing the genetic architecture of those populations (Rose and Charlesworth 1981a, 1981b). Subsequent studies with these long-established laboratory populations have provided tremendous insight into how evolution potentially can work (Service et al. 1985; Leroi et al. 1994a, 1994b; Chippendale et al. 1996, 1997, 1998; Shiotsugu et al. 1997; Deckert-Cruz et al. 1997), but we still need to turn to natural populations to gain insight into how evolution actually has worked.

Our approach has been to recreate the organism's natural habitat in the laboratory, including both its micro- and macroenvironment, and then to study the genetic architectures of very recently colonized populations. We have used the mosquito, *Wyeomyia smithii*, which completes its preadult development only within the leaves of the carnivorous purple pitcher plant, *Sarracenia purpurea*, wherein it lives on the decomposition products of its host's prey. From the Gulf of Mexico to northern Canada, *W. smithii* is a single species of mosquito that exploits exclusively the water-filled leaves of a single species of plant. The larvae are captive in this habitat, which defines the thermal (W. E. Bradshaw 1980), photic (W. E. Bradshaw and Phillips 1980), and trophic (W. E. Bradshaw 1983; W. E. Bradshaw and Holzapfel 1986) environment for this stage of the mosquito. All of these variables may be reproduced faithfully in the laboratory by rearing the mosquito in the leaves of intact plants in controlled environment rooms that provide the light, temperature, humidity, and nutritional resources encountered by *W. smithii* in the field (W. E. Bradshaw 1986; W. E. Bradshaw and Holzapfel 1989, 1996; W. E. Bradshaw et al. 1997, 1998a, 2000). Herein, we use this ability to rear *W. smithii* under controlled, but near-natural conditions to explore the evolution of its genetic architecture.

Our research focuses primarily on traits that affect fitness in seasonal environments. Fitness in natural populations at temperate latitudes depends upon a successful alternation of seasonal strategies. Demographic traits—such as growth, development, and reproduction—are generally associated with continuous life cycles and they contribute directly to ecological success. Phenological traits—such as dormancy and migration—generally disrupt or delay continuous life cycles, and are usually invoked seasonally by specific direct (temperature, moisture, food) or indirect (photoperiod) cues (Lees 1955; Danilevskii 1965; Beck 1980; Tauber et al. 1986; Danks 1987). In short, temperate insects deploy demographic traits to capitalize upon the opportunities provided by warm, humid summers of varying duration, and they deploy phenological traits to avoid or mitigate the exigencies imposed by cold, dry winters of varying duration and intensity. Herein, we shall consider both types of traits and show how they have been modified phenotypically and genetically during the invasion and dispersal into North America by the formerly tropical *W. smithii*. We shall show that both dominance and epistasis have contributed to the evolution of demographic and phenological traits. Finally, we shall discuss how the genetic differentiation of natural populations of this mosquito contrasts with the views of adaptive evolution as envisioned by Ronald Fisher and Sewall Wright.

Ecological and Evolutionary Background of *W. smithii*

Natural History and Phylogeography

Wyeomyia is a genus of some 50-plus neotropical species of Sabethine mosquitoes, many of which complete their preadult development in a variety of natural, water-filled containers such as fruit husks, tree holes, bromeliads, *Heliconia* bracts, and pitcher plants. Two species, *W. mitchelli* and *W. vanduzeei*, occupy bromeliads in peninsular Florida. Only one species, *W. smithii*, extends its range into temperate North America. The range of *W. smithii* closely approximates that of its host plant, *Sarracenia purpurea*, and extends from the Gulf of Mexico (30°N) in the south to Labrador and Saskatchewan (54°N) in the north (Fig. 15.1). Evidence from multiple sources indicates that *W. smithii* invaded North America from South America, and has subsequently dispersed from south to north; i.e., Gulf Coast populations are ancestral and more northern populations are progressively more derived (Ross 1964; W. E. Bradshaw and Lounibos 1977; Istock and Weisburg 1987; W. E. Bradshaw and Holzapfel 1990). Based on 10 variable allozyme loci, latitudinally disparate populations of *W. smithii* fall into three distinct clades (Armbruster et al. 1998). First, there is a distinct split between the populations from the Gulf Coast and lowland North Carolina (including the coastal plain and Piedmont), similar to the patterns of mtDNA and allozyme variation found in a variety of marine, freshwater, and terrestrial taxa (Avice 1992). Second, there is an even deeper split between a southern group that includes the Gulf Coast and North Carolina populations and a northern clade that extends from New Jersey to Maine

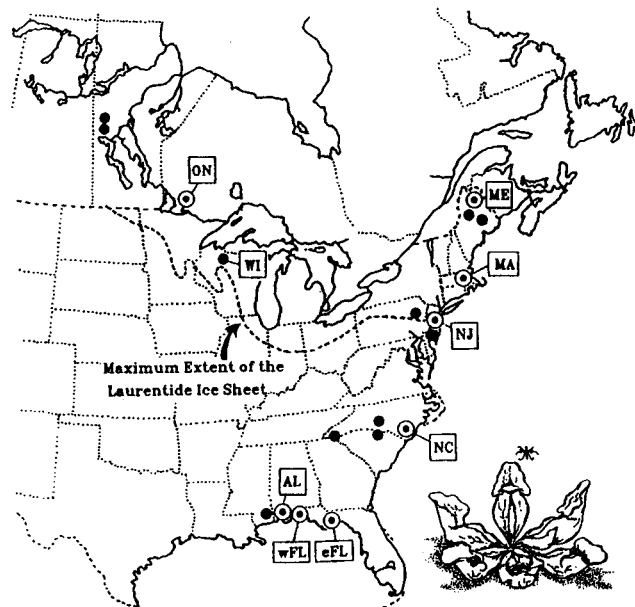
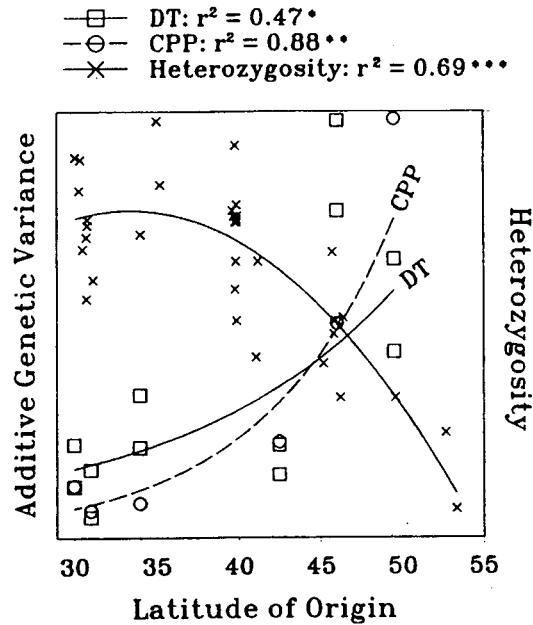


Figure 15.1 Origin of populations referred to in the text. Populations used in experimental studies are denoted with a circled dot; additional populations used to evaluate allozyme variation are denoted with a filled circle (see Fig. 15.2). (Some populations are close enough to be covered with a single symbol.)

Figure 15.2 Genetic variation within and among populations of *Wyeomyia smithii*. Additive genetic variance of preadult development time (DT, after W. E. Bradshaw et al. 1997), critical photoperiod (CPP, from Hard et al. 1993a), and average heterozygosity at 10 allozyme loci (from Armbruster et al. 1998). The units of each plot have been adjusted to fit to the same maximum and minimum scale. In *W. smithii*, long days promote continuous development or terminate dormancy (diapause); short days initiate and maintain diapause. The critical photoperiod is defined as the number of hours of light per day that induces and maintains diapause in 50% of an experimental cohort and, conversely, averts or terminates diapause in 50% of the cohort.



and westwards to Manitoba. This latter split reflects the southern limit of the Laurentide Ice Sheet (Pielou 1991). Average allozyme heterozygosity remains relatively high from the Gulf of Mexico to New Jersey (30–40°N) but declines with increasing latitude thereafter (Fig. 15.2).

Wyeomyia smithii is a weak-flying species, highly prone to death by desiccation. Adults fly mainly within the boundary layer of bogs, swamps, and wet pine savannahs that are surrounded by inimical woodland habitats. Within a bog, populations approach panmixia, but there is restricted gene flow even between nearby bogs (Istock and Weisburg 1987). The decreasing allozyme heterozygosity with increasing latitude (Fig. 15.2), and concomitant low levels of isolation by distance (Armbruster et al. 1998), provide our most direct evidence that invasion of *W. smithii* into the formerly glaciated regions of North America (> 40°N) has taken place by a series of founder events that have sequentially depleted structural gene heterozygosity. This same argument has been used frequently to account for reduced allozyme variability in previously glaciated areas relative to more southern populations or to glacial refugia (Highton and Webster 1976; Bellemin et al. 1978; Cwynar and MacDonald 1987; Boileau and Hebert 1991; Stone and Sunnuck 1993; Demelo and Hebert 1994; Lewis and Crawford 1995; Green et al. 1996), including *W. smithii*'s host plant, *Sarracenia purpurea* (Schwaegerle and Schaal 1979).

Evaluation of Genetic Differences between Populations

To examine differences between populations in the genetic architecture that underlies quantitative fitness traits, we (Hard et al. 1992, 1993a; Lair et al. 1997) have performed line crosses between two parents and have evaluated additive and nonadditive genetic differences between them by the use of joint-scaling tests (Box 15.1) derived from Mather and Jinks (1982; Hayman 1958, 1960b; Lynch and

Box 15.1 The joint-scaling test

The joint-scaling test is a goodness-of-fit test of observed generation means (parents, F_1 , F_2 , backcross, etc.) to the generation means expected if the parents differ in additive, dominance, or other genetic effects. By way of example, suppose we cross two diploid lines homozygous for different alleles (A and a) at a single locus. We use the Mather and Jinks (1982) notation:

d = the phenotypic deviation of AA or aa from the midpoint (m) between them;

h = the departure in phenotype of the heterozygote from m .

If we use m as our reference point, then we can describe expected phenotypic deviations from m in terms of additive (d) and dominance (h) effects, as shown in Table B15.1.

Notice that, because of independent assortment of the F_1 gametes, the recombining F_2 and backcross (B_1 and B_2) generations lose half the heterozygosity and, consequently, express half the dominance effects of the F_1 generation. This example can be extended to any number of loci, and this leads to composite expectations of m , h , and d in the hybrids between two populations or lines (Fig. B15.1). The joint-scaling test uses the method of least-squares to "fit" the

Table B15.1

Generation	Genotype	Expected Deviation from m Due to:		Expected Generation Mean
		Additive Effects	Dominance Effects	
P_1	AA	$-1d$		$m - 1d$
P_2	aa	$+1d$		$m + 1d$
F_1	Aa		$+1h$	$m + 1h$
F_2	$1AA:2Aa:1a$		$+1/2h$	$m + 1/2h$
B_1	$1AA:1Aa$	$-1/2d$	$+1/2h$	$m - 1/2d + 1/2h$
B_2	$1aa:1Aa$	$+1/2d$	$+1/2h$	$m + 1/2d + 1/2h$

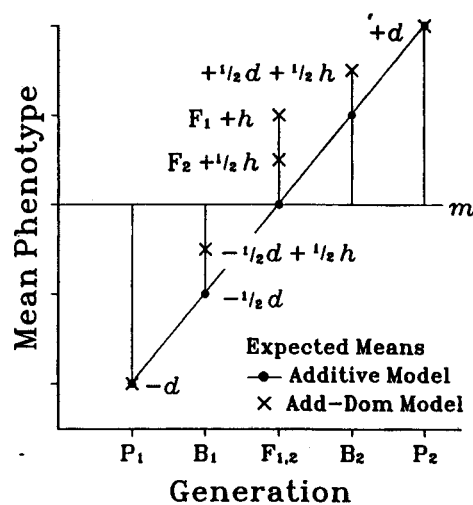


Fig. B15.1

(continued)

Box 15.1 (continued)

observed generation means to the expected means by assuming only additive effects or additive and dominance effects. Epistasis is indicated by a significant departure (χ^2 ; $p < .05$) from these additive–dominance expectations.

By including the mean phenotypes of the reciprocal F_1 , B_1 , and B_2 generations, we can estimate the components of digenic epistasis (additive \times additive, additive \times dominance, and dominance \times dominance interactions), estimate the additive and dominance maternal effects, and test for the goodness-of-fit to the combined additive–dominance–maternal–digenic epistasis model (Lair et al. 1997).

Walsh 1998). The joint-scaling test uses the method of least-squares to test for goodness of fit (χ^2 statistic) of generation means and variances to models that incorporate purely additive, or additive and dominance, effects (Fig. 15.3). Detection of differences due to dominance between parent populations requires both parents and their F_1 hybrids; detection of differences due to epistasis requires, additionally, at least the F_2 generation. The inclusion of the first backcross generations ($B_1 = F_1 \times P_1$ and $B_2 = F_1 \times P_2$) permits estimation of the components of digenic epistasis: additive \times additive, additive \times dominance, and dominance \times dominance interactions (Hard et al. 1992, 1993a). The inclusion of all possible reciprocals permits incorporation of maternal-additive and maternal-dominance effects into the model (Lair et al. 1997). We proceed with the joint-scaling test in a hierarchical manner. First, we test for goodness-of-fit to a model that incorporates only additive effects. Acceptance of the additive model indicates that additive effects alone are sufficient to explain the genetic divergence of the parental populations. Rejection of the additive model leads us to test for goodness-of-fit to an additive–dominance model. Acceptance of the additive–dominance model indicates that additive and dominance effects without epistasis are sufficient to explain the genetic divergence of the parent populations. Rejection of the additive–dominance model indicates the presence of epistatic genetic differences between the parent populations.

There are four main caveats concerning this approach. (1) Joint-scaling tests investigate genetic differences *between* populations. They do not reveal anything

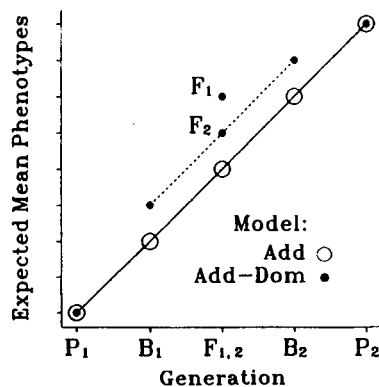


Figure 15.3 Expected generation means from line crosses (see Box 15.1) that show expected values under the additive (Add) and additive–dominance (Add–Dom) models. Deviations from the additive–dominance expectation in the recombining generations (---) indicate directional epistasis.

about the genetic architecture within populations. They are therefore useful to explore how populations have diverged genetically in the past, but not how they might evolve in the future. (2) In the presence of substantive epistasis, estimation of differences due to additive or dominance effects is unreliable (Hayman 1960a). (3) Estimates of the number of loci, or minimum number of effective factors, that contribute to the differences in mean phenotype between two populations are biased by nonadditive differences between them (Lande 1981; Mather and Jinks 1982; Zeng et al. 1990). Consequently, in the presence of significant dominance or epistasis between populations, estimates of the minimum number of effective factors are unreliable. (4) Hybrid means are composites of all genetic effects and, if these effects differ in sign, they may cancel each other out. Joint-scaling tests are therefore prone to Type II error because they detect only net directional dominance or net directional epistasis. This caveat does mean, however, that the detection of nonadditive difference between populations is very robust.

Differences in Genetic Architecture that Underlie Fitness

To examine differences in genetic architecture within and between disparate latitudes, Armbruster et al. (1997) performed crosses between two southern populations (Fig. 15.1) in eastern (eFL) and western (wFL) Florida (Nei's genetic distance \pm SE: $D = 0.020 \pm 0.004$), between two northern populations in Maine (ME) and Ontario (ON) ($D = 0.007 \pm 0.001$), between the Maine and eastern Florida populations ($D = 0.404 \pm 0.085$), and between the Ontario and western Florida populations ($D = 0.386 \pm 0.069$). For each cross, Armbruster et al. (1997) determined a composite index of fitness, capacity for increase

$$r_c = \frac{\ln(\text{juvenile survivorship} \times \text{eggs per enclosed female} \times \text{fraction eggs hatching})}{\text{cohort mean generation time}}$$

in five replicate cohorts within each of the parental, F_1 , and F_2 generations at near-optimal low-density and at a high density sufficient to reduce fitness by about 50%. They sought primarily to ascertain the contribution of nonadditive genetic differences (dominance and epistasis) between ancestral populations (eastern \times western FL), between descendent populations (ME \times ON), and between ancestral and derived populations (wFL \times ON and eFL \times ME) at densities encountered by ancestral (high) and derived (low) populations. Several patterns emerge (Fig. 15.4). First, there was no significant difference in mean fitness between the two parents in any cross; yet, there were genetic differences in r_c between populations that involved dominance in three of four crosses at high density and epistasis in two of four crosses at low-density. Consistency of mean fitness across disparate populations of *W. smithii* does not necessarily imply stasis of the underlying genetic architecture. Hybrid incompatibility can be due more to the modification of the genetic architectures of populations than to differences in population means (Goodnight 1999, and chap. 8, this volume).

Second, the contribution of dominance and epistasis to hybrid fitness depends on larval density. At high density, significant nonadditive genetic differences in r_c

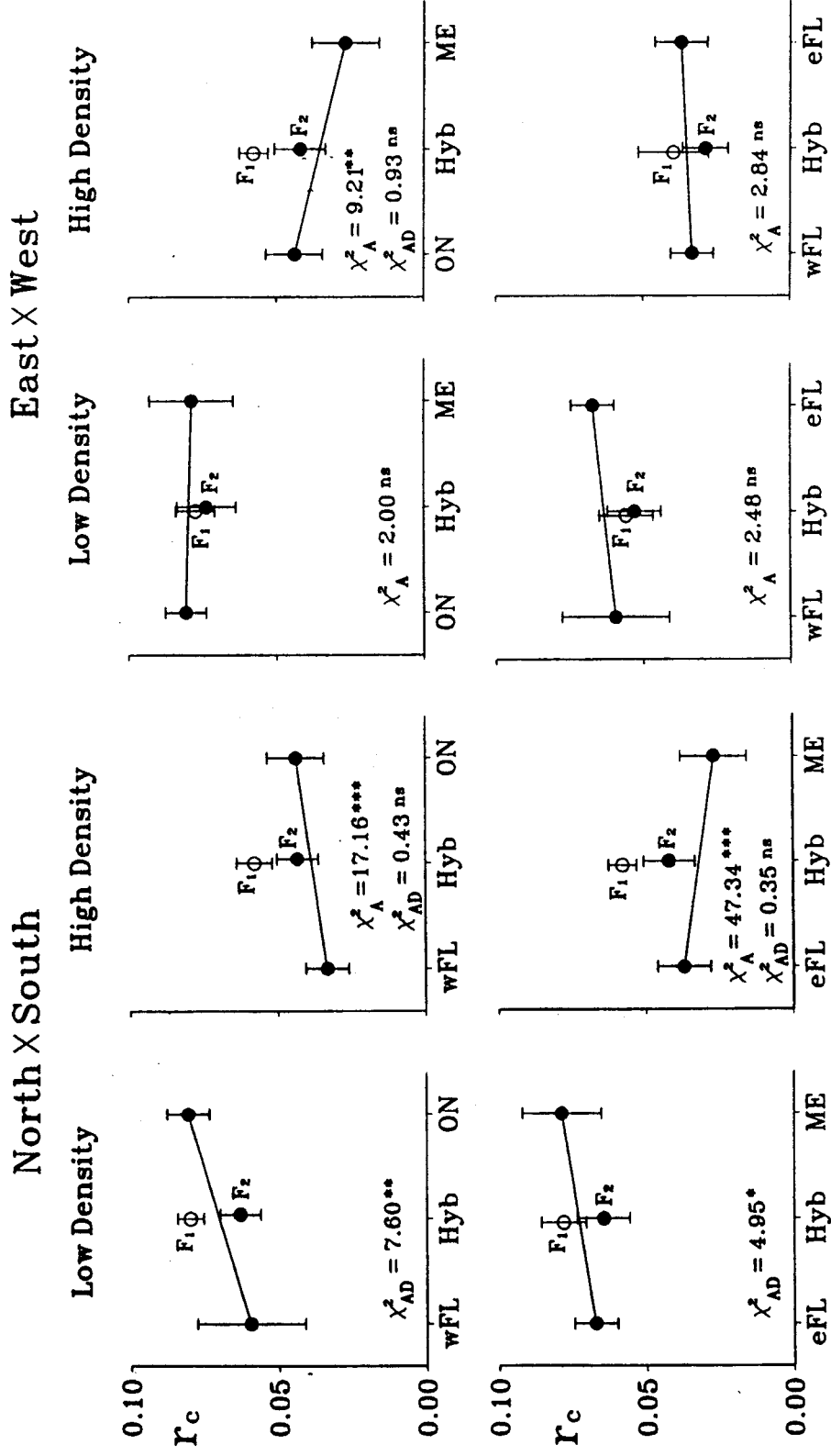


Figure 15.4 Capacity for increase ($r_c \pm 2SE$) of northern and southern populations of *W. smithii* and their F_1 and F_2 hybrids (from Armbruster et al. 1997). Density refers to larvae reared on a fixed resource at high or low-density. Joint-scaling tests for goodness-of-fit to the additive (χ^2_A) or, if that is rejected ($p < .05$), to the additive-dominance (χ^2_{AD}) model are shown in each plot. $^{ns} p > .05$, $^* p < .05$, $^{**} p < .01$, $^{***} p < .001$.

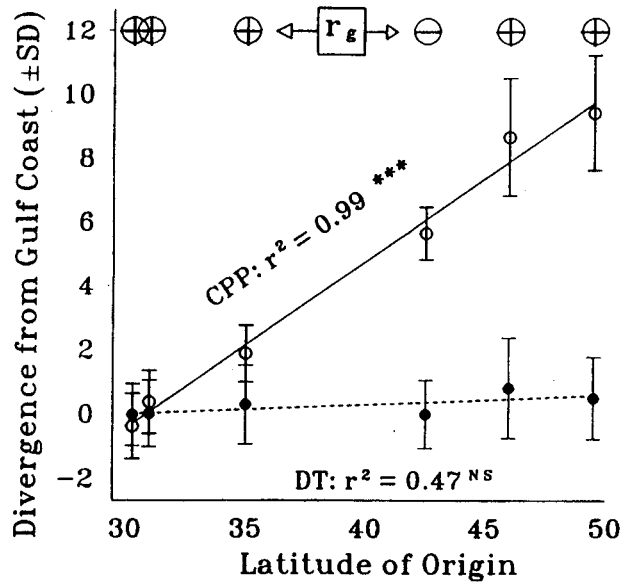
involve only dominance and, in each case, result in improved fitness of the F_1 generation over the additive expectation. At low-density, significant nonadditive differences in r_c involve epistasis and, in each case, result in lower fitness of the F_2 generation below the additive-dominance expectation. Thus, under stressful conditions, the advantages gained by heterozygosity clearly outweigh any disadvantages incurred through the breakdown of favorable genic interactions. Previous studies have demonstrated that genetic architectures can differ according to environmental conditions (Jinks et al. 1973; Barnes et al. 1989; Blows and Sokolowski 1995). Furthermore, extensive data from the animal-breeding literature (Barlow 1981) and evolutionary genetic studies (Hoffmann and Parsons 1991) indicate that levels of heterosis tend to increase under increasingly stressful environmental conditions. The results shown in Figure 15.4 make it clear that the phenotypes of F_2 hybrids between genetically differentiated populations represent a balance between the effects of epistasis and the effects of dominance.

Epistasis has been shown to be an important component of the genetic architecture of individual life-history traits (Vetukhiv 1953; Wallace and Vetukhiv 1955; Templeton et al. 1976; Burton 1990a, 1990b; Brown 1991; Parker 1992; Hard et al. 1992, 1993a). However, the perception of epistatic differences among populations depends critically on the particular trait examined (Armbruster et al. 1997). The results in Fig. 15.4 are especially pertinent to the evolution of natural populations for three principal reasons. First, r_c is a composite index of fitness that spans the entire life cycle of experimental cohorts and it incorporates any effects of compensating tradeoffs. Second, r_c is determined from cohorts reared in the leaves of intact pitcher plants under near-natural conditions, so that the results in Fig. 15.4 are directly relevant to populations in nature. Third, southern (Florida) populations encounter year-round, density-dependent constraints to development, and these constraints abate with increasing latitude or altitude (W. E. Bradshaw and Holzapfel 1986). Our evaluation of fitness at high and low densities then represents a comparison of genetic differences between populations under ancestral and derived conditions, respectively. It is under the environmental conditions of reduced density-dependent development encountered by the derived populations that genetic differences due to epistasis emerge between ancestral and derived populations of *W. smithii*.

Seasonal Coordination of Life History

Wyeomyia smithii overwinter as diapausing larvae like a vast array of other temperate arthropods (Andrewartha 1952; Lees 1955; Danilevskii 1965; Tauber et al. 1986; Danks 1987; Leather et al. 1993). The onset, maintenance, and termination of their diapause is mediated by daylength (photoperiod). Long days promote continuous development or terminate diapause; short days initiate and maintain diapause (Smith and Brust 1971; W. E. Bradshaw and Lounibos 1972; Evans and Brust 1972). The daylength that induces and maintains diapause in 50% of an experimental cohort and, conversely, averts or terminates diapause in 50% of an experimental cohort, is termed the critical photoperiod. As one proceeds north in latitude or upwards in altitude, winter arrives earlier, the optimal time to switch

Figure 15.5 Phenotypic divergence of critical photoperiod and preadult development time in units of the average standard deviation of the two southernmost (ancestral) populations. Top: genetic correlation (r_g) between critical photoperiod and development time within populations that show positive (+) and negative (-) correlations, recalculated from original data from experiments described in Hard et al. (1993b).



to diapause should occur earlier when days are longer, and, consequently, the critical photoperiod should increase with latitude and altitude of origin. This prediction is borne out in a large number of arthropods, including *W. smithii* (Fig. 15.5; W. E. Bradshaw 1976; W. E. Bradshaw and Lounibos 1977; Taylor and Spalding 1986; Table 24 in Danks 1987).

Individuals that develop faster effectively have a longer favorable season than individuals that develop slower. Faster developing individuals should then initiate diapause later in the season and, consequently, use a shorter photoperiod to cue the switch from direct development to diapause (Taylor 1980). When there is genetic variation for both photoperiodic response and development time, these two traits should be positively genetically correlated, that is, genotypes with longer development times should switch to diapause earlier in the season, at longer photoperiods (Istock et al. 1976; Taylor 1980; Istock 1983). Such a positive genetic correlation does indeed occur within most populations of *W. smithii* (Istock et al. 1976; Hard et al. 1993b; Fig. 15.5) and this correlation can retard short-term response to selection against the correlation (Scheiner and Istock 1991).

Over the range of *W. smithii*, there is stabilizing selection on photoperiodic response for a local optimum, but, there is directional selection on a continental scale for longer photoperiods at more northern latitudes that mediate the switch from direct development to diapause. Critical photoperiod has diverged 10 standard deviations between the Gulf of Mexico and Canada (Fig. 15.5), while mean development time has evolved less than one standard deviation [for traits plotted on a common scale of standard deviations from the ancestral (southern) phenotype]. In this case, the independent evolution of critical photoperiod and development time has occurred despite their underlying genetic correlation. Phenotypic correlations among populations do not necessarily reflect even persistent genetic correlations within populations, and the evolution of genetically correlated traits need not follow the “genetic lines of least resistance” as found by Schluter (1996).

The Genetic Architecture of Photoperiodic Response

Critical photoperiod is usually evaluated on the basis of percentage development or diapause in an experimental cohort, and, hence, as a threshold trait. By virtue of *W. smithii*'s being photoperiodic while in diapause (W.E. Bradshaw and Lounibos 1972), it is possible to determine the photoperiodic response of individuals. We rear cohorts of *W. smithii* on short days to induce and maintain diapause. Diapausing larvae are exposed to short days that are incremented 3 min per day by electronic timers. At some point, each individual larva perceives a transition from diapause-maintaining to diapause-terminating daylength, resumes development, and eventually pupates. We then define the critical photoperiod of an individual as the daylength on the day that it pupates, and the critical photoperiod of an experimental cohort as the mean daylength of pupation with its associated standard error. When treated in this manner in successive generations, offspring-parent regressions yield estimates of the heritability and additive genetic variance of critical photoperiod within populations. Additive genetic variance for critical photoperiod increases with latitude of origin (Fig. 15.2). This result is paradoxical because (1) the northern, derived populations have undergone progressively more recent directional selection on critical photoperiod since recession of the Laurentide Ice Sheet 18–7 thousand years before present, (2) local, stabilizing selection is, if anything, stronger in the north than in the south (Hard et al. 1993a), and (3) average heterozygosity at allozyme loci shows exactly the opposite relationship with geography (Fig. 15.2). The decrease in heterozygosity with increasing latitude indicates that invasion of at least the formerly glaciated regions of North America by *W. smithii* has involved multiple episodes of migration, isolation, and drift.

When nonadditive genetic effects contribute to gene expression, theoretical investigations suggest that genetic drift can increase additive genetic variance following a bottleneck (Robertson 1952; Griffing 1960; Cockerham 1984; Bryant et al. 1986a; Goodnight 1987; Hard et al. 1993b; Whitlock et al. 1993). Empirical studies indicate that populations that survive bottlenecks do not necessarily lose genetic variance (Sene and Carson 1977; Powell 1978; Craddock and Johnson 1979; Schwaegerle and Schaal 1979; Ringo et al. 1985; Bryant et al. 1986b; Carson and Wisotzkey 1989; Fleischer et al. 1991; Bryant and Meffert 1993, 1995), but evidence for increased additive genetic variance following a bottleneck is still scant (Lints and Bourgois 1982; Bryant et al. 1986a, 1986b; López-Fanjul and Villaverde 1989; Cheverud and Routman 1996; Meffert, chap. 11, this volume). We have already shown that dominance and epistasis have contributed to genetic differences in capacity for increase among populations of *W. smithii* (Fig. 15.4). We now use our ability to assess photoperiodic response of individual *W. smithii* to examine whether epistasis has been involved in the genetic divergence in critical photoperiod among populations.

Hard et al. (1992, 1993a) examined genetic differentiation derived from ancestral populations by determining the contribution of dominance and epistasis to genetic differences in critical photoperiod between two Florida populations separated by 300 km (Fig. 15.1: eFL, wFL) and progressively more northern populations in North Carolina (NC), Massachusetts (MA), Maine (ME), and Ontario (ON). They

performed line crosses, including the F_1 , F_2 , and both first backcross generations, with all of their possible reciprocals (14 total lines per cross). In these experiments, Hard et al. (1992, 1993a) found that epistasis made a significant contribution to genetic differences in critical photoperiod between each of the ancestral (Florida) and each of the more derived, northern populations. Digenic epistatic effects involved primarily additive \times additive and dominance \times dominance interactions, but not additive \times dominance interactions. The magnitude of composite epistatic differences between populations did not, however, increase with the geographic distance between them, or with the difference in mean phenotype. Hard et al. argued that epistatic variance, especially additive \times additive epistatic variance, may interact with genetic drift to increase levels of additive genetic variance in descendent populations.

Hard et al. (1992, 1993a) focused on the genetic differentiation of populations along a latitudinal gradient that also reflected their historical dispersal into North America. Lair et al. (1997) found significant differences due to epistasis in a cross between two ancestral Gulf Coast populations (Fig. 15.1: AL \times eFL), but they found significant differences in only one of the three crosses performed between the more recently derived and less differentiated northern populations (only ME \times ON, and not NJ \times ON or ME \times WI). Differences due to epistasis are apparent between two southern populations separated by 400 km (AL, eFL), but neither dominance nor epistasis contribute to genetic differences between a New Jersey (NJ) and an Ontario (ON) population separated by 2,500 km. These results also suggest that differences in composite additive and dominance effects arise early during the genetic divergence of populations (as within the northern region), while differences due to epistasis accumulate after more prolonged isolation (as within the more ancient Gulf Coast region, or between southern and northern regions).

When the joint-scaling test indicates significant effects of epistasis, directional epistasis is measured by the deviation of the recombining generations from the additive–dominance expectation. Figure 15.6 shows critical photoperiods for north–south and east–west crosses of *W. smithii* analogous to those for r_c in Fig. 15.4. We consider directional epistasis to be significant whenever the generation mean falls more than two standard errors above or below the additive–dominance expectation. Directional epistasis toward a shorter critical photoperiod is evident in all cases (Fig. 15.6): in the B_2 generation of the AL \times FL cross; in the F_2 , B_1 , and B_2 generations of the ME \times ON cross; in the F_2 and B_2 generations of the eFL \times ON cross; and in the F_2 , B_1 , and B_2 generations of the wFL \times ON cross. Hence, whenever evolved differences in epistatic interactions between populations are disrupted by recombination, the directional effect is consistently toward shorter critical photoperiods. These observations indicate that stabilization of critical photoperiod within the southern populations is adaptive, and that evolution of longer critical photoperiods at northern latitudes involves epistatic masking of a short-day response. Concomitantly, adaptation of photoperiodic response to more northern latitudes has involved a declining contribution of the circadian pacemaker to photoperiodic response and a greater reliance on a day-interval timer (Wegis et al. 1997; W. E. Bradshaw et al. 1998b). We therefore propose that adaptive evolution of photoperiodic response in *W. smithii* has been accomplished by epistatic down-regulation of the circadian pacemaker that contributes to photoperiodic time measurement.

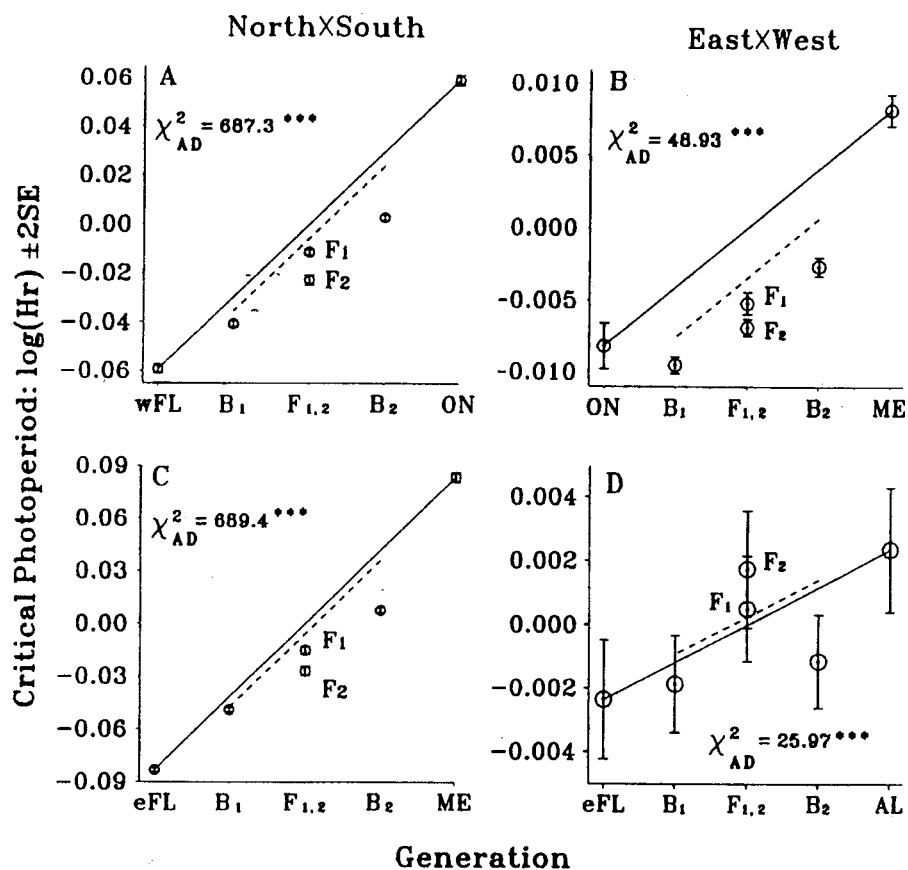


Figure 15.6 Critical photoperiod of northern and southern populations of *W. smithii* and their hybrids. The expected mean phenotypes from an additive–dominance model in the recombining generations (F₂, B₁, B₂) are indicated by the dashed line. Joint-scaling tests are denoted as in Fig. 15.4. Figures are replotted from data in experiments described in (A, C) Hard et al. (1992, 1993a) and (B, D) Lair et al. (1997). All critical photoperiods are plotted as deviation from the mid-parent value, and the large error bars in part (D) reflect the expanded scale of that plot.

Evolution of the Genetic Architecture in *W. smithii*

Our studies lead us to conclude that *W. smithii* comprises genetically differentiated populations spread across a wide geographic range. Even though we observed regional among-bog similarities in allozyme frequencies in *W. smithii*, populations that are virtually indistinguishable from their allozyme frequencies (Armbruster et al. 1998: Nei's genetic distance < 0.001) may reveal complex genetic differentiation that underlies quantitative traits (Armbruster et al. 1997; Lair et al. 1997). Indeed, the geographic pattern of allozyme heterozygosity is the inverse of that for the additive genetic variation that underlies both preadult development time and critical photoperiod (Fig. 15.2). The specific components of digenic epistasis by which populations differ in critical photoperiod or a more inclusive index of fitness (r_c) are virtually unique to each cross between geographical populations and are unrelated to the historical range expansion of *W. smithii* in North America (Hard et al. 1993a; Armbruster et al. 1997; Lair et al. 1997). Genetic differences between

Box 15.2 Evolution of novel genetic architectures following founder events

A. Sequence of events in a small founder population in which the effects of drift initially exceed the effects of selection:

- Decreased heterozygosity at structural gene loci exposes recessive alleles. Release of additive from epistatic variance exposes new genetic variation. Altered genetic correlations break down antagonistic pleiotropic relationships, facilitating the independent evolution of formerly "constrained" traits.
- Altered genetic background alters average effects of alleles, creating a novel array of advantageous, neutral, and maladaptive gene combinations.
- Internal genetic environment is a stronger selective force than external environment.
- **Genetic coadaptation predominates in small to modest populations.**

B. Sequence of events in the larger growing populations in which there is an increasing effect of mass selection:

- Local adaptation exceeds genetic coadaptation as external ecological factors become increasingly important in the new habitat. Rare advantageous alleles spread in the descendent population.
- Evolution of new pleiotropic relationships and new allelic and genic interactions.
- **Novel genetic architectures become established in the descendent population, even if the new habitat is congruent with the ancestral habitat.**

populations have accumulated in a stochastic, rather than deterministic, manner along the evolutionary trajectory of *W. smithii* in North America. We have argued above that these geographic patterns of genetic variation in structural gene loci and in quantitative traits are best explained by an historical dispersal by *W. smithii* in a series of founder-flush episodes with a concomitant release of additive from epistatic variance (Hard et al. 1992, 1993a, 1993b; Armbruster et al. 1997, 1998; Lair et al. 1997).

Because of their strict host specificity, *W. smithii* cannot invade a new locality until *S. purpurea* has become established. We therefore view the northward adaptive radiation of *W. smithii* as the successive colonization by a few individuals into a wide-open habitat, followed by drift, rapid population growth, and mass selection. If dispersal ability of seeds, eggs, and weak-flying adults is limited, founders are few in number and are more likely to land in nearby habitats than distant ones. While *W. smithii*'s habitat is always a single species of host plant, we do not see this situation as being qualitatively different from any specialist that invades a fragmented, patchy habitat. Successful dispersal to a new patch implies the preexistence of the appropriate habitat, which also provides a similar seasonal climate if it is geographically close. The result should be rapid population growth in the new habitat, unimpeded by intraspecific competition and with low, but not necessarily zero, selection pressure for adaptation to a new local climate.

There are several immediate consequences of drift (Box 15.2). First, there is the familiar decline in heterozygosity at structural gene loci. Second, there can be altered gene frequencies at loci that affect the expression of quantitative traits. Drift should deplete preexisting additive genetic variance for quantitative traits, but it

may also expose new additive genetic variation that was previously hidden from selection by epistasis (Mayr 1954; Carson 1968; Wright 1977; Templeton 1980a; Wade and McCauley 1984; Bryant et al. 1986a, 1986b; Goodnight 1987, 1988, and chap. 8, this volume). The resulting altered gene frequencies can drastically alter genetic correlations and, at least temporarily, may facilitate the independent evolution of traits that were previously constrained in their evolution by antagonistic pleiotropy (Bohren et al. 1966; Sheridan and Barker 1974; Nordskog 1977; Lande 1980; Mitchell-Olds and Shaw 1987; Rose et al. 1990; Slatkin and Frank 1990; Stearns et al. 1991; Shaw et al. 1995; Pigliucci 1996). From theoretical arguments (Via and Lande 1985; Zeng 1988), the genetic correlation between two traits may affect their short-term covariation and adaptation, but, unless the correlation is absolute (i.e., 1.0), it should not prevent their independent evolution in the long-term. We have argued that "long-term" means the differentiation of populations within a species, and that the alteration of genetic correlations by drift after a founder event can accelerate the independent evolution of previously genetically correlated traits (Hard et al. 1993b). The potential for independent evolution does not mean that the genetic correlation was maladaptive in the ancestral habitat. A positive genetic correlation between development time and critical photoperiod should be adaptive locally, but it does constrain the independent response of each trait to selection (Scheiner and Istock 1991). Such a correlation has not prevented the traits' independent evolution on a continental scale (Fig. 15.5). Our results do not show that isolation and drift actually degraded preexisting genetic correlations or that nonadditive genetic covariation facilitated the process. Our results do provide strong evidence that isolation and drift have been important events in the establishment of derived populations (Fig. 15.2); they do show that populations of *W. smithii* differ dramatically in the genetic architecture that involves dominance and epistasis, as well as additive effects of genes (Figs. 15.4, 15.6); and they do show evolutionary independence of genetically correlated traits that differ in epistasis among populations (Fig. 15.5).

Third, we propose that, following isolation and drift, genetic coadaptation will transiently exceed local adaptation while populations are still of moderate size. If isolation and drift alter genetic correlations and genetic interactions, they will break down the internal genetic coordination (Schlichting and Pigliucci 1998). Alleles that have strictly additive effects can vary in their effect on fitness according to the genetic background in which they occur (Lande 1980). Nonadditive effects can have a more drastic effect and can severely alter the epigenetic landscape (Cheverud et al. 1997), even if the new environment is identical to the old one. A founder-flush episode therefore provides an opportunity for the reordering of the average effects of alleles (Lande 1980), thereby facilitating major changes in some traits while alleviating negative pleiotropic effects through the accumulation of modifier loci (Weber 1996): namely, epistasis.

Fourth, selection during population increase should be more effective at fixing advantageous alleles than it is in established populations (Slatkin 1996). Whether these alleles are relics from the ancestral population or are unmasked by drift from allelic or genic interactions does not matter. Rare advantageous alleles that survive or emerge as a consequence of drift should be widely represented in the descendent population.

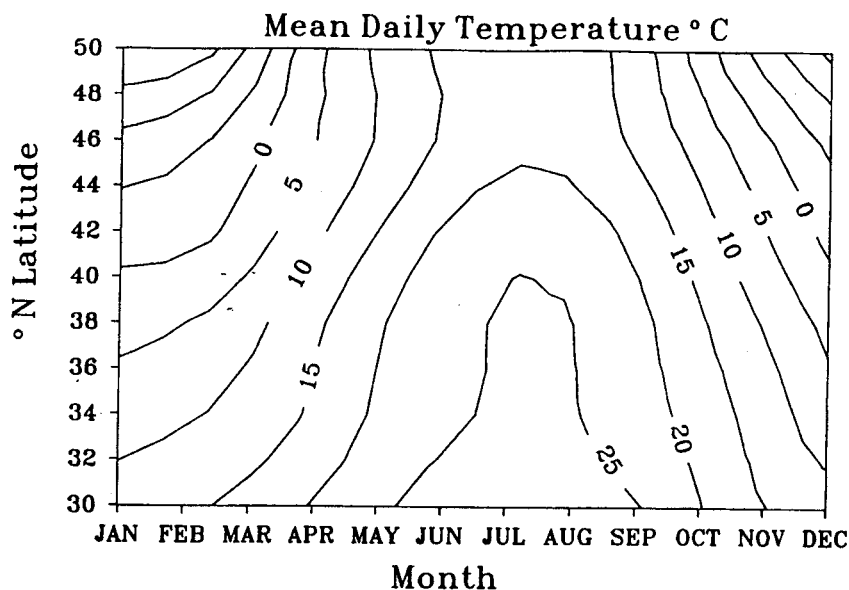


Figure 15.7 Mean daily isotherms from 25 localities in the eastern United States (NOAA 1968; data smoothed with a locally weighted regression, TriMetrix 1993). Note that the low-temperature isotherms tend to converge at northern latitudes, which, consequently, experience a shorter growing season.

Finally, mass selection following buildup of the population to large numbers can affect local adaptation. On a continental scale, however, what are the major variations in local microhabitat? With species such as *W. smithii* that exhibit strong host fidelity, there should be minor variations in local habitat and the major geographic variable would be environmental temperature. In eastern and central North America, temperature varies with latitude and season (Fig. 15.7). Three patterns emerge from the isotherms in Fig. 15.7. (1) There is little variation in midsummer temperatures over wide latitudinal distances. (2) There is a strong decline in midwinter temperature with increasing latitude. (3) The length of the summer season declines with increasing latitude (e.g., the 15°C isotherm ranges from 255 days at 30°N to 105 days at 50°N). The first pattern implies that there should be little selective pressure for modification of temperature-dependent growth, development, and reproduction during the summer in a seasonal organism such as *W. smithii*. It is therefore not surprising that we find little correlation between geography and r_c or its components (W. E. Bradshaw and Holzapfel 1989, 1990; Hard et al. 1993b). The fact that we do find consistent differences in mean phenotype and genetic architecture between populations in these same traits (W. E. Bradshaw and Holzapfel 1989, 1990; Armbruster et al. 1997) shows that these traits are not evolutionarily static, but that climate has been a potent force in directing their evolution (W. E. Bradshaw et al. 2000). The last two patterns imply, respectively, that range expansion into progressively more northern latitudes should involve two separate responses to temperature: (1) adaptations to the duration and intensity of winter cold and (2) adaptations to the timing of seasonal events: that is, the “fitting” of growth, development, and reproduction into the available growing season. Capacity for increase (r_c) declines about 60% during the “overwintering” generation in a 30-week simulated winter under controlled

conditions in the laboratory (W. E. Bradshaw et al. 1998a). Despite the high cost of overwintering, there is no latitudinal cline in fitness among populations from Florida to Ontario (30–50°N) through the same simulated winter (W. E. Bradshaw et al. 2000). By marked contrast, photoperiodic response, involved in the timing of seasonal development, shows a strong correlation with geography ($r^2 \geq 96\%$ in separate studies: W. E. Bradshaw 1976; Hard et al. 1993a; Lair et al. 1997). From these results, we conclude that the historical dispersal of a formerly tropical mosquito from the Gulf of Mexico into Canada has involved the genetic differentiation of populations in both demographic and phenological traits, but only the latter show a clear correlation between phenotype and the climate of North America, and even then only a correlation with the *timing* aspect of climate and not the absolute temperature.

The unusual opportunity afforded by *W. smithii* to quantify the photoperiodic response of individuals has enabled us to explore the genetic architecture of this highly adaptive trait over the evolutionary trajectory of this species. Patterns of allozyme heterozygosity and additive genetic variance of quantitative traits lead us to conclude that at least the northern (> 40°N) populations of *W. smithii* were established by a series of founder events with successive episodes of isolation and drift (Armbruster et al. 1998). Genetic differences between ancestral (Gulf Coast) and progressively more derived populations consistently involve epistasis (Hard et al. 1992, 1993a). Genetic differences among the derived populations themselves may involve only additive effects; additive and dominance effects; or additive, dominance, and epistatic effects (Lair et al. 1997). Differences due to additive and dominance effects probably arise early in the genetic differentiation of populations, and differences due to epistasis become established after more prolonged isolation of populations.

Ronald Fisher and Sewall Wright Encounter *W. smithii*

Fisher (1958) envisioned adaptive evolution as the result of mass selection that operates primarily on very large numbers of loci, each of which contributes a small, mainly additive effect. Wright (1932, 1977), by contrast, envisioned adaptive evolution as the result of selection that operates in episodic rearrangements of reticulate interactions within and among loci. In the Fisherian view, gene effects are largely independent of one another and selection operates on individual loci, whereas in the Wrightian view, pleiotropy and epistasis are omnipresent and selection operates on networks of interacting genes (Brodie, chap. 1, this volume). Because genetic background can change the average effects of alleles and because certain genic interactions are likely to be more favorable than others, Wright envisioned that combinations of interactions affect fitness differentially. Thus, selection would lead to improved fitness within the context of a given genetic background, even though other gene combinations might lead to higher fitness in other genetic backgrounds. Maximization of fitness in any one panmictic population is contingent on the initial genetic context, and it limits the ability of the population genetically to explore other, potentially more favorable gene combinations. Instead of the smooth adaptive landscape envisioned by Fisher, the Wrightian adaptive landscape is rugged, and

populations can get “stuck” on peaks of lesser fitness because they are separated by valleys of less favorable gene combinations.

The question remains, “How are these valleys traversed?” Wright’s shifting-balance theory was his answer to this question. Wright proposed that populations existed in semi-isolated demes that arose through a series of founder events. Isolation and drift would reorder the average effect of alleles on fitness and fragment formerly favorable genic interactions. Isolation and drift provided the opportunity to traverse fitness valleys and start selection anew on the foothills of a new, potentially higher fitness peak. Differential migration of favorable gene combinations among demes would then enable the broader population to escape confinement from peaks of lesser fitness.

The shifting-balance theory depends critically on the traverse of adaptive valleys. As pointed out by Whitlock et al. (1995), the existence of populations that differ in genetic architecture on different fitness peaks demonstrates that genetic landscapes are rugged, but it does not demonstrate that the populations ascended separate fitness peaks by traversing valleys of maladaptive gene combinations. Rather, different adaptive peaks (1) may be connected by adaptive ridges (Gavrilets 1997), (2) may have been connected in the past by an adaptive ridge that no longer exists, or (3) may have arisen as a consequence of environmental change that lowered the peaks, thereby facilitating the traverse of a former fitness valley (Price et al. 1993; Whitlock 1997). Consequently, it may be impossible to show that extant populations that currently reside on distinct adaptive peaks have arrived at those peaks by traversing a fitness valley. Consequently, the shifting-balance theory may be an inherently untestable hypothesis.

Untestability of the shifting-balance theory does not, however, erase the difference between Fisher and Wright which “emanated from their different views of evolution in nature and not in their differences in quantitative modeling” (Provine 1986, p. 491). In the final analysis, the tension between Fisher and Wright may have arisen as a need by each to be distinctive. Fifteen years after Fisher’s death, Wright was no less a proponent of his shifting-balance theory, but he did seem to have a more fundamental rapprochement with Fisher:

If environmental conditions differ significantly in different parts of the (species’) range, correspondingly different interaction systems tend to be established. The resulting pattern is difficult to distinguish from one arrived at wholly by local mass selection, but the interaction systems should be more adaptive than mere gene substitutions.

(Wright 1977, p. 472)

Coyne et al. (1997) provide a thorough critique of Wright’s shifting-balance theory and conclude that it does not provide an important explanation for the evolution of adaptations. We agree with Coyne et al. (1997) that no one study has demonstrated that a transition across an adaptive valley was responsible for variation within or between-species. But, we also believe that resolution of the Fisher–Wright controversy cannot be reduced simply to refuting the shifting-balance theory or to concluding that it is an untestable hypothesis. The shifting-balance theory was Wright’s answer to his quandary of how to traverse a fitness valley, not the basis for

his fundamental view of adaptive evolution. Wright's most fundamental view was that stochastic events involved in the subdivision of natural populations led to those populations residing on a rugged genetic landscape and differing in complex, interactive patterns of pleiotropy and epistasis.

We have repeatedly argued that genetic differences between populations of *W. smithii* have accumulated in a stochastic, rather than in a deterministic, manner. We base this argument on two observations. First, the relative contribution of additive, dominance, and epistatic effects to genetic differences in fitness and its components is unique to each cross and unrelated to isolation-by-distance (Armbruster et al. 1997, 1998). Second, when epistasis contributes to genetic differences in photoperiodic response between populations, the magnitude and sign of additive \times additive, additive \times dominance, or dominance \times dominance epistasis change without regard to each other or to the evolution of the mean phenotype (Hard et al. 1992, 1993a; Lair et al. 1997). Hugh Dingle (1992, personal communication) has pointed out to us that mutation itself is, after all, a stochastic process, so that these patterns could have arisen as a consequence of allelic substitution driven by mass selection. We cannot show that such a process did not take place, but we point out that beneficial mutations must then have occurred at potentially interacting loci, and not only at loci with independent effects.

Isolation and drift are fundamental processes in the Wrightian view of the differentiation of natural populations. As we have discussed, the contrasting patterns of allozyme variation and additive genetic variance that underlie critical photoperiod and preadult development time (Fig. 15.2) argue strongly that isolation, drift, and the release of additive from epistatic variance have been integral processes to *W. smithii*'s adaptive northward dispersal, especially north from the maximum extent of the Laurentide Ice Sheet. *Wyeomyia smithii* therefore provides an example of the differentiation of natural populations where isolation and drift have been important and have involved the reorganization of potentially interacting loci. We have no evidence to show that any population has crossed an adaptive valley in this process; however, we do show results that are difficult to explain by invoking mass selection that operates on allelic substitutions at loci with independent effects on fitness. Fisher's view of the evolutionary processes in natural populations is not wrong, it is incomplete; Wright's view of the evolutionary processes in natural populations adds a significant and important dimension to that of Fisher. Natural populations of *W. smithii* exist on a rugged genetic landscape, and even closely related populations differ by a reticulate pattern of interacting genetic effects on traits that are intimately associated with fitness in a seasonal environment. We need not reject this Wrightian view simply because the shifting-balance theory resolves itself into a difficult or untestable hypothesis.

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